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CONTENTS Page

Editorial

Original Articles

CONTENTS **Page**

Systematic / Narrative Review Article

Letter to the Editor

Acknowledgement

What is the difference between Metabolic Dysfunction-Associated Steatotic Liver Disease, Eosinophilic Esophagitis and Gastroesophageal Reflux Disease?

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ABSTRACT

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is emerging as a key hepatic manifestation of metabolic syndrome that affects nearly 40% of the global population. While links between MASLD and conditions such as type 2 diabetes and cardiovascular disease are well recognized, recent evidence suggests a potential connection with eosinophilic esophagitis (EoE) and gastroesophageal reflux disease (GERD). This editorial explores overlapping pathophysiology and inflammatory mechanisms shared by MASLD, EoE, and GERD, drawing from the current global literature and a multicenter U.S. cohort study. This editorial highlights how systemic inflammation, oxidative stress, and gut microbiota imbalance may drive these associations. Notably, MASLD was associated with a 2.38-fold increased risk of EoE and a modest but significant association with GERD independent of obesity. These findings underscore the importance of considering MASLD beyond liver-specific pathology and call for further research on shared immunometabolic pathways. An improved awareness of these relationships may guide diagnostic and therapeutic strategies in clinical practice.

INTRODUCTION

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), an updated nomenclature for Non-Alcoholic Fatty Liver Disease (NAFLD), is gaining recognition as a hepatic manifestation of metabolic syndrome (MetS), encompassing a wide range of hepatic pathologies, ranging from hepatic steatosis to cirrhosis.[1] The term 'metabolic-associated fatty liver disease (MAFLD)" is a refined alternative and more accurate descriptor than NAFLD, intended to be a more accurate underlying metabolic dysfunction commonly present in affected individuals.[2] Concurrently, eosinophilic esophagitis (EoE) and gastroesophageal reflux disorder (GERD) have emerged with substantial symptom overlap and complex inflammatory underpinnings, where EoE may lead to GERD by reducing the ability of the esophagus to clear normal reflux, while GERD might contribute to EoE by damaging the epithelial barrier and allowing allergens to trigger inflammation.[3] This editorial explores the potential associations between MASLD, EoE, and GERD, drawing upon findings from a recent multicenter retrospective cohort study conducted in the United States, along with insights from global research.

Understanding MASLD and Its Systemic Reach

The MASLD reflects the liver-specific manifestation of MetS, which is marked by hepatic steatosis and is strongly associated with insulin resistance. To meet these criteria, an individual must have either one or more of the following conditions: excess weight including overweight or obesity, type 2 diabetes, or other features of metabolic dysfunction, as described by Sangro et al., with the presence of hepatic steatosis.[1] Meta-analyses conducted by Chan et al. revealed that MASLD affects over a third of the global population, with a notable proportion of cases occurring in individuals with a body mass index (BMI) within the normal range, among whom metabolic conditions, such as hypertension and type 2 diabetes, are commonly and significantly associated. The worldwide prevalence of MASLD has been reported at 38.77%, with rates of approximately 55.33% in certain regions such as Europe.[2] Its pathophysiology involves chronic low-grade inflammation, oxidative stress, and altered lipid metabolism.[4] As MetS continues to increase, its systemic effects, such as diabetes and cardiovascular disease, are increasingly mirrored in the liver through conditions such as MASLD, which is now recognized as a hepatic manifestation of these metabolic disturbances.[2] These effects extend beyond the liver and implicate other organs, suggesting MASLD's relevance as a driver of systemic disease.[5]

EoE and GERD: Distinctions and Diagnostic Convergence

EoE is a long-standing condition marked by eosinophilic infiltration of the esophageal mucosa, which is driven by a Th2-driven immune reaction triggered by food or environmental allergens, cytokine activity (interleukin (IL)-4, IL-5, and IL-13), and epithelial barrier dysfunction.[3,6] According to studies by Dellon et al., the clinical features of EoE in adults include dysphagia (about 60% to 100%), heartburn (about 30% to 60%), and non-cardiac chest pain (approximately 8% to 44%). These individuals also frequently have coexisting allergic conditions (food allergies, allergic rhinitis, sinusitis, asthma, and atopic dermatitis).[3] In contrast, GERD occurs when backward movement of gastric

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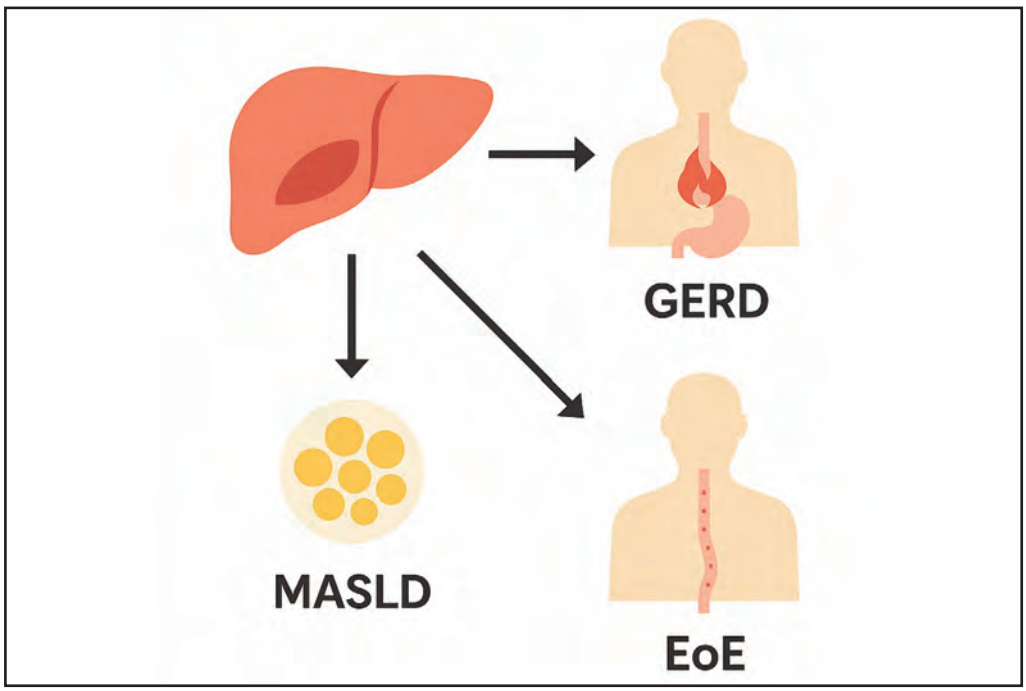

Fig. 1: This figure visually represents the proposed associations between MASLD and two esophageal conditions: GERD and EoE

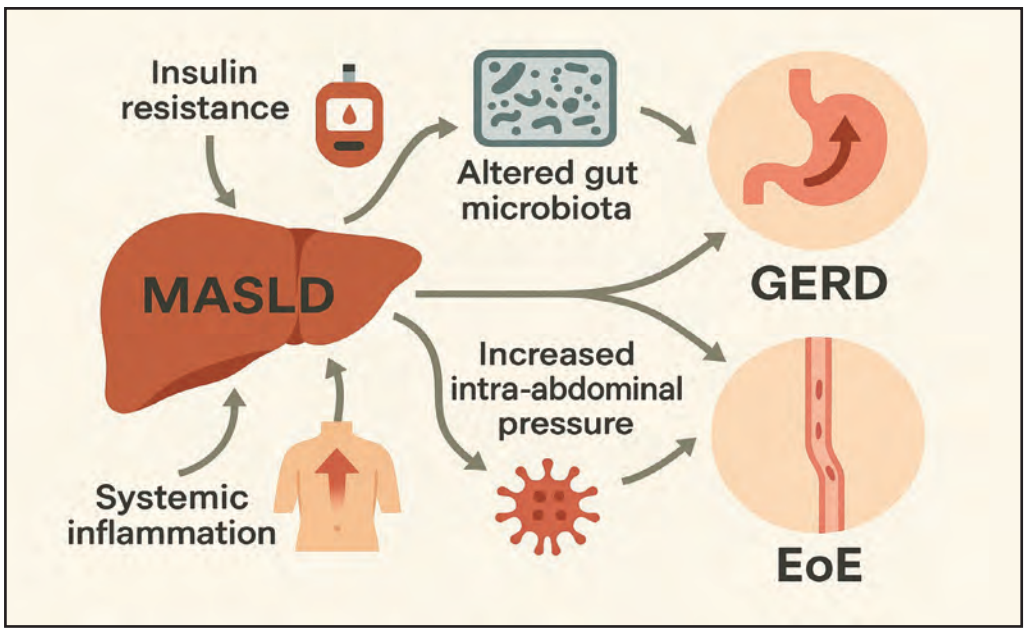

Fig. 2: This figure illustrates the proposed pathophysiological links between MASLD and esophageal disorders such as GERD and EoE

and duodenal contents into the lower esophagus leads to the development of a chronic condition.[4] Despite differing pathogenesis, GERD and EoE often present overlapping symptoms.[3,7] PPI-responsive esophageal eosinophilia (PPI-REE) and EoE share overlapping clinical, endoscopic, and histological features, which makes differentiation challenging. Standard diagnostic tools, such as pH monitoring and endoscopy, are often inadequate, as both conditions exhibit similar inflammatory mediators and molecular markers.[3] A trial on PPI therapy is required before confirming the diagnosis of EoE. According to the current definitions, patients whose esophageal eosinophilia resolves with this treatment are excluded from EoE diagnosis.[3] However, studies have shown that up to 74% of patients with esophageal eosinophilia respond to PPIs.[3]

Interlinking MASLD with GERD: Epidemiologic and Mechanistic Evidence

Research spanning multiple continents, including longitudinal cohorts and meta-analyses, has demonstrated a consistent association between NAFLD/MASLD and GERD.[5] In a Korean cohort of over 34,000 individuals, NAFLD was

initially linked to an increased risk of reflux esophagitis; however, the association weakened after adjusting for BMI, further highlighting the mediating role of obesity.[8] Conversely, meta-analyses by Xue et al. support that MASLD remains significantly associated with GERD even after adjusting for metabolic risk factors, indicating that the association persists regardless of age, sex, or obesity.[5] Xue et al. also reported an odds ratio estimated at 1.28, yielding a 95% CI between 1.12 and 1.44, and the association persisted in both adjusted and unadjusted models.[5]

Mechanistically, visceral obesity may increase intragastric and transesophageal pressures, leading to structural changes at the gastroesophageal junction, such as hiatal hernia formation and shortening of the lower esophageal sphincter (LES). Additionally, systemic inflammation is driven by adipose tissue and resident immune cells through the secretion of proinflammatory cytokines, which may result in esophageal mucosal injury. Both mechanisms promote reflux[4] Moreover, increased oxidative stress, as evidenced by elevated biomarkers, has been associated with overweight and MetS. In GERD, reactive oxygen species (ROS) combined with acid exposure may aggravate the damage to the esophageal lining[4]

Emerging Link Between MASLD and EoE: A Novel Frontier
Using the U.S. National Inpatient Sample, Kohli et al. conducted a multicenter cohort analysis and found that patients presenting with MASLD had more than double the odds of acquiring EoE, which is independent of obesity and other metabolic factors, with an adjusted odds ratio of 2.38 was reported with a 95% CI ranging from 1.82 to 3.11, and a p-value of less than 0.001. The study reported a 6.1% incidence of MASLD in patients with EoE compared to 2.9% in those without EoE.[7] Lamb et al. additionally reported a higher prevalence of radiographic hepatic steatosis in approximately 26% of patients with EoE compared to 21% in controls.[9] In patients with EoE, reduced HIF-1α signaling may impair oxygen-sensing pathways and compromise epithelial barrier integrity by affecting the expression of tight junction proteins, such as claudin-1.[6] Additionally, individuals with EoE and GERD have shown changes in their microbiomes, which include a general reduction in microbial diversity in EoE patients. In models of high-fat intake, saturated fats reaching the distal intestine are associated with gut microbial shifts, particularly an elevated Firmicutes-to-Bacteroidetes ratio. These microbiota disturbances may contribute to increased cytokine expression, potentially driving the shared inflammatory responses observed in both EoE and MASLD.[7]

Shared Mechanisms and Immunometabolic Crosstalk
All three disorders, MASLD, EoE, and GERD, have convergence in inflammatory signaling, oxidative stress, and free radicals at the cellular level.[7] For example, changes in the microbiome, esophagus, or gut occur with EoE, and MASLD can lead to downstream overexpression of cytokines, resulting in similar pro-inflammatory changes in EoE and MASLD.[7]

In addition, ROS are believed to contribute to the pathophysiological mechanisms underlying gastrointestinal diseases including GERD.[4] Patients with GERD were observed to exhibit elevated sensitivity to H2O2 and lipid peroxidation when compared to controls, implying a multifactorial mechanism involving acid exposure and the resulting generation of ROS as a contributing factor to mucosal damage and might be involved in hepatocellular damage and inflammation.[4] Cytokines such as IL-8 and platelet-activating factor (PAF) are upregulated in the esophageal mucosa of individuals with GERD.[4] In addition, elevated serum levels of IL-6 and IL-8 have been observed in both experimental animal models and individuals with NAFLD.[4]

The patatin-like phospholipase domain contains (PNPLA3) protein gene, a powerful modulator of lipid droplet deposition observed in both hepatocytes and hepatic stellate cells, which has demonstrated a strong connection to the disease mechanism of NAFLD due to overexpression of downstream inflammatory pathways.[7] Interestingly, PNPLA3 was found to be a genetic locus associated with EoE (odds ratio, 1.343).[7] Apart from genetics, MASLD, EoE, and GERD involve a complex interplay of pathways that include the overexpression of cytokines.[7]

Clinical and Translational Implications
Higher rates of MASLD were found in the EoE group than in those without EoE, with rates of 6.1% and 2.9%, respectively ($p < 0.001$). When uncontrolled factors were controlled for, MASLD was associated with a 2.38-fold increased likelihood of developing EoE, with a 95% confidence interval of 1.82 to 3.11 and a p-value of less than 0.001.[7] Patients must be initiated on PPI therapy prior to excluding the diagnosis of EoE; responders with esophageal eosinophilia do not have EoE as presently defined.[3] Heartburn occurs in 30%-60% of patients with EoE.[3] In adults with reflux symptoms that are resistant to PPI, the etiology is EoE in 1–8% of cases.[3] Other factors that have been linked to a higher risk of EoE include younger age, Caucasian ethnicity, irritable bowel syndrome (IBS), GERD, inflammatory bowel disease (IBD), and celiac disease (CD).[7] A meta-analysis of observational studies provides evidence of a strong positive correlation between NAFLD and GERD risk that remained even after controlling for age, sex, BMI, diabetes, triglycerides, and other metabolic risk factors.[5]

LIMITATIONS AND FUTURE DIRECTIONS

There is no therapy yet for MASLD to halt disease progression to liver fibrosis or to reduce established fibrosis because biological drug targets are difficult to find owing to the pathophysiology of MASLD complexity.[1] A meta-analysis of observational studies provides evidence for a strong correlation between NAFLD and the risk of GERD, but the temporal association between GERD and NAFLD has not been definitively established.[5] Another question concerns the phenotype of EoE. It is unclear whether EoE may progress from one phenotype to another or whether the phenotypes are stable.[3] The causal association between NAFLD and GERD remains uncertain and requires confirmation in future large-scale cohort studies.[5] At present, it is uncertain whether NAFLD is an independent pathogen in the pathogenesis of GERD, irrespective of obesity. Further prospective studies are required to confirm this correlation are required.[7]

CONCLUSION

Briefly, MASLD increases the risk of both GERD and EoE. There are numerous overlapping symptoms of GERD and EoE. GERD can also cause increased infiltration of the esophagus by eosinophils, making it extremely difficult to distinguish between GERD and EoE. EoE may induce GERD (because of impaired ileal clearance) and GERD can induce EoE (through augmented epithelial permeability and antigen presentation). Patients with MASLD had a 2.38-fold greater risk of indicating a strong association with EoE (95% confidence interval: 1.82 to 3.11; $p < 0.001$). MASLD and EoE share parallel pathologies that are possibly linked by metabolic or microbiome-mediated mechanisms. MASLD was linked to a heightened risk of GERD, with a pooled OR of 1.28 and a 95% confidence interval ranging from 1.12 to 1.44, suggesting a modest but significant risk elevation. GERD manifestations were significantly associated with elevated BMI and MetS. However, NAFLD was significantly associated with GERD independent of MetS.

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Correlation of bacterial biofilm profile based on optical density cut-off with clinical severity in patients with chronic suppurative otitis media tubotympanic type

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ABSTRACT

Introduction: Chronic suppurative otitis media (CSOM) is a middle ear infection with a high incidence in ear cases, is often recurrent, and causes hearing impairment. Bacteria in the CSOM frequently form biofilms, which enhance antibiotic resistance and contribute to disease progression. The aim of this study was to determine the correlation of bacterial biofilm profiles based on optical density cut-off with the clinical picture of patients with tubotympanic type CSOM.

Materials and Methods: This was a cross-sectional study using a descriptive analytical design. The study was conducted at the tertiary teaching hospital of Hasanuddin University and the network hospital in Makassar, Indonesia, from July 2023 to July 2024. The study population consisted of patients with the CSOM tubotympanic type who met the inclusion criteria. Bacterial cultures and biofilm examinations were performed using the tissue culture plate method. Data were analyzed using SPSS® version 28.

Results: A total of 53 patients with the CSOM tubotympanic type were included in this study. The mean age of the patients was 30±14 years. Pseudomonas aeruginosa was the most dominant bacterium (32.1%), with 20 other bacteria, and all these bacteria formed biofilms with either weak or moderate strength. There was a significant association between biofilm formation and nature of secretion (r=0.395, p=0.003). The chronicity of the disease (r=0.407, p=0.002) and the degree of hearing impairment (r=0.294, p=0.032) were also significant. A significant positive association was found between total clinical score and biofilm formation (r=0.429, p=0.001).

Conclusion: All bacteria found in the tubotympanic CSOM formed biofilms. The correlation analysis revealed a significant positive relationship between several clinical variables and biofilm formation. The substantial formation of biofilms may account for the fact that patients with elevated scores frequently experience infections that are challenging to manage with conventional antibiotic treatments.

KEYWORDS:
Biofilm, chronic suppurative otitis media, tubotympanic type, clinical characteristics

INTRODUCTION

Globally, CSOM often occurs, especially in developing countries, affecting between 65 to 330 million people. It is estimated that there is an annual incidence of 31 million new cases, a fifth of which occur in children under the age of 5.[1] *Staphylococcus aureus* is the most commonly identified microorganism is *Staphylococcus aureus* (including MRSA). Other similar bacteria, including *Pseudomonas aeruginosa, Proteus spp., Klebsiella spp., Bacteroides spp.,* and *Fusobacterium spp.*, can cause this disease.[2]

Bacteria are generally considered microorganisms that live individually; however, most form complex organizations and adhere to surfaces. This phenomenon is known as biofilm formation.[3] Biofilms have been shown to play a significant role in otitis media and have been identified in direct biopsy specimens from the middle ear. Many bacteria commonly found in CSOM exist in biofilm states under favorable conditions.[4] Bacteria within biofilms are 10–1,000 times more resistant than when they are not in biofilms.[5] Numerous studies have reported the presence of biofilm bacteria in CSOM, highlighting their impact on bacterial persistence and infection treatment. The presence of biofilm bacteria may explain the occurrence of resistance to systemic and topical antibiotics.[6]

MATERIALS AND METHODS

This was a cross-sectional study that was conducted at the Ear, Nose and Throat (ENT) clinics of Hasanuddin University Hospital and Network Hospital in Makassar from July 2023 to July 2024. The study population consisted of patients with tubotympanic-type CSOM who underwent treatment at an outpatient clinic.

The inclusion criteria were as follows: patients with tubotympanic type CSOM who were over the age of 17 years

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and had never undergone ear surgery. Exclusion criteria included CSOM patients accompanied by immunocompromised disorders, such as malignancy, malnutrition, diabetes mellitus, and CSOM tuberculosis.

The study's protocol involved patients with CSOM attending the outpatient clinic, where history-taking and physical examination were conducted. This included assessment of the severity and duration of the disease and hearing examination using pure tone audiometry. CT scan examinations serve as supplementary examinations that complement ENT assessments to establish a diagnosis of tubotympanic CSOM and to eliminate the possibility of cholesteatoma. Following the satisfaction of the inclusion criteria, the patient was deemed eligible for further consideration to be enrolled in the study.

The next stage of the process involved the collection of ear secretion samples for culture and bacterial identification. These samples were then analysed using the Microtiter Plate Assay method to detect biofilm.

An optical density (OD) examination of the biofilm was performed with a micro ELISA autoreader (Model 680, Bio-Rad, UK) at a wavelength of 620 nm. The results were then interpreted based on the Stepanovic criteria. The threshold value (ODc) was calculated from the mean OD of the negative control plus 3×SD. The presence of biofilms was classified as weak (<2×ODc), moderate (2-4×ODc), and strong (>4×ODc).

Data were obtained from patient histories, physical examinations, audiometric results, bacterial cultures, and bacterial biofilm examination. The data were analyzed using SPSS® software version 28 with Chi-square and Spearman tests and are presented in the form of tables and diagrams.

RESULTS

In this study, an analysis was conducted on 53 patients with tubotympanic CSOM. The results of the data analysis included the distribution of sex, age, types of bacteria, biofilm profiles, and the relationship between clinical severity and biofilm profiles. The majority of respondents were female (64.15%), while males accounted for only 35.8%. The average age of the patients was 35 years (median, 17 – 77 years). The clinical picture of patients with CSOM tubotympanic includes mucopurulent secretions in 27 (50.94%) of cases and mucoid secretions in 26 (49.05%) of cases. The intensity of otorrhea is predominantly categorized as intermittent in 43 (81.1%) patients and continuous in 10 (18.8%) patients. Regarding the volume of secretions, 36 (67.9%) patients experience slight otorrhea (limited to the middle ear) and 17 (32.07%) experience significant otorrhea (extending to the ear canal). In terms of chronicity of the illness, 30 (56.6%) patients have suffered for more than 3 years, 15 (28.3%) for between 1 to 3 years, and 8 (15.09%) for less than one year. Regarding the type of hearing impairment, 42 (79.2%) patients suffered from conductive hearing loss, 8 (15.09%) from mixed hearing loss, 1 (1.88%) from sensorineural hearing loss, and 2 (3.77%) with no hearing impairment. The degree of hearing impairment is predominantly moderate in 35 (66.03%) patients, mild in 9 (16.9%) , severe in 4 (7.54%) , very severe in 3 (5.66%), and with no hearing impairment in 2 (3.77%).

Table I shows the bacteria responsible for the tubotympanic type of CSOM. Among the 21 identified bacterial species, 11 (52%) were gram-negative and 10 (48%) were gram-positive. *Pseudomonas aeruginosa* was the most dominant pathogen (32.1%), followed by *Staphylococcus aureus* (11.3%). Other identified bacteria included *Proteus mirabilis* (7.5%), *Achromobacter xylosoxidans* (5.7%), and several other species, indicating the involvement of a diverse range of pathogens.

The relationship between the bacterial species and biofilm formation was classified into three categories: weak, moderate, and strong. The majority of bacteria (81.1%) formed weak biofilms (43 isolates), whereas 18.8% formed moderate biofilms (10 isolates), with no samples exhibiting strong biofilm formation. The bacteria responsible for moderate biofilm formation include *Pseudomonas aeruginosa, Achromobacter xylosoxidans, Burkholderia cepacia, Staphylococcus epidermidis,* and *Corynebacterium amycolatum*. (Table I).

In terms of discharge characteristics, the weak biofilm group was predominantly associated with mucoid discharge (60.47%), whereas the moderate biofilm group was mostly associated with mucopurulent discharge (90.00%). This difference was statistically significant (p=0.004), suggesting that moderate biofilms were more likely to produce mucopurulent discharge (Table II).

In terms of the intensity of otorrhea, the majority of patients in both the weak (83.72%) and moderate biofilm (70.00%) groups experienced intermittent otorrhea; however, no significant difference was observed between the two groups (p=0.318). Regarding the volume of discharge, both the weak and moderate biofilm groups predominantly exhibited small amounts of discharge (69.77% and 60.00%, respectively); however, the difference was not statistically significant (p=0.551) (Table II).

Regarding disease chronicity, the weak biofilm group exhibited varied disease duration, with 18.60% of cases having a duration of less than one year, 34.88% between 1 and 3 years, and 46.51% with a duration of ≥3 years. In contrast, all patients in the moderate biofilm group had a disease duration of ≥3 years. Pearson's correlation test showed a moderate correlation (r=0.515, p<0.001), confirming that stronger biofilms were associated with a longer disease duration (Figure 1).

Regarding the severity of hearing loss, both weak and moderate biofilm groups were predominantly associated with moderate hearing loss (65.12% and 70.00%, respectively). Pearson's test revealed a low correlation between biofilm strength and hearing loss severity (r=0.281, p=0.015), indicating that stronger biofilms were associated with more severe hearing loss (Figure 2).

Based on Chi-Square test, most patients in both the weak (81.40%) and moderate (70.00%) biofilm groups had

Table I: Bacteria responsible for CSOM tubotympanic type

	Bacterial Species	Biofilm form		n (%)
		weak	moderate	
Gram- Negative	Pseudomonas aeruginosa	12	5	17 (32.1)
	Proteus mirabilis	4	0	4 (7.5)
	achromobacter xylosoxidans	1	2	3 (5.7)
	Pseudomonas Putida	2	0	2 (3.8)
	Acinetobacter baumannii	2	0	2 (3.8)
	Eschericia coli	2	0	2 (3.8)
	Klebsiella pneumoniae	2	0	2 (3.8)
	Providencia stuartii	1	0	1 (1.9)
	Citrobacter freundii	1	0	1 (1.9)
	Burkholderia cepacia	0	1	1 (1.9)
	Pandoraea ssp	1	0	1 (1.9)
Gram-Positive	Staphylococcus aureus	6	0	6 (11.3)
	Staphylococcus haemolyticus	3	0	3 (5.7)
	Arcanobacterium haemolyticum	1	0	1 (1.9)
	Staphylococcus hominis	1	0	1 (1.9)
	Staphylococcus cohnii	1	0	1 (1.9)
	Staphylococcus epidermidis	0	1	1 (1.9)
	Streptococcus Agalactiae	1	0	1 (1.9)
	Gemella morbillorum	1	0	1 (1.9)
	Corynebacterium Striatum	1	0	1 (1.9)
	Corynebacterium amycolatum	0	1	1 (1.9)
TOTAL		43	10	53 (100)

Table II: Correlation of biofilm profiles with discharge characteristics and type of hearing impairment in patients with CSOM tubotympanic type based on chi-square test

	Variable	Biofilm Profile		Total n (%)	p-value
		Weak n (%)	Moderate n (%)		
Type	Mucoid	26 (60.47)	1 (10.00)	27 (50.94)	0.004
	Mucopurulent	17 (39.53)	9 (90.00)	26 (49.06)	
Intensity	Intermittent	36 (83.27)	7 (70.00)	43 (81.13)	0.318
	Continuous	7 (16.28)	3 (30.00)	10 (18.87)	
Volume	Slight (Middle ear only)	30 (69.77)	6 (60.00)	36 (67.92)	0.551
	plenty (Ear canal)	13 (30.23)	4 (40.00)	17 (32.08)	
Type of hearing impairment	Normal hearing	2 (4.65)	0 (0.00)	2 (3.77)	0.165
	Conductive	35 (81.40)	7 (70.00)	42 (79.25)	
	Sensorineural	0 (0.00)	1 (10.00)	1 (1.89)	
	Mixed	6 (13.95)	2 (20.00)	8 (15.09)	

Chi Square Test

conductive hearing loss. However, no statistically significant difference was observed in the type of hearing loss between the two groups (p=0.165) (Table II).

A significant relationship was found between bacterial biofilm profiles and clinical severity in the CSOM tubotympanic type. According to the graph, the correlation between biofilm strength and overall clinical presentation was 0.373, representing a low but statistically significant correlation (p=0.002). This indicates a positive relationship between biofilm strength and clinical presentation, in which stronger biofilms are linked to more severe clinical manifestations. This significant biofilm formation may help explain why patients with higher clinical scores often present with infections that are difficult to treat with standard antibiotic therapies (Figure 3).

DISCUSSION

The results of this study provide significant insights into the clinical severity influenced by biofilm profiles in patients with tubo tympanic CSOM. In the analysis of the 53 CSOM isolates, 21 bacterial species were identified. The variety of bacterial species indicates that despite the dominance of certain pathogens, CSOM infections may be caused by a broad spectrum of microorganisms. Among the identified bacteria, 52% were gram-negative and 48% were gram-positive. This finding may serve as a reference for the choice of antibiotic therapy in patients with tubotympanic type CSOM before the results of microbial culture are obtained.

In terms of microbiological findings, *Pseudomonas aeruginosa* was identified as the most dominant pathogen (32.1%), underscoring its significance as a major pathogen in chronic ear infections (CSOM). This bacterium is known for its ability to form biofilms, which contributes to resistance to a variety of antibiotics.[7] Biofilms formed by *Pseudomonas aeruginosa* act as protective barriers against the host immune system and enhance antibiotic resistance, making infection difficult to treat. These findings align with those of Ha et al. (2018), who showed that biofilms formed by *Pseudomonas aeruginosa* in chronic infections play a significant role in treatment

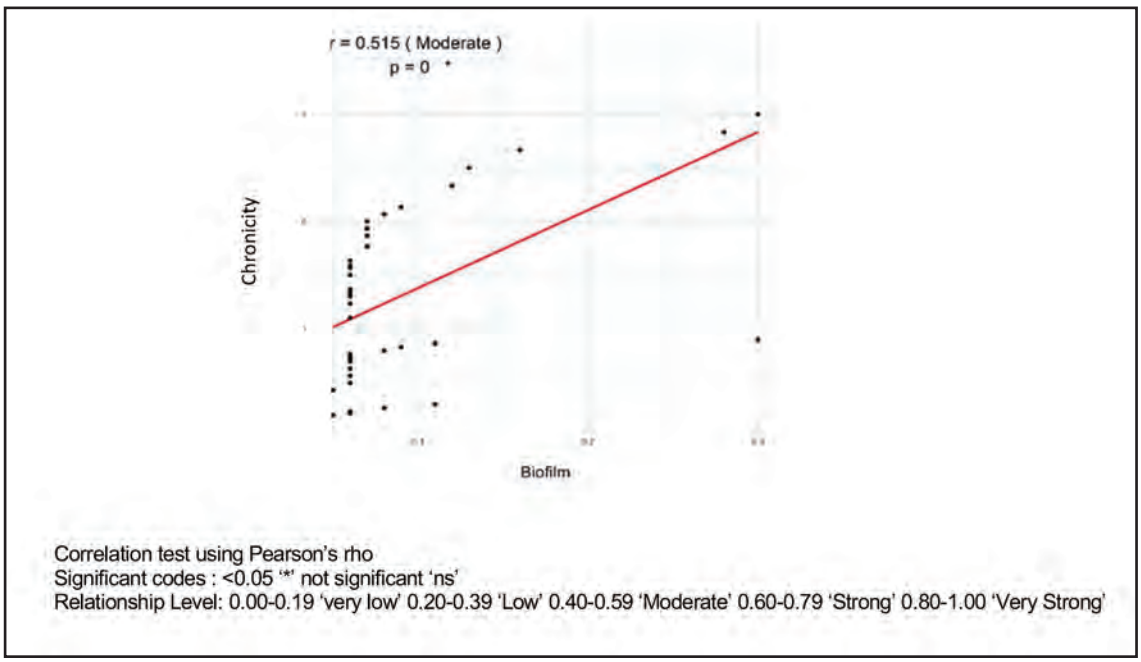

Fig. 1: Correlation of biofilm profiles with disease chronicity in patients with chronic otitis media tubotympanic based on Pearson's Test

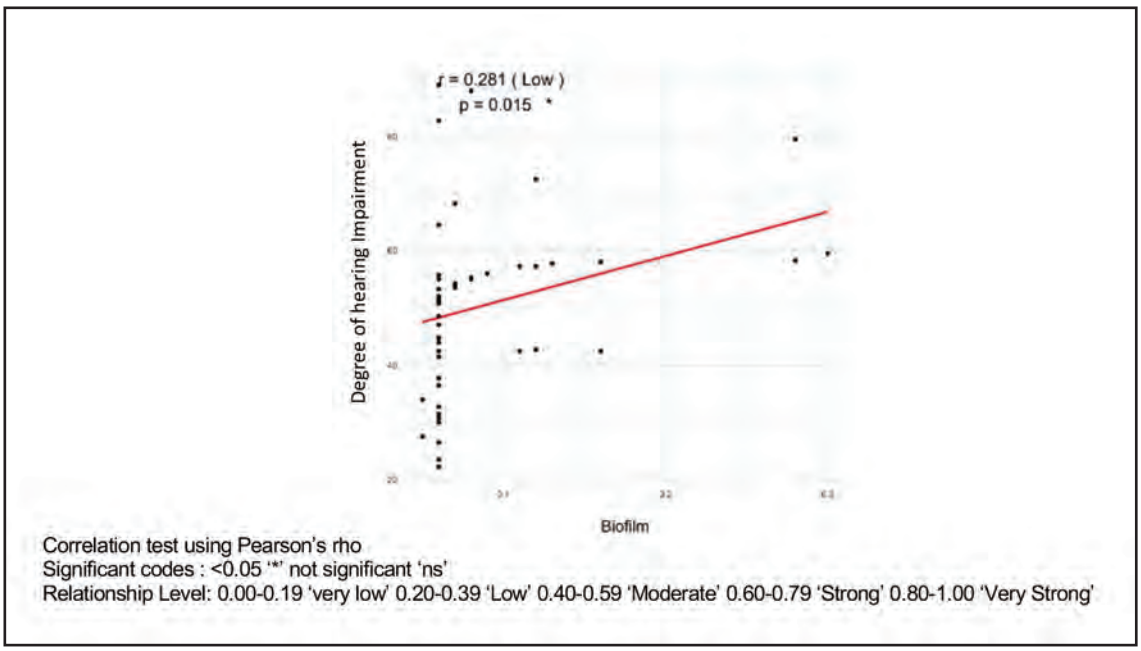

Fig. 2: Correlation of biofilm profiles with degree of hearing impairment in patients with chronic otitis media tubotympanic based on Pearson's Test

resistance and are associated with poorer clinical outcomes. *Staphylococcus aureus* has long been recognized as a pathogen involved in chronic infections, particularly because of its ability to form biofilms that protect the bacteria from antibiotic therapy and immune responses.[8] However, in the present study, the biofilm formed by *Staphylococcus aureus* was weak. Becker et al. found that biofilms formed by *Staphylococcus aureus* in chronic infections enhance inflammation and prolong healing. In the context of CSOM, these biofilms may exacerbate clinical symptoms such as otorrhea and tympanic membrane perforation.[9]

Among the various bacterial species responsible for CSOM, all are capable of biofilm formation. Ten isolates formed moderate biofilms, including *Pseudomonas aeruginosa* (5 out of 17 samples, 29.4%), Achromobacter xylosoxidans (2 out of 3 samples, 66.6%), and other species such as *Burkholderia cepacia*, *Staphylococcus epidermidis,* and *Corynebacterium amycolatum,* which also exhibited severe clinical severity. Biofilm formation plays a crucial role in persistence of chronic infections. Although some bacteria form weak biofilms, their presence remains a significant factor in exacerbating infections. In vitro studies have shown that TSB

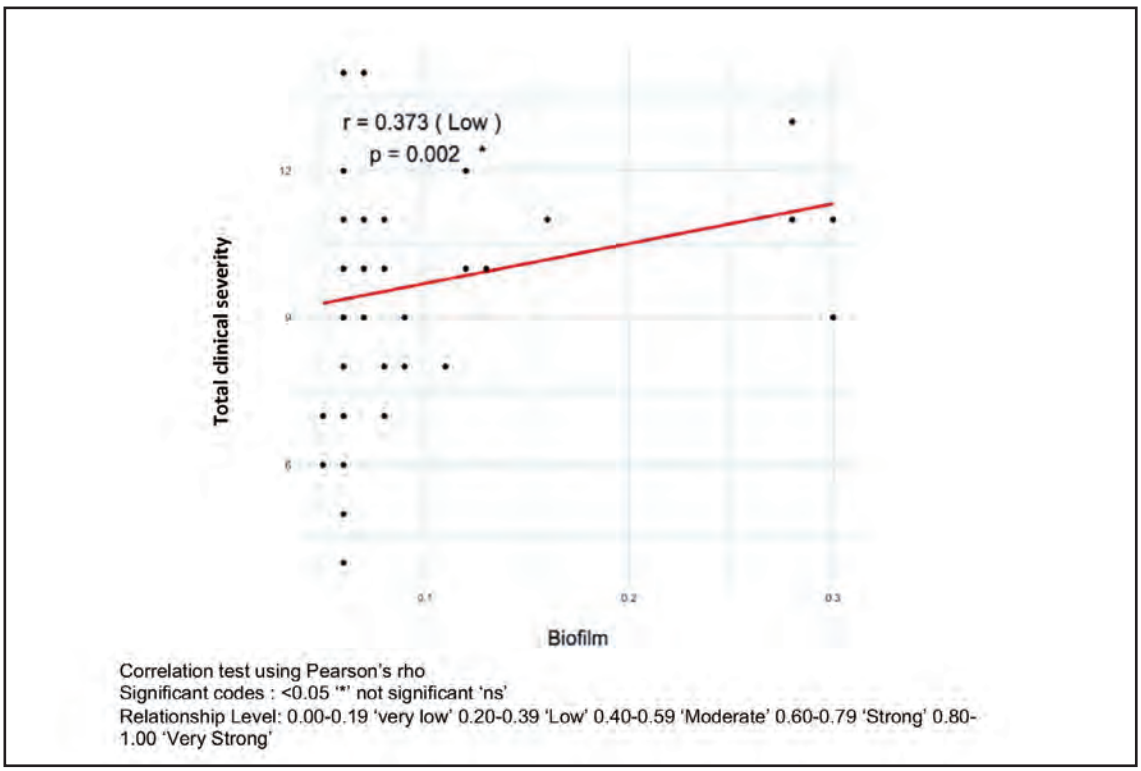

Fig. 3: Correlation between bacterial biofilm profile and total clinical severity in patients with chronic suppurative otitis media tubotympanic type based on Pearson's test

supplemented with glucose can support strong biofilm formation, which can be reproducibly quantified.[10] Moreover, weak biofilms still affect therapeutic outcomes and worsen infections.

The intensity of otorrhea and quantity of discharge did not show a significant relationship, suggesting that these factors may not be influenced by the biofilm profile. Biofilm formation, whether weak or moderate, enables bacteria to survive for extended periods at the infection site, leading to persistent clinical symptoms. Otorrhea, often caused by ongoing inflammation and secretion in the ear, may be associated with the ability of biofilms to create an environment conducive to recurrent infections. Hall-Stoodley et al. demonstrated that biofilms enhance bacterial resistance to the immune system, making it difficult to resolve inflammation and fluid production. Additionally, tympanic membrane perforation, commonly observed in CSOM, may be linked to the ability of bacteria within the biofilm to damage local tissues. Biofilms protect bacteria by enabling them to continue producing enzymes or toxins that can harm tissue structures, slow the natural healing process, and cause further damage to the tympanic membrane.[11] This is in line with findings by Jensen et al. who showed that bacteria within biofilms produce proteases and other bioactive components that can damage local tissues and exacerbate the infection.[12]

The most statistically significant finding was the relationship between disease chronicity and biofilm formation ($p<0.001$), indicating that stronger biofilms correlated with longer disease duration. This is consistent with the research by Edward and Novianti (2023), which emphasizes the crucial role of biofilm formation in maintaining chronic infections and impeding the response to treatment.[13]

The degree of hearing loss also showed a correlation coefficient ($r=0.281$), indicating low correlation strength, but the correlation was statistically significant ($p=0.015$). This suggests that stronger biofilms are associated with more severe hearing impairment. Individuals with more severe hearing loss may have this condition because of the chronic nature of the disease, which is influenced by biofilm formation. This finding is consistent with reports by Triola et al. state that chronic otitis media is a major cause of hearing loss, especially when the infection persists. In chronic infections, biofilms facilitate bacterial colonization of the middle ear structures, causing chronic inflammation that disrupts normal auditory function.[14] Alhede et al. (2019) found that bacteria within biofilms are frequently resistant to conventional antibiotics, resulting in persistent hearing loss due to uncontrolled inflammation in the region.[15]

In this study, two patients did not exhibit hearing loss, which could be related to the fact that eight patients had a disease duration of less than one year. Additionally, this could be associated with excellent hearing levels. Therefore, when tympanic membrane perforation occurs due to CSOM, there is a reduction in hearing function, but it has not yet reached the level of mild hearing loss. Furthermore, one patient was found to have sensorineural hearing loss, which warrants further investigation to determine whether there are diseases or other disorders besides CSOM that cause this condition. Overall, the results of this study indicate a significant

relationship between the clinical symptoms of patients with tubotympanic type chronic suppurative otitis media and bacterial biofilm profiles. Biofilms formed by various types of bacteria in these patients contribute to the persistence and exacerbation of the clinical symptoms. Generally, the primary symptoms of CSOM, such as otorrhea, hearing loss, and chronicity, can be worsened by the presence of biofilms, which protect bacteria from both the body's immune response and antibiotic treatment. The clinical severity of CSOM tubotympanic type is strongly associated with the presence of bacterial biofilms. Biofilms not only prolong the infection and increase resistance to treatment but also play a crucial role in exacerbating the clinical manifestations of the infection, making it difficult to treat and often requiring more aggressive and prolonged therapies.[16] In this study, participants who were selected were those who did not have comorbid conditions such as immunocompromised disorders, in order to avoid bias caused by other factors that could affect the severity of the disease aside from pathogens and biofilms

The results of this study indicate that all bacteria are capable of forming biofilms, highlighting the importance of considering additional therapeutic strategies for managing CSOM. Ear irrigation with antiseptic solutions, as well as the use of adjunctive anti-biofilm therapies and quorum sensing inhibitors, are believed to enhance the success of treatment in CSOM. Ear irrigation can help to clear debris, pus, and microorganisms, thereby improving the effectiveness of topical medications. Antiseptic solutions such as 2% acetic acid and hydrogen peroxide are commonly used. Acetic acid inhibits the formation and eradication of *Pseudomonas aeruginosa* biofilms in CSOM.[6] Hydrogen peroxide (H_2O_2) is used as an antiseptic irrigation solution because of its ability to generate reactive oxygen species, which can damage bacterial cell walls and biofilm structures, making it effective in killing microorganisms and disrupting biofilm integrity.[17]

Several studies have shown that certain agents can inhibit biofilm formation or destroy the existing biofilms. Blasi and Page (2016) demonstrated in vitro that N-acetylcysteine has antibacterial properties and can inhibit biofilm formation. N-acetylcysteine blocks the production of exopolysaccharides, a major component of the biofilm matrix, thus preventing biofilm formation and accelerating biofilm degradation.[18] In addition, N-acetylcysteine induces oxidative stress in bacterial cells, contributing to cell death and biofilm disruption.[19] Ethylenediaminetetraacetic acid (EDTA) can chelate divalent cations such as calcium and magnesium, which stabilize the biofilm matrix. The removal of these ions weakens the biofilm structure and increases its permeability, making the bacteria more susceptible to antimicrobial agents.[20,21] The combination of N-acetylcysteine and EDTA synergistically disrupted the biofilm matrix and enhanced the effectiveness of antimicrobial therapy. However, clinical use must consider potential side effects and compatibility with other therapeutic agents.

Quorum sensing (QS) is a form of bacterial communication that allows bacteria to collectively coordinate gene expression, including genes involved in biofilm formation and virulence factor production. Nur et al (2006) explored several agents that inhibit enzymes involved in the production of QS signaling molecules known as autoinducers.[22] Specific enzymes, such as halogenated furanones from *Delisea* pulchra algae, N-(heptylsulfanylacetyl)-L-homoserine lactone from *Allium sativum*, and flustramine from the bryozoan *Flustra foliacea*, can inhibit and degrade autoinducers, thereby preventing gene expression and activation of quorum sensing pathways. These findings highlight the importance of understanding the clinical and microbiological characteristics of patients with CSOM and the relationship between these factors and biofilm formation. This understanding could inform the development of more effective treatment strategies, taking into account the interaction between bacterial pathogens and the clinical conditions of patients. Further research is needed to explore the underlying mechanisms of this relationship and to assess its impact on treatment and patient prognosis.

CONCLUSION

This study successfully analyzed the clinical and microbiological characteristics of patients with tubotympanic type chronic suppurative otitis media, focusing on biofilm formation. The main findings indicated that 21 types of bacteria were identified, predominantly gram-negative bacteria, with the most prevalent being Pseudomonas aeruginosa, followed by *Staphylococcus aureus* and *Proteus mirabilis*. Correlation analysis revealed a significant positive relationship between the biofilm profile and several clinical variables, indicating that the stronger the biofilm profile, the more severe the clinical presentation of the tubotympanic type of CSOM.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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ORIGINAL ARTICLE

Velopharyngeal function and nasalance score in post-radiation nasopharyngeal carcinoma patients

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ABSTRACT

Introduction: Voice production and speech impairment in head and neck cancer patients can be experienced due to tumors or therapy such as radiotherapy. Velopharyngeal fibrosis in post-radiation nasopharyngeal carcinoma (NPC) patients can disrupt the velopharyngeal closure during speech, causing hypernasality. This study aims to determine the characteristics and proportions of the nasalance score in post-radiation NPC patients with or without resonance disorder.

Materials and Methods: This research is a descriptive study using cross-sectional techniques, followed by retrospective data collection of post-radiation NPC patients at Dr. Cipto Mangunkusumo General Hospital for the period July-August 2023. The parameter assessed is the nasalance score using a nasometer, the velopharyngeal dysfunction assessed with flexible laryngoscopy, and the hypernasality assessed by a 15 years' experienced speech therapist.

Results: The nasalance score in the Gajah 1 test obtained a median of 14 (7-22), for the mean value of Hantu 1 test was 39.8% ± 4.5, and for the mean value of Sengau test was 62.2 ± 6.9, with a nasalance score cut point in Gajah 1 test between normal resonance and hypernasal was 15.5% and in Hantu 1 test was 42.5%. Gender and radiation dose to the pharyngeal constrictor muscle tend to have a significant relationship with resonance disorder in post-radiation NPC patients.

Conclusion: A prospective study is needed in NPC patients with pre- and post-radiation assessment and follow-up evaluation to assess the effects of radiation which includes all relevant functional aspects of voice and speech.

KEYWORDS:
Nasopharyngeal carcinoma, radiation, nasalance score, hypernasality, velopharyngeal dysfunction

INTRODUCTION

Voice production is essential for verbal communication and social interaction, serving as a reflection of an individual's identity and personality, which significantly impacts their well-being and quality of life. [1,2]

The velopharynx (VP) plays a vital role in speech and voice generation. Dysfunction in the velopharynx, whether caused by nerve issues, structural abnormalities, or functional impairments, can lead to resonance problems such as hypernasality.[3,4] Additionally, individuals with head and neck cancer may experience difficulties in voice production and speech due to tumors or treatments like radiotherapy.

Radiotherapy works by inhibiting tumor cell growth through various molecular mechanisms and can be used alone or in combination with surgery and/or chemotherapy.[5] According to Dorr et al. and Kraaijenga et al.[6] the risk of side effects on normal tissues near the targeted area depends on the radiation dose and the amount of healthy tissue exposed.[7] High doses of radiation not only destroy tumor cells but can also affect normal cells, potentially causing tissue fibrosis, hypovascularity, and hypocellularity.[8] In patients with nasopharyngeal carcinoma (NPC), VP is at risk of radiation side effects due to its proximity to the tumor being targeted. A study by Xiao-song et al.[9] examined 16 post-radiation NPC patients with velopharyngeal dysfunction who had received an average radiation dose of 70 Gy. The dysfunction resulted in velopharyngeal insufficiency caused by atrophy and fibrosis, the common side effects of radiotherapy.

Nasometry, an acoustic tool that measures speech nasality through a nasalance score, is often used to assess the impact of therapies or procedures on speech. Numerous studies have explored velopharyngeal function and resonance in head and neck cancer patients. However, there is still no data on the characteristics and proportions of nasalance scores in post-radiation NPC patients, whether they have resonance disorders or not. Therefore, research is needed to assess nasalance scores and velopharyngeal dysfunction in these patients.

MATERIALS AND METHODS

Study design and participants

This descriptive study was conducted using a cross-sectional approach at the Ear, Nose, Throat, Head, and Neck Surgery Outpatient Clinic and Radiation Oncology Unit of Cipto Mangunkusumo General Hospital. The study was conducted from June to September 2023 and involved 37 post-radiation NPC patients.

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Table I: Subject Distribution of Study Population (N=37)

Characteristics of study population	Frequency	Percentage (%)
Gender		
Male	23	62.2
Female	14	37.8
Age Group		
18 – 45 years old	17	45.9
46 – 59 years old	20	54.1
Median (Range) Age	47.0	18 – 59
Treatment Modality		
Radiation	1	2.7
CRT	13	35.1
NAC and CRT	16	43.2
CRT and adjuvant chemotherapy	6	16.2
NAC, CRT, and adjuvant chemotherapy	1	2.7
Tumor size		
T1	5	13.5
T2	15	40.5
T3	7	18.9
T4	10	27
Time from the last radiation		
3 months - 1 year	17	45.9
More than 1 year	20	54.1
Median (Range) Time from the last radiation in month	14	3 – 120
Resonance disorder		
Normal	29	78.4
Hypernasal	8	21.6
Velopharyngeal dysfunction		
Velopharyngeal dysfunction	13	35.1
Coronal	5	38.5
Circular	4	30.8
Sagittal	4	30.8
Normal VP	24	64.9
Nasalance score (Median/Mean and SD/Range)		
Median (Range) Gajah 1 test	14,0	7 – 22
Mean ± SD Hantu 1 test	39.8	± 4.5
Mean ± SD Hantu 1 test	62.2	± 6.9
Radiation dose (Median/Mean and SD/Range)		
Mean ± SD PCM radiation dose cGy	6091.3	± 311.7
Median (Range) Soft palate radiation dose cGy	6836.0	5535 – 7125

CRT, chemoradiation; NAC, neo-adjuvant chemotherapy; PCM, pharyngeal constrictor muscle; VP, velopharynx.

Table II: Subject distribution by resonance disorder (N=37)

Distribution	Resonance Disorder		p-value
	Hypernasal (N=8)	Normal (N=29)	
Gender			
Male	2	21	0.035[a]
Female	6	8	
Age Group			
18 – 45 years old	3	12	>0.999[a]
46 – 59 years od	5	17	
NAC			
Yes	5	12	0.428[a]
No	3	17	
Adjuvant chemotherapy			
Yes	2	5	0.631[a]
No	6	24	
Time from the last radiation in month (Median and Range)	15 (4-85)	12 (3-120)	0.502[b]
PCM radiation dose cGy (Mean ± SD)	6292.66 ± 277.2	6035.77 ± 301.6	0.037[c]
Soft palate radiation dose cGy (Median and Range)	6909 (6752-7070)	6919 (6045-7125)	0.957[b]
Velopharyngeal dysfunction			
Coronal	3	2	
Sagittal	2	2	
Circular	2	2	
Normal velopharynx	1	23	

NAC, neo-adjuvant chemotherapy; PCM, pharyngeal constrictor muscle
[a]Fisher's exact test, [b]Mann-Whitney test, [c]Independent t-test

Table III: Characteristics of study population with velopharyngeal dysfunction (N=37)

Characteristic	Velopharyngeal dysfunction		p-value
	Velopharyngeal dysfunction (N=13)	Normal VP (N=24)	
Gender			
Male	6	17	0.171[a]
Female	7	7	
Age Group			
18 – 45 years old	6	9	0.730[a]
46 – 59 years old	7	15	
Time from the last radiation in month (Median and Range)	14 (3-78)	13,5 (3-120)	0.838[b]
PCM radiation dose cGy (Mean ± SD)	6195 ± 334.6	6035 ± 290.4	0.139[c]
Soft palate radiation dose cGy (Median and Range)	6941 (6752-7125)	6918 (6045-7111)	0.276[b]

PCM, pharyngeal constrictor muscle.
[a]Fisher's exact test, [b]Mann-Whitney test, [c]Independent t-test

Table IV: Nasalance score based on type test and resonance disorder (N=37)

Nasalence score (%)	Resonance disorder				p-value
	Hypernasal (N=8)		Normal (N=29)		
	Mean	SD	Mean	SD	
Gajah 1 test	17.5	± 3.9	13.3	± 4.2	0.01
Hantu 1 test	44.0	± 5.1	38.6	± 5.6	0.02
Sengau test	65.3	± 8.5	61.4	± 6.3	0.15

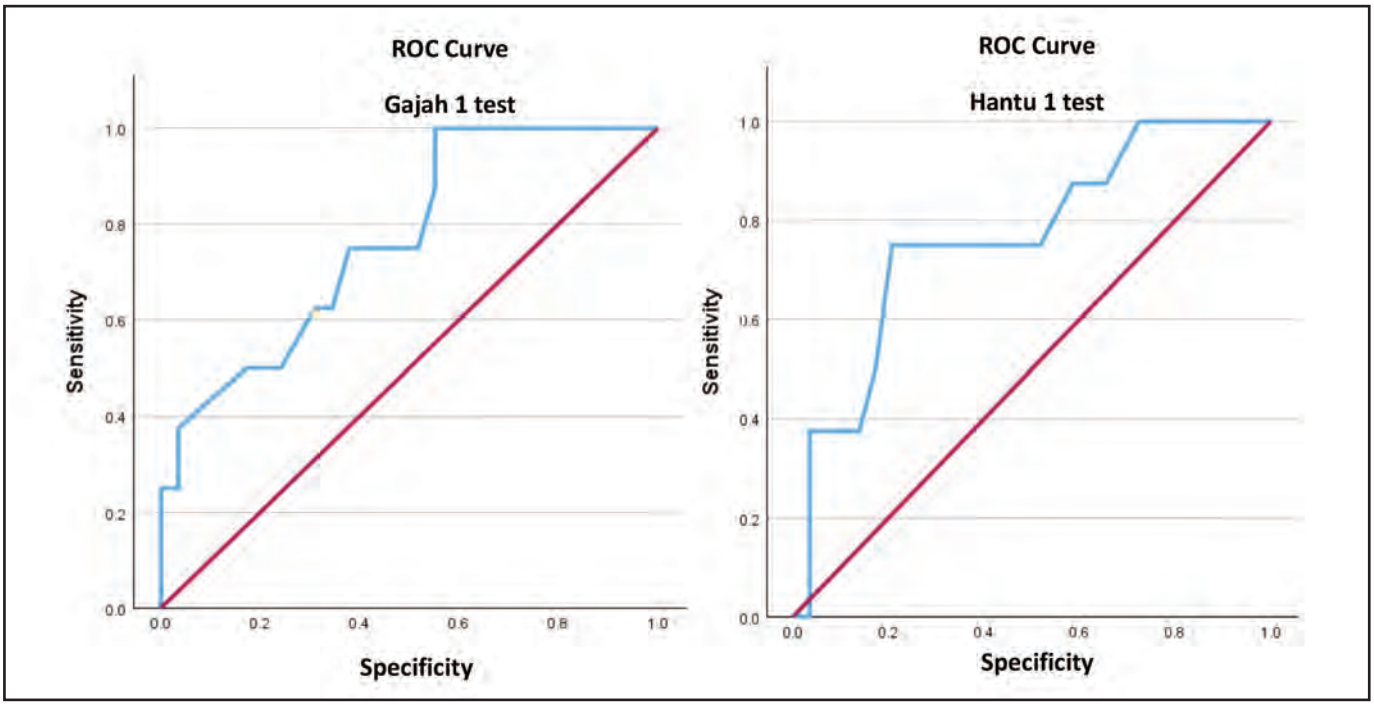

Fig. 1: ROC curve for Gajah 1 test and Hantu 1 test based on resonance disorder

The inclusion criteria for this study were NPC patients aged 18–60 years who had completed definitive radiation therapy with no residual mass in the nasopharynx and at least three months since the last radiation session. Exclusion criteria included: (1) patients with other malignancies, (2) those with progressive or degenerative nerve disorders, (3) acute nerve injuries, (4) tracheostomies, (5) anatomical abnormalities in the nasal cavity or throat unrelated to radiation, (6) a history of severe bilateral hearing loss, (7) prior nasopharyngectomy, and (8) acute infections or allergies in the nose or sinuses during the examination. All participants provided written informed consent for the study.

Study procedure and outcomes

The study subjects underwent clinical evaluations, including age, gender, clinical symptoms (ear, nose, throat, and neck), NPC treatment history, and resonance disorders assessed by an experienced speech and language therapist. Flexible laryngoscopy (Olympus Visera OTV-S7 videoscope, 3 mm diameter, Maxenon Xi 300 light source) was used to examine

nasal and throat structures and evaluate VP function. An Otorhinolaryngology consultant with over 15 years of experience reviewed and validated the nasopharyngoscopy videos for velopharyngeal function.

Nasometry was performed using the Pentax Model 6500, which involved placing a computer-based device with a headset and microphone on the nose and mouth. Patients read Indonesian passages, including the Sengau test, Gajah 1 test, and Hantu 1 test, to calculate the average nasalance score by comparing acoustic energy in the nasal and oral cavities. The Gajah 1 test corresponds to zoo passages, the Hantu 1 test to rainbow passages, and the Sengau test to nasal sentences. A speech and language therapist with over 20 years of experience evaluated and validated resonance disorders using perceptual speech assessments and nasometry.

Statistical analysis

Descriptive data were presented as frequencies and proportions for categorical variables and as mean ± standard deviation (SD) for continuous variables. Associations between age, gender, treatment type, time since last radiation, and radiation doses to the pharyngeal constrictor muscle (PCM) and soft palate with resonance disorders and velopharyngeal dysfunction were analyzed using Fisher's exact test, Mann-Whitney test, or Independent t-test. Sensitivity, specificity, and the area under the curve (AUC) were calculated, and a receiver operating characteristic (ROC) curve was plotted when a correlation between nasalance score and resonance disorder was identified.

Ethics approval

The study protocol has been approved by the Health Research Ethics Committee, Faculty of Medicine Universitas Indonesia and Dr. Cipto Mangunkusumo National General Hospital.

RESULTS

Characteristics of study population

A total of 37 post-radiation NPC patients were assessed at the Ear, Nose, Throat, and Head and Neck Surgery Outpatient Clinic during this study. We evaluated age, sex, treatment type, tumor size, and time since the last radiation. Normality tests were conducted on numerical variables, including age, radiation doses to the pharyngeal constrictor muscles and soft palate, time since the last radiation, and results from the Gajah 1, Hantu 1, and Sengau tests. Variables that showed a normal distribution included the Gajah 1 test, Sengau test, and PCM radiation dose. The distribution of the study population is presented in Table I.

Resonance Disorder and Velopharyngeal Dysfunction

Gender and radiation dose to the pharyngeal constrictor muscle were found to significantly contribute to resonance disorder, with p-values of 0.035 and 0.037, respectively. The distribution of treatment modalities related to resonance disorder is shown in Table II. Velopharyngeal dysfunction with hypernasality was observed, with 3 subjects having a coronal closure pattern, 2 having a sagittal pattern, and 2 having a circular pattern. One subject had a normal velopharyngeal closure pattern.

Velopharyngeal dysfunction was observed in 13 (35.1%) of the study subjects. No significant association was found between age, sex, radiation dose to the pharyngeal constrictor muscle, radiation dose to the soft palate, or time since the last radiation and velopharyngeal dysfunction (Table III).

Nasalance score of study population

The nasalance scores for each test type in patients with normal resonance and hypernasality are shown in Table IV. In the subsequent analysis, the Gajah 1 and Hantu 1 tests were included for determining the nasalance cut-off scores and confidence intervals, as only these two tests demonstrated statistically significant differences between normal and hypernasal perceptual speech groups.

The cut-off point for the Gajah 1 test nasalance score, distinguishing normal resonance from hypernasality, is 16.5%, with a sensitivity of 62.5% (95% CI: 30.6%–86.3%) and a specificity of 69% (95% CI: 50.8%–82.8%). Similarly, the cut-off point for the Hantu 1 test nasalance score is 42.5%, with a sensitivity of 75% (95% CI: 40.9%–92.9%) and a specificity of 79.3% (95% CI: 61.6%–90.1%).

DISCUSSION

This study found that the prevalence of NPC was higher in males (67.8%) than in females (32.2%). According to Global Cancer Statistics10 and Beyene et al.[11], males are 2-3 times more at risk than females. Adham et al.[12] reported that from 1995 to 2005, the male-to-female ratio of NPC patients at Cipto Mangunkusumo General Hospital was more than 2.4:1. The higher incidence of NPC in men is likely due to biological or lifestyle factors, such as smoking and exposure to carcinogens. The median age in this study was 42.97 years, with the 45-60 age group being the most affected. Yu et al.[13] noted that NPC incidence increases with age, possibly due to genetic factors and early Epstein-Barr virus (EBV) infection. Long-term environmental factors may impair the immune control of EBV over time, leading to the development of NPC. Velopharyngeal dysfunction occurred in 35.1% of subjects, with 5 having a coronal pattern, 4 a sagittal pattern, and 4 a circular pattern. Sun-Yung Bak et al.[8] noted that head and neck cancer treatments not only affect tumor cells but also normal cells. Wang et al.[14] highlighted that collagen deposition causes hypovascularity, leading to fibrosis and making these areas more vulnerable to physical damage, ischemia, and eventual loss of function, atrophy, or necrosis. In velopharyngeal function, radiation can cause soft palate dyskinesia, including muscle atrophy and sclerosis, as well as hard palate osteonecrosis and perforation. These side effects may develop later due to hypovascularity and hypocellularity from radiation exposure, resulting in fibrosis and scar tissue that interfere with VP movement when opening and closing the nasopharynx.

Resonance disorder, specifically hypernasality, was found in 8 subjects. Kraaijenga et al.[6] reported resonance abnormalities in 64% of 22 post-radiation head and neck cancer patients. Radiation can cause resonance disorders by affecting the laryngeal tissue, leading to edema during treatment and fibrosis afterward. An inadequate VP closure

during speech, with a velopharyngeal gap greater than 0.1 mm, can cause hypernasality. Warren et al.[15] noted that inadequate VP closure leads to hypernasality, which also reduces oral muscle mobility, affecting both speech and swallowing functions. Gender and radiation dose to the PCM were found to be significantly associated with resonance disorders in post-radiation NPC patients. Although no studies have focused on the impact of gender on speech resonance in these patients, a study by Pearsell et al.[16] found that gender influences speech perception in individuals with normal hearing and cognition. The pharyngeal constrictor muscle helps close the velopharynx during speech by moving anteromedially, along with the superoposterior movement of the velum. Radiation-induced fibrosis in this muscle can affect VP function.

Jordan HN et al.[17] suggests sex differences in velopharyngeal closure patterns with the increased velar length observed in males compared with females. Kumar et al18 found significant increases in the nasalance values during the menstruation phase. The findings indicate that hormonal and other related changes occurring during menstruation leads to a significant change in the resonance characteristics of voice.

Late-onset side effects after radiation in head and neck cancer patients are influenced by various factors. Kraaijenga et al.6 conducted a study to assess voice, speech, and quality of life in head and neck cancer patients 10 years after chemoradiation. The study found that voice and speech dysfunction were common problems in this population. Jacobi et al.[1] reviewed the literature and found that voice and speech often decreased during chemoradiation but improved within 1 to 2 months, continuing to improve for up to a year or more after therapy. However, voice and speech assessments did not return to normal levels, either before or after treatment.

Larger or more advanced tumors are associated with greater toxicity compared to early-stage tumors due to higher radiation doses and broader radiation exposure.[19] Stelzle et al.[20] found that tumor size was linked to speech intelligibility, though it is important to consider that tumor removal may lead to fibrosis, which is worsened by radiotherapy. Radiation doses above 40 Gy in NPC can damage the oral, pharyngeal, or glandular tissues in the mucous and submucous layers. Jacobi et al.[21] stated that radiation to the base of the tongue and velopharynx can alter speech by affecting the strength, movement, and balance between the muscles, which impacts articulation after treatment. According to Kraaijenga et al.[6], radiotherapy for non-laryngeal cancers can affect voice and speech due to changes in the anatomy of the vocal tract, such as scar tissue, edema, and fibrosis in surrounding structures, leading to less clear speech and poor articulation. This can affect daily activities and social interactions, leading to functional and psychosocial issues and a reduced quality of life. Patients receiving Intensity-Modulated Radiotherapy (IMRT) generally experience fewer voice and speech problems than those who receive conventional radiotherapy.[6,8]

Chemotherapy helps tumors and surrounding tissues more sensitive to radiation, which can worsen radiation-related side effects. Morton et al.[22] reported that speech impairment worsened in head and neck cancer patients undergoing multimodal treatment. Chemotherapy is known to cause cytotoxicity, leading to conditions like xerostomia and oral mucositis, which can affect speech function.[23,24]

Individual factors can cause variations in nasalance scores. In this study, the mean nasalance scores for post-radiation NPC patients were as follows: 14% (7% - 22%) for the Gajah 1 test, 39.8% ± 4.5 for the Hantu 1 test, and 62.4% ± 6.9 for the Sengau test. NPC patients with hypernasality had higher mean nasalance scores than those with normal resonance across all three tests. Nasometry is used to assess the impact of therapy or procedures on speech and helps differentiate between hypernasal and hyponasal speech, as well as determining the severity of hypernasality.[25] In post-radiation head and neck cancer, radiation can cause edema and muscle fibrosis in the oral and nasal structures, influencing resonance and nasalance scores. The study found that the Hantu 1 test had higher sensitivity 75% (95% CI: 40.9%–92.9%) and specificity 79.3% (95% CI: 61.6%–90.1%) than the Gajah 1 test with sensitivity 62.5% (95% CI: 30.6%–86.3%) and specificity 69% (95% CI: 50.8%–82.8%). However, this study did not assess nasalance scores and resonance before radiation, which could be a potential bias affecting the results.

CONCLUSION

Radiotherapy is the primary treatment for NPC because it is a radiosensitive cancer. However, while effective, radiation can have side effects that impact resonance speech and velopharyngeal function in head and neck cancer patients. These side effects may develop gradually, requiring long-term follow-up for post-radiation NPC patients. Nasalance scores serve as a valuable quantitative tool for identifying individuals at risk of hypernasality, enabling timely and targeted interventions. High nasalance scores, particularly in high-risk groups, can act as early indicators of velopharyngeal dysfunction. By identifying high-risk patients early, clinicians can implement preventative measures or interventions at the beginning of the treatment course, reducing the long-term impact of velopharyngeal dysfunction and enhancing overall communication outcomes.

This study had a few limitations. Hypernasality may be influenced by various factors, including hormonal levels, psychological conditions, and detailed anatomical variations. Furthermore, the current study offers only a cross-sectional perspective, without investigating longitudinal changes in hypernasality or nasalance scores. Cultural and linguistic differences in speech patterns may also impact both the perception and measurement of hypernasality. As initial resonance characteristics prior to radiation were not captured, drawing conclusions about radiation-induced changes remains challenging. To comprehensively evaluate the effects of radiation on all functional aspects of voice and speech, a prospective study incorporating pre- and post-radiation resonance assessments, followed by longitudinal evaluations, is warranted.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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ORIGINAL ARTICLE

Unmasking nasal basal cell carcinoma: Strategies for defect coverage

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ABSTRACT

Introduction: Many reconstruction methods have been introduced for the reconstruction of basal cell carcinoma (BCC) post excision however no study has described the preferred reconstruction method in the Malaysia setting. Variations in resource availability and surgical training between regions may affect reconstructive choices. This study intends to find out our preferred method for reconstruction in nasal BCC patients post excision in our centre.

Materials and Methods: We conducted a retrospective chart review of patients undergoing different reconstruction methods and assessing outcomes for a series of patients with BCC post-resection, conducted in Hospital Universiti Sains Malaysia (HUSM) and Hospital Raja Perempuan Zainab II, Kelantan, from 2012 to 2024.

Results: A total of seven patients were identified in this retrospective study, comprising five females and two males. The ages of these seven patients range from 60 to 77 years old. All seven patients who underwent excision postoperatively underwent immediate soft tissue reconstruction with either a local or regional flap, a free flap, or a combination of flaps. Among those seven patients, only one developed flap-related complications. All patients were followed up for at least 3 months, with a range of 3-38 months. Functional and cosmetic assessments over the resected area post-reconstruction were good.

Conclusion: Local flaps remain the preferred option for small and medium nasal BCC defects, while forehead flaps and free flaps are reserved for larger or complex defects. In Asian patients, thicker skin and pigmentation influence flap design and thinning to optimize outcomes.

KEYWORDS:
Basal cell carcinoma, nasal reconstruction, local flap, wide local excision

INTRODUCTION

Basal cell carcinoma (BCC) is the most common cancer in the United States, and increasing incidence rates have been noted worldwide. An annual incidence of 2 million BCC cases has been reported in Americans.[1-2] BCC is the most common cancer among non-melanoma skin cancers, followed by squamous cell carcinoma. The increased incidence rate of BCC also poses an increase in healthcare burden in terms of expenditure. An estimated $2-4 billion annual cost was reported in a U.S. study in treating non-melanoma skin cancer.[2]

BCC was found to originate from keratinocytes of the basal layer of the epidermis and pluripotent cells of the hair follicles. BCC occurs more commonly on sun-exposed areas, with the head and neck accounting for approximately 80% of cases. Among those BCC involving the head and neck region, 25-30% were found on the nose.[3] BCC rarely metastasises (<0.1% incidence); however, 30-50% recur within 5 years, and nasal BCC was noted to have a higher risk of recurrence.[4]

Resection of BCC involving the nose will leave a soft tissue defect, which poses a challenge in reconstruction, aiming to achieve both good functional and cosmetic outcomes. A good understanding of nasal anatomy, as well as preoperative planning, is necessary for successful nasal reconstruction. Various soft tissue reconstruction methods for nasal defects have been introduced throughout the past few decades, ranging from primary closure to free flaps and wound coverage, depending on the size, depth, orientation, and location of the defect on the nose.[5] We present a series of cases of different methods of soft tissue reconstruction for nasal BCC post-resection involving different areas of the nose.

MATERIALS AND METHODS

We conducted a retrospective review of patients who underwent nasal reconstruction after resection of nasal BCC using various techniques from 2012 to 2024 in Hospital Universiti Sains Malaysia (HUSM), and Hospital Raja Perempuan Zainab II (HRPZ II). Patients with nasal BCC who underwent wide resection with a 3mm resection margin, followed by immediate reconstruction, were reviewed to illustrate different techniques used.

A 3 mm surgical margin was adopted for clinically well-defined, low-risk lesions, in line with our institutional protocol and supported by evidence that this margin achieves adequate clearance in most cases while preserving tissue in cosmetically sensitive areas such as the nose. Wider margins, as recommended by the NCCN (4–5 mm), were avoided to minimize functional and aesthetic compromise. For ill-defined or recurrent lesions, wider margins or intraoperative frozen section control were considered to ensure complete excision. All excised specimens were submitted for histopathological examination to confirm margin clearance.

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Reconstruction was done with either a free or local flap, depending on the size and location of the defects. All patients were followed up for at least 6 months to assess their functional status and any recurrence of disease. All patient data, clinical information, surgical techniques, pathology results, radiology results, and follow-up information were reviewed.

Ethics approval

The study adhered to the principles outlined in the Declaration of Helsinki. The local ethics committee approved this study – JEPEM USM, with JEPeM Code: USM/JEPeM/KK/24040349, and the Medical Research and Ethics Committee, with code NMRR ID-24-02556-UED. Photo publication consent was obtained from patients.

RESULTS

A total of 7 patients were identified in this retrospective study, comprising five females and two males (Table I). The age of these seven patients ranges from 60 to 77 years old. All patients have lesions over their nasal region, which include three on the dorsum of the nose, one on the nasal ala, two on the nasal bridge, and one over the whole nose, as well as the right cheek.

Wide local resection was performed in all cases, with a 3 mm lateral margin and a deep margin extended to the pre-fascial layer or deeper, depending on the layers of tissue involved. The majority of the cases we encounter are primary lesions, which account for 6 cases, and the remaining case is due to local recurrence after resection. Post-resection histopathology examination revealed that the margins were clear in 5 cases, whereas 2 cases were noted to have inadequate resection margins.

All seven patients' post-excision underwent immediate soft tissue reconstruction with either a local or regional flap, a free flap, or a combination of flaps. Only one patient developed flap-related complications, characterized by partial necrosis of the flap tip, which was treated conservatively.

All patients were followed up for at least 7 months, with a range of 7-38 months. Postoperative outcomes were assessed at follow-up visits based on both functional recovery and cosmetic appearance. Functional outcomes—such as nasal breathing, speech, and oral competence—were evaluated clinically by the surgical team. Cosmetic outcomes were assessed subjectively, based on the operating surgeon's clinical judgment and patient satisfaction, using standard postoperative photographs and discussions during outpatient reviews. Functional and cosmetic assessments over the resected area post-reconstruction were good. Adjuvant radiotherapy was offered to 2 patients who had inadequate resection margins. One out of 7 patients developed new lesions over the same region of the body, which was found to be histopathologically proven BCC as well.

DISCUSSION

Basal cell carcinoma is the most common non-melanoma skin cancer, and its annual incidence rate has been rising in the past few decades worldwide. In our experience, we have treated BCC mostly in the head and neck region, which corresponds to what has been reported, where 80% of BCCs involve the head and neck region, and out of those, 25-30% are found on the nose.[3] BCC is characterised as a locally invasive skin malignancy. It rarely metastasises (accounts for < 0.1%).[1] In our encounter, none of the cases we encountered had distant metastasis. Some cases showed substantial local destruction involving up to cartilage, bone, or even the dura mater, which required craniectomy.

Our series demonstrated a preference for local and regional flaps in nasal reconstruction because they provide a superior color and texture match. Six out of seven patients underwent wound coverage with local and/or regional flaps. However, one patient with extensive soft tissue defects post-tumour resection required a free flap for wound coverage. Skin grafting and healing by secondary intention were avoided whenever possible because of poor aesthetic outcomes and contour irregularities.[6] However, in elderly patients with multiple comorbidities who are unable to undergo operation under general anaesthesia, skin grafting is a possible wound coverage option for them.

For small to medium–sized defects (up to 2 cm in diameter) over the upper third of the nose, we performed a transposition glabella flap for wound coverage. It was first introduced by Von Graefe in 1818, and subsequently, multiple modifications have been reported.[7] The advantages of this flap include a single-stage procedure, which can be done under local anaesthesia, and the donor site can be closed primarily.

For a small to medium-sized defect involving the upper third of the nasal sidewall, we performed a cheek advancement flap for wound coverage. This flap was described by Beare in 1969 and subsequently modified by Mustarde, Schrudde, and Beinhoff for facial reconstruction.[8] The single-stage procedure, ability to camouflage the scar between aesthetic facial lines, and robust blood supply are all advantages of this flap; thus, it is also considered the first-choice technique for nasal sidewall reconstruction by other authors.[8-9]

A combination of cheek flaps with other flaps is not uncommon and has been used in large defects affecting the nasal sidewall, dorsum nasal, and medial cheek subunit.[3,10] This was performed on one of our patients (Figure 1) with a full-thickness defect size of 5x3cm post-wide resection with a margin of 3mm of BCC lesion involving the nasal sidewall and dorsum nasal subunit. A Mustarde rotational cheek flap with a subcutaneously pedicled island forehead flap was performed for outer skin coverage. In contrast, a conchal chrondrocutaneous graft was harvested and inset as the inner lining as well as for cartilage reconstruction for support. For small lesions (less than 1cm in diameter) over the distal third of the nose, we performed other types of transposition flaps. A Zitelli's bilobed double transposition flap was performed for a small nasal dome defect of 1.6cm. The bilobed flap was first introduced by Esser in 1918, and later, modifications to the technique were introduced by Zitelli in 1989 to reduce the incidence of pincushioning or trapdoor deformity.[11] For a patient with a nasal alar defect (Figure 2), we performed a transposition nasolabial flap, which was first

Table I: Overview of cases in this study

No	Patient (age, sex)	Location	Primary/ recurrence	Tumor size (cm^2)	Defect size (cm^2)	Margin of resection (mm)	Margin involved	Reconstruction method	Operation-related Complication	Follow-up time (months)	Recurrence (HPE proven)
1	70, F	Dorsum of nose	Primary	4.6	7.5	3	Clear	Forehead flap	None	7	None
2	77, F	Right nasal alar	Primary	1.5	3.0	3	Clear	Nasolabial flap with concha cartilage graft	None	7	None
3	64, F	Left nasal bridge	Primary	0.8	1.82	3	Clear	Cheek advancement flap	None	7	None
4	62, M	Right nasal dorsum	Primary	1.4	4.5	3	Clear	Glabellar flap	Tip of flap necrosis	7	None
5	70, M	Left nasal dorsum	Primary	1.0	2.56	3	Clear	Bilobed flap	None	26	None
6	60, F	Nasal bridge and right nasojugal	Primary	10	15	3	Margin involved	Right cheek Mustardė flap + forehead flap + conchal chrondrocutaneous graft + FTSG	None	10	None
7	65, F	Midface	Recurrence	35.3	81.6	10	Margin involved	Free LD flap + capular bone flap	None	38	Yes, local

LD – latissimus dorsi, FTSG – full-thickness skin grafting, HPE – histopathological examination

Table II: Reconstructive Options for Nasal BCC Defects Based on Size and Location

Defect Location	Defect Size	Preferred Flap	Advantages	Limitations
Upper third	< 2cm	Glabellar flap	Single stage, good color match, donor site closes primarily	Limited reach, risk of medial brow scar
Nasal sidewall	< 2 cm	Cheek advancement flap	Excellent scar concealment along facial lines, robust blood supply	May distort adjacent aesthetic units if large
Nasal tip/dome	<1.5–2cm	Bilobed flap	Good color match, preserves contour	Risk of trapdoor deformity if poorly designed
Nasal ala (full-thickness)	< 2 cm	Nasolabial flap with cartilage graft	Good texture match, reliable vascularity	May require secondary debulking, staged if interpolated
Multi-subunit or large defect	> 2 cm	Forehead flap (paramedian)	Excellent color/texture match, robust flap	Requires 2–3 stages, visible donor site scar
Extensive/through-and-through	> 4–5 cm or composite	Free flap	Allows bone/cartilage reconstruction, fills large dead space	Technically demanding, longer operative time

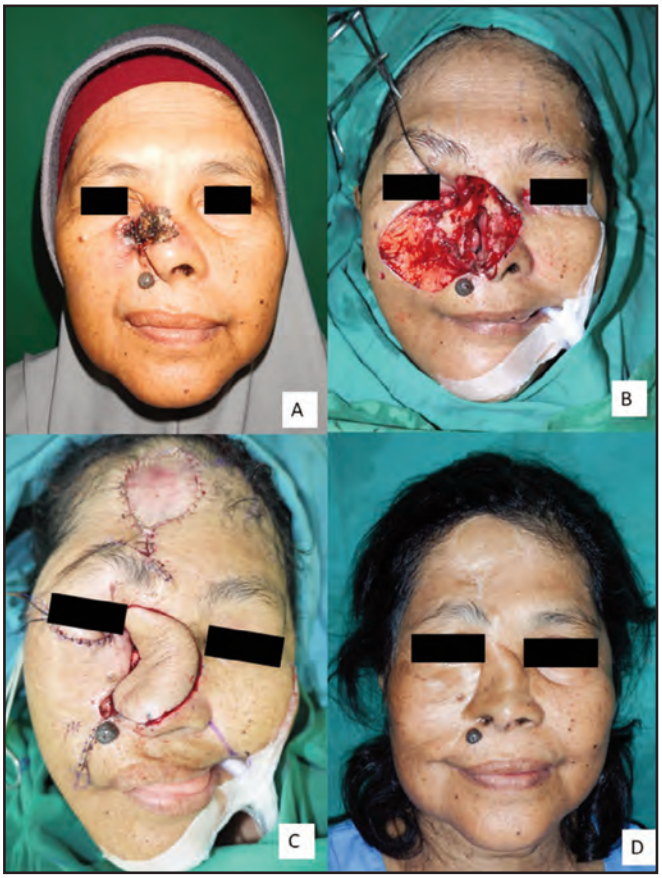

Fig. 1: Case no. 6 – 60 years old lady with right nasal sidewall BCC
A). BCC lesion preoperation, B). post resection with 3mm margin taken, C). post Mustarde rotational cheek flap with forehead flap and conchal chrondrocutaneous graft, D). post operation 1 year

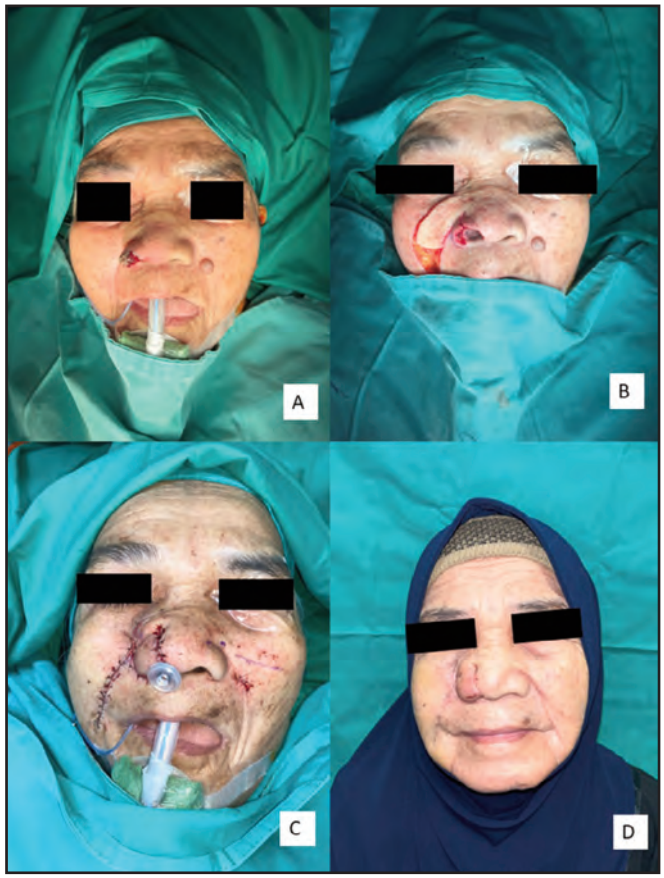

Fig. 2: Case no.2 – 77 years old lady presented with full thickness right nasal alar BCC
A). Lesion pre-operation, B). post-wide local excision and superiorly-based right nasolabial flap elevation, C). post flap inset with conchal cartilage graft and closure of donor site, nasal stent was inserted to maintain the right nostril patency temporarily, D). 1 month post-operation

described by Johann Friedrich Dieffenbach, a German surgeon, in 1846.[12] Our patient has a full-thickness nasal alar defect involving all three layers of the nasal alar; thus, a single-stage superiorly based, turned-in nasolabial flap was performed, with a concha graft inserted between to maintain nostril patency.

For patients with larger defects (>2cm) over the distal third of the nose involving multiple aesthetic subunits, a two-stage interpolated forehead flap was performed (Figure 3). The forehead flap is one of the oldest surgical techniques recorded for nasal reconstruction. It was described in the Sushruta Samhita in 700 BC. Subsequently, Millard, Gilles, and Converse refined the techniques, and it remains a workhorse in nasal reconstruction today.[13] The forehead flap is performed under general anesthesia and requires two to three stages, spaced a few weeks apart, to complete the nasal reconstruction; however, it provides an excellent color-texture match for nasal reconstruction.

For a patient with neglected recurrent giant BCC involving the whole nose and right cheek with infiltration into the sinonasal and overlying skin loss, we performed a free flap for wound coverage post-resection. The large size of the defect post-resection, as well as its involvement of the maxillary sinus, which necessitates a maxillectomy, renders local and regional approaches infeasible in this case. A free chimeric myocutaneous latissimus dorsi and scapular bone flap was performed instead in this case. The scapular bone was anchored over the pterygoid plate to separate the oral cavity from the nasal cavity. In contrast, the myocutaneous latissimus dorsi flap was used to obliterate the dead space post-resection of the lesion. This flap was introduced by Deraemaeker back in 1988 and has been used in head and neck reconstruction.[14] The advantages of this flap include a long pedicle, the ability to include scapular bone as a chimeric flap, a reliable vascular system, and the ability to provide a bulk of tissue for cavity obliteration, and thus was chosen for our patient.

Out of the seven patients, only one had partial flap necrosis, which was left to heal with secondary intention, and all other patients did not experience any operation-related complications. The majority of our patients are also satisfied with both the aesthetic and functional outcomes following their operations. Patients in this series were followed up for at least 7 months (ranging from 7 to 38 months), and only one patient with a giant BCC developed local recurrence, which was histopathologically proven to be BCC as well.

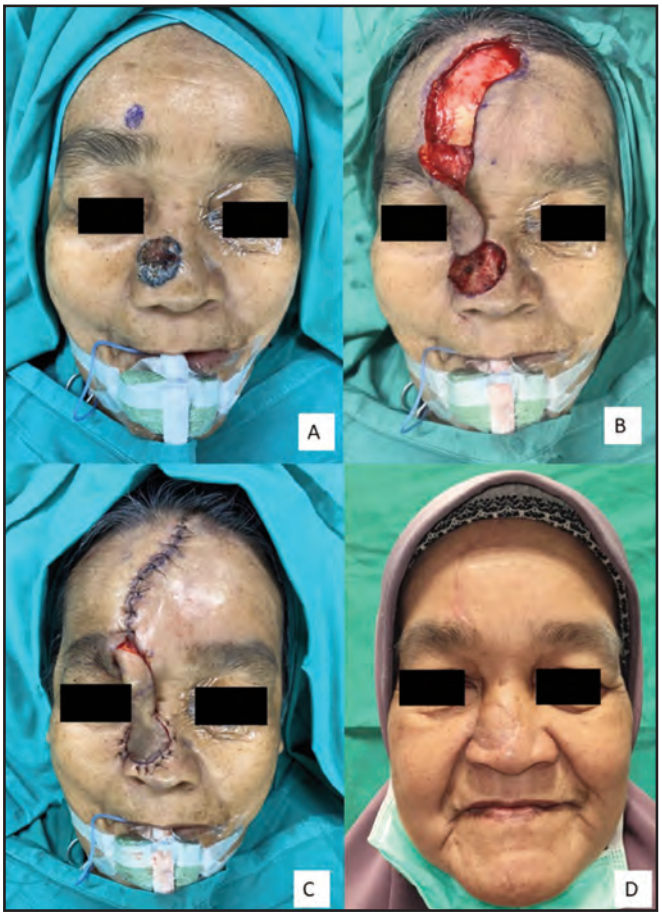

Fig. 3: Case no. 1- 70 years old lady presented with nasal dorsum BCC
A). Lesion over right nasal dorsum pre-operation, blue dot was marked over supratrochlear artery, B). elevation of interpolated forehead flap, C). after flap inset and closure of donor site, D). 2 months after division of flap

While surgical principles are similar globally, certain considerations apply to Malaysian patients. Thicker sebaceous skin in Asian patients can lead to bulkier flaps, requiring meticulous thinning for optimal contour. Additionally, increased pigmentation in Malaysian patients makes scar camouflage critical, favoring local flaps over skin grafts. Limited availability of Mohs surgery in many Malaysian centers often necessitates conventional wide excision, influencing reconstructive choices toward more robust flaps with predictable vascularity.

In summary, small and medium nasal defects can be effectively managed with local flaps, while large or full-thickness defects may require staged forehead flaps or free tissue transfer (Table II). Reconstruction should aim to restore both function and aesthetics while minimizing donor site morbidity.

CONCLUSION

Nasal BCC reconstruction should be individualized based on defect size and location. Local flaps provide excellent results for small to medium defects, while forehead flaps and free tissue transfer are reserved for larger or complex cases. In Asian patients, thicker skin and pigmentation require meticulous planning to optimize contour and scar camouflage.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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Adaptation and validation of the Sleep Quality Scale among Saudi population (A-SQS)

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ABSTRACT

Introduction: The quality of sleep has a significant impact on an individual's health and overall well-being. Given the variability of factors that impact sleep quality and their varying degrees of significance between individuals, the utilization of a self-report approach becomes necessary. The Sleep Quality Scale (SQS) is a widely used self-report measure designed to evaluate sleep quality. It consists of six distinct techniques and encompasses a total of 28 items. The aim of this study was to translate and validate the SQS in the Saudi population.

Materials and Methods: A cross-sectional approach was applied to evaluate the reliability, validity, and cross-cultural suitability of the Arabic adaptation of the Sleep Quality Scale (A-SQS) in a sample consisting of 402 individuals, with 33.9% representing females.

Results: The test-retest reliability was found to be significant, with a coefficient of 0.88 at a 15-day interval. Additionally, the principal component factor (PCF) analysis revealed five factors, that accounted for 56.29 % of the total variance. The Cronbach's alpha coefficient was 0.90 for internal consistency.

Conclusion: This result determined that the A-SQS possesses a valid and reliable 5-factor structure when applied to the Saudi population. These therefore renders the scale a valid and reliable instrument in both clinical practice and clinical research.

KEYWORDS:
Reliability, sleep quality scale, validity, Saudi Arabia

INTRODUCTION

One of the key functions of sleep is to allow the body to rest and restore energy. Sleep disorders or insufficient sleep contribute to physical and mental health problems as well as affect the quality of life.[1-3] In addition, sleep is an individual experience influenced by factors such as age, gender, dietary habits, and overall physical and psychological well-being. The assessment of sleep quality is crucial as its components and significance vary among individuals.[4] Therefore, sleep quality measurements are essential not only in clinical practise but also in research.[3] A diagnosis of insomnia is primarily based on the evaluation of self-reported symptoms, according to the International Classification of Sleep Disorders, third edition (ICSD-3) Sateia[5], and the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) Reynolds III and O'Hara[6], the sleep diary has become a standard tool to assess the patient's self-reported insomnia perception. The use of structured and semi-structured clinical interviews to assess sleep is becoming more common in clinical practice.

Several instruments have been improved in order to explore sleep quality among individuals and its possible influencing factors. For instance, Pittsburgh Sleep Quality Index (PSQI)[4], the Stanford Sleepiness Scale (SSS)[7], and the Sleep Quality Scale (SQS).[3] Even though objective tools, for example the multiple sleep latency test (MSLT), are effective in diagnosing individuals' sleep quality, previous studies reported that they are not as convenient and reasonable as self-reported scales.[8-9] In addition, technical training is needed and it is expensive as well as requires much time for measuring and reporting data. Moreover, one of the difficult points is testing sleep quality because a lot of equipment is required for this process.[3] On the other hand, sleep scales have multidimensional features, for example SQS is able to evaluate sleep quality from multiple perspectives to comprehensively reflect the association between sleep and other psychological variables, for example well-being and depression.[10] In addition, Differ sleep quality experiences can be assessed by self-report methods, for example, sleep diary, sleep log, and sleep questionnaire, and attempt to measure both quantitative and qualitative features of sleep.[11] Therefore, these subject methods are inexpensive, easily administered, and appropriate for large surveys.

Yi et. al. reported that some sleep quality scales have been utilised before but demonstated numerous limitations for example, few all-inclusive assessment scales, items that are unassociated with sleep quality, or they exclude necessary items.[3] Moreover, few scales provide a total score.[3] The SQS was developed in South Korea in 2006, in order to measure the sleep status of individuals in the past month. It is one of the most popular self-report sleep quality scales. The SQS has a 28-item assessment of the sleep quality of individuals across six factors/domains: daytime dysfunction, restoration after sleep, difficulty in falling asleep, difficulty in getting up, satisfaction with sleep, and difficulty in maintaining sleep. The SQS demonstrated satisfactory reliability in a Korean sample population.[3]

In terms of usage, SQS has commonly been used in English and other languages. In South Korea, SQS was developed and used for two samples. The initial sample consisted of 629

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people between the ages of 18 and 59 who were residing in the community. The second sample consisted of 110 subjects who were university students and had completed four years of education, 43.1% were male and 56.9% were female, with an average age of 20.6 years. SQS, which consisted of 28 questions and six covariates, explained 62.6% of the overall variance. The construct validity of the SQS score was validated by a significant difference (t=13.8, p=0.000) between insomniacs and normal participants. Cronbach's alpha coefficient demonstrated a high level of internal consistency, with a value of 0.92. Additionally, the test-retest reliability was found to be strong, as indicated by a correlation coefficient of 0.81 across a 2-week interval.[3]

In China, the SQS was used for 522 Chinese people aged from 18 to 56 years old. The result illustrated that the new version of SQS included 23 items across four factors/domains. The four factors were difficulty in getting up (2 items), difficulty in falling asleep (5 items), sleep recovery (6 items), and daytime dysfunction (10 items). In addition, men had lower scores on the element pertaining to the difficulty in initiating sleep, while displaying greater scores on the aspect related to sleep recovery, in comparison to women.[12]

In Indonesia, the SQS was administered to 90 cancer patients aged 18 to 65 years. The result demonstrated the same original instrument SQS 28 items, with six factors. The authors presented that the Indonesian QSQ version had an adequate level of internal consistency and stability and can be used for both clinical and general population.[13]

In Turkish, a cross-cultural adaptation of SQS study were conducted by Dereli M et. al , to determine the validity and reliability of the Turkish version of SQS in 238 adults aged from 18-65; 152 (63.9%) were female, and 86 (36.1%) were male.14 The findings of the study indicate that the SQS is a valid and reliable tool that may be effectively employed for assessing the sleep quality of Turkish adults who are in good health.

In Saudi Arabia, several studies were conducted in order to evaluate the sleep quality. For example, a cross-sectional study among 440 university students, to assess the association between poor sleep quality and physical inactivity using PSQI.[15] Another study in Saudi Arabia evaluated the sleep quality and academic performance among 95 medical students using PSQI. The results illustrated that poor sleep was prevalent in 63.2% of students; it was higher among students who were physically inactive and spent more time on screens Moreover, results showed that poor sleepers demonstrated significantly higher academic performance compared to adequate sleepers (p=0.04).

In addition, the PSQI was used to assess the sleep quality during COVID-19 for 790 Saudi population. The results demonstrated that poor sleep quality was reported by 54.4% and 55.5% of respondents in the two groups, respectively. Female gender and marital status were linked to lower overall PSQI, sleep quality, sleep distribution, sleep latency, and daytime dysfunction.[16]

The aim of this study was to evaluate the psychometric properties of the Arabic version of the QSQ and identify patterns of sleep quality in the Saudi population.

MATERIALS AND METHODS

The Sleep Quality Scale (SQS), which consists of 28 items, assesses six domains of sleep quality: daytime symptoms, sleep restoration, problems initiating and maintaining sleep, difficulty waking, and sleep satisfaction. The developers hoped to create a scale that could be used as a general, efficient measure suitable for evaluating sleep quality in a variety of patient and research populations. Respondents indicate how frequently they exhibit certain sleep behaviours using a four-point Likert-type scale (0 = "few," 1 = "sometimes," 2 = "often," and 3 = "almost always"). Scores on items from factors 2 and 5 (restoration after sleep and sleep satisfaction) are reversed before being tallied. Total scores range from 0 to 84, with higher scores indicating more severe sleep issues. 3, conducted a psychometric evaluation and discovered an internal consistency of 0.92 and test-retest reliability of 0.81. The SQS is highly correlated with the Pittsburgh Sleep Quality Index results. The insomnia sample scored significantly higher than the controls, indicating good construct validity. The subscales and their items are listed in Table I.

Translation

The Sleep Quality Scale (SQS) was translated from English to Arabic and then back to English by another translator. In the current study, a Brislin's back-translation model was used.[17] The scale was then administered in small groups to ensure that all items were clear and understandable. Four Saudi psychologists fluent in both English and Arabic were involved in the translation process in this study. Following that, the experts were asked to look for inconsistencies and changes to the original item, as well as to assess whether the items were suitable for measuring sleep quality among Saudis. There have been no changes made to fit the scale items with the Saudi context. The final scale was administered to 30 participants (15 males and 15 females) to determine how clear and understandable the scale was. The participants were asked whether the items were readable and understandable. The current study made use of the final version of the Arabic Sleep Quality.

Procedure

The researcher, who is a native Arabic speaker, collected questionnaires via the internet using an online survey. After 15 days, 38 participants were tested for test-retest reliability of the total scale score and both subscales on the first and second test.

Data Analysis

Using SPSS version 22.0 software, data analyses were performed on 403 participants with complete data. The A-SQS scale structure was evaluated using factor analysis. Cronbach's coefficient was calculated to assess the A-SQS scale's internal consistency. Pearson's correlation coefficient was calculated to investigate test-retest reliability as well as correlations between the subscales and the overall A-QSQ scale score.

RESULTS

Participants in this study were 402 Saudi male and females aged from 18 to 59 years old (mean= 33.76 ± 8.37). To represent the Saudi population, participants were recruited from different regions in Saudi Arabia. Participants included individuals of both genders with varying educational backgrounds. All participants volunteered to participate in this study. Table I describes participants' characteristics for the sample of this study.

Factor structure (Principal Components Analysis (PCA))

The 6 factors produced in the study data did not fit the structure advocated. Therefore, the total scores of the QSQ scale were obtained by summing across all items. Following this, a test of normality was carried out. Multivariate normality of the items was assessed statistically on Mardia's normalized estimate of multivariate kurtosis in the form of the critical ratio of kurtosis in the output. An exploratory factor analysis of the scale was performed using the principal components method with Equamax rotation. Initially, the sampling adequacy and sphericity were tested; the Kaiser-Meyer-Olkin (KMO) value was 0.897, exceeding the value of 0.6, while the value of Bartlett's test of sphericity was statistically significant ($p<0.0001$), supporting the factorability of the correlation matrix. These two tests showed that the data were suitable for factor analysis. A 5-factor solution resulted and explained 56.29% of the variance Table II. SQS was developed using item and factor analysis on items with content validity. SQS, composed of 28 items and five factors, accounted for 56.29 % of the total variance. remaining 27 items and omit one item No.(10) (poor sleep gives me headache) because the loading was less than 0.35, and the total variance became only 55.47. A 5-factor structure incorporating is more appropriate with a minimum loading of 0.35; 1-Day time dysfunction (DD) that includes 11 items (11, 14,15,17,19,21,22, 23,24, 26, 28). 2-Restoration after sleep (RA) that include (6) items (8,13,16,18,20,27) 3-Difficulty in getting up (DG) that include (2) items (12, 25) 4-Difficulty in maintaining sleep (DI) that include (5) items (1,2, 3,5,6) 5-Difficulty to sleep after getting up at night (DM) that include(3) items (4,7,9). Table II below presents the 5-factors structure.

Internal consistency

In order to examine the internal consistency of the A-QSQ scale, Cronbach's alpha was used. The alpha scores are presented in Table III below. The minimum acceptable reliable score of the scales of only two items is 0.50. The scores of the A-QSQ scale ranged from 0.58 to 0.88.

Confirmatory Factor Analysis (CFA) with path diagrams

The validity and reliability of the A-QSQ scale was tested. It was then important to determine the fit of the A-QSQ model (Table IV). The results of the CFA for the adapted A-QSQ scale as presented in Figure 1 show a good fit between the data (N=402) and the measurement model. The measurement model has a chi-square of 397,793 $p<0.000$. The ratio of the relative chi-square to its degree of freedom, χ 2/df, was 1.447. The data revealed that the fit statistics for the revised measurement model is good compared to the hypothesised measurement model. All of the fit indicators in Table III, the CFI=0.954 and TFI=0.962, fulfil the threshold of 0.90, the standard deemed important for model fit. Nevertheless, the root-mean-square error of approximation (RMSEA=0.033) indicated a good fit of the hypothesised model. As a result of a good fit based on the goodness-of-fit indices, this model has to be revised.

Test-retest reliability

Test-retest reliability was computed to confirm that the Arabic QSQ was constant across time. Twenty-three male and female participants were again recruited after 15 days to complete the scale. The results demonstrated that the correlations between the test and retest were strong, with a total score of .88. The test-retest reliability of the four clusters ranged from .90 for 'DD', .90 for 'RA'.84 for 'DF', .96 for 'DI' and .92 for 'DM'. These findings suggest that the Arabic QSQ scale has acceptable reliability over time.

DISCUSSION

This study found that the A-SQS, as a self-report measurement can be used to assess the sleep quality among Saudi Arabic populations. The items of the A-SQS were clear and understandable for an Arabic-speaking population, and the participants reported no difficulty in understanding or

Table I: Demographic characteristics of the participants (N=402)

Characteristic	n (%)	Mean (SD)
Total sample (N = 402)		
Age (years)		33.76 (8.37)
Gender		
Men	269 (66.9)	
Women	134 (33.1)	
Education level		
High School	107 (26.7)	
Undergraduate	224 (55.7)	
Postgraduate	71 (17.6)	
Statue/Occupation		
Student	118 (29.2)	
Employed	229 (57)	
Unemployed	56 (13.8)	
Marital status		
Single	144 (35.8)	
Married	259 (64.2)	

Table II: A-SQS subscales and their loadings

N	Items	Component A-SQS new subscales				
		DD	RA	DG	DI	DM
11	Poor sleep makes me irritated	.763				
14	Poor sleep makes me lose my appetite	.701				
15	Poor sleep makes hard for me to think	.663				
17	Poor sleep makes me lose interest in work or others	.660				
19	Poor sleep causes me to make mistakes at work	.636				
21	Poor sleep makes me forget things more easily	.630				
22	Poor sleep makes it hard to concentrate at work	.598				
23	Sleepiness interferes with my daily life	.570				
24	Poor sleep makes me lose desire in all things	.465				
26	Poor sleep makes me easily tired at work	.428				
28	Poor sleep makes my life painful	.409				
8	I feel refreshed after sleep		.791			
13	My sleep hours are enough		.774			
16	I feel vigorous after sleep		.732			
18	My fatigue is relieved after sleep		.648			
20	I am satisfied with my sleep		.630			
27	I have a clear head after sleep		.623			
12	I would like to sleep more after waking up			.714		
25	I have difficulty getting out of bed			.545		
1	I have difficulty falling asleep				.667	
2	I fall into a deep sleep				.598	
3	I wake up while sleeping				.570	
5	I wake up easily because of noise				.469	
6	I toss and turn				.459	
4	I have difficulty getting back to sleep once I wake up in middle of the night.					.839
7	I never go back to sleep after awakening during sleep					.807
9	I feel unlikely to sleep after sleep					.518

Table III: Internal consistency of the A-QSQ scale

No	Factors	Items	Cronbach's alpha
1	Day time dysfunction (DD)	11	0.889
2	Restoration after sleep (RA)	6	0.818
3	Difficulty in getting up (DG)	2	0.588
4	Difficulty in maintaining sleep (DI)	5	0.632
5	Difficulty to sleep after getting up at night (DM)	3	0.715
total		27	0.90

Table IV: Goodness-of-fit indices for the A-QSQ model

Goodness-of-fit indices	E-service quality model
χ 2	397.793
DF	275
χ 2/DF	1.447
RMR	0.053
RMSEA	0.033
CFI	0.934
AGFI	0.910
NFI	0.911
IFI	0.971
TFI	0.962

Note: RMR: Root Mean Square Residual; RMSEA = Root-Mean-Square Error of Approximation; CFI = Comparative Fit Index; AGFI: Adjustment Goodness Fit Index ; NFI = Normed Fit Index; IFI = Incremental Fit Index.

reading the items. Moreover, to maximise generalisability, the participants – both males and females – were recruited from different population regions within Saudi Arabia, with ages ranging from 18 to 65 years, and of differing education levels.

In addition, this study assessed the psychometric properties the A-SQS and the factor analysis yielded a revised 27-item version with five factors, including daytime dysfunction, restoration after sleep, difficulty in falling sleep, difficulty in maintaining sleep, difficulty to sleep after getting up at night. The range of score is from 0 to 81, with a higher score showing a lower sleep quality.

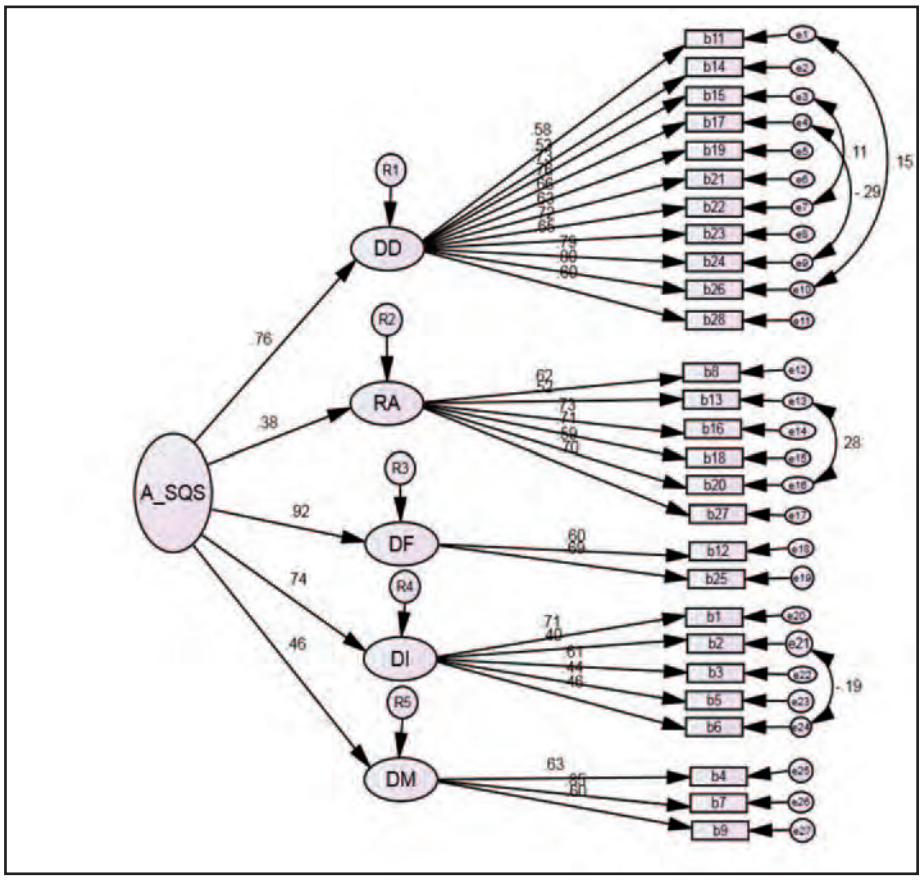

Fig. 1: Parameter estimates for the sample (N=402)

The original SQS had a 6-factor structure, with factors for example, Satisfaction with Sleep and Difficulty in Falling Asleep, which are not retained as distinct domains in the A-SQS. Notably, the A-SQS merges or redistributes several items, potentially reflecting culturally specific patterns in the perception and experience of sleep. For example, Difficulty in Falling Asleep and Difficulty Maintaining Sleep in the original scale appear consolidated into two broader categories: DI and DM in the A-SQS. In addition, the factor "Satisfaction with Sleep" from the original (3) items was not retained as an independent domain in the A-SQS, possibly due to overlapping variance with other constructs for example, Restoration After Sleep. Therefore, the A-SQS offers a psychometrically acceptable structure for the Saudi context, and the reclassification of items and change in the number of factors support questions about cross-cultural construct equivalence.

In factor one day time dysfunction, item number 11(Headache due to poor sleep) was omitted because of low minimum loading of 0.3. This factor has 11 items with an appropriate loading and internal consistency, and this result consist with Yi H et. al,study and supports the poor sleep and daytime dysfunctions related.[3] In the current study, restoration after sleep factor includes six items compared with SQS which has only four items. Items "satisfaction with sleep " and " deep sleep" from the satisfaction with sleep factor in SQS moved in restoration after sleep factor in A-SQS with internal consistency of 0.818 and a goodness of fit indices. Therefore, this factor is accepted regarding name and items because satisfaction with sleep meaning and restoration after sleep related to a concept of good sleep, according to a study, which reported that perceived calmness of sleep and sleep efficiency formed an index of sleep quality.[18]

On the other hand, the third element of the A-SQS in the present study consisted of a limited set of two items only that pertained to the challenge of getting up. Zwick WR et. al argues that for interpretation to be relevant, a component should consist of a minimum of three items.19 The selection of this component was based on the observation that those who experienced bad sleep encountered challenges in waking up after sleep, as noted by Yi H et. al,.[3] Additionally, it has been established that sleep continuity is closely associated with sleep quality, as highlighted by another two studies.[18,20] Therefore, it will be imperative to develop additional resources pertaining to the difficulty of getting up after sleep in future study endeavors.

The current study identified five items for the factor "difficulty in maintaining sleep," showing adequate loadings and reliability. This is consistent with Yi H. et al[3]., although their SQS version included only two items; the A-SQS expanded this factor by adding three additional items. Moreover, study by DJ B et. al.[4], reported that normal subjects, for example depressives, disorders of initiating and maintaining sleep, and disorders of excessive somnolence correlated.[4] Therefore, in this study, items "difficulty falling asleep, wake up while sleeping, wake up easily because of noise, toss and turn, and

fall into a sleep" including in this factor. The final factor in this study A-SQS "difficulty to sleep after getting up at night," has three items with an appropriate loading from 0.51 to 0.83 and internal consistency 0.71. Two items came from factor three, "difficulty in failing asleep" in the SQS study, while one item from factor four " difficulty in getting up". The items in this factor consisting with both meaning and statistical validity and reliability. This finding is supported by Yi H et. al,, a study which incorporated a greater number of items such as challenges associated with waking up and experiencing numerous dysfunctions during the day can be attributed to poor sleep. Therefore, the concept validity was established using a similar approach to the prior scales or questionnaires.

In the current study, the assessment of reliability was conducted using two distinct methodologies. Initially, it is important to note that the Cronbach's alpha coefficient for homogeneity yielded a value of 0.90, signifying a substantial level of internal consistency. In addition, the findings of the confirmatory factor analysis revealed the anticipated factor structure consisting of three elements. The adequacy of the 5-factor structure is supported by the favourable fit indices, including the RMSEA and standardised RMR. Furthermore, the study also assessed the test-retest reliability to determine the consistency of the repeated measures. The correlation coefficient of 0.88 provides empirical evidence supporting the instrument's high level of stability.

One further constraint of this research is the examination of outcomes across several studies investigating the composition of the A-SQS. The applications exhibit inconsistency in various dimensions, including socioeconomic class, gender, levels of education, and sample size. However, it is important to note that the study's sample size consisted of 402 participants. It is worth mentioning that a sample size of ≥300 or more is generally considered adequate for conducting a confirmatory factor analysis on a population model.

The A-SQS employed a methodical approach in conducting a cross-cultural study, ensuring that sociocultural variations were taken into account when adapting the instruments. In this study, the A-SQS applied to the general population in Saudi Arabia. Furthermore, it should be noted that the individuals involved in the study might not experienced any overtly stressful situations. Moreover, it appears that there is a lack of easily accessible, detailed data regarding sleep quality within the Saudi population. Nevertheless, it is widely recognised that the quality of sleep can be impacted by a multitude of circumstances, including but not limited to lifestyle choices, job schedules, levels of stress, and availability of healthcare resources. Hence, future research endeavours ought to encompass Saudi individuals from many circumstances and locations, employing a combination of qualitative and quantitative methodologies to comprehensively investigate the multidimensional nature of the A-SQS.

Furthermore, while the study appropriately emphasizes cultural adaptation, it does not sufficiently investigate how specific cultural factors unique to Saudi Arabia—for example prevalent lifestyle patterns, typical work schedules (e.g., late-night work or prayer routines), or social norms regarding sleep and rest—may influence both actual sleep quality and respondents' interpretation of scale items. A deeper analysis of these contextual influences is critical to ensure that the A-SQS accurately captures culturally embedded experiences of sleep and wakefulness. Without this exploration, there is a risk of cultural oversimplification, which could limit the scale's ecological validity and generalizability within the local context. Moreover, prior research in Middle Eastern contexts suggests that factors, for example, high rates of caffeine consumption in the evening, gender-specific roles and obligations, and environmental conditions (e.g., urban noise or heat) can significantly shape sleep behaviours and perceptions. Addressing these variables in the adaptation process could improve the cultural sensitivity and psychometric fidelity of the instrument.[21-22]

While the study offers preliminary evidence for the utility of the A-SQS in assessing sleep quality, its reliance solely on self-reported data is a notable limitation. Self-report measures are inherently subjective and may be influenced by factors, for example mood, memory bias, or individual interpretation of sleep experiences. In contrast, objective measures, for example polysomnography and actigraphy provide quantifiable and physiologically based assessments of sleep parameters. Several studies using these methods have revealed discrepancies between perceived and actual sleep quality—particularly in populations with insomnia or other sleep disorders, where individuals often underestimate or overestimate their sleep duration and efficiency.[21,23] Without a comparison to such objective benchmarks, it is difficult to determine the extent to which the A-SQS reflects actual sleep behaviour versus subjective perception. Including such validation would greatly strengthen the interpretive power and generalizability of the study's findings. Moreover, future research should consider longitudinal methodologies to assess the predictive validity of the A-SQS and to capture changes in sleep quality across different life stages or contexts.

In addition, the sample size of 23 participants for the test-retest reliability analysis aligns with other preliminary scale validation studies that have used similarly small samples to estimate temporal stability (e.g., Carmines & Zeller, 1979). While a larger sample would strengthen generalizability, the observed reliability coefficient provides an initial indication of the A-SQS's consistency over time.

CONCLUSION

In summary, the A-SQS version has inadequate psychometric qualities for the six subscales as documented in the original SQS. In the present work, the A-SQS demonstrated a five-factor structure that exhibited satisfactory psychometric qualities. The A-SQS version has demonstrated efficacy as an assessment tool in clinical care settings and has the potential for versatile application. Moreover, this culturally tailored version of the Arabic Sleep Quality Scale (A-SQS) offers a specific tool for assessing sleep quality among individuals in Saudi Arabia and other Arabic-speaking populations. In addition, future research should include cross-national validation studies to evaluate the scale's psychometric

properties across diverse Arabic-speaking populations. Such work is essential to ensure the tool's broader utility and cultural fairness, and, Future studies should adopt a mixed-methods approach to better capture participants' perspectives, particularly during the early stages of cultural adaptation and scale refinement.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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ORIGINAL ARTICLE

A national survey on percutaneous tracheostomy practice in Malaysian adult general intensive care units

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ABSTRACT

Introduction: Percutaneous tracheostomy (PT) has gained increasing acceptance over surgical tracheostomy (ST) in the last few decades due to lower rates of postoperative infections, less bleeding, and cost-effectiveness. However, there has been little information regarding the PT practice in Malaysian adult general intensive care units (ICU). The objective of the study was to assess the current practice of PT in Malaysia.

Materials and Methods: This observational cross-sectional study used a validated questionnaire with 15 items. A total of 61 ICUs consisting of adult general ICUs under Ministry of Health (MOH) hospitals and adult general ICUs in university teaching hospitals were recruited into the study whereas ICUs in private hospitals and specialist ICUs were excluded from this study. The questionnaire was subsequently distributed to the heads of those 61 ICUs through existing WhatsApp or Telegram groups and the data collection period lasted four months.

Results: Fifty-three out of 61 ICUs participated. Ninety point six percent of the responses came from MOH hospitals, whereas 9.4% came from university hospitals. The heads in participating ICUs comprised 35.8% intensivists and 64.2% anaesthetists. At the time of the survey, 45.3% of ICUs were still practicing PT, 13.2% had performed PTs in the past but stopped whereas 41.5% were not. The rate of PT (both actively practising and formerly practised combined) in intensivist-led ICUs was 94.7% compared to 38.2% in anaesthetist-led ICUs. Intensivists performed PTs in almost two-thirds of ICUs, while anaesthetists did so in another two-thirds. The vast majority of assistants were medical officers at 96.8%. The Ciaglia Blue Rhino technique was the predominant technique (71.0%) while airway management during the technique was solely via endotracheal tube. Ninety-six point eight percent of the ICUs employed routine infiltration of local anaesthetics prior to PT. Thirty-eight point seven percent of performers of PT routinely used fibreoptic bronchoscopy but only 6.4% used ultrasonography. Seventy-four point two percent used tracheostomy tubes with inner cannulae and 83.9% routinely followed up with patients post-discharge from the ICU. Seventy-nine point two percent of respondents believed PT was the method of choice for elective tracheostomy in the ICU but only 49.1% perceived PT to be safer compared to ST.

Conclusion: PT is commonly practised in intensivist-led ICUs. PT is generally preferred for elective tracheostomy but there is a variability in perceptions regarding its safety compared to ST.

KEYWORDS:
Tracheostomy, surveys and questionnaires, Malaysia, intensive care units, attitude

INTRODUCTION

Tracheostomy is reported in the medical literature as one of the oldest surgical operations and was almost exclusively performed in emergency settings until half a century ago.[1] It is used to protect airways, facilitate long-term mechanical ventilation, including weaning, relieve upper airway obstruction, and provide frequent bronchial toileting.[2] Many studies have found tracheostomy to be superior to long-term endotracheal intubation in terms of intensive care units (ICU) stay duration, infection rates, sedation requirements, patient comfort, laryngeal trauma, nursing care, early oral feeding, and resource utilisation in the ICU.[2-5]

First described in 1955, percutaneous tracheostomy (PT) did not gain traction in medical practice until 1985, when Ciaglia et al. introduced the Percutaneous Dilatational Tracheostomy technique, and since then, other variations have been introduced.[6-7] Many studies recommended PT due to the fact that it can be performed quickly at the bedside without the need for potentially hazardous patient transfers.[6] Moreover, PT was associated with lower rates of postoperative infections and bleeding and also cost-effective.[8]

National surveys conducted in multiple geographically close European countries showed that the use of PT in clinical practice varied but shared common methodologies.[9-19] Outside of Europe, its practice was heterogeneous and country-specific.[20] Guidelines for PT at the international and national levels are rare, and in the absence of a set of recommendations, clinical practice is often guided by rules of thumb, expert opinions, and case reports.[21]

The latest clinical audit by the Malaysian Registry of Intensive Care (MRIC) showed that in 2020, 4.7% of 21,071 patients receiving MV in 57 ICUs had undergone tracheostomy, with 76.1% of them performed surgically rather than percutaneously.[22] Likewise, in 2021, 1.8% of

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25,807 mechanically ventilated patients required tracheostomies, with 82.7% of them being surgical tracheostomy (ST). Apart from that, there has been little information regarding practice variation of PT in Malaysian ICUs. A search for "Percutaneous Tracheostomy in Malaysia" on PubMed yielded limited results, despite widely published recommendations supporting its use. An audit by Rao et al. in 2003 reported that PT was the technique of choice for tracheostomy in the ICU of Hospital Kuala Lumpur, whereas in 2004, Tan et al. concluded in a prospective study at Hospital Sultanah Aminah, Johor Bahru, that PT was a safe alternative to ST.[23,24] Neither of those studies evaluated the daily practice of PT in accordance with operators, assistants, techniques, adjuncts, and follow-ups.

Based on past surveys evaluating ICU tracheostomy practices, we suspected that its practice in Malaysian adult general ICUs varies considerably. The purpose of this national survey was to ascertain the current practice of PT in Malaysian adult general ICUs. Specifically, the study aimed to determine the operators of PT, the frequency of different techniques of PT, the procedural adjuncts used during PT, the practice of post-PT follow-up care, and the current opinion on the technique of PT.

MATERIALS AND METHODS

Study Design and Protocol

This was an observational cross-sectional study based on a national survey of PT practice in Malaysian ICUs conducted from 01/10/2023 till 31/01/2024. This study employed total population sampling, which is a type of purposive sampling. The inclusion criteria were the adult general ICUs under Ministry of Health (MOH) hospitals that participated in the MRIC Annual Report 2020-2021 and the adult general ICUs in university teaching hospitals. Specialist ICUs (such as paediatric, cardiothoracic or neurosurgical ICUs), ICUs in private hospitals, and ICUs not listed in the MRIC Annual Report were excluded from the study.

Study Instruments

A questionnaire consisting of 15 items with various question formats (i.e., single-answer questions, multiple-answer questions, yes/no/sometimes, open-ended questions) was developed for this study. The following items were recorded: hospital category; ICU category; PT use in clinical practice; the operator; the assistants; preferred PT technique; method of airway management; use of local adjuncts; use of endoscopic guidance; use of neck ultrasound; use of tracheostomy tubes with inner cannulae; follow-up care for patients; and opinions on safety and attitudes towards PT. To ensure validity of the survey instrument, the questionnaire was reviewed by a panel consisting of five consultant intensivists registered with the National Specialist Registry of Malaysia. The questionnaire was also piloted in five ICUs to assess clarity and ease of use before it was distributed and directed to the heads of the ICUs.

Study Administration

A total of 61 ICUs were identified, which included 55 ICUs in MOH hospitals that participated in the MRIC Annual Report 2020-2021, as well as six ICUs in university teaching hospitals. A QR code linked to a Google Form based on the questionnaire was distributed to the heads of the ICUs through existing WhatsApp or Telegram groups. A participant information sheet and informed consent were included on the first page of the questionnaire, and all participants were assured of confidentiality and anonymity. Participants were given a duration of four months (01/10/2023 till 31/01/2024) to answer the questionnaire. The QR code was distributed again at a monthly interval during the period of data collection to act as a reminder to the participants who had not answered the survey.

Statistical Analysis

The data were exported from Google Forms into Microsoft Excel for cleaning before analysis. A descriptive analysis was performed on the data using the Statistical Package for the Social Sciences (SPSS) version 28.0 for Windows. Categorical variables were expressed as frequency and percentage and were also analysed using the crosstabs subroutine with the chi-squared (χ^2) test or Fisher's exact test, where appropriate, for statistical comparison between the groups. Statistical significance was set at a p value of less than 0.05.

Ethical approval

Each participant provided informed consent before completing the survey. The study was registered in the National Medical Research Register (NMRR ID-23-01950-ALC) and approved by the Medical Research Ethics Committee prior to the commencement.

RESULTS

Out of the 61 ICUs that were identified and included in this study, 53 responded to our questionnaire, resulting in a response rate of 86.9%, while the remaining eight ICUs, which did not respond, accounted for 13.1%. Table I shows the distribution of PT practice status among the 53 ICUs that responded to our survey according to hospital type and ICU type as well as their association. Of the 53 responding ICUs, 48 (90.6%) were from MOH hospitals, while five (9.4%) were from university hospitals. As illustrated by the table, there were equal numbers of ICUs in MOH hospitals that were actively practising and that had never practised PT, each accounting for 21 hospitals or 43.8%, whereas another six, or 12.4%, of MOH hospitals had practised PT in the past but had stopped. As for university hospitals, three (60.0%) ICUs were still actively performing PT, one (20.0%) had stopped practising PT, whereas another one (20.0%) had never practised it. There was no statistically significant association between hospital type and PT practice status, as the Fisher's exact test yielded $p \approx 0.2956$ ($p > 0.05$). Based on the same responses obtained from the 53 ICUs, the PT practice status was also categorised according to the specialty/background of the head of each ICU: 19 (35.8%) intensivist-led ICUs and 34 (64.2%) anaesthetist-led ICUs. In the former group, 16 (84.2%) intensivists were still performing PT, and two (10.5%) had done it in the past, but one (5.3%) had never practised it. In contrast, among the 34 ICUs led by anaesthetists, only eight (23.5%) were actively involved in PT. Five (14.7%) ICUs had stopped carrying out PT by the time of the study, but the majority (21) had never attempted PT, accounting for 61.8% of the anaesthetist-led units. In contrast, there was a

statistically significant association between ICU type and PT practice status (χ^2=19.5000, p<0.0001), indicating that intensivist-led and anaesthetist-led ICUs differed in their PT practice patterns.

Factors Behind Non-Practice of PT in ICUs
Of the 53 respondents, ICUs that formerly practised and had stopped practising provided various reasons for not practising PT at the time of the study: Eight ICUs mentioned budget/equipment constraints, while another eight noted that the main issue was a limitation/lack of expertise. Two ICUs stated that all tracheostomies in their units were managed by ENT specialists, with only the surgical method being employed by that team. One ICU reported that time constraints, due to both clinical and academic responsibilities, complicated efforts for PT.

Personnel, Clinical Practices, and Procedural Aspects of PT in ICUs
Tables II and III summarise the additional responses from the 31 ICUs that had experience with PT, comprising 24 ICUs actively practising PT and seven ICUs that formerly practised it.

Respondents were allowed to report more than one main operator and/or more than one assistant. For the main operators of PT, intensivists performed PT in nearly two-thirds of the ICUs (20 or 64.5%), with anaesthetists also performing PT in the same proportion (20 or 64.5%). Additionally, one (3.2%) ICU reported that general surgeons were involved, while another (3.2%) employed an ENT surgeon. Two (6.4%) ICUs allowed medical officers to serve as the main operator. In contrast, regarding assistants for PT, the majority of the 31 ICUs involved medical officers (30 or 96.8%), followed by anaesthetists assisting in 20 or 64.5% ICUs. Intensivists assisted in six (19.4%) ICUs, while nurses also served as assistants in the same number of ICUs (six or 19.4%). Lastly, only two (6.5%) ICUs employed medical assistants to assist with PT.

PT Technique
The most commonly used technique for PT was Ciaglia Blue Rhino, accounting for 22 or 71.0% of the ICUs. This was followed by the Basic Ciaglia technique, employed in five (16.0%) ICUs, while the remaining 4 (13.0%) ICUs used Griggs technique for the procedure.

Airway Management
Regarding the routine airway maintenance method during PT, the sole technique used in all 31 (100%) ICUs was the endotracheal tube. None of the respondents reported the use of a laryngeal mask airway as a method of airway maintenance during PT.

Use of Local Medications
For medications routinely administered prior to PT, 23 or 74.2% of respondents used a combination of local anesthetics and vasoconstrictors, while seven (22.6%) applied only local anesthetics. Only one ICU (3.2%) reported not using any medications.

Use of Fibreoptic Bronchoscopy
When it came to the use of fibreoptic bronchoscopy during PT, 12 out of 31 respondents routinely implemented it, representing 38.7% of the ICUs. However, 14 or 45.2% did not incorporate fibreoptic bronchoscopy in their PT practice. Meanwhile, five (16.1%) ICUs only sometimes used it, specifically to manage potentially difficult airways.

Use of Ultrasonography
Similarly, the majority of ICUs, comprising 22 or 71.0%, did not routinely use ultrasonography during PT, while only two (6.4%) ICUs consistently used it. Nonetheless, seven (22.6%) ICUs indicated that ultrasonography was sometimes employed due to difficult surface landmarks and possible aberrant vasculatures or goitre.

Use of Tracheostomy Tubes with Inner Cannulae
Regarding the implementation of tracheostomy tubes with inner cannulae, over half of the ICUs (23 or 74.2%) incorporated them as part of their routine practice, seven (22.6%) ICUs did not use them, and only one ICU (3.2%) reported using them occasionally, depending on the availability provided by the PT kit.

Post-Procedure Care
Similarly, a significant majority of ICUs (26 or 83.9%) routinely arranged follow-ups for their post-PT patients after discharge from the ICU, whereas post-discharge visits were not part of PT practice in five (16.1%) ICUs.

Opinions on PT as the Method of Choice and its Safety
All respondents were asked about their opinions on PT as the method of choice for elective tracheostomy in ICUs and its safety profile compared to ST, regardless of the status of PT practice in their ICUs. Tables 4 and 5 summarise these findings and their association with ICU type. As shown in Table IV, 42 out of 53 respondents (79.2%) indicated that PT was their preferred method for elective tracheostomy in ICUs, while 11 (20.8%) did not agree that PT was the better option in this context. There was a statistically significant association between ICU type and PT being the preferred method of choice for elective tracheostomy (Fisher's exact test, $p \approx 0.0045$), with intensivist-led ICUs more frequently reporting PT as the preferred method. Despite the majority favouring PT for elective cases, Table V shows that less than half (26 out of 53 ICUs, or 49.1%) believed that PT was safer than ST. Interestingly, 27 ICUs (50.9%) disagreed with this view. There was no statistically significant association between ICU type and the perception of PT being safer than ST ($\chi^2 = 3.3180$, $p = 0.0685$).

Some respondents provided additional comments. Thirteen emphasised the importance of patient selection and safety to avoid complications associated with percutaneous tracheostomy (PT). They generally preferred PT for straightforward cases without difficult airways, while surgical tracheostomy was considered a better option for patients with potentially challenging airways. Eleven responses highlighted that PT was valuable in saving operating theatre time and assisting ICU bed turnover, as it could be quickly performed in the ICU without needing to book OT slots. However, seven respondents noted that PT required

Table I: Respondent Profile - Association of Hospital Type and ICU Type with PT Practice (N=53)

	Total	PT practice status			Chi-squared (χ^2) test / Fisher's exact tes
		Still practising	Formerly practised	Never practised	
Valid respondents	53/53 (100%)	24/53 (45.3%)	7/53 (13.2%)	22/53 (41.5%)	
Type of hospital					$p \approx 0.2956$
MOH hospital	48/53 (90.6%)	21/48 (43.8%)	6/48 (12.4%)	21/48 (43.8%)	
University hospital	5/53 (9.4%)	3/5 (60.0%)	1/5 (20.0%)	1/5 (20.0%)	
Type of ICU					
Intensivist-led	19/53 (35.8%)	16/19 (84.2%)	2/19 (10.5%)	1/19 (5.3%)	$\chi^2 = 19.5000$
Anaesthetist-led	34/53 (64.2%)	8/34 (23.5%)	5/34 (14.7%)	21/34 (61.8%)	$p < 0.0001$

Table II: Profile of Routine Personnel Involved in PT - Performers and Assistants (N=31)

	Total
Valid respondents	31 (100%)
Personnel routinely performing PT (multiple answers)	
Intensivist	20/31 (64.5%)
Anaesthetist	20/31 (64.5%)
General surgeon	1/31 (3.2%)
Ear, nose & throat surgeon	1/31 (3.2%)
Medical officer	2/31 (6.4%)
Personnel routinely assisting PT (multiple answers)	
Intensivist	6/31 (19.4%)
Anaesthetist	20/31 (64.5%)
Medical officer	30/31 (96.8%)
Medical assistant	6/31 (19.4%)
Nurse	2/31 (6.5%)

Table III: Practices and Techniques Used for PT Among Respondents (N=31)

	Total
Valid respondents	31 (100%)
Main technique of PT used	
Ciaglia Blue Rhino	22/31 (71.0%)
Basic Ciaglia	5/31 (16.0%)
Griggs	4 /31 (13.0%)
Method of airway management routinely used during PT	
Endotracheal tube	31/31 (100%)
Laryngeal mask airway	0/31 (0%)
Medication(s) routinely administered for PT	
Local anaesthetics	7/31 (22.6%)
Vasoconstrictors	0/31 (0%)
Local anaesthetics and vasoconstrictors	23/31 (74.2%)
None	1/31 (3.2%)
Fibreoptic bronchoscopy routinely used during PT	
Yes	12/31 (38.7%)
No	14/31 (45.2%)
Sometimes	5/31 (16.1%)
Ultrasonography routinely used during PT	
Yes	2/31 (6.4%)
No	22/31 (71.0%)
Sometimes	7/31 (22.6%)
Tracheostomy tubes with inner cannulae routinely used for PT	
Yes	23/31 (74.2%)
No	7/31 (22.6%)
Sometimes	1/31 (3.2%)
Post-discharge follow-ups routinely arranged for PT	
Yes	26/31 (83.9%)
No	5/31 (16.1%)

Table IV: Association Between ICU Type and PT as the Method of Choice for Elective Tracheostomy (N=53)

	Total	PT as the method of choice for elective tracheostomy in ICU		Fisher's exact test
		Yes	No	
Valid respondents	53 (100%)	42/53 (79.2%)	11/53 (20.8%)	p=0.0045
Intensivist-led ICU	19/53 (35.8%)	19/19 (100%)	0/19 (0%)	
Anaesthetist-led ICU	34/53 (64.2%)	23/34 (67.6%)	11/34 (32.4%)	

Table V: Association Between ICU Type and Perception of PT Safety Compared to ST (N=53)

	Total	PT perceived to be safer compared to ST		Chi-squared (χ2) test
		Yes	No	
Valid respondents	53 (100%)	26/53 (49.1%)	27/53 (50.9%)	χ^2=3.3180
Intensivist-led ICU	19/53 (35.8%)	13/19 (68.4%)	6/19 (31.6%)	p=0.0685
Anaesthetist-led ICU	34/53 (64.2%)	13/34 (38.2%)	21/34 (61.8%)	

experienced staff, costly equipment, and questioned its viability in certain settings where responsibility for follow-up care could be a limiting factor. On a similar note, one respondent stated that PT may only suit hospitals with high OT workloads and high ICU bed occupancy rates, while another suggested the need for ENT follow-up on PT patients. Four respondents reiterated that PT and surgical tracheostomy were similar in terms of safety and efficacy.

DISCUSSION

Our study achieved a high response rate of 86.9% among the target ICUs in both MOH and university hospitals, indicating that the results accurately and reliably reflect PT clinical practice in Malaysia. Nevertheless, the fact that 13.1% of respondents did not reply to our inquiry could introduce some bias to our findings. However, this limitation may potentially be mitigated by the standardised training pathways for ICU heads in Malaysia, whether for intensivist or anaesthetist, which follow common syllabi overseen by national conjoint boards, which likely minimise variations in clinical practice. Therefore, we believe that we have successfully sampled a wide cross-section of ICUs, further validating our results.

Of our respondents, 58.5% had experience performing PT, while 41.5% had never practised it. This indicates a low PT rate in Malaysia, despite its widespread acceptance since introduction, as shown by many past studies in Europe; the Netherlands (61.8%), Germany (86%), Spain (82%), Italy (89%), and the UK (75%-100%).[8,11,13-18] Respondents reported that a lack of training among staff and limited resources in their settings were the major obstacles for PT. To address this, both implementing training programs and adequately allocating resources specific to PT in all ICUs must be considered to increase the PT rate.

The absence of a statistically significant association between hospital type and PT practice status may reflect shared constraints across both MOH and university hospitals. Both types of institutions may face similar issues, such as budget limitations, lack of equipment, or shortage of expertise, making the type of hospital less decisive. Furthermore, there might be variation within each hospital type. For example, some MOH hospitals may be better resourced than others, while some university hospitals face similar limitations, thus making broad categorisation less predictive. In fact, as reported by the respondents, some ICUs depended on ENT specialists who only perform surgical tracheostomies, while others were affected by time constraints due to both clinical and academic demands. These findings suggest that PT practice patterns are determined more by local factors and available resources rather than by hospital type alone.

However, our study found that intensivist-led ICUs (94.7%) had more experience performing PT compared to anaesthetist-led ICUs (38.2%), a trend similarly reported in national surveys conducted in Europe.[13,14,17] The difference was statistically significant ($p<0.05$), indicating a strong association between the specialty of the ICU head and the likelihood of performing PT. This may likely be because PT is a procedural skill intensivists are expected to attain during their training, whereas it is not part of the core procedures among Malaysian-trained anaesthetists. While training more intensivists can lead to more PT being performed, implementing PT training or credentialing programs in anaesthetist-led units can also increase its adoption rate in ICUs overall. However, it is noteworthy that some intensivist-led ICUs that formerly practised PT had since stopped. While the presence of trained intensivists increases the likelihood of adopting PT, maintaining its practice depends on factors like resource availability, local priorities, and departmental decisions, as highlighted in the previous paragraph.

In relation to that, despite the lower PT rate in ICUs led by anaesthetists, an equal proportion of intensivists and anaesthetists served as primary PT operators. This suggests that anaesthetists demonstrate general competence in performing PT, further reinforcing the need for specific PT training programs to support broader adoption in anaesthetist-led ICUs.

Regarding PT assistants, an overwhelming majority were medical officers working in ICUs, likely reflecting the generally low numbers of specialised doctors in Malaysian ICUs, whether intensivists or anaesthetists. This basically highlights the need for non-specialists to act as assistants. Therefore, it is important to extend PT training to medical officers to improve outcomes and reduce associated risks and complications.

In terms of technique preferences, most ICUs favoured the Ciaglia Blue Rhino technique over others, such as the Basic Ciaglia and Portex Griggs. This aligns with practices seen in Germany (69.4%) and the UK (55%-64%), where Ciaglia Blue Rhino had become the most popular PT technique as it was technically simpler, user-friendly, less time-consuming, and less traumatic.[13,17,18,25]

For airway maintenance, 100% of the ICUs with PT experience relied solely on endotracheal tube as the primary method, a higher rate than that reported in the UK (92%-95%) and Italy (83%).[14,17,18] Although we did not inquire about the reasons for such a homogenous practice, we infer that endotracheal tube was preferred due to its secure airway properties, particularly in potentially difficult airways. In the UK, laryngeal mask airways and microlaryngeal masks had been used in small numbers of cases (2%-5%) as described by Krishnan et al.[17] However, reasons for such practice were not inquired by the authors.

Regarding adjuncts routinely used in PT practice, nearly three-quarters of respondents reported using a combination of local anaesthetics and vasoconstrictors in their ICUs, while the remainder preferred only local anaesthetics. This ratio (combination 95% vs. local anaesthetics only 5%) is similar to figures reported by Veenith et al in a British study.[18] Nevertheless, no other studies surveyed this aspect of PT probably because the choice is unlikely to significantly affect aspect of PT practice as intravenous agents are commonly used to control pain in ICU patients.

For the use of fibreoptic bronchoscopy during PT, only 38.7% of ICUs practised it routinely, comparable to rates from surveys in the Netherlands (36%) and Spain (16%).[8,11] This contrasts with trends in other major European countries, particularly the UK, where successive national PT practice studies have shown a progressive adoption of fibreoptic bronchoscopy.[13-18] Fibreoptic bronchoscopy has been shown to decrease the risk of iatrogenic damage and misplacement of the PT tube, but in less experienced hands, it can compromise ventilation and increase costs.[8,16,26-28] The low fibreoptic bronchoscopy usage rate in Malaysian ICUs may be due to resource limitations, underscoring the importance of appropriate support in these settings.

Seventy-one percent of units did not favour the use of ultrasonography in routine PT practice, unlike findings reported by Vargas et al. in Italy (10.7%).[14] Although the midline of the neck is assumed to be avascular, this is not always the case, and ultrasonography is essential to identify aberrant vessels.[16,29] In cases involving obese patients, ultrasonography had proven useful; one author successfully performed PT on a patient weighing over 200 kg with the aid of ultrasonography.[16]

The incorporation of tracheostomy tubes with inner cannulae and post-ICU discharge follow-ups into PT practice was high, at 74.3% and 83.9%, respectively. Tracheostomy tubes with inner cannulae are important as they have been shown to reduce infection and blockage rates.[17,30] Follow-ups help to minimise peri- and post-surgical complications and identify technique-associated sequelae, which can then be corrected and improved.[8] Surveys from Europe have reported lower follow-up rates, ranging from 7% in the Netherlands to 52% in the UK.[8,11,13,15-18] Some Malaysian ICUs do not conduct follow-ups, which may indicate staffing limitations. Indeed, some ICUs that had stopped carrying out PT reportedly did so due to a lack of coordination with ENT on follow-up protocols. This highlights the need for strengthened intra- and inter-department efforts, e.g. a tracheostomy team, to sustain PT practices and follow-up care.

A majority (79.2%) of units preferred PT for elective tracheostomy, given the many advantages of PT. With a statistically significant association found between ICU type and PT preference ($p<0.05$); intensivist-led ICUs were more likely to favour PT. This likely reflects the stronger procedural training in PT among intensivists compared to anaesthetists. Despite this, only about half of them thought it was safer than ST and no statistically significant association was observed between ICU type and the perception of PT being safer. This lack of association may be due to shared concerns across ICUs, such as the importance of patient selection, the need for experienced staff, and the risks in complex cases like difficult airways, as highlighted by respondents in their survey comments. A similar discrepancy was observed in the Netherlands, Spain, and Germany, where large majorities of ICUs preferred PT for elective tracheostomy but did not agree it was safer than ST.[8,11,13] Krishnan et al. found that 66.6% of the clinicians still favoured ST for morbidly obese patients while 50% of them used it in difficult airway cases.[17]

CONCLUSION

Our study provides an overview of PT practices in Malaysian ICUs. With a high response rate of 86.9%, we found that PT implementation in intensivist-led units was significantly greater than that of anaesthetist-led units, despite both groups being equally involved as operators in PT. Notable trends included the reliance on medical officers as assistants and limited use of FOB and USG during PT, underscoring the impact of staffing and resource limitations. Practices such as the preference for the CBR technique, use of ETT for airway maintenance, and the combination of local anesthetics with vasoconstrictors align closely with findings from previous studies. Additionally, Malaysian ICUs were found to be more regular in follow-up care compared to their European counterparts. Nevertheless, while PT was the preferred method for elective tracheostomy in critically ill patients, only half of the ICUs considered it safer than surgical tracheostomy.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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Sleep Goal Index (SGI) – A new success outcome criteria on 618 OSA patients

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ABSTRACT

Introduction: Sleep-Goal Index (SGI) comprises of Blood Pressure, AHI (number of apnoea and hypopnea events per hour), T90 (duration of oxygen below 90% and BMI (body mass index). This study aims to demonstrate SGI as a holistic, comprehensive and practical measurement of treatment outcomes in OSA (obstructive sleep apnoea) management.

Materials and Methods: A prospective 10-center clinical trial of 618 OSA patients, who underwent nose, palate and/or tongue surgery. Pre- and post-operative data were analyzed and compared with the Sher's criteria (AHI reduction 50% and <20) and the Sleep Goal Index.

Results: There were 514 males and 104 females, mean age of 45.8±13.1 years. Mean snore VAS improved from 7.6±1.9 to 2.8±2.1 (p<0.001), mean Epworth score (ESS) improved from 11.5±4.8 to 5.4±3.5 (p<0.001), mean BMI decreased from 28.6±4.8 to 27.3±5.3 (p<0.001), gross weight decreased from 82.4±14.2kg to 78.1±13.3kg (p<0.001). Mean AHI decreased 37.4±25.7 to 16.4±14.6 (p<0.001), mean LSAT improved 74.5±18.4% to 85.4±7.6% (p<0.001), and mean T90 (time spent <90%) decreased from 27.7±8.9 minutes to 9.7±2.1 minutes (p<0.001). Mean SBP decreased from 130.4±19.4 to 121.1±14.6mmHg, mean DBP decreased from 84.7±13.4 to 79.5±12.3mmHg. The overall success rate (Sher's criteria) was 55.7%. Based on McNemar's test, comparing Sher's criteria and SGI (4 parameters – BP, BMI, T90, AHI), it was demonstrated that fulfilling any 2 out of 4 SGI parameters would be just as sensitive as Sher's criteria, whilst being more holistic and representative of the patients' oxidative stress. From McNemar's test, the overall duo-paired combination and permutations of these 4 SGI parameters ranged from 41.8% to 60.9%.

Discussion: AHI as a single parameter to measure OSA treatment success can be unreliable. The SGI is a holistic, comprehensive, easily measured and better patient appreciated measurement index reflecting true end-organ function/improvement.

KEYWORDS:
OSA, sleep apnea, surgical outcomes, success rate, AHI, Sleep Goal Index

INTRODUCTION

Obstructive sleep apnoea (OSA) is a common sleep disorder that affects 9% of middle age men and 3% of women in North America.[1] This upper airway disorder causes recurrent hypoxic events during sleep and has been shown to affect the patient's neuro-cardiovascular system, resulting in strokes, heart attacks, arrythmias, and even sudden cardiac death. Some studies estimate that 93% of females and 82% of males with moderate to severe OSA remain undiagnosed.[2] Many scientific studies have shown strong correlation and causation between OSA and hypertension,[3] cardiovascular diseases,[4] and congestive heart failure.[5]

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It is widely accepted that the level 1, overnight full polysomnography is the gold standard test for OSA, the foreign sleeping environment makes it difficult for the patient to sleep. Traditionally, the severity of the OSA is classified based on the number of apnoea and hypopnea events per hour (AHI). The effectiveness of any intervention for OSA has been based on a specific arbitrarily proposed 50% reduction in pre-operative AHI and an AHI below 20 (known as the Sher's success criteria).[6]

The over-reliance on the AHI has resulted in inconsistencies of measurement being reported. There is discordance between AHI used to denote outcomes/success of therapy and real-world clinical outcomes like, quality of life (QoL), patient perception of disease, daytime tiredness, snoring, cardiovascular measures (e.g., blood pressure, oxygen saturation), and/or survival.[7]

A fundamental issue of AHI is the basic definition of hypopnoea varies from one sleep laboratory to another sleep laboratory system. Other variables include the monitoring system (thermistors versus transducers), the subjective scoring of each epoch by the sleep technologist, the intrinsic human sleep night-to-night variability[8-11] and the usage of different sleep monitoring system/laboratory/equipment[12] pre-operative and post-operatively.

This parameter AHI is not intuitively informative to the patient; no patient would seek a consultation with a sleep specialist complaining that "my AHI is high". Too much weightage has been given to this single parameter (AHI) that is well known for its variability. Patients are more concerned and affected by "real tangible" issues like loud snoring, daytime sleepiness, uncontrolled hypertension, obesity, high glucose levels; these are the effects of OSA as a systemic disease affecting end-organs, manifesting as these patient related symptoms or complaints. Hence, we propose measuring, assessing and utilizing these end-organ effects of OSA in assess outcomes of intervention.

We had proposed the SLEEP-GOAL outcome parameters previously with good acceptance amongst sleep specialists13. The SLEEP-GOAL success criteria is more holistic, comprehensive and inclusive of patient' complaints compared to AHI alone. We present a more compendious version of the Sleep-Goal outcome parameters known as the Sleep-Goal Index (SGI) comprising of the Blood Pressure, Gross Weight (BMI), Oxygen Time Spent below 90% (T90), and AHI.

MATERIALS AND METHODS

Study Design

This was a non-randomised prospective ten-centre (10) clinical trial of consecutive OSA patients who consulted the sleep/ENT clinic for snoring and/or symptoms of OSA. These patients met the inclusion criteria, and subsequently underwent upper airway surgery, in the form of either nose, palate and/or tongue surgery, single or multi-level surgery. Patients were recruited from ten tertiary clinical centres from ten countries from June 2016 to December 2023 (however, due to the pandemic, patient recruitment was very low from 2020 to 2022).

Patient Selection

All patients had comprehensive clinical assessment including a physical examination, naso-endoscopy, and an overnight polysomnography pre- and post-surgery. Parameters included the time spent oxygen saturation below 90% (T90), AHI, gross weight/BMI, systolic (SBP) and diastolic blood pressure (DBP). Patients completed the Epworth Sleepiness Scale (ESS) and a visual analogue scale (VAS) for snoring pre- and post-surgery. Quality of Life (QoL) was assessed using at least one of the following instruments the 36-Item Short Form Survey (SF36), the Functional Outcomes of Sleep Questionnaire (FOSQ10), Sleep Apnea Quality of Life Index (SAQLI), and/or the Pittsburgh Sleep Quality Index (PSQI) questionnaires.

Clinical examination included neck circumference, body-mass index (BMI), and blood pressure (pre- and post-operative); an endoscopic assessment of the nasal cavity, posterior nasal space, oropharyngeal area, soft palatal redundancy, uvula size and thickness, tonsillar size and Mallampati grade. Flexible naso-endoscopy was performed for all patients and collapse during a Mueller's manoeuvre was graded for the soft palate, lateral pharyngeal walls and base of tongue. Blood pressure measurements recorded were pre-operative average blood pressure readings at the clinic on two to four separate occasions and/or blood pressure readings at home on four separate occasions. The blood pressure measurements, BMI, gross weight calculations, and polysomnographic measurements were all done after a minimum of 6 months post-operatively, onwards. All patients had pre-operative and post-operative sleep test done in the same respective centres with the same level of study done. All patients had a level 1 sleep test done.

Inclusion criteria were patients >18 years old, AHI >5, all Friedman stage, all Mallampati grades, all multi-level collapse, all BMI, and all combinations of nose surgery alone, nose with palate surgery and/or nose with palate and tongue surgery. All patients were offered continuous positive airway pressure (CPAP) therapy, and those patients who chose CPAP were subsequently excluded from the study. We excluded patients who had previous upper airway surgery and/or had any pillar implants or hypoglossal nerve implant inserted previously. The study protocol and methodology were reviewed and approved by the hospital Ethics Committee/Institutional Review Board of their respective countries.

Study Intervention

All patients enrolled had either nasal, palatal and/or tongue surgery performed as a single level or multilevel surgery. Nasal surgery included either functional endoscopic sinus surgery, septoplasty, turbinate reduction and/or turbinoplasty. Palate surgery performed was either uvulopalatopharyngoplasty, anterior palatoplasty, z-plasty, uvulo-palatal flap, barbed phayngoplasty and/or the expansion sphincter pharyngoplasty. Tongue surgeries included radiofrequency tongue base ablation, midline tongue glossectomy, or tongue base coblator channelling. Surgeries were decided by surgeon discretion, best practices, highest standard of care and the anatomy of the patient. Post-operatively, patients were on soft liquid diet for 2 weeks duration (due to the palate surgery), with subsequent dietary

and nutritional counselling for every patient (in order to encourage weight reduction and a holistic health program).

Outcome Measures

Sleep-Goal Index

The SLEEP-GOAL[13] outcome measures published in 2020, relates closely with the end-organ effects/parameters of the OSA patient (Table I). It reflects the cardiovascular and neuro-cognitive effects of the OSA disease process, oxidative stress and the OSA disease load. Based on the medical evidence on these parameters, Pang et al[13] had assigned SLEE as minor criteria and PGOAL as the major criteria. Successful improvement post treatment is denoted by :-

S = Snoring – VAS reduction by 50%
L = sleep Latency – increase by 50% time latency
E = ESS – a reduction of 50% and < 10
E = Execution time – an improvement by 50%
P = blood Pressure – reduction of either SBP or DBP by 7mmHg or both by 5mmHg
G = Gross weight / BMI – reduction of GW by 8% or drop in BMI by 2 points
O = Oxygenation (time spent < 90%) – improvement by 50%
A = AHI – reduction by 50%
L = Life quality (QOL) score – improvement by 50%

The Sleep-Goal Index (SGI) is the more condensed and concise use of the main major criteria of the Sleep-Goal parameters, it consists of blood pressure, gross weight/BMI, time spent oxygen saturation <90%, and AHI.

P = blood Pressure – reduction of either SBP or DBP by 7mmHg or both by 5mmHg
G = Gross weight / BMI – reduction of GW by 8% or drop in BMI by 2 points
O = Oxygenation (time spent < 90%) – improvement by 50%
A = AHI – reduction by 50%

Statistical Analysis

All analyses were performed using SPSS 28.0 with statistical significance set at $p<0.05$. Descriptive statistics for numerical variables were presented as mean±sd and frequency (%) for categorical variables. The comparison of pre-operative and post-operative variables were compared using Paired T test. The McNemar's Tests were performed to compare the discriminant capabilities of the various Sleep Goal Indexes with the traditional Sher's Criteria.

Ethical approval

Ethical approval: This article does not contain any studies with animals performed by any of the authors. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. There were no recognisable data or patient/human profiles within the article.

RESULTS

The 618 OSA patients were recruited from the ten tertiary clinical centres in ten countries. There were 514 males and 104 females, mean age of 45.8±13.1 years. The overall mean snore VAS based on bed partner rating improved from pre-operative 7.6±1.9 to post-operative 2.8±2.1 ($p<0.001$). The mean daytime sleepiness Epworth score (ESS) improved from pre-operative 11.5±4.8 to post-operative 5.4±3.5 ($p<0.001$). The mean BMI had decreased from a pre-operative value of 28.6±4.8 to 27.3±5.3 post-operatively ($p<0.001$), the range of height was 1.50 metres to 1.98 metres, and the mean weight was 81.9±14.3kg. The mean gross weight decreased from pre-operative 82.4±14.2kg to a post-operative mean gross weight of 78.1±13.3kg ($p<0.001$). The mean pre-operative AHI decreased from 37.4±25.7 to post-operative AHI 16.4±14.6 ($p<0.001$), while the mean pre-operative LSAT increased from pre-operative 74.5±18.4% to post-operative 85.4±7.6% ($p<0.001$), and mean T90 (oxygen time spent / duration <90%) decreased from a high pre-operative duration of 27.7±8.9 minutes to an impressive lower duration of 9.7±2.1 minutes, post-operative ($p<0.001$). The mean SBP decreased from pre-operative 130.4±19.4 to a post-operative 121.1±14.6mmHg, and the mean DBP decreased from pre-operative 84.7±13.4 to post-operative 79.5±12.3mmHg ($p<0.001$).

The overall success rate for these 618 OSA patients (based on Sher's criteria) was 55.7%. Based on McNemar's test, comparing Sher's criteria and the Sleep-Goal Index (SGI) (4 parameters – blood pressure, gross weight, BMI, time spent oxygen <90%, T90, AHI), it was demonstrated that fulfilling any 2 out of 4 SGI parameters would be just as sensitive as the Sher's criteria, whilst being more holistic and representative of the patients' end-organ effects and oxidative stress (Table II) and real-world experience. For the purpose of simplicity and comparison in this paper, we assign the SGI parameters into (A) blood pressure, (B) gross weight reduction, BMI, (C) T90 – time spent / oxygen duration below 90%, and (D) AHI. Out of the 618 OSA patients, 36.7% of the patients had reduction of either SBP or DBP by 7mmHg or both by 5mmHg, 25.9% had reduced their gross weight by 8% or reduced their BMI by 2 points, 52.2% reduced the oxygen duration below 90% by half (T90), and 59.0% reduced the AHI by half.

Referring to Table II, we note that the overall success rates (rate that fulfils the criteria stipulated by the SGI), in paired combinations that fulfilled the respective SGI criteria, were as follows – A and B – 41.8%, A and C – 56.2%, A and D – 55.8%, B and C – 54.5%, B and D – 56.7%, C and D – 60.9% (all of which were very similar and close to Sher's criteria of a success rate of 55.7%, indicating that any of these 2 out of the 4 SGI parameters combined, would be as sensitive as the Sher's criteria).

In the column "Success Met by Sher but Missed by SGI", the percentage of 618 patients who met the Sher's criteria but were missed by the SGI criteria pairs are as follows: A and B – 1.0%, A and C – 1.0%, A and D – 0.0%, B and C – 2.0%, B and D – 0.0%, C and D – 0.0% ($p<0.001$). This data illustrated that the SGI criteria pairs included 98-99.0% of all the patients who also satisfied the Sher's criteria.

In the column "Success Met by SGI but Missed by Sher's", the percentage of 618 patients who met the SGI criteria pairs but were missed by the Sher's criteria were as follows: A and B – 26.3%, A and C – 34.7%, A and D – 26.3%, B and C – 29.4%,

Table I: Sleep Goal Index criteria

SLEEP GOAL INDEX – SGI
A. reduction of either SBP or DBP by 7mmHg or both combined by 5mmHg
B. reduction of gross weight by 8% or a BMI drop by 2 points
C. a reduction of 50% of the Oxygen duration below 90%
D. AHI reduction of 50% (from pre-op)

Table II: Comparison of the SLEEP GOAL INDEX to Sher's criteria (using the McNemar's test)

Method	Both Yes & Yes Success Met	Success met by Sher but Missed by SGI	Success met by SGI but Missed by Sher	p-value
Sher criteria	55.7%	-	-	-
A	36.7%	19.1%	21.9%	0.329
B	25.9%	29.5%	11.0%	< 0.001
C	52.2%	5.3%	25.4%	< 0.001
D	59.0%	10.0%	10.9%	< 0.001
A X B	41.8%	1.0%	26.3%	0.001
A X C	56.2%	1.0%	34.7%	< 0.001
A X D	55.8%	0.0%	26.3%	< 0.001
B X C	54.5%	2.0%	29.4%	< 0.001
B X D	56.7%	0.0%	17.0%	< 0.001
C X D	60.9%	0.0%	27.1%	< 0.001

Any 2 out of the 4 parameters is as stringent as the Sher's Criteria.

B and D – 17.0%, C and D – 27.1% (p<0.001). We note that the Sher's criteria were not in concordance with a fair number of patients (17.0% to 34.7%) who were noted to have had a successful outcome based on the criteria of SGI combination pairs.

DISCUSSION

Sher's success criteria were arbitrarily based on a single parameter of AHI as the sole success rate indicator of treatment has been used since 1996. Pang et al[13] had illustrated the short-comings of the AHI and the close association between OSA and with blood pressure, gross weight, BMI, quality of life (QOL), hypoxemia (T90), neuro-cognitive and the cardio-vascular systems. The Pang et al[13] discussion had detailed the reasons for the utilisation of the SLEEP-GOAL as a suitable outcome measure and to illustrate the inadequacies of the single parameter of AHI. Pang et al[13] had also explained the inaccuracies for some of the parameters, for example, Epworth Sleepiness Scale (ESS) can vary from night to night, and week to week, depending on the duration of the sleep that particular night/day/week; moreover, the commonest cause of high ESS is sleep deprivation and not OSA. With this background, we wish to discuss the advantages of using the SGI criteria pairs as a measure of treatment outcome as follows.

The Reliable or "Liable" AHI

The level 1 overnight in-hospital polysomnogram is cumbersome, uncomfortable, resource intensive, costly, with long waiting lists and intense labour requirements. It has several issues of inconsistency:

Firstly, night-to-night variability affects the pre-operative and post-operative AHI results. Chediak et al8 reported that 32% of their patients had a difference of AHI≥10 in two consecutive nights of PSG. Levendowski et al[10] reported a weak correlation (r=0.44) between overall AHI from the two PSG studies conducted approximately 40 days. However, Stepnowsky et al[11] demonstrated in 1091 patients that the night-to-night Pearson correlation coefficients ranged between 0.88 and 0.90 for each pair of nights. Secondly, the in-lab overnight polysomnogram and the home-based test would also affect AHI results. The patient should have the identical sleep test performed pre-operative and post-operative.

Thirdly, the different definitions of hypopnea in the laboratory systems and the criteria based on a 4% desaturation are different sleep laboratories. Hypopnea is usually defined as reduction in ventilation of at least 50% that results in a decrease in arterial saturation of 4% or more due to partial airway obstruction. Some sleep centres define hypopnea as clinically significant when there is a ≥30% reduction in nasal airflow lasting for 10 seconds or longer with an associated ≥4% oxygen desaturation and/or if these result in an arousal. Medicare's definition strictly follows ¤ 5% or more of oxygen desaturation. Finally, different monitoring equipment during the sleep test affects sensitivity of airflow detection; e.g., nasal thermistors versus nasal airflow pressure sensors.

OSA and Blood Pressure

Patients with OSA are "non-dippers", after a period of suffering from OSA; normal patients have a typical 10-20% dip in nocturnal blood pressure.[14-16] Scientific research has shown the strong association between OSA and neuro-cardiovascular effects, like increased risk of stroke, heart failure, arrhythmias, and myocardial infarction.[16-18] Patients with OSA have a higher incidence of hypertension, as high as 1.5 to 2.7 times.[18-20], and treatment of these OSA patients with CPAP have consistently and reliably shown a decrease in blood pressure, likely due to the improvement of vascular function.[21,22] The significance of a blood pressure reading is easily understood by a patient.

Gross Weight / BMI and OSA

Obese and OSA patients have higher oxidative metabolic changes/stress and are more prone to diabetes, hypertension, hypercholesterolaemia and obstructive sleep apnea.[23] It is also known that patients with OSA may not be obese.[23] Simplistically, the anatomy of the upper airway is essentially a balance between the soft tissues and its skeletal framework. Studies have also showed that in Asian patients a cranio-facial restriction (small jaw, retrognathia) is commonly associated with OSA (making gross weight a better reflection compared to BMI), compared to Caucasian patients where fat deposition is common.[23] Research also demonstrate that a BMI>40 is also a predictor of poorer surgical outcomes,[24] and that obesity is significantly associated with fat deposition in the posterior tongue.[25] Kim et al., had recently showed that the tongue fat percentage was higher in OSA patients compared to normal (matched BMI) subjects (42% versus 24%).[26] Parapharyngeal fat pads have also been shown to be enlarged in apneics and to contribute to airway narrowing.[27] Sleep specialist appreciate that a reduction in BMI would not only reduce the overall oxidative metabolic stress but also, inadvertently also increase the upper airway space in totality.

Sleep Goal Index (SGI)

The AHI is a not an intuitively informative concept, patients do not complain of a raised AHI. Patients are bothered by real life clinical symptoms like excessive sleepiness, loud snoring, poor memory/concentration, irritability and loss of libido; or its systemic disease like high blood pressure and cardiovascular morbidity, yet, such parameters are underutilised and unaccounted for in evaluating treatment outcomes. Consider patient A with AHI of 95 who, after treatment, has a post-operative AHI 21; this patient would likely experience clinical symptomatic improvement with decrease in oxidative stress level, even though he would have been classified as a "failure" based on Sher's AHI criteria. Consider another patient B, with pre-operative AHI 35, and post-operatively AHI < 14, this is considered a "successful" AHI outcome (based on Sher's AHI criteria) even though the impact might be minimal, compared to patient A. Intuitively, patient A benefitted significantly more than patient B.

From our data, the overall success rate for these 618 OSA patients (based on Sher's criteria) was fairly low at 55.7%. We anticipated this lower success rate, as our data included OSA patients who had all forms of upper airway surgery, including nose surgery alone (a single surgical modality not expected to show much improvement in AHI). This discordance was intentionally planned so that the SGI could be tested and compared to the Sher's criteria for both surgical "success" and "failures".

SGI is compared with Sher's criteria using the McNemar's test. The Sleep-Goal Index (SGI) utilizes 4 more holistic parameters – blood pressure, gross weight, BMI, oxygen time spent / duration <90%, (T90) and AHI. Based on these 4 parameters, it was noted that fulfilling any 2 out of 4 SGI parameters would be just as sensitive as the Sher's criteria, with additionally being more holistic and representative of the patients' end-organ effects and oxidative stress (Table II).

The overall success rates of various SGI pairs that fulfilled SGI criteria as "success" (under the column "both yes & yes success met") , were as follows – A and B – 41.8%, A and C – 56.2%, A and D – 55.8%, B and C – 54.5%, B and D – 56.7%, C and D – 60.9% (all of which were very similar and close to Sher's criteria of a success rate of 55.7%, indicating that any of these 2 out of the 4 SGI parameters combined, would be as sensitive as Sher's criteria), with reference to Table I.

With reference to Table II and the column "Success Met by Sher but Missed by SGI", we note that the percentage of these 618 patients who met the Sher's criteria but was missed by the SGI criteria was: A and B – 1.0%, A and C – 1.0%, A and D – 0.0%, B and C – 2.0%, B and D – 0.0%, C and D – 0.0% ($p<0.001$). From this table, we can conclude that the SGI criteria included 98-99.0% of all the patients who also satisfied the Sher's criteria.

With reference to Table II and the column "Success Met by SGI but Missed by Sher", we note that the percentage of these 618 patients who met the SGI criteria but was missed by the Sher's criteria were as follows, A and B – 26.3%, A and C – 34.7%, A and D – 26.3%, B and C – 29.4%, B and D – 17.0%, C and D – 27.1% ($p<0.001$). We note that the Sher's criteria is not comprehensive and did not encompass the patients who had benefited from surgery, as Sher's criteria only used one parameter, AHI. Hence, Sher's criteria had missed between 17.0% to 34.7% of patients whose treatment outcomes were successful on the SGI by 2 out of 4 parameters, and who had actually benefited from surgery.

Hence, based on these validated parameters of the SGI, we propose that any patient who meets the criteria of 2 out of these 4 SGI parameters, would be deemed as clinical success for that respective intervention. In addition, we also illustrated that had we utilized the old Sher's criteria to these 618 patients, the patients who had encouraging post-intervention results in terms of blood pressure decrease, BMI/gross weight reduction, and significance reductions in the duration below 90% oxygen saturations (T90) would have been mis-classified as failures.

We acknowledge and recognize some possible limitations and short comings of this study. This includes that fact that the numbers are not large, and some centres may have had patients that were lost to follow up and as with multi-centre studies, the surgeon performing the procedure, might have a slightly different technique and may contribute to the slight difference in success rates. However, we noted that the objective of the paper was not to compare success rates of the various procedures or techniques, but to compare the two different methods of evaluating success rate, namely Sher criteria and the SGI. Furthermore, surgical techniques that are employed by each surgeon might differ; however, this paper's objective was not to analyse the success rates of techniques but the type of outcome measures used. In addition, the method and device used for assessing sleep may vary. The device software may have slightly different definitions of hypopnea and oxygen desaturation definitions in each country. This is the objective of this study, to illustrate the over-reliance of the AHI which in turn has wide variability.

We also noted a few other limitations. Firstly, different centres practise different pre-operative protocols. Some centres use DISE routinely, where other centres might not. The inclusion of pre-operative DISE might also affect the success rates and surgical outcome.

Finally, we are comparing SGI to Sher's criteria, demonstrating that because SGI has 4 parameters instead of only one very unreliable parameter AHI (as we had discussed), SGI would intuitively be more holistic and non-inferior to the AHI. However, the disclaimer is that this work may not have demonstrated that SGI is superior. However, instinctively, all sleep physicians are aware of the pitfalls of the AHI, and are also aware of that the SGI provides a more holistic approach through blood pressure, gross weight, BMI and oxygen levels, compared to only one AHI parameter alone.

CONCLUSION

The SGI parameters are easy to measure, consistent and reproducible. The SGI is realistic and holistic for OSA patients undergoing treatment for OSA. The patient's treatment outcome could already be measurable by 2 out of the 4, SGI criteria. We would like to propose the use of Sleep Goal Index as a treatment outcome measure as it is holistic, comprehensive, easily measured and better patient-appreciated as a treatment outcome measure.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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Autologous serum skin test in chronic spontaneous urticaria: Evaluation of the relationship with disease activity and autoimmune antibodies

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ABSTRACT

Introduction: Chronic spontaneous urticaria (CSU) is a multifactorial, mast cell driven disorder characterized by wheals, angioedema, or both, lasting for more than six weeks. Autoimmunity, particularly Type IIb autoimmunity, involving IgG autoantibodies directed against either IgE or its high affinity receptor (FcεRI) on mast cells and basophils, plays a significant role in CSU pathogenesis. The Autologous Serum Skin Test (ASST) is a practical tool for detecting IgG autoantibodies and may be associated with the disease severity and the presences of autoimmune antibodies. Nonetheless, previous studies on ASST responses and the clinical features of patients with CSU have conflicting results.

Materials and Methods: This study aimed to establish the relationship between ASST positivity and disease activity, assessed by the Urticaria Activity Score 7 (UAS7) and to determine the associations with autoimmune antibodies including anti-thyroid peroxidase (anti-TPO), anti-thyroglobulin antibodies, and antinuclear antibodies (ANA). This cross- sectional study was conducted over a five months period, from January to May 2024, at the Department of Dermatology, in the tertiary hospital located in the capital city of Malaysia. Participants underwent ASST, laboratory evaluation for autoimmune antibodies, and assessment of disease activity using UAS7.

Results: In this study, 24 of the 59 patients were ASST positive, resulting in a prevalence rate of 41%. ASST positive patients demonstrated significantly higher disease activity, with a mean UAS7 score of 23.96 ± 10.55, compared to 13.51 ± 10.88 in ASST negative individuals (p = 0.001). A significant association was also found between ASST positivity and higher UAS7 severity categories (p = 0.011). Furthermore, a significant gender difference was observed with females more likely to exhibit ASST positivity (p = 0.016). Nevertheless, no significant associations were found between ASST results and presence of angioedema (p =1.0), atopy (p = 0.968), or autoimmune antibodies including ANA, anti-TPO, and anti-thyroglobulin antibodies (p > 0.05)

Conclusion: The significant association between ASST positivity and increased UAS7 scores heightened interplay between autoimmunity, disease severity, and clinical characteristics in CSU, particularly Type IIb autoimmunity subtype. Hence, ASST is a practical clinical tool for identifying autoimmune profile in CSU patients, and aids dermatologist in prognosis assessment and treatment strategies.

KEYWORDS:
Chronic spontaneous urticaria, autologous serum skin test, urticaria activity score 7, autoimmune antibodies

INTRODUCTION

Chronic spontaneous urticaria (CSU) is mast cell driven skin disorder characterized by recurrent wheals, angioedema, or both, persisting for more than six weeks.[1] The pathogenesis of CSU is multifactorial and complex. Several mechanisms have been contributing to the pathogenesis of CSU, including infections, food intolerance, coagulation cascade, genetic factors, and autoimmunity. Nowadays, increasing evidence suggest that autoimmunity plays a significant role in a subset of CSU patients. It is estimated that between 30 to 50% of CSU cases are autoimmune in nature, referred to as chronic autoimmune urticaria (CAU).[2-3] In these patients, the autoimmune response is primarily driven by functional autoantibodies that target mast cell and basophil receptors, leading to the mast cells degranulation and release of proinflammatory mediators responsible for the clinical manifestations of urticaria and angioedema.

According to the EAACI/GA²LEN/EuroGuiDerm/APAAACI guidelines published in 2021,[4] the pathogenesis of chronic urticaria can be categorized into different mechanisms, with Type I and Type IIb autoimmune pathways, with Type IIb being particularly relevant in chronic autoimmune urticaria.[4] Type I autoimmunity is characterized by the formation of IgE antibodies against allergens, which activate mast cells and basophils, commonly seen in allergic urticaria. In contrast, Type IIb autoimmunity involves IgG autoantibodies as the central players. These autoantibodies target IgE and FcεRIα receptors on mast cells and basophils. The binding of IgG autoantibodies to the receptors lead to mast cell degranulation and basophil activation, even in the absence of allergens, causing the release of histamine and other inflammatory mediators. The presence of these autoantibodies in Type IIb autoimmunity is a key feature of autoimmune CSU, and they can be detected using diagnostic tests such as the autologous serum skin test and the basophil histamine release assay.[3]

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Basophil histamine release assay (BHRA) remains the gold standard for detecting these autoantibodies in Type IIb autoimmunity. However, its complexity and limited availability necessitate simpler diagnostic alternatives. The autologous serum skin test (ASST) has emerged as a practical and widely accessible test to assess auto reactivity.[5-6]

Previous studies have demonstrated that patients with CSU and ASST positivity often experience greater disease activity, longer disease duration, diminished quality of life, and a higher frequency of concomitant angioedema.[6-8] However, some studies have failed to demonstrate significant correlation. This study aims to establish the association between ASST positivity and disease severity in patients with CSU, as well as its correlation with autoimmune antibodies in our study population. These findings may offer valuable insights for prognosis, guide treatment decisions, and support long term disease management in CSU patients.

The primary objective of this study is to establish the relationship between ASST positivity and disease activity, as measured by the UAS7, in patients diagnosed with CSU. UAS7 is a validated tool and widely use in both clinical practice and research by evaluating the number of wheals and the intensity of pruritus in patients with CSU.[4]

The secondary objective is to establish the association between ASST positivity and the presence of autoimmune biomarkers, including anti thyroid peroxidase (anti-TPO) antibodies, anti thyroglobulin antibodies, and antinuclear antibodies (ANA). These analyses aim to provide a deeper understanding of the immunological profile and disease severity within the study population

MATERIALS AND METHODS

This cross sectional study was conducted over a five months period, from January to May 2024, at the Skin Specialist Clinic Department of a tertiary hospital in a Malaysian state capital.

Ethical approval from the Medical Research and Ethics Committee (MREC) of the Ministry of Health (MOH) Malaysia, ID-23-02988-AEP (IIR), was obtained prior to the initiation of the study. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and the Malaysian Good Clinical Practice (GCP) guidelines

Eligible participants were adults aged 18 years or older who provided written informed consent. All participants had a confirmed diagnosis of chronic spontaneous urticaria (CSU), or CSU with concurrent inducible urticaria, with symptoms lasting for at least six weeks prior to enrolment. Participants were excluded if they met any of the following criteria: pregnancy or breastfeeding; needle phobia; severe, uncontrolled urticaria requiring continuous antihistamine use; chronic inducible urticaria without coexisting CSU; urticarial vasculitis; urticaria associated with autoinflammatory conditions such as Schnitzler syndrome or cryopyrin associated periodic syndromes; active malignancy; or active autoimmune disease on treatment. In addition, patients receiving high dose oral corticosteroids (more than 15 mg/day), cyclosporine, omalizumab or other immunosuppressive therapy such as methotrexate, azathioprine were also excluded.

Prior to undergoing the ASST, participants were instructed to discontinue antihistamines for at least 72 hours. They were also advised to avoid consuming any known foods that could trigger urticaria or allergic reactions.

The ASST was conducted following the standardized protocol recommended by the EAACI/GA²LEN task force consensus report to ensure accuracy and consistency.[7] Each participant was interviewed to collect demographic data, disease duration, triggering factors, and details about urticaria symptoms, including any episodes of angioedema or systemic involvement.

Venous blood samples were collected for laboratory investigations, including complete blood count, thyroid function tests, and autoimmune antibodies such as anti-thyroid peroxidase (anti-TPO), anti-thyroglobulin, and antinuclear antibodies (ANA). An additional blood sample was drawn into a plain tube to obtain serum for the ASST. This sample was allowed to clot at room temperature for 30 minutes and then centrifuged promptly. Fresh serum was used immediately to reduce the risk of contamination.

The ASST was performed on the volar side of the forearm that had been free from wheals for at least 24 hours. The skin was cleaned with normal saline, intradermal injections were administered using a 27G sterile syringe, spaced 3 cm apart. The test included three injections: 0.05 ml of normal saline as a negative control, 0.05 ml of the patient's serum, and a histamine solution as a positive control.

After 30 minutes, the injection sites were examined. The largest perpendicular diameters of the wheals were measured. A positive ASST result was defined as a serum-induced wheal that was at least 1.5 mm larger than the one from the normal saline control. The test was only considered valid if the histamine control produced a visible wheal.

Following the ASST, participants were asked to complete the Urticaria Activity Score 7 (UAS7) diary over the next seven days. Participants were asked to avoid antihistamines during this period.

Statistical Analysis

Data were cleaned and analyzed using SPSS version 26.0. The distribution of continuous variables was assessed through measures of skewness and kurtosis, as well as visual inspection of histograms. Continuous variables were presented as mean ± standard deviation when normally distributed, and as median when the data were not normally distributed. Categorical variables were presented as frequency and percentage.

The association between the Urticaria Activity Score 7 and the autologous serum skin test, disease duration and eosinophilia were analysed using independent sample t-tests, Kruskal-Wallis tests, Fisher's exact tests, and correlation

analyses. Additionally, the relationship between ASST results and the presence of autoantibodies was assessed using Fisher's exact test. All tests were two-sided, with statistical significance set at $p < 0.05$.

Ethics Approval

Ethical approval from the Medical Research and Ethics Committee (MREC) of the Ministry of Health (MOH) Malaysia, ID-23-02988-AEP (IIR), was obtained prior to the initiation of the study. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and the Malaysian Good Clinical Practice (GCP) guidelines

RESULTS

The study included a total of 59 participants, with a mean age of 47 years. The majority of the sample were female, constituting 76.3% of the study population, while males accounted for 23.7%. The ethnic composition was diverse, with Malay (49.2%), Chinese (35.6%), Indian (13.6%), and Filippino (1.7%) represented. The reported comorbidities encompassed metabolic disorders (45.7%), cardiovascular conditions (6.7%), hypothyroidism (6.7%), and connective tissue disorders (6.7%) and neurological disease (1.7%). Notably, no participants had a history of vitiligo, type 1 diabetes, or inflammatory bowel disease (Table I).

The study found that 40.7% of the participants had a personal history of atopic conditions. Additionally, 30.5% of the participants reported a family history of atopy, 23.7% had a family history of chronic urticaria, and 22% had a family history of autoimmune diseases (Table I).

The clinical characteristics of the patients are summarized in Table II. The median duration of disease activity was 12 months. The distribution of urticarial lesions varied among patients, with the lower limbs being the most frequently affected site, observed in 94.9% of cases. This was followed by involvement of the upper limbs in 93.2% of patients, the trunk in 89.8%, and the face in 52.5%. A significant proportion of patients experienced angioedema, 35 patients (59.3%) reported a history of at least one episode of angioedema (Table II).

Regarding laboratory findings, elevated eosinophil counts were detected in 6 patients (10.2%), while abnormal thyroid function tests were observed in 2 patients (3.4%). The presence of autoantibodies was also noted, with anti-thyroid peroxidase (anti-TPO) antibodies in 16.9%, and anti-thyroglobulin antibodies in 22.0% of patients and antinuclear antibodies (ANA) detected in 16.9% of patients (Table II).

In this study, 24 patients (40.7%) exhibited a positive ASST result, while the remaining 59.0% had a negative ASST result (Table II). ASST was performed to assess the presence of autoreactivity in patients with chronic urticaria. ASST is a widely used diagnostic tool that evaluates the presence of circulating histamine-releasing autoantibodies, which contribute to the pathophysiology of chronic spontaneous urticaria (CSU).

In this study, the mean UAS7 score was 17.76 (standard deviation [SD]: 11.84), reflecting a broad spectrum of disease severity among participants. 22.0% of participants were classified as having well-controlled disease (UAS7: 0–6), mild disease activity (UAS7: 7–15) was observed in 25.4% of patients, while 30.5% exhibited moderate disease severity (UAS7: 16–27). Notably, 22.0% of participants experienced severe urticaria (UAS7: 28–42), characterized by frequent and intense symptoms significantly impacting daily life (Table II).

The study found a statistically significant difference in the autologous serum skin test results between genders. The data showed that 55.6% of the female participants had a positive ASST, compared to only 14.3% of the male participants. This difference was found to be statistically significant, with a p-value of 0.016. This suggests that female participants with chronic spontaneous urticaria were more likely to exhibit a positive ASST response compared to male participants (Table III).

The results of our analysis did not indicate a statistically significant relationship between the occurrence of angioedema and the outcome of the autologous serum skin test. Among participants with history of angioedema, 51.4% exhibited a positive ASST result, while 50% of those without angiodema also showed a positive ASST. This finding suggests that the presence or absence of angioedema did not significantly influence the ASST results (Table III).

The analysis revealed that among participants with a positive autologous serum skin test, 45.8% had a personal history of atopic diseases. In contrast, a higher proportion of 54.2% of participants with negative ASST had a personal history of atopy. However, the p-value of 0.968 indicates a lack of statistical significance in the association between atopy and ASST positivity. This suggests that the ASST results may be more reflective of the autoimmune mechanisms underlying chronic spontaneous urticaria, rather than being primarily driven by IgE mediated mast cell degranulation (Table III).

Patients who tested positive for the ASST exhibited significantly higher USA7 scores compared to those with negative ASST results. The mean USA7 score for patients with a negative ASST result was 13.51 ± 10.88, while for those with a positive ASST, the mean score was 23.96 ± 10.55 ($p = 0.001$). This indicates that patients with positive ASST results had a notably higher disease severity, as reflected by the USA7 scores, which assess the severity of skin involvement (Table IV).

In addition, a higher proportion of patients with a negative ASST test were found to have well controlled or mild disease severity. In contrast, patients with positive ASST results tended to show higher proportions of moderate to severe disease severity. Therefore, a statistically significant association was observed between the USA7 score categories and ASST results ($p = 0.011$) (Table IV).

In this study, the results of the positive ASST was compared to the auto antibody markers (Anti Nuclear Antibody (ANA), Anti Thyroid Peroxidase (Anti-TPO) and Anti-thyroglobulin) using chi square test. It was found that there was no

Table I: Demographics of study population

Characteristic	Findings	N (%)
Age in years, mean ± SD	47.1 ± 15.1	
Gender	Female	45 (76.3)
	Male	14 (23.7)
Ethnicity	Malay	29 (49.1)
	Chinese	21 (35.6)
	Indian	8 (13.6)
	Filippino	1 (1.7)
Comorbidities	Metabolic disease	27 (45.7)
	Heart disease	4 (6.7)
	Thyroid disease	4 (6.7)
	Connective tissue disease	4 (6.7)
	Neurological disease	1 (1.7)
	Vitiligo	0 (0)
	Type 1 diabetes mellitus	0 (0)
	Inflammatory bowel disease	0 (0)
Personal history of atopy	Yes	24 (40.7)
	No	35 (59.3)
Family history	Atopy	18 (30.5)
	Chronic urticaria	14 (23.7)
	Autoimmune disease	13 (22.0)

Table II: Clinical characteristics of study population

Characteristics	Findings	N (%)
Duration of disease in months, Median	2 to 120	12 months
Distribution of urticaria	Lower limb	56 (94.9)
	Upper limb	55 (93.2)
	Trunk	53 (89.8)
	Face	31 (52.5)
History of angioedema	Yes	35 (59.3)
	No	24 (40.7)
ASST	Postive	24 (40.7)
	Negative	35 (59.3)
UAS 7 Mean score ± SD	17.76 ± 11.84	
USA 7 in severity category	Well controlled (1-6)	13 (22.0)
	Mild (7-15)	15 (25.5)
	Moderate (16-27)	18 (30.5)
	Severe (28-42)	13 (22.0)
Eo0sinophil count	Normal (> 0.5 x10^9/L)	53 (89.8)
	Elevated (< 0.5 x10^9/L)	6 (10.2)
Thyroid function test	Normal	57 (96.6)
	Abnormal	2 (3.4)
Anti thyroid peroxidase	Normal	49 (83.1)
	Elevated	10 (16.9)
Anti thyroglobulin	Normal	47 (78.0)
	Elevated	13 (22.0)
Antinuclear antibody	Negative	49 (83.1)
	Positive	10 (16.9)

Table III: Association of autologous serum skin test and gender, angioedema and personal atopy disease

Characteristics	ASST positive N (%)	ASST negative N (%)	p-value
Gender			0.016
• Female	25 (55.6%)	20 (44.4%)	
• Male	2 (14.3%)	12 (85.7%)	
Angioedema			1
• Yes	18 (51.4%)	17 (48.6%)	
• No	12 (50%)	12 (50%) 1	
Atopy disease			0.968
• Yes	11 (45.8%)	13 (54.2%)	
• No	16 (45.7%)	19 (54.3%)	

Table IV: Association of autologous serum skin test with disease activity and autoimmune autoantibodies

Disease severity	ASST positive N (%)	ASST negative N (%)	p-value
UAS 7 score, mean ± SD	23.96 ± 10.55	13.51 ± 10.88	0.001
UAS 7 in severity category			
• Well controlled	1 (4.2)	12 (43.3)	
• Mild	5 (20.8)	10 (28.6)	0.011
• Moderate	9 (37.5)	9 (24.7)	
• Severe	9 (37.5)	4 (11.4)	
ANA			
• Non reactive	21(87.5)	28 (80.0)	0.506
• Reactive	3 (12.5)	7 (20.0)	
Anti TPO			
• Normal	20 (83.3)	29 (82.9)	> 0.950
• Elevate	4(16.7)	6 (17.1)	
Antithyroglobulin			
• Normal	19 (79.2)	27 (77.1)	>0.950
• Elevate	5 (20.8)	8 (22.9)	

Table V: Association of elevated eosinophils, presence of autoantibodies with disease activity based on UAS 7

Blood parameters	Well controlled	Mild	Moderate	Severe	p-value
Eosinophil count					0.126
• Normal	11(84.6)	14 (93.3)	18 (100.0)	10 (76.9)	
• Elevate	2(15.4)	1 (6.7)	0 (0.0)	3 (23.1)	
ANA					0.195
• Non reactive	9 (69.2)	12 (80.0)	15 (83.3)	13 (100.0)	
• Reactive	4 (30.8)	3 (20.0)	3 (16.7)	0 (0.0)	
Anti TPO					0.313
• Normal	9 (69.2)	12 (80.0)	17 (94.4)	11 (84.6)	
• Elevate	4 (30.8)	3 (20.0)	1(5.6)	2 (15.4)	
Antithyroglobulin					0.356
• Normal	9 (69.2)	10 (66.7)	16 (88.9)	11 (84.6)	
• Elevate	4 (30.8)	5 (33.3)	2 (11.1)	2 (15.4)	

statistical significant difference with the ANA (p=0.51), Anti-TPO (p=0.99) and Anti-thyroglobulin (p=0.99)(Table IV).

In this study, we aimed to investigate the relationship between elevated eosinophil levels, the presence of autoantibodies, and disease severity, as assessed by the UAS7 score. Despite our analysis using Fisher Exact test, no significant correlations were observed between these factors and the severity of the disease. All results yielded a p-value greater than 0.05, indicating the lack of a statistical significant association. (Table V).

The analysis revealed that the mean duration of the disease was shorter in the severe group compared to the other groups. However, this difference was not statistically significant, with a p-value of 0.147.

DISCUSSION

The current study aims to provide better insight into the clinical characteristics of CSU, the relationship between the outcomes of ASST with the clinical presentation, disease activity and the presence of autoimmune auto-antibodies.

Our study demonstrated a statistically significant gender different in ASST positivity among CSU patients, with females representing 76.3% of ASST positive cases (p = 0.016). This observation is consistent with earlier studies reporting a higher prevalence of CSU in women, which may be influenced by hormonal factors.[8-9] Women have higher levels of oestrogen and progesterone, whereas men exhibit increased levels of dehydroepiandrosterone sulphate (DHEAS), a hormone with anti inflammatory and immuno-modulatory properties. Serum concentrations of DHEAS in CSU patients are significantly lower than those in healthy subjects and are associated with positive responses to ASST.[10] These hormonal differences are believed to influence immune responses and may contribute to the greater autoimmune activity seen in female CSU patients, potentially explaining their higher ASST positivity.

Angioedema is the clinical manifestation of urticaria, located within the subcutis. Although angioedema is commonly observed in CSU, occurring in 30-50% of cases.[3] The relationship between angioedema and the outcomes of the autologous serum skin test remains unclear. Some studies have suggested that CSU patients with angioedema may experience a more prolonged and severe disease course.[8-9] This has been attributed to the potential role of functional autoantibodies, particularly those targeting IgE and FcεRI, in triggering stronger and more prolonged mast cell activation, which could increase the risk of severe urticaria and angioedema. Type IIb autoimmunity characterized by these autoantibodies has been associated with severe CSU and recurrent, prolonged angioedema, especially in individuals with positive ASST results.[3,11-12] However, the current study did not find a statistically significant association between the

presence of angioedema and ASST positivity. This lack of significance may be attributed to sample size limitations or individual variability in immune responses.

Previous studies have shown that patients with chronic urticaria exhibit a higher prevalence of atopic conditions, such as allergic rhinitis, asthma, and atopic dermatitis, compared to control groups.[13-14] Our study corroborates these findings, with 40.6% of participants reporting a personal history of atopic disorders and 30.5% having a family history of atopy. However, further analysis did not reveal a significant association between a personal history of atopy and positive results on the autologous serum skin test. This is due to difference autoimmune mechanism in between Type 1 and Type IIb autoimmunity. Type I CSU is linked to IgE mediated mechanisms, with patients often exhibiting higher total IgE levels and more pronounced atopic features. In contrast, Type IIb CSU is associated with the presence of autoantibodies, such as IgG or IgM targeting the IgE receptor and FcεRI, and is frequently characterized by low total IgE levels and a positive autologous serum skin test.[15] Therefore, in our study, the positive ASST findings suggest the presence of Type IIb autoimmunity in CSU, which is driven by autoantibodies rather than atopic predisposition.

The participants in our study were well distributed across different disease severity levels based on the Urticaria Activity Score 7 (UAS7), a validated tool used to assess disease activity in CSU. The UAS7 score assesses the frequency and intensity of wheals and pruritus over severe days. The majority of our participants with positive ASST fell into the moderate and severity category, with ($p = 0.011$). According to a study by Alyasin et all, patients with a positive ASST had more severe CSU, characterized by larger wheal size, longer disease duration, and higher attack frequency.[16] Our finding align with these observations, indicating that individuals with positive ASST results demonstrated significantly higher mean UAS7, with a statistically significant p value of 0.001. This suggests that these individuals exhibited more severe disease symptoms compared to those with negative ASST results. The presence of autoantibodies, such as IgG and IgM directed against the IgE receptor and FcεRI, may contribute to the increased severity and persistence of symptoms in chronic spontaneous urticaria patients.[17-19]

In addition, ASST is an effective clinical screening tool for detecting functional circulating autoantibodies in patients with CSU. It has demonstrated approximately 70% sensitivity and 80% specificity in identifying the autoimmune subset of CSU.[6] This screening test has a negative predictive value of approximately 82.5±14%, indicating that in CSU patients with a negative ASST response, there is a high likelihood that no functional circulating autoantibodies are present in their serum.[9,20-22]

Chronic spontaneous urticaria is strongly associated with various autoimmune conditions, including autoimmune thyroiditis, celiac disease, rheumatoid arthritis, Graves' disease, vitiligo and type 1 diabetes.[7,23] Among these, thyroid disease is the most frequently reported autoimmune condition in CSU patients.[24-25] Individuals with thyroid dysfunction often experience a more severe and prolonged course of CSU compared to those without thyroid abnormalities.[12,26] Type IIb autoimmunity, characterized by the presence of functional autoantibodies such as IgG anti thyroid peroxidase, is increasingly recognized as a key driver of autoimmune CSU.[3] Even clinically euthyroid CSU patients may have persistent anti-thyroid antibodies, indicating an underlying autoimmune mechanism.

A study by Ismail et al in Malaysia, found that 23% of chronic urticaria patients had anti TPO antibodies compared to 8% in the control group, reinforcing the higher prevalence of thyroid autoimmunity in CSU.[10] The activation of the complement system by thyroid autoantibodies may exacerbate urticaria, leading to increased inflammation and prolonged disease activity. This suggests that the presence of these autoantibodies, as detected by ASST, could contribute to the severity and persistence of CSU symptoms. While our study did not find a statistically significant association between the presence of autoantibodies, such as ANA, anti-TPO, and anti-thyroglobulin, and the results of the autologous serum skin test, this discrepancy may be attributed to the relatively small sample size and heterogeneity of the study population. Further large scale studies are needed to assess the complex relationships between autoantibodies, disease activity, and clinical features in patients with CSU.

CONCLUSION

This study showed the interplay between autoimmunity, disease severity, and clinical characteristics in chronic spontaneous urticaria. Our findings support the association between positive ASST and increased CSU severity, with ASST positive individuals exhibiting significantly higher UAS7 score. Furthermore, the observed gender disparity suggests a potential hormonal influence on ASST reactivity, leading to a higher prevalence of positive ASST results among female participants. However, no significant associations were observed between ASST positivity and atopy, angioedema, or thyroid related autoimmune antibodies. Given its simplicity, low cost, and wide availability, the ASST remains a valuable tool for evaluating disease severity and supporting clinical decision making in the management of CSU.

CONFLICT OF INTEREST

The authors declare no conflicts of interest regarding the research, no relevant financial or non-financial interest to disclose.

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ORIGINAL ARTICLE

Exploring prenatal risk factors associated with congenital anomalies among newborns in national referral hospital, Indonesia

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ABSTRACT

Introduction: Congenital anomalies (CAs) account for approximately 8 to 15% of perinatal deaths and 13 to 16% of neonatal deaths. Congenital anomalies are a significant public health issue in Indonesia, affecting approximately 59.3 per 1,000 live births. The three most frequent malformations were hydrocephalus (21%), cleft lip and cleft palate (9.2%) and Down Syndrome (9.2%).

Materials and Methods: A retrospective case-control study was conducted at Dr. Cipto Mangunkusumo General Hospital, Jakarta, between September 2023 and October 2024. Data from 552 births were analysed, including 97 cases of congenital anomalies (CAs). Maternal, fetal, and environmental factors were assessed using medical records and documented clinical histories. Statistical analyses included descriptive statistics, cross-tabulations, binary logistic regression, and multivariable logistic regression.

Results: The prevalence of CAs was 17.6%. Significant maternal risk factors included a history of congenital anomalies (OR = 3.7, 95% CI: 0.88–16.00) and severe anemia (OR = 4.37, 95% CI: 2.48–7.69). Environmental risks, such as drug use in the first trimester (OR = 3.43, 95% CI: 2.01–5.86), passive smoking (OR = 4.10, 95% CI: 1.89–8.90), and pesticide exposure (OR = 3.92, 95% CI: 1.26–12.17), were also significant. Folic acid supplementation showed a significant protective effect against congenital anomalies (OR = 0.56, p = 0.001), although the usage rate remained low (35.5%).

Conclusion: This study found a significant association between congenital anomalies and risk factors such as passive smoking, exposure to pesticides, and chemicals. It highlights the importance of ongoing community health education to prevent and manage these predisposing risk factors.

KEYWORDS:
Congenital anomaly, maternal factors, epigenetics

INTRODUCTION

Congenital anomalies (CAs), commonly referred to as birth defects, are prenatal conditions characterized by structural, functional, behavioral, or metabolic abnormalities that develop during fetal development. Present at birth, these abnormalities can significantly affect an infant's health, growth, and ability to thrive. They pose a significant global health challenge, contributing to pregnancy losses, stillbirths, and neonatal deaths, while also causing lifelong disabilities that affect individuals, families, and healthcare systems.[1-2] Globally, an estimated 8 million infants are born each year with major congenital anomalies, accounting for approximately 6% of all live births and leading to nearly 300,000 deaths in the first month of life.[3] According to the Centers for Disease Control and Prevention (CDC), approximately one in 33 infants is affected by a congenital anomaly, contributing to 8–15% of perinatal deaths and 13–16% of neonatal deaths.[4-5] Congenital anomalies are a significant public health concern in Indonesia, with an estimated prevalence of 59.3 per 1,000 live births, translating to approximately 263,154 affected infants annually. A study conducted at Dr. Cipto Mangunkusumo General Hospital in Jakarta reported that 8 out of every 1,000 live births involved congenital heart disease (CHD), with approximately 50,000 infants born with CHD annually in Indonesia.[6] The three most frequent malformations were hydrocephalus (21%), cleft lip and cleft palate (9.2%) and Down's Syndrome (9.2%).[6] Congenital anomalies continue to represent a substantial global health burden, with emerging regional data indicating a rising trend in prevalence. Notably, in South Korea, the prevalence of congenital anomalies doubled between 2006 and 2014, reflecting broader global epidemiological patterns.[7-8] Similar increases have been observed in Indonesia, where records from Dr. Cipto Mangunkusumo General Hospital show a 1.5-fold increase in cases compared to 2016. These trends highlight the urgent need for further research and intervention, particularly in low- and middle-income countries where congenital anomalies are often overlooked as a public health priority.[9]

The causes of congenital anomalies are diverse, ranging from genetic and environmental factors to maternal health conditions. Known prenatal risk factors include maternal infections such as cytomegalovirus, rubella, and toxoplasmosis; exposure to hazardous substances like chemicals, radiation, air pollution, pesticides, and heavy metals; and maternal characteristics such as advanced age, smoking, obesity, chronic illnesses, and gestational diabetes.[10-12] Despite advances in understanding these factors, 40–60% of congenital anomalies still have no clearly identified cause.[13]

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Genetic testing is not part of routine screening in Indonesia and is not covered by national health insurance, limiting access to this essential diagnostic tool for many individuals. In Indonesia, however, research into the prenatal risk factors contributing to congenital anomalies remains limited, leaving significant gaps in understanding and prevention strategies. Few studies have examined the roles of genetic, environmental, and maternal health factors in influencing the prevalence of congenital anomalies. This study aims to address these gaps by exploring prenatal risk factors associated with congenital anomalies, with the goal of informing effective preventive measures and improving prenatal care practices in Indonesia.

MATERIALS AND METHODS

This retrospective case-control study was conducted at Dr. Cipto Mangunkusumo General Hospital, Jakarta, to investigate prenatal risk factors associated with congenital anomalies. Data collection included cases documented between September 2023 and October 2024. Participants were selected based on medical records and previously documented clinical information from the hospital. Inclusion criteria included individuals diagnosed with specific congenital anomalies, such as spina bifida, anencephaly, meningo-/encephalocele, congenital cataract, cleft palate, cleft lip, cleft lip and palate, hypospadias, epispadias, talipes, reduction deformity, atresia ani with or without fistula, omphalocele, gastroschisis, and conjoined twins. Patients with incomplete medical records or those not meeting these diagnostic criteria were excluded from the study.

Data were obtained by reviewing medical records for the specified period. The data collection process was conducted continuously and rigorously, with daily monitoring by trained data collectors and oversight from the principal investigator and supervisory team to ensure completeness and accuracy. Following collection, the data underwent cleaning, coding, and entry into EpiData Manager, and were subsequently exported to SPSS Version 25.0 for statistical analysis. The outcome variable—fetal congenital anomalies—was examined in relation to the mode of delivery. Classification of congenital anomalies was based on the International Classification of Diseases, 10th Revision (ICD-10). Prevalence was calculated by dividing the number of documented congenital anomaly cases (numerator) by the total number of live and stillbirths (denominator) within the study setting and time frame. Descriptive and inferential statistics were employed, including frequency distribution, cross-tabulations, binary logistic regression, and multivariable logistic regression analyses. Exposure variables with a p-value ≤ 0.20 in bivariate analysis were included in the multivariable model to assess their association with congenital anomalies. Adjusted odds ratios (AOR) with corresponding 99% confidence intervals and p-values were reported. Statistical significance was determined based on 99% confidence intervals that did not include the null value, and results were presented in both textual and tabular formats.

RESULTS

A total of 552 births were recorded between September 2023 and October 2024 at Dr. Cipto Mangunkusumo General Hospital, with 97 cases of congenital anomalies (17.6%). The median maternal age was 27 years, ranging from 14 to 45 years. The majority of mothers of affected infants were aged 26–35 years (38%), had a low level of education (55.7%), and were in the low-to-middle socioeconomic category (58.8%). Among deliveries, caesarean sections accounted for 63% of cases, and diabetes was observed in 5.97% of mothers. Table I summarize the sociodemographic characteristics.

Maternal Factors

Maternal factors such as a history of congenital anomalies in previous pregnancies and severe anaemia were strongly associated with an increased risk of congenital anomalies, as shown in Table II. Among the mothers included in the study, 25% had a history of a malformed child, and notably, 25% of these mothers gave birth to another child with a congenital anomaly. Similarly, severe anaemia (Hb ≤ 7 g/dL) was identified as a significant factor, with 32.97% of the mothers experiencing severe anemia and resulting in malformed infants.

Foetal Factors

As presented in Table III, foetal factors such as birth weight, maturity, and type of birth were examined. Congenital anomalies were more common in preterm infants, with preterm birth showing a significant association (OR = 17.052, 95% CI: 10.95–26.54). Infants with a birth weight under 1,500 grams had an incidence of 0.97%, while anomalies occurred in 72% of live births and 40% of preterm infants. Stillbirths were more frequent in cases than controls (OR = 14.58, 95% CI: 8.98–23.68), although this did not reach statistical significance. Gender showed no notable association.

Environmental, Family History, Exposure to Different Chemicals, and Maternal Illness

Environmental exposures, family history, and maternal conditions were assessed for their association with congenital anomalies, as shown in Table IV. Factors significantly contributing to congenital anomalies included the absence of folic acid supplementation, drug use during the first trimester, and pesticide exposure. Mothers who did not take folic acid had a higher likelihood of congenital anomalies (OR = 0.56, 95% CI: 0.39–0.83).

The main reason for non-compliance is the lack of adequate antenatal care (ANC). Women who miss regular ANC visits often lack information about the importance of folic acid, leading to lower adherence. This issue is especially common in rural and underserved areas, where logistical barriers and financial constraints limit access to essential prenatal care. Socioeconomic factors, such as the cost of prenatal vitamins, hinder folic acid uptake, especially among low-income women.[14]

Moreover, side effects such as nausea, bloating, and gastrointestinal discomfort discourage some women from adhering to folic acid supplementation.[15] Additionally, misinformation and lack of awareness contribute

Table I: Sociodemographic characteristics of the participants of the study

Characteristics	Group	n (%)	
		Cases	Controls
Age (years)	≤20	3 (3.1)	22 (4.8)
	21–25	31 (32.0)	159 (35.0)
	26–35	37 (38.1)	152 (33.4)
	≥36	26 (26.8)	122 (26.8)
Education	<12 years	54 (55.7)	254 (55.8)
	≥12 years	43 (44.3)	201 (44.2)
Socioeconomic status	Low–Middle	57 (58.8)	191 (42.0)
	High–Very High	40 (41.2)	264 (58.0)
ANC visits	Regular	19 (20.5)	304 (66.8)
	Irregular	78 (79.5)	151(33.2)
Delivery	Caesarean section	58 (63)	354 (77.8)
	Spontaneous	39 (37)	101 (22.1)
Maternal comorbidities	Diabetes mellitus	5 (5.97)	9 (1.9)
	Asthma	1 (1.49)	91 (20.0)
	Graves' disease	2 (2.99)	63 (13.8)
	Preeclampsia	2 (2.47)	131 (28.8)
	Autoimmune	3 (2.50)	68 (14.9)
	None	84 (64.18)	93 (20.4)

Table II: Maternal factors associated with congenital anomalies

Characteristics	n (%)		OR (95% CI)
	Cases	Controls	
Age (years)			0.43 (0.22 to 0.83)
≤20	3 (3.1)	22 (4.8)	
21–35	68 (70.1)	311 (68.4)	
≥35	26 (26.8)	122 (26.8)	
Socioeconomic status			1.51 (0.92 to 2.50)
Low–Middle	57 (58.8)	191 (42.0)	
High–Very High	40 (41.2)	264 (58.0)	
History of malformation			34.1 (28.36 to 58.12)
Yes	25 (25.7)	15 (3.3)	
No	72 (74.3)	440 (96.7)	
Severe anaemia (Hb ≤7 g/dL)			6.95 (4.36 to 11.23)
Yes	32 (32.9)	22 (4.8)	
No	65 (67.1)	433 (95.1)	

Note: OR = odd ratio

Table III: Foetal factors associated with congenital anomalies

Characteristics	n (%)		OR (95% CI)
	Cases	Controls	
Birth weight			1.21 (0.62 to 2.38)
<2500 g	39 (40.1)	282 (62)	
≥2500 g	58 (50.9)	173 (38)	
Type of birth			14.58 (8.98 to 23.68
Live births	70 (72.2)	410 (98.4)	
Stillbirths	27 (27.8)	45 (1.6)	
Gender			0.81 (0.63 to 1.44)
Male	45 (47)	282 (62)	
Female	52 (53)	173 (38)	
Maturity			17.05 (10.95 to 26.54)
Preterm	68 (70.9)	182 (40)	
Full term	29 (29.1)	273 (60)	

Note: OR = odd ratio

Table IV: Environmental, family history, exposure to different chemicals, and maternal illness

Characteristics	n (%)		OR (95% CI)
	Cases	Controls	
Folic acid			0.56 (0.39-0.83)
Yes	34 (35.1)	223 (49)	
No	63 (64.9)	232 (51)	
Drug use in 1st trimester			3.0 0(1.88-5.07)
Yes	39 (40.2)	39 (8.7)	
No	58 (59.7)	416 (91.3)	
Smoking			5.31 (0.50 to 56.24)
Yes	29 (30)	45 (9.9)	
No	68 (70)	410 (90.1)	
X-ray exposure			0.69 (0.05-8.48)
Yes	27 (28)	5 (1)	
No	70 (72)	450 (99)	
Pesticide exposure			
Yes	39 (40)	47 (10.3)	1.46 (0.80 – 2.28)
No	58 (60)	408 (89.7)	
Diabetes mellitus			
Yes	43 (45)	212 (46.6)	1.12 (0.77-1.62)
No	54 (55)	243 (53.4)	
Maternal illness			
Yes	51 (53)	173 (38)	1.30 (0.80-2.10)
No	46 (47)	282 (62)	

Note: OR = odd ratio

Table V: Multivariate analyses of factors associated with congenital anomalies

Characteristics	AOR	95% CI
Age	2.35	1.036–5.642
History of malformation	3.7	0.88–16.00
Severe anaemia	4.37	2.48-7.69
Birth weight	2.65	1.15-8.63
Maturity	2.39	2.30-2.49
Drug use during the 1st trimester	3.43	2.01–5.86
Smoking	4.10	1.89–8.90
Folic acid use	0.63	0.24–0.74
Pesticide exposure	3.92	1.26–12.17

Note: AOR = Adjusted Odd ratio

significantly to low folic acid intake. Cultural beliefs and traditional practices also play a role in minimizing the perceived need for modern supplements. Studies indicate that women with limited knowledge about folic acid supplementation are less likely to follow medical recommendations and may rely on non-medical remedies16 Drug use during the first trimester was strongly associated with anomalies (OR = 3.0, 95% CI: 1.88–5.07). Pesticide exposure also increased the risk, though the effect size was moderate (OR = 1.46, 95% CI: 0.80–2.28).

Several pesticides have been associated with fetal anomalies. Organophosphates, such as chlorpyrifos, are linked to developmental neurotoxicity, including lower IQ and motor impairments in offspring. Triazines, such as atrazine, have been associated with low birth weight and defects in the heart, urinary system, and limbs.

Although smoking and x-ray exposure were observed more frequently in cases, they did not show statistically significant associations. Similarly, maternal diabetes and other illnesses did not demonstrate strong correlations with congenital anomalies in this study population.

Multivariate Analyses

The Cox multivariate model identified several significant factors associated with congenital anomalies, as shown in Table V. Unidentified medication used during the first trimester demonstrated a strong association with congenital anomalies (OR=3.43, 95% CI: 2.01–5.86). Passive smoking was the most significant factor, with an adjusted odd ratio of 4.10 (95% CI: 1.89–8.90), followed by pesticide exposure (OR=3.92; 95% CI: 1.26–12.17). While factors such as severe anaemia, low birth weight, maturity, and folic acid use showed trends toward significance, they did not retain statistical significance in the multivariate model.

DISCUSSION

This study identified key factors associated with CAs, highlighting maternal, foetal, and environmental contributors. A history of congenital anomalies and severe anaemia in mothers were significant risks, with severe anaemia linked to nearly one-third of cases. Preterm birth showed the strongest foetal association, while other factors like low birth weight and stillbirths were less significant. Environmental risks included unidentified medication use during the first trimester, passive smoking, and pesticide

exposure, with passive smoking showing the highest hazard ratio. Notably, 64.5% of mothers in this study did not receive folic acid supplementation, potentially reflecting gaps in antenatal care and knowledge, as evidenced by the lack of antenatal care follow-up in a significant portion of both cases and controls. While the absence of folic acid supplementation showed a protective trend, it did not retain significance in the multivariate model.

Teratogens disrupt organ development during the critical period of organogenesis in early pregnancy, a stage when the embryo is highly susceptible to environmental exposures despite being protected by extra-embryonic membranes.[17-18] These agents can penetrate the placenta and interact with maternal and fetal genetic profiles, modifying biochemical pathways and morpho-functional patterns, which influence susceptibility to malformations. Mechanisms such as oxidative stress, endocrine disruption, hyperacetylation, and alterations in folate metabolism are common pathways through which teratogens induce developmental disruptions.[19] For example, pesticide exposure during the first eight weeks of gestation can interfere with neuronal proliferation, synaptogenesis, and neurotransmitter regulation, increasing the risk of structural and neurodevelopmental anomalies.[20-22]

Maternal behaviors such as smoking further exacerbate these risks. Active and passive smoking during early pregnancy increase oxidative stress, leading to cellular damage and disruptions in essential pathways like Notch and Wnt, which are crucial for embryonic development.[23] Additionally, inadequate folic acid intake significantly raises the likelihood of congenital anomalies, particularly neural tube defects, due to its role in DNA synthesis and cell division during organogenesis.[24-25] A recent meta-analysis has demonstrated that folic acid supplementation reduces the risk of congenital anomalies by up to 77% (OR 0.23; 95% CI: 0.16–0.32).[26]

Our study identified several maternal, foetal, and environmental factors associated with congenital anomalies, many of which align with findings from previous research. Similar to the study by Maritska et al conducted in Indonesia, we observed that maternal smoking and exposure to chemicals, such as pesticides, were significant risk factors.[27] Additionally, studies conducted in Iraq and Egypt also reported a strong association between maternal smoking—both active and passive—during the first three months of pregnancy and the occurrence of birth defects, particularly cleft lip with or without cleft palate.[28-29] The differences in the prevalence of smoking-related congenital anomalies between these regions and Indonesia may be due to cultural variations in smoking practices and second-hand smoke exposure. Additionally, Maritska et al. reported congenital digestive system anomalies as the most prevalent type, whereas our study focused more broadly on risk factors and did not categorize specific anomaly types.[27]

Several studies have shown that gestational diabetes is strongly associated with foetal growth abnormalities, as maternal hyperglycaemia leads to increased glucose levels in the embryo, resulting in oxidative stress and apoptosis.[30-32] However, our findings did not reveal a significant association between diabetes mellitus and congenital anomalies. This lack of association may be attributed to the fact that most diabetes patients in our study population were already under the care of internal medicine specialists before pregnancy, potentially achieving better glycaemic control.

Sunitha et al.'s research in South India also highlighted maternal age and consanguinity as significant contributors to congenital anomalies, particularly in high-risk pregnancies.[33] Our study identified maternal age >35 years as a risk factor but did not examine consanguinity due to cultural and demographic differences. Indonesia, being a predominantly Muslim country, does not permit consanguineous marriages. As a result, there were no cases of consanguinity recorded in our dataset, and therefore this variable was not included in the analysis. However, in Indonesia, TORCH screening remains relatively expensive and is not covered by government health insurance, resulting in limited available data; therefore, it was not included in our analysis.

Findings from African studies, including Moges et al and Abebe et al, also resonate with our results.[26,34] Moges et al identified folic acid deficiency, maternal illness, and drug use as significant risk factors, findings consistent with our study's emphasis on the protective role of folic acid and the risks associated with unidentified medication use.[26] Abebe et al specifically noted pesticide exposure and passive smoking as major contributors, similar to our results. Interestingly, while smoking did not appear significant in bivariate analysis in our study, it emerged as a significant factor in multivariate analysis.[34]

The umbrella review by Lee et al reinforced the global relevance of environmental and genetic risk factors.[35] Congenital anomalies were linked to maternal exposure to air pollution, toxic chemicals, and smoking, all of which align with our findings on pesticides and smoking. The review also emphasized the preventive role of folic acid supplementation, consistent with our study's findings. The observed association between genetic factors and congenital anomalies in Lee et al.'s review was not within the scope of our study, suggesting an area for further exploration in future research.[35]

Cultural practices and healthcare accessibility in Indonesia influence the findings of this study, particularly the high exposure to passive smoking despite low rates of active smoking among mothers and the limited folic acid supplementation, reflecting gaps in antenatal care and awareness. These findings highlight the need for public health campaigns to reduce passive smoking, regulate pesticide use, and promote safe medication practices during pregnancy. Improving antenatal care to ensure consistent folic acid supplementation and addressing teratogenic risks can significantly reduce the burden of congenital anomalies. However, the study's single-hospital design limits generalizability, and potential recall bias from self-reported data may affect accuracy. Future research should explore multi-center studies for a broader understanding of congenital anomalies in Indonesia.

CONCLUSION

Maternal socio-demographic factors, such as education, socioeconomic status, and ANC visits, were not significantly associated with CAs. However, maternal smoking, pesticide and chemical exposure, and unidentified medication use during the first trimester were significant risk factors, while folic acid supplementation showed a protective effect despite low usage rates in Indonesia. Improving antenatal care, promoting folic acid supplementation through food fortification, and ensuring safe medication use during pregnancy are essential for congenital anomalies prevention.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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Evaluating the efficacy of transrectal povidone-iodine application for infection prevention in transrectal ultrasound-guided prostate biopsy: A single-center retrospective study

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ABSTRACT

Introduction: Prostate cancer diagnosis via transrectal ultrasound-guided (TRUS) biopsy carries a significant risk of infectious complications due to potential contamination from the rectal microbiome. This study aimed to evaluate the efficacy of transrectal 10% povidone-iodine application, in combination with antibiotic prophylaxis, in reducing infectious complications following TRUS biopsy.

Materials and Methods: A retrospective analysis was conducted on 643 patients who underwent TRUS biopsy at a single center in a tertiary hospital in Kuala Lumpur between January 2017 and December 2023. Patient records were reviewed for demographic data, biopsy indications, type of antibiotic prophylaxis, and post-biopsy complications. Patients were categorized into two groups: those who received antibiotic prophylaxis alone and those who received both antibiotic prophylaxis and transrectal povidone-iodine. Statistical analyses, including chi-square tests and logistic regression, were performed to compare outcomes and assess the impact of povidone-iodine on infection rates.

Results: Of the 643 patients, 285 received antibiotic prophylaxis combined with transrectal povidone-iodine, was associated with a significantly lower infection rate from 2.23% to 0.7% (P<0.05). There were no significant differences between the povidone-iodine and non–povidone-iodine groups in terms of patient demographics, including age, prostate volume, Prostate Specific Antigen (PSA) levels, and histopathological findings. Logistic regression analysis further confirmed the significant effect of povidone-iodine in reducing post-biopsy infections presenting as fever >37.5 within 30 days after TRUS biopsy.

Conclusion: The results indicate that the use of transrectal 10% povidone-iodine alongside antibiotic prophylaxis is an effective approach for reducing infectious complications following TRUS biopsy.

KEYWORDS:
Prostate biopsy, sepsis, urosepsis, povidone-iodine, prophylactic antibiotic, rectal cleansing

INTRODUCTION

Prostate cancer is the second most prevalent cancer globally, following lung cancer.[1-2] In Malaysia, it ranks as the third most common cancer among men, with incidence rising from 1,186 cases in 2014 to 1,807 cases in 2018, accounting for 8.8% of all cancers in Malaysian men.[3] The increase in case detection is largely due to screening programs that incorporate Prostate Specific Antigen (PSA) continues to be the most crucial and commonly utilized biomarker for prostate cancer.[4] Elevated serum PSA levels, or with abnormal findings from a digital rectal examination (DRE), are primary indicators for performing a prostate biopsy to confirm prostate cancer.

Prostate biopsies can be performed using either the transrectal or transperineal approach. The transperineal method, often supplemented by multiparametric magnetic resonance imaging (mpMRI), has emerged as a viable option for diagnosing prostate cancer in modern clinical practice.[5] This technique minimizes exposure to the rectal microbiome, potentially reducing the risk of infectious complications compared to the transrectal approach. Studies comparing the two methods have shown that the transperineal approach provides diagnostic outcomes comparable to those of TRUS biopsy.[6]

Although transperineal biopsies may offer safety advantages, they present challenges such as the need for general anesthesia, higher costs, longer procedure times, and specialized equipment. As a result, the transrectal ultrasound-guided 12-core systematic biopsy remains the most commonly used method for the initial diagnosis and grading of prostate cancer.[7] However, due to the high density of bacterial flora in the rectum, this approach carries an increased risk of infectious complications, primarily resulting from bacterial contamination during the biopsy procedure.[8]

TRUS biopsy is associated with various complications, with bleeding being the most common. Hematuria and hematospermia occur in approximately 60% of cases, followed by rectal bleeding in 20%.[9] These complications are typically mild and self-limiting. However, infectious complications such as urinary tract infections, epididymitis, orchitis, and prostatitis, pose a more significant risk.

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Although rare, cases of sepsis, septic shock, and even death have been reported, with incidence rates of 5.7%, 0.45%, and 0.2%, respectively.[9]

Various strategies have been implemented to reduce the risk of infectious complications following TRUS biopsy, including the use of oral or intravenous antibiotic prophylaxis. These measures are consistent with the recommendations of the European Association of Urology (EAU) and the American Urological Association (AUA) guidelines.[10] Additionally, transrectal application of povidone-iodine has shown promising results in lowering infection rates. Povidone-iodine, widely recognized for its effectiveness in preventing infections in colorectal surgery and wound care, has also been used alongside prophylactic antibiotics prior to TRUS biopsy to further reduce infection risk.[11] Despite supporting evidence, transrectal povidone-iodine cleansing is not universally adopted in clinical practice due to lack of standardized protocol and logistical barriers to implementation.[12-13] This study aims to provide real-world data on its effectiveness when combined with antibiotic prophylaxis, further supporting its role in infection prevention within a contemporary patient cohort.

Previous research has consistently shown that combining povidone-iodine with antibiotic prophylaxis effectively reduces the risk of infectious complications following TRUS biopsy.[14] Therefore, this study aims to assess whether the application of transrectal 10% povidone-iodine in combination with prophylactic antibiotic prior to the procedure at our center can further decrease the incidence of infectious complications.

MATERIALS AND METHODS

Study Population

A retrospective analysis was conducted on the records of all patients (n = 643) who underwent TRUS biopsy at our center between January 2017 and December 2023. Data collected included patient age, DRE findings, PSA levels, prostate volume, type of antibiotic prophylaxis, histopathological findings, and post biopsy complications. For patients who experienced infectious complications, additional information was collected on comorbidities, culture results, duration of hospitalization, type of antibiotic treatment, and severity of complications.

Study Design

The medical records of 643 patients who underwent TRUS biopsy at a tertiary hospital in Kuala Lumpur between January 2017 and December 2023 were reviewed retrospectively. Indications for biopsy included a PSA level above 4.0 ng/mL and/or suspicious findings on prostate examination. Patients were excluded if they had abnormal coagulation, immunodeficiency (specifically patients undergoing chemotherapy or HIV infection), severe hemorrhoids, indwelling urinary catheters, or known hypersensitivity to povidone-iodine.

All patients received prophylactic antibiotics, either ciprofloxacin (500 mg twice daily) for 5 days starting the day before the procedure, or fosfomycin (3 g once daily) for 2 days starting on the day of the procedure. Additionally, all patients were administered a sodium chloride–glycerine enema (glycerine 25%, sodium chloride 15%) two hours prior to the procedure.

During the procedure, patients were positioned in the left lateral decubitus position with the left knee flexed. The external anal mucosa and surrounding skin were cleansed with 10% povidone-iodine, and sterility was maintained by draping the procedural area. A lubricating gel (Cathejell; 2% lignocaine, 0.05% chlorhexidine) was introduced into the rectum. In addition to external cleansing, 10 mL of 10% povidone-iodine was instilled into the rectum using a 10 mL syringe. Local anesthesia was administered via a periprostatic nerve block. The biopsy procedure commenced after five minutes of povidone-iodine exposure. Transrectal ultrasound was performed to assess the prostate for cystic or suspicious nodular lesions, and prostate volume was recorded. A standard 12-core prostate biopsy was then performed using a 16G biopsy needle with an automatic biopsy gun. Additional cores were taken if suspicious areas were identified during TRUS biopsy. After the procedure, patients were observed in a supine position for approximately 15 minutes and discharged the same day.

Patients were advised to return to the emergency department if they experienced urinary retention, fever, hematuria, dysuria, rectal bleeding, or persistent pain following the procedure. A follow-up appointment at the urology outpatient clinic was scheduled two weeks post-biopsy to review pathology results and assess for infectious or non-infectious complications. Minor complications were defined as self-limiting conditions such as hematuria, rectal bleeding, dysuria, and anal pain. Infectious complications were defined as fever (>37.5°C) occurring within 30 days post-biopsy, accompanied by chills or at least one lower urinary tract symptom (dysuria, urgency, frequency, hematuria, or perineal pain), or a positive urine or blood culture. Sepsis was defined as a systemic infection with hemodynamic instability.

Statistical Analysis

Patient data including age, DRE findings, prostate volume, PSA values, histopathology results, and instances of hospitalization due to post-biopsy fever—were analyzed as basic demographic and clinical information. Categorical variables (e.g., benign vs. suspicious DRE findings and pathology results indicating malignancy) were compared using the Chi-square test, while continuous variables (e.g., age, prostate volume, PSA values) were compared using the t-test. These analyses aimed to assess differences between two groups: one that received antibiotic prophylaxis combined with transrectal povidone-iodine and another that received antibiotic prophylaxis alone.

A multivariate logistic regression analysis was conducted to assess the impact of several factors on the likelihood of developing infectious complications following TRUS biopsy. These factors included the type of prophylaxis (antibiotic prophylaxis with or without transrectal povidone-iodine), patient age, DRE findings, prostate volume, PSA level, and histopathological outcome (malignancy: yes/no). Odds ratios

Table I: Combined statistical results for demographic parameters and infection rates

Variable	Povidone Group (n=285)	Non-Povidone Group (n=358)	Total (n=643)	p-value
Infection Rate	2/285 (0.7%)	8/358 (2.23%)	10/643	0.008
Age (mean ± SD)	70.45 ± 6.21	73.06 ± 6.72	643	0.102
DRE Findings				0.030
- Nodular	105	103	208	
- Smooth, Benign	180	255	435	
Prostate Volume (cc)				0.781
- Mean ± SD	58.41 ± 31.31	55.16 ± 26.43	643	
PSA Level (ng/mL)				0.162
- Mean ± SD	103.19 ± 393.13	115.17 ± 685.51	643	
HPE Results				0.116
- Benign	165	229	394	
- Adenocarcinoma	120	129	249	

Table II: Results of multivariate logistic regression analysis

Variable	Odds Ratio (OR)	95% CI	p-value
Age	1.042	0.944 - 1.152	0.709
DRE	1.314	0.601 - 2.875	0.133
PSA Level	0.999	0.996 - 1.003	0.048
Prostate Volume	0.999	0.976 - 1.023	0.880
HPE	0.911	0.692 - 1.200	0.770
Povidone-Iodine	0.550	0.082 - 3.690	0.149

(ORs) with 95% confidence intervals (CIs) were calculated to determine the strength of these associations. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), Version 23.0 (SPSS Inc., Chicago, IL), with a P-value of <0.05 considered statistically significant.

Ethics Approval

This retrospective study was approved by the Research Ethics Committee of the National University of Malaysia (IRB no. JEP-2024-572). In accordance with institutional policy, the requirement for individual written informed consent was waived due to the retrospective nature of the study.

RESULTS

A total of 643 patients underwent TRUS biopsy, with 285 receiving transrectal povidone-iodine in addition to antibiotic prophylaxis, and 358 receiving antibiotic prophylaxis alone. The infection rate was significantly lower in the group that received povidone-iodine, decreasing from 2.23% (8 out of 358 patients) in the non-povidone group to 0.7% (2 out of 285 patients) in the povidone group (P = 0.008) (Table I).

Among the 10 cases of post-TRUS biopsy infection, all complications were mild (Clavien-Dindo Grade II), with no instances requiring ICU admission or intubation. Five of the cases had underlying diabetes mellitus, while the other five had underlying hypertension and dyslipidemia. Most infections responded well to antibiotic treatment, either empirically or based on culture results. Only two cases yielded positive cultures: one blood culture grew Proteus mirabilis, and one urine culture grew Escherichia coli. No patient required hospitalization for more than 10 days.

The combined analysis of demographic and clinical variables, as shown in Table 1, revealed a significant difference between the povidone-iodine and non–povidone-iodine groups only in DRE findings (p=0.030). Other variables, including age (p=0.102), PSA level (p=0.162), prostate volume (p=0.781), and histopathological examination (HPE) results (p=0.116), showed no statistically significant differences between the two groups.

Multivariate logistic regression analysis was performed to evaluate the influence of various factors including the use of povidone-iodine, age, DRE findings, prostate volume, PSA level, and HPE results on the likelihood of developing post-biopsy fever. The analysis identified PSA level as a significant predictor of infection (p=0.048), while other factors, including the use of povidone-iodine, did not reach statistical significance (Table II).

DISCUSSION

Infectious complications following TRUS biopsy have been reported in 0.1% to 7.0% of cases, with sepsis rates ranging from 0.3% to 3.1%.[15] To reduce the risk of post-biopsy infections, various preventive strategies have been implemented, with antimicrobial prophylaxis being one of the most widely supported. Although there is considerable variability in clinical practice regarding the choice and duration of prophylaxis, strong evidence supports the effectiveness of antimicrobial agents in reducing infection risk.[16] A systematic review further confirmed that antimicrobial prophylaxis significantly decreases the incidence of infectious complications, particularly when fluoroquinolones are used.[17]

Fluoroquinolones are preferred for prophylaxis due to their broad-spectrum activity against intestinal flora and their ability to achieve high concentrations in prostatic tissue following oral administration.[18] However, the increasing prevalence of fluoroquinolone resistance has prompted the

exploration of alternative antibiotics, such as fosfomycin, which has shown promising results in patients with fluoroquinolone-resistant infections.[19] Studies have indicated that fosfomycin not only results in fewer septic complications but also has a side effect profile comparable to that of quinolone-based prophylactic regimens for TRUS biopsy.[20] In our study, all patients received either ciprofloxacin (a second-generation fluoroquinolone) or fosfomycin, both of which have demonstrated efficacy in preventing post-biopsy infections.

The role of adjunct measures such as pre-biopsy rectal cleansing enemas in infection prevention remains controversial. Enemas are intended to reduce the rectal microbial load before biopsy, thereby decreasing the number of bacteria introduced during the procedure.[21-23] However, the use of enemas alone has been found to be insufficient in preventing infections following TRUS biopsy.[24] In our study, all patients received an enema the night before the procedure and another two hours prior, which not only helped reduce fecal content but also improved the acoustic window for the biopsy.

Recent guidelines from the EAU recommend the use of rectal povidone-iodine preparation as part of the infection prevention protocol for TRUS biopsy. Our study aimed to evaluate and further support this guideline-recommended practice. While the use of rectal povidone-iodine has been previously reported, this study provides updated real-world data, particularly in the context of rising fluoroquinolone resistance and the increasing use of alternative prophylactic antibiotics.

Comparisons between povidone-iodine and chlorhexidine for rectal mucosal cleansing have also been explored.25 While the effectiveness of povidone-iodine may be reduced in the presence of mucus and feces, which can limit its bioavailability, chlorhexidine in its alcohol-based form may offer better mucosal and skin penetration. However, studies have shown no significant difference between the two agents in preventing infections. Povidone-iodine may be the safer option, as it has been associated with a lower risk of complications such as hematuria, rectal bleeding, and urinary retention.[25]

Substantial evidence supports the transperineal approach for prostate biopsy, as it carries a lower risk of infection.[26] However, recent meta-analyses have shown that infection rates following transperineal and transrectal biopsies are comparable.[27] Widespread adoption of this method particularly in developing or transitioning economies remains challenging. Barriers include the need for general anesthesia (despite the availability of local anesthesia alternatives), limited access to necessary equipment, inadequate reimbursement, and insufficient training during residency. Consequently, efforts to reduce infection risks associated with the transrectal approach remain a priority.

Our study has several limitations. As a retrospective, non-randomized investigation based on consecutive patient data, it is inherently subject to bias. Data were collected through patient questionnaires rather than direct clinical observation, which may have introduced inconsistencies particularly for patients who did not return for follow-up at our institution due to insurance affiliations with other centers. Additionally, evaluations were limited to symptomatic patients, potentially overlooking asymptomatic or mildly symptomatic cases.

While the sample size of 643 patients provides meaningful insight, it may be insufficient to detect very small differences in infection rates. Moreover, the single-center nature of the study limits generalizability, underscoring the need for validation through larger, multi-center prospective randomized trials.

Another limitation is the use of two different antibiotic regimens (ciprofloxacin and fosfomycin) without subgroup analysis. Future prospective studies should stratify outcomes based on antibiotic type to better determine whether variations in infection rates are attributable to the specific regimen used.

CONCLUSION

Our study concludes that rectal cleansing with transrectal 10% povidone-iodine injection, when combined with antibiotic prophylaxis, is an effective, affordable, and easily implementable strategy to reduce infectious complications following TRUS biopsy. This approach aligns with current guidelines and offers a practical solution, particularly in settings where antibiotic resistance is an increasing concern.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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ORIGINAL ARTICLE

Carotid endarteretomy: A single vascular centre experience in Malaysia

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ABSTRACT

Introduction: Carotid artery stenosis remains one of the leading causes of major stroke. Carotid endarterectomy (CEA) has proven effective in preventing debilitating major stroke. However, the data on CEA in Malaysia is still lacking. University of Malaya Medical Centre, Kuala Lumpur, Malaysia first embarked on CEA since 2017. We are reporting the outcomes of CEA performed in our centre.

Materials and Methods: This was a retrospective case series of 20 patients who underwent CEA from the year 2017 until 2024. Patients having asymptomatic (≥60-99%) and symptomatic carotid artery stenosis (≥50-99%) were selected for the procedure. All patients received best medical treatment, which include antithrombotic medications, lipid lowering therapy, blood pressure management, diabetes mellitus management and lifestyle modifications especially smoking cessation. All the patients underwent CEA under general anaesthesia. Shunting was done routinely. Preoperative, intraoperative, and postoperative data were collected and evaluated. Mortality, myocardial infarction, stroke, postoperative bleeding, surgical site infection and cranial nerve injury at 30 days were the outcomes investigated. We also evaluated restenosis after CEA.

Results: Most patients in our series were males 70% (n = 14) compared to 30% (n = 6) females. There were more symptomatic patients (n = 14) than asymptomatic patients (n = 6). There was one 30-day mortality among the symptomatic patients, while there was no 30-day mortality in the asymptomatic patients. The 30-day myocardial infarction was 5% (n = 1), which was the same symptomatic patient who died. In this cohort, only one patient had 30-day stroke (5%), which was a symptomatic patient. The patient recovered from the stroke after two weeks. Cranial nerve injuries happened in four patients (20%), where the commonest nerve injured was recurrent laryngeal nerve (n = 3). Only one patient had postoperative bleeding which did not need any reintervention. No surgical site infection was noted on all patients. Three patients developed restenosis, which was noted at two to six months post CEA. Two of the patients had symptomatic restenosis (more than 50% stenosis) which resulted in them being reoperated.

Conclusion: The uptake of CEA in Malaysia is still slow. By sharing the outcomes data, hopefully it will create awareness among medical practitioners on the importance of early referral for carotid artery stenosis. Long term outcomes are very much needed.

KEYWORDS:
Carotid artery stenosis, stroke, carotid endarterectomy, Malaysia

INTRODUCTION

Stroke is the third leading cause of death, and probably the most important cause of long-term disability, burdening the patients, their families and societies.[1] 85% of strokes are ischaemic in nature.[2] Carotid artery disease is a recognized cause of ischaemic stroke. Atherosclerotic plaques can rupture and lead to thrombosis and emboli, resulting in stroke if they occur in a carotid artery.[3]

In Malaysia, stroke is the third most common cause of death.[4] Stroke patients in Malaysia were generally younger, with the mean age of stroke onset between 54.5 and 62.6 years.[5-10] This trend is alarming as this will lead to loss of productive age, which will jeopardize the national income. Up to two-third of reported stroke cases in Malaysia were of ischaemic in origin.[6-11] However, the data on carotid artery stenosis causing ischaemic stroke in Malaysia is still lacking.

Carotid endarterectomy (CEA) is one of the interventions offered to prevent stroke. There have been abundant improvements ever since the first CEA described by Eascott et al, in 1994.[12] CEA has now been shown to be superior to carotid artery stenting (CAS) in several randomized studies.[13-14] To our knowledge, there is no review of outcomes of CEA done in Malaysia as of now. We are reviewing the outcomes of the CEA procedures done in University Malaya Medical Centre, Kuala Lumpur, Malaysia from 2017 until 2024. University Malaya Medical Centre is a 1600-bedded tertiary hospital, receiving vascular referrals from Peninsular Malaysia.

MATERIALS AND METHODS

We report a retrospective case series of 20 patients who underwent CEA in University Malaya Medical Centre from October 2017 until July 2024. Institutional Review Board approval was taken for the study. Preoperative duplex ultrasound was used initially to measure the severity of stenosis. We adopted the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method, in which the residual lumen diameter is used as the numerator and the

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diameter of disease free internal carotid artery (ICA) above the stenosis, where vessel walls were parallel is used as the denominator.[15] In all patients, computed tomography (CT) angiography of the carotids or magnetic resonance angiography (MRA) were done to corroborate the duplex ultrasound findings.

The decision to operate on each patient was brought to multidisciplinary team (MDT) discussions involving the vascular surgeons, neurologists, interventional radiologists, anesthetists and occasionally the ear, nose, and throat (ENT) surgeons. The indication of surgery was classified into symptomatic and asymptomatic. For symptomatic carotid artery stenosis, the threshold of carotid artery revascularization should be more than 50% until 99% of stenosis. The symptomatic patients were being divided into either transient ischaemic attack (TIA), stroke or chronic ocular ischaemia syndrome. The symptoms should be within the past six months. If a patient presented with stroke, the severity of symptoms should be scored using the modified Rankin Score (mRS). For patients who experienced disabling stroke and have a mRS of >3, we did not offer any carotid revascularization as to minimize the risk of postoperative parenchymal hemorrhage. Meanwhile, for asymptomatic carotid artery stenosis, the threshold should be more than 60% until 99% of stenosis. Carotid artery total occlusion was not intervened. All patients received best medical treatment (BMT), which include antithrombotic medications, lipid lowering therapy, blood pressure management, diabetes mellitus (DM) management and lifestyle modifications especially smoking cessation.

All the patients underwent CEA under general anaesthesia (GA). All the patients received prophylactic antibiotics prior to operation. The incisions were a longitudinal anterior sternomastoid incision, while the carotid artery was exposed via antegrade approach. We adopted the routine shunting approach. Our technique for CEA was conventional patched endarterectomy where the patch used was made of bovine pericardium. Heparin was given pre carotid clamping (80units/kilogram body weight). No protamine reversal was given. All patients had active drain placed and it would be removed only if the output was less than 30ml/day. Every patient was managed in intensive care unit (ICU) postoperatively.

Data regarding patient demographics, degree of stenosis, indications for surgery, intraoperative data, and post-operative outcomes were collected and analyzed. The outcomes that we investigated were 30-day mortality, 30-day myocardial infarction (MI), 30-day stroke, 30-day cranial nerve injury (CNI), 30-day postoperative bleeding, 30-day surgical site infection (SSI) and restenosis.

RESULTS

The data summary of the population studied is summarized in Table I. A total of 20 CEA was performed. Majority was male (70%). The commonest age group we operated on was from age of 60-69 years old (60%) followed by age group 70-79 years old (20%). Mean age was 65 years old. There were more symptomatic patients who underwent CEA (n = 14) than asymptomatic patients (n = 6). Five of the symptomatic patients had stroke within the past six months. Their mRS was either one or two. Seven of the symptomatic patients suffered from TIA, while two had chronic ocular ischaemia syndrome.

The percentage of stenosis was 60-90% for symptomatic patients, while 70-90% for asymptomatic patients. Three of the patients had contralateral carotid total occlusion (two symptomatic and one asymptomatic). One patient had bilateral carotid artery stenosis operated as a staged procedure where the symptomatic side was operated first followed by the asymptomatic side six months later. One patient had post radiation carotid artery stenosis. The patient had nasopharyngeal cancer post radiotherapy and was asymptomatic with stenosis of 70%. The contralateral carotid had total occlusion. However, three years later, restenosis occurred and at that time, the patient suffered from multiple TIA. As a result, we performed re do CEA for the patient. Unfortunately, this patient was still symptomatic despite the redo operation, hence we resorted to CAS for the next reintervention.

85% of the patients had hypertension while 55% had DM. Two patients had coronary artery disease (CAD) and one had non-dialysis-dependent chronic kidney disease (CKD). 45% of the patients identified themselves as smokers. There was no standardized protocol for antithrombotic medications prior to CEA. 70% of the patients were started on aspirin 100mg daily and clopidogrel 75mg daily. Three of them were commenced on only aspirin 100mg daily prior to CEA. One patient was on aspirin 100mg daily and ticagrelor 90mg twice daily before the CEA. This patient was asymptomatic and had contralateral CAS 18 months prior in another centre for symptomatic stenosis. Another patient was already on apixaban before the CEA as there was sigmoid sinus and internal jugular vein thrombosis before.

The timing of surgery for symptomatic patients was recorded. This is defined as time from onset of symptoms until the date of surgery. Only one patient was operated within seven days of symptoms onset. Three patients were operated from eight days to 14 days of symptoms onset while 10 patients were operated after more than 15 days. All the symptomatic patients were operated within six months. The mean operative time for CEA was 173 minutes. The average pre shunt clamp time was five minutes, while post shunt clamp time was six minutes. Median ICU stay was one day, and median length of hospital stays were three days. Just like the preoperative antithrombotic medications, the postoperative antithrombotic medications were also not standardized. 45% of them continued to take aspirin and clopidogrel after the CEA. The rest of the patients were reduced to just single antiplatelet, either aspirin (30%) or clopidogrel (20%).

The outcomes of each population studied including the subgroup analysis are summarized in Table II and III. 30-day mortality happened in only one patient (5%). This patient was symptomatic (TIA). The patient already had background of CAD. The clamping time were three minutes each for pre and post shunt. This patient died five days after CEA from MI. The same patient also had haematoma at operation site

Table I: Summary of the patients' population

Variables	N, % in parentheses
Age	
40-49 years old	2 (10)
50-59 years old	2 (10)
60-69 years old	12 (60)
70-79 years old	4 (20)
Gender	
Male	14 (70)
Female	6 (30)
Indications of surgery	
Symptomatic	14 (70)
Asymptomatic	6 (30)
Symptomatic patients' presentations (n = 14)	
Transient ischaemic attack	7 (50)
Stroke	5 (35.7)
Chronic ocular ischaemia syndrome	2 (14.3)
Percentage of stenosis of operated side	
60-69%	5 (25)
70-79%	7 (35)
80-89%	3 (15)
90-99%	5 (25)
Contralateral carotid lesion	
No lesion	10 (50)
20-70% stenosis	7 (35)
Total occlusion	3 (15)
Aetiology of carotid artery stenosis	
Atherosclerotic	18 (90)
Post radiation	2 (10)
Comorbidities	
Diabetes mellitus	11 (55)
Hypertension	17 (85)
Coronary artery disease	2 (10)
Chronic kidney disease	1 (5)
Smoker	9 (45)
Preoperative antithrombotic medications	
Aspirin and Clopidogrel	14 (70)
Aspirin and Ticagrelor	1 (5)
Aspirin only	3 (15)
Apixaban	1 (5)
Postoperative antithrombotic medications	
Aspirin only	6 (30)
Clopidogrel only	4 (20)
Aspirin and Clopidogrel	9 (45)

Table II: Patients' outcomes in this study

Study parameters	N, % in parentheses
30-day mortality	1 (5)
30-day myocardial infarction	1 (5)
30-day stroke	1 (5)
30-day cranial nerve injury	Recurrent laryngeal nerve palsy = 3 (15) Hypoglossal nerve palsy = 1 (5)
30-day postoperative bleeding	1 (5)
30-day surgical site infection	0 (0)
Restenosis	3 (15)

which did not require any operative intervention. The only patient who had stroke post CEA was symptomatic preoperatively. The patient developed new left precentral gyrus infarct presented with hemiparesis. Nevertheless, this stroke was not disabling. After intensive physiotherapy, the patient was able to move independently two weeks postoperatively.

CNI occurred in four patients. Three of them suffered from recurrent laryngeal nerve injury. They presented with hoarseness of voice after CEA. All of them were referred to the ENT team and managed conservatively. All of them recovered from the symptoms within six months. One patient had hypoglossal nerve injury presented with deviation of tongue. Management was also conservative, and the patient recovered within six months. In terms of restenosis, three

patients developed restenosis, which was noted at two to six months post CEA. Two of the patients were symptomatic restenosis (more than 50% stenosis) which resulted in them being reoperated. One patient was asymptomatic with less than 70% stenosis hence no operative intervention was offered.

DISCUSSION

Meta-analysis of 6092 patients was performed by The Carotid Endarterectomy Trialists Collaboration (CETC) which revealed that CEA conferred benefit in symptomatic patients with moderate (50-69%) and severe (70-99%) stenoses compared to BMT alone.16-18 Regarding CEA versus CAS in symptomatic patients, a meta-analysis of 4754 patients from four large trials (>500 patients) showed that CAS was associated with higher 30-day stroke and death as compared to CEA.[19-22] Meanwhile, in asymptomatic patients, Asymptomatic Carotid Surgery Trial (ACST-1) and Asymptomatic Carotid Atherosclerosis Study (ACAS) found that CEA conferred notable reductions in any stroke at five years compared to BMT alone.[23-24] CAS was found to have higher rate of 30-day stroke and death compared to CEA in asymptomatic patients.[25] However, CAS had lower 30-day MI.[25] Following this evidence, we opted for CEA as first option of carotid revascularization in our centre. The MDT discussion remains pivotal in deciding this. There are instances where despite the patient having previous neck scar or radiation, we still proceeded with CEA as CAS was deemed technically challenging.

It is interesting to note on the six asymptomatic patients who underwent CEA. Two of them were symptomatic on the contralateral carotid and had revascularization before by CEA and CAS. Hence, they were already screened for both carotids. The patient with nasopharyngeal cancer was detected to have carotid artery stenosis by surveillance CT scan. Another patient was referred by colorectal team as the patient had to go for rectal cancer surgery but had TIA three years prior. Thus, carotid duplex was done as screening prior to non-cardiac surgery. Society of Vascular Surgery (SVS) in its guideline advised on carotid screening for patients with risk factors such as peripheral arterial disease, age > 65 years with CAD, smoking, or hypercholesterolaemia.[26] Patients undergoing major non-cardiac surgery with three to four cardiovascular risk factors such as age, CAD, CKD, hypertension, DM, smoking, body mass index (BMI) > 35 kg/m^2, chronic obstructive pulmonary disease (COPD), prior stroke/TIA had a 0.7% risk of peri-operative stroke.[27-28] The SVS guidelines stated that patients with carotid disease undergoing non-cardiac surgery should have the same indications for intervention as the general population.[26] In our centre, we do not practice routine screening for carotid stenosis in the asymptomatic patients with risk factors as mentioned above. However, if a patient was already intervened before being it CEA or CAS, the patient would be screened for contralateral carotid stenosis. Some patients were referred after six months of symptoms which considered them asymptomatic. We did performed CEA if the threshold were more than 60% until 99% of stenosis.

European Society of Vascular Surgery (ESVS) guideline on antithrombotic therapy stated that protocols for antiplatelet therapy for symptomatic patients prior to CEA should be made by local teams.[29] A retrospective study by Donners et al.found that the effectiveness and safety of double antiplatelet therapy (DAPT) did not differ from single antiplatelet therapy (SAPT) in patients undergoing CEA.[30] Despite excluding patients going for CEA, two randomized controlled trials (RCT), POINT and CHANCE, showed that DAPT reduced the risk of stroke, MI, and cardiovascular death by 30%, compared with aspirin alone for patients with TIA or minor stroke.[31-32] This formed the basis of us mainly using DAPT (aspirin and clopidogrel) before CEA. Despite DAPT, there was only one patient of us that experienced postoperative hematoma. There is no RCTs that evaluated clopidogrel monotherapy or combination antiplatelet therapy in asymptomatic patients undergoing CEA. We extrapolated the results of POINT and CHANCE trials to our asymptomatic patients by initiating clopidogrel and aspirin before CEA.

CEA in symptomatic patients confers maximum benefit if performed within 14 days of symptoms onset.[16-18] Even ESVS recommended that in symptomatic patients with a 50-99% stenosis, carotid intervention should be performed within 14 days of symptom onset.[15] In contrast to that, majority of our symptomatic patients were operated after 15 days. The main reason for operative timing after 15 days was due to late referrals by the referring team. Moreover, the patients who were referred need preoperative cardiac/anesthetic assessment with the optimization of preoperative status, which delayed the procedure even further. Certainly, the timing of surgery needs further improvement. The awareness among the referring teams, such as the neurology, ENT, ophthalmology, and family medicine must be reinforced. In this modern and digital age, social media holds a very important yet exciting role in disseminating awareness and information to health personnel and general population. We also believe that a key performance indicator (KPI) for timing of carotid revascularization in Malaysia will need to be established. Reflecting on UK National Vascular Registry, CEA was performed in only 10% of patients within 2 weeks of the index event in 2008, rising to 37% in 2009 and 58% in 2014.[33] By setting a national standard for timing of carotid revascularization, it will be obligatory for each Malaysian vascular centre to work towards achieving this goal.

It is advised that the 30-day risk of stroke/ death when performing CEA in patients reporting ipsilateral carotid territory symptoms of less than six months should be 6% or less.[34] For asymptomatic patients, it should be 3% 30-day risk of stroke/death.[34] This number is not only important in setting a worldwide standard in centres intending to embark in CEA, but it also acts as a reminder for the performing surgeons whenever they are counseling their patients. The performing surgeons should quote to patients their own procedural risks especially pertaining to death and stroke. The major cause of stroke in CEA is embolism. Few steps were described in literature to prevent embolism from happening. The administration of intravenous heparin prior to clamping has become a standard of care and our centre is not an exception. Hannan et al reported that all surgical specialties

that performed CEA used heparin extensively with 97.5% of all patients received heparin.[35] Another strategy described was by Pratesi and Bourke whereby early distal control of internal carotid artery was achieved.[36-37] They demonstrated that the strategy was independently associated with a lower risk of developing intraoperative neurological deficit.[36-37] 'Flow-control' CEA technique was described by Yoshida et al where they clamped the proximal common carotid artery (CCA), external carotid artery and superior thyroid artery, then dissected the bifurcation of the CCA and ICA before clamping the distal ICA.[38] New embolic lesions as detected by diffusion-weighted MRI were significantly decreased compared with the conventional method of CEA.[38] In our cohort of patients, all of dissection started from antegrade, whereby CCA was dissected first. Another limitation in our cohort is that we did not specify the sequence of clamp applied which may influence the risk of stroke.

Based on a meta-analysis, cranial nerves most injured during CEA are recurrent laryngeal (4.2%), hypoglossal (3.8%), mandibular branch of facial nerve (1.6%), glossopharyngeal (0.2%), and the spinal accessory (0.2%).[39] In our cohort of patients, CNI happened in 20% of the patients (three recurrent laryngeal and one hypoglossal nerve). All the nerve injuries resolved within six months after CEA. Most of these injuries were caused by excessive retraction. During carotid artery dissection, trauma may occur if the dissection is not kept close to the wall of the artery.[35] A careful retraction and early identification of the cranial nerves remain paramount in preventing CNI. Pertaining to recurrent laryngeal nerve, indirect laryngoscopy is not a routine in our centre. It was only reserved for those who has previous scars over the neck and those who had radiation to the head and neck. If the patient had previous contralateral CEA, total/partial thyroidectomy, or radical neck surgery, indirect laryngoscopy is a must to exclude contralateral recurrent laryngeal nerve palsy as bilateral nerve injuries can be fatal.[15] CAS should be considered if there is already presence of unilateral recurrent laryngeal nerve palsy.[15]

There is currently no concrete evidence to support routine surveillance post CEA.[15] Nonetheless, we decided to do duplex ultrasound surveillance at three months, six months then annually for all our CEA patients. For symptomatic restenosis where there was 50-99% stenosis, we attempted redoing CEA or CAS. Meanwhile, the threshold for reintervention for asymptomatic restenosis was above 70% stenosis. We had three patients who had restenosis after CEA. Two of them needed reintervention due to persistence of symptoms despite CEA. These were the patients who had radiation therapy-induced carotid stenosis (RCIS). Questions remain whether CEA or CAS will be better for RCIS in terms of restenosis. In a meta-analysis, CAS had a higher rate of restenosis compared to CEA in RCIS patients, however CEA had more temporary CNI40. In RCIS, since it is different from atherosclerotic stenosis, a more careful patient selection is important in determining which patient need intervention and which intervention is the best.

This study has its limitations. The number of patients analyzed was only 20. This is low compared to other countries' data. A multicentre review of outcomes in CEA performed in Malaysia is very much required for us to better counsel our patients for the operation. The data collected is mainly limited to 30-day post-surgery. A prospective study looking at long term complications and outcomes are needed especially on the ones looking at restenosis rate and recurrence of symptoms. It is also interesting to see a randomized controlled trial comparing outcomes of CEA and CAS being conducted in Malaysian setting. With that, participation of various disciplines will be needed especially among the vascular surgeons, neurologists and interventional radiologists.

CONCLUSION

CEA remains the first choice of intervention for symptomatic and asymptomatic carotid artery stenosis. However, its uptake in Malaysia is still poor despite all the evidence shown in literature. To our knowledge, we are the first centre in Malaysia to report on CEA outcomes. A prospective study looking at long term complications and outcomes are needed, especially in Malaysian setting.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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Systematic review of challenges of telehealth-based intervention in managing cancer pain

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ABSTRACT

Introduction: Understanding the challenges of telehealth interventions is essential to determining their future direction in cancer pain management, as these are considered complex interventions. This systematic review aimed to identify the challenges associated with telehealth-based interventions in cancer pain management.

Materials and Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed. A systematic search was conducted from January 19 to February 2, 2022, covering the past 10 years. Databases searched included PubMed and EBSCO. Inclusion criteria were articles published in English focusing on cancer pain in patients with any cancer diagnosis. Data were extracted on participants, interventions, and outcomes, with a particular focus on challenges reported in each study. A total of 320 publications were retrieved and screened; 38 articles met the inclusion criteria.

Results: The most reported challenge was limited or slow Internet access, followed by lack of technological expertise among healthcare teams and low computer literacy. Human resource-related challenges were also frequently reported, including inadequate reimbursement mechanisms, concerns over malpractice, increased staff workload, and absence of formal organisational structures. In studies conducted after the COVID-19 pandemic, data-related issues such as data security and management were also highlighted.

Conclusion: Telehealth is a rapidly growing technology with the potential to transform healthcare delivery. Addressing the challenges identified in this review may help guide the development and implementation of more effective telehealth interventions in cancer pain management.

KEYWORDS:
Cancer, challenge, pain management, telehealth

INTRODUCTION

Technological innovations are full of exciting opportunities in the direction of novel approaches to enhance clinical care delivery, and one of the innovations that has recently grasped the attention of the medical fraternity is telehealth. Telehealth uses telecommunications technology as a modality to deliver clinical care to populations with limited access to care.[1] Common approaches for telehealth are live video teleconferencing, remote monitoring, text, email, mobile health applications, and store-and-forward technology.[2] In the pre-pandemic era, telehealth was mainly used for primary care needs only, but now specialized and urgent care health services are being utilized more than ever before, and this also includes cancer pain management.[1-3]

Cancer is a global health concern. In terms of mortality, cancer is the second cause of death globally (8.97 million deaths) after ischemic heart disease but will probably become the first in 2060 (18.63 million deaths).[4] Regardless of the type of cancer, the potential symptoms of cancer can be a challenging experience for patients, and pain is probably one of the most burdensome of all cancer symptoms for patients and their families.[5-7] Cancer pain is a product of complex interactions among the central and peripheral nervous systems, the immune system, and cancer cells.[7] Cancer cells and the local immune cells produce a variety of biochemical substances that interact with pain receptors.[7]

We believe telehealth is the next milestone in the health delivery system and utilizing it to its full advantage in cancer pain management could lessen the cancer burden faced by cancer patients and their families. While telehealth has improved drastically, especially after the pandemic, there are still some challenges to be addressed to fully utilize it. This systematic review was carried out with the aim of identifying those challenges. This review can facilitate the development of a better remote healthcare delivery system to lessen the cancer burden faced by cancer patients and their families. By addressing the challenges, we also can establish personalized care and able to make sure the patient receives appropriate and timely care when needed, without putting the patient at risk.

MATERIALS AND METHODS

Search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were adopted for the literature search.[8] From January 19 to February 2, 2022, the search for articles was conducted. A research protocol was

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Table I: PICO concepts used in the review

PICO	Concept
Population	cancer patients
Intervention	Telehealth based intervention
Control	Not applicable
Outcome	Challenge in managing pain

Table II: Keywords and MeSH terms used in the search in PubMed

Free keywords	MESH terms
Growth' OR 'tumor' OR 'malignancy' OR 'sarcoma' OR 'carcinoma' OR 'neoplasm' OR 'melanoma' OR 'tumour' OR 'lymphoma' OR 'myeloma' OR 'fibroadenoma' OR 'meningioma' OR 'metastasis' OR 'neurofibroma' OR 'teratoma' OR 'neoplasia' OR 'malignant growth' OR 'cancerous growth' OR 'malignant tumor' OR 'lump' OR 'polyp' OR 'tumefaction disease' OR 'bump' OR 'excrescence' OR 'outgrowth'	("Neoplasms"[Mesh] AND "Thyroid Cancer, Papillary"[Mesh] AND "Breast Cancer Lymphedema"[Mesh] AND "Cancer-Associated Fibroblasts"[Mesh] AND "Prostatic Neoplasms, Castration-Resistant"[Mesh] AND "Neoplasms, Second Primary"[Mesh] AND "Head and Neck Neoplasms"[Mesh] AND "Colorectal Neoplasms, Hereditary Nonpolyposis"[Mesh] AND "Uterine Cervical Neoplasms"[Mesh] AND "Colitis-Associated Neoplasms"[Mesh] AND "Urologic Neoplasms"[Mesh] AND "Sigmoid Neoplasms"[Mesh] AND "Liver Neoplasms"[Mesh] AND "Unilateral Breast Neoplasms"[Mesh] AND "Urogenital Neoplasms"[Mesh] AND "Testicular Neoplasms"[Mesh] AND "Stomach Neoplasms"[Mesh] AND "Pharyngeal Neoplasms"[Mesh] AND "Oropharyngeal Neoplasms"[Mesh] AND "Gallbladder Neoplasms"[Mesh] AND "Ear Neoplasms"[Mesh] AND "Endometrial Neoplasms"[Mesh] AND "Vulvar Neoplasms"[Mesh] AND "Vaginal Neoplasms"[Mesh] AND "Uterine Neoplasms"[Mesh] AND "Urethral Neoplasms"[Mesh] AND "Ureteral Neoplasms"[Mesh] AND "Tonsillar Neoplasms"[Mesh] AND "Thymus Neoplasms"[Mesh] AND "Splenic Neoplasms"[Mesh] AND "Rectal Neoplasms"[Mesh] AND "Prostatic Neoplasms"[Mesh] AND "Penile Neoplasms"[Mesh] AND "Pelvic Neoplasms"[Mesh] AND "Pancreatic Neoplasms"[Mesh] AND "Ovarian Neoplasms"[Mesh] AND "Nose Neoplasms"[Mesh] AND "Nasopharyngeal Neoplasms"[Mesh] AND "Mouth Neoplasms"[Mesh] AND "Mediastinal Neoplasms"[Mesh] AND "Lung Neoplasms"[Mesh] AND "Laryngeal Neoplasms"[Mesh] AND "Kidney Neoplasms"[Mesh] AND "Intestinal Neoplasms"[Mesh]) AND ("Granulosa Cell Tumor"[Mesh] OR "Endocrine Gland Neoplasms"[Mesh] OR "Esophageal Neoplasms"[Mesh] OR "Colonic Neoplasms"[Mesh] OR "Breast Neoplasms"[Mesh] OR "Urinary Bladder Neoplasms"[Mesh] OR "Appendiceal Neoplasms"[Mesh] OR "Adrenal Cortex Neoplasms"[Mesh] OR "Carcinoma, Ovarian Epithelial"[Mesh] OR "Triple Negative Breast Neoplasms"[Mesh] OR "Neoplasms, Germ Cell and Embryonal"[Mesh] OR "Jejunal Neoplasms"[Mesh] OR "Ileal Neoplasms"[Mesh] OR "Gastrointestinal Neoplasms"[Mesh] OR "Anus Neoplasms"[Mesh] OR "Duodenal Neoplasms"[Mesh] OR "Adrenal Gland Neoplasms"[Mesh] OR "Inflammatory Breast Neoplasms"[Mesh] OR "Muscle Neoplasms"[Mesh] OR "Trophoblastic Neoplasms"[Mesh] OR "Tongue Neoplasms"[Mesh] OR "Thyroid Neoplasms"[Mesh] OR "Skin Neoplasms"[Mesh] OR "Salivary Gland Neoplasms"[Mesh] OR "Pituitary Neoplasms"[Mesh] OR "Parotid Neoplasms"[Mesh] OR "Parathyroid Neoplasms"[Mesh] OR "Lip Neoplasms"[Mesh] OR "Jaw Neoplasms"[Mesh] OR "Heart Neoplasms"[Mesh] OR "Eye Neoplasms"[Mesh] OR "Digestive System Neoplasms"[Mesh] OR "Cecal Neoplasms"[Mesh] OR "Brain Neoplasms"[Mesh] OR "Biliary Tract Neoplasms"[Mesh] OR "Bile Duct Neoplasms"[Mesh] OR "Non-Muscle Invasive Bladder Neoplasms"[Mesh] OR "Retinal Neoplasms"[Mesh] OR "Breast Neoplasms, Male"[Mesh] OR "Neoplasms, Squamous Cell"[Mesh] OR "Neoplasms, Basal Cell"[Mesh] OR "Neoplasms, Post-Traumatic"[Mesh] OR "Carcinoma, Merkel Cell"[Mesh] OR "Retinoblastoma"[Mesh] OR "Paranasal Sinus Neoplasms"[Mesh] OR "Maxillary Sinus Neoplasms"[Mesh] OR "Carcinoma, Hepatocellular"[Mesh] OR "Fallopian Tube Neoplasms"[Mesh] OR "Bone Neoplasms"[Mesh] OR "Prostate cancer, familial" [Supplementary Concept] OR "Thyroid cancer, Hurthle cell" [Supplementary Concept] OR "Hematologic Neoplasms"[Mesh] OR "Infratentorial Neoplasms"[Mesh] OR "Colorectal Neoplasms"[Mesh] OR "Supratentorial Neoplasms"[Mesh] OR "Otorhinolaryngologic Neoplasms"[Mesh] OR "Meningeal Neoplasms"[Mesh] OR "Hypothalamic Neoplasms"[Mesh] OR "Cerebellar Neoplasms"[Mesh] OR "Hypopharyngeal Neoplasms"[Mesh] OR "Carcinoma, Non-Small-Cell Lung"[Mesh] OR "Carcinoma, Renal Cell"[Mesh])
'Web-based intervention' OR 'technology intervention' OR 'internet intervention' OR 'tele-health intervention' OR 'telecare' OR 'telehealth' OR 'tele-dermatology' OR 'teleradiology' OR 'tele-education' OR 'e-health' OR 'tele-medicine' OR 'tele-mental'	"Telemedicine"[Mesh] AND "Telerehabilitation"[Mesh]
'Pain control' OR 'numbing' OR 'analgesia' OR 'pain killing' OR 'pain relief' OR 'pain control' OR 'pain therapy' OR 'opiate' OR 'morphine' OR 'anesthesia'	"Acute Pain"[Mesh] AND "Pain Management"[Mesh] AND "Breakthrough Pain"[Mesh] AND "Musculoskeletal Pain"[Mesh] AND "Chronic Pain"[Mesh] AND "Visceral Pain"[Mesh] AND "Nociceptive Pain"[Mesh] AND "Eye Pain"[Mesh] AND "Pain, Referred"[Mesh] AND "Flank Pain"[Mesh] AND "Shoulder Pain"[Mesh] AND "Complex Regional Pain Syndromes"[Mesh] AND "Pelvic Pain"[Mesh] AND "Neck Pain"[Mesh] AND "Low Back Pain"[Mesh] AND "Abdominal Pain"[Mesh] AND "Facial Pain"[Mesh] AND "Chest Pain"[Mesh] AND "Back Pain"[Mesh] AND "Pain, Procedural"[Mesh] AND "Cancer Pain"[Mesh] AND "Pain"[Mesh]
'Challenges OR 'limitations' OR 'barriers' OR 'issues' OR 'concerns' OR 'control' OR 'restriction' OR 'control'	Not applicable.

Table III: Inclusion and exclusion criteria used in the review

Inclusion criteria	Exclusion criteria
Patient with any type of cancer	Animal test subject
Studies involved cancer pain only	Patient who underwent nerve ablation procedure.
Peer reviewed conference proceedings, journal, or preprints	Not peer reviewed articles
Papers Written in English	Articles in any language other than English
Papers translated to English	
Any article published between 2012 and 2022	

agreed upon before the review. There was no pre-registration or publication of the research protocol.

Both PubMed and EBSCO were searched for relevant articles. To construct a search syntax, we employed the Population, Intervention, Control, and Outcome (PICO) framework. The PICO concept was used in a search query to focus on current questions in a clinical setting.[9] The PICO framework was used to choose keywords for this study (Table I).

The keywords and MeSH terms were used to search PubMed for articles for this systemic review based on the PICO concept (Table II). Whereas, the EBSCO search solely utilised free keywords.

Selection of studies
A set of inclusion and exclusion criteria were utilized in this review (Table III). Due to our review's emphasis on peer-reviewed publications in academic journals, the grey literature was left out. English-language publications with publication dates between 2012 and 2022 comprised the articles chosen from these databases.

Data extraction, synthesis and analysis
There were three phases to the screening process with peer reviewing. Three reviewers independently screened the titles and abstracts of all publications identified by the search during the first stage, and the results were compared. To decide whether a certain publication should be included, differences were discussed.

The full texts of publications identified as relevant in the first phase were reviewed by three reviewers during the second screening phase, and differences were discussed. The authors of several of the articles in the publications that were screened were contacted to obtain the full version of their works because they weren't readily available. Some authors sent us their full papers in response to our request.

The reference lists of the articles chosen in the second phase were reviewed during the third screening phase to determine if any relevant publications had been missed. The same inclusion and exclusion criteria were used for all three screening steps (Figure 1).

In this study, Excel 2019 was used for data extraction. The extraction fields included the study characteristics (year of publication, author, countries which were involved in the study, study design), challenges of telemedicine-based intervention addressed in the study and effect of the challenges of telemedicine-based intervention.

The Excel method is efficient, cost-free, and able to generate clear and comprehensive reports on systematic reviews. It is a credible substitute for the systematic reviews created by cutting-edge software and equipment.[1] After the data extraction, the information was synthesised and presented narratively.

Quality assessment
All publications included in the review were assessed for risk of bias qualitatively. The assessment included risk of bias in reporting and evidence selection, as well as risk of bias in the primary study, detection, performance, attrition, and outcome reporting bias. The Cochrane Collaboration Risk of Bias Tool 2.0 for interventional studies and the Newcastle-Ottawa Scale for observational studies are two tool that were used to evaluate the validity and reliability of the studies used in this review paper. A thorough evaluation was performed for each study by four authors of this paper.

RESULTS

Study Description
A total of 320 publications were retrieved and then assessed based on our inclusion and exclusion criteria. Of those publications, 27 articles were removed as duplications, and 258 were filtered out as they did not meet the inclusion criteria for this review. There was no automation tool used for exclusion or detection of duplication. Thus, 38 of the 320 articles were accepted for review (Table IV).

Summary of Evidence
The findings are presented according to year, as we believed the advancement of telehealth in a yearly manner may influence the challenges possessed by it (Table VI).[11] The most reported challenge, regardless of year, was limited or slow Internet access, followed by a lack of technological expertise among the healthcare team and computer literacy (Table VI). An interesting finding from the review was the human resource-related challenges, including reimbursement mechanisms for healthcare providers, concerns regarding malpractice-related issues, longer staff time, and a lack of formal organisational structures (Table VI). In studies conducted after the COVID-19 pandemic (2021 and 2022), data-related deterrents, including data security and data management, were some of the challenges reported (Table VI).

DISCUSSION

Main Challenges in Telehealth-Based Cancer Pain Management
The challenges of telehealth-based intervention in cancer

Table IV: Selected article's characteristics

Publication Number	Title	Author	Year of Publication	Type of study	Country	Reference
1.	Supportive Care Interventions for People With Cancer Assisted by Digital Technology: Systematic Review	Michael Marthick, PhD, Deborah McGregor, MHS, Jennifer Alison, PhD, Birinder Cheema, PhD, Haryana Dhillon, PhD, and Tim Shaw, PhD	2021	Systematic Review	Australia	25
2.	Improving health-related quality of life in women with breast, blood, and gynaecological Cancer with an eHealth-enabled 12-week lifestyle intervention: the women's wellness after Cancer program randomised controlled trial	Charrlotte Seib, Debra Anderson, Amanda McGuire, Janine Porter-Steele, Nicole McDonald, Sarah Balaam, Diksha Sapkota, and Alexandra L. McCarthy	2022	RCT	Australia	53
3.	Use of home telehealth in palliative cancer care: a case study	Anita Stern‡, Ruta Valaitis*, Robin Weir*† and Alejandro R Jadad‡1	2012	RCT	Canada	37
4.	The eCALM Trial-eTherapy for cancer appLying mindfulness: online mindfulness-based cancer recovery program for underserved individuals living with cancer in Alberta: protocol development for a randomized wait-list controlled clinical trial	Kristin A Zernicke1,2, Tavis S Campbell1,2, Michael Speca1,2,3, Kelley McCabe-Ruff4 , Steven Flowers5,6, Dale A Dirkse1,2 and Linda E Carlson1,2,	2013	RCT	Canada	28
5.	Development of a mHealth RealTime Pain Self-Management App for Adolescents With Cancer: An Iterative Usability Testing Study	Lindsay A. Jibb, PhD, RN1,2 , Joseph A. Cafazzo, PhD, PEng2,3 , Paul C. Nathan, MD, MSc1,2 , Emily Seto, PhD, PEng2,3 , Bonnie J. Stevens, PhD, RN1,2 , Cynthia Nguyen, MPH1 , and Jennifer N. Stinson, PhD, RN-EC1,2	2017	Cohort study	Canada	22
6.	Wearable Respiratory Monitoring and Feedback for Chronic Pain in Adult Survivors of Childhood Cancer: A Feasibility Randomized Controlled Trial From the Childhood Cancer Survivor Study	Nicole M. Alberts, PhD1,2; Wendy M. Leisenring, ScD3 ; Jessica S. Flynn, MS1 ; Jillian Whitton, MSc3 ; Todd M. Gibson, PhD4 ; Lindsay Jibb, PhD, RN5 ; Aaron McDonald, PhD1 ; James Ford, PhD1 ; Neema Moraveji, PhD6 ; Blake F. Dear, PhD7 ; Kevin R. Krull, PhD1 ; Leslie L. Robison, PhD1 ; Jennifer N. Stinson, RN, PhD5 ; and Gregory T. Armstrong, MD, MSCE1	2020	RCT	Canada	45
7.	Nurse-led telehealth interventions for symptom managementin patients with cancer receiving systemic or radiation therapy: a systematic review and meta-analysis	Chanel Kwok, Charlena Degen, Narges Moradi, and Dawn Stacey	2022	systematic review	Canada	49
8.	Development of mobile health–based self-management support for patients with lung cancer: A stepwise approach	Xiaosha Ni1,2 | Yan Lou1 | Wenyi Hu3 | Hemei Wang4 | Hong Xu1 | Shuaini Li5 | Yunxian Zhou6 | Yisha Ni1	2021	structured interactions	China	50
9.	Efficacy of virtual reality-based interventions for patients with breast cancer symptom and rehabilitation management: a systematic review and meta-analysis	Huayi Zhang, Hui Xu, Zhen-xiang Zhang, and Qiushi Zhang	2022	Sytematic review and Meta-analysis	China	57
10.	Approaches and best practices for managing cancer pain within the constraints of the COVID-19 pandemic in India	A. Damani, A. Ghoshal, N. Salins, S. Bhatnagar, P. Sanghavi, V. Viswanath, S. Ostwal, G. Chinchalkar and N. Vallath	2020	structured interactions	India	16
11.	Management of Cancer Patients in the COVID-19 Crisis Using Telemedicine: A Systematic Review	Fatemeh SALEHIa , Leila MASHHADIb , Kamran KHAZENIc , Zahra EBRAHIMId,1	2022	Systematic review	Iran	31
12.	Telerehabilitation and Monitoring Physical Activity in Patient with Breast Cancer: Systematic Review	Leila Keikha 1, Elham Maserat 2, Zeinab Mohammadzadeh	2022	Systematic Review	Iran	23
13.	Satisfaction with Telemedicine for Cancer Pain Management: A Model of Care and Cross-Sectional Patient Satisfaction Study	Marco Cascella 1 , Sergio Coluccia 2 , Mariacinzia Grizzuti 1 , Maria Cristina Romano 1 , Gennaro Esposito 1 , Anna Crispo 2,* and Arturo Cuomo	2022	cross-sectional study	Italy	40
14.	Providing Supportive and Palliative Care Using Telemedicine for Patients with Advanced Cancer During the COVID-19 Pandemic in Mexico	YANIN CHÁVARRI-GUERRA , a WENDY ALICIA RAMOS-LÓPEZ, b ALFREDO COVARRUBIAS-GÓMEZ, b SOFÍA SÁNCHEZ-ROMÁN, c PAULINA QUIROZ-FRIEDMAN, c NATASHA ALCOCER-CASTILLEJOS, c MARÍA DEL PILAR MILKE-GARCÍA, d MÓNICA CARRILLO-SOTO, e ANDREA MORALES-ALFARO, f MILDRED MEDINA-PALMA, f JOSÉ CARLOS AGUILAR-VELAZCO, f KAREN MORALES-BARBA, d ANDREA RAZCON-ECHEGARAY, d JENNY MALDONADO, d ENRIQUE SOTO-PÉREZ-DE-CELISf	2020	cohort study	Mexico	

Table IV: Selected article's characteristics

Publication Number	Title	Author	Year of Publication	Type of study	Country	Reference
15.	The effect of weekly specialist palliative care teleconsultations in patients with advanced cancer –a randomized clinical trial	Patrick D. Hoek1*, Henk J. Schers2 , Ewald M. Bronkhorst3 , Kris C. P. Vissers1 and Jeroen G. J. Hasselaar1	2017	RCT	Netherlands	20
16.	Telehealth system (e-CUIDATE) to improve quality of life in breast cancer survivors: rationale and study protocol for a randomized clinical trial	Noelia Galiano-Castillo1*, Angelica Ariza-García1,2, Irene Cantarero-Villanueva1 , Carolina Fernández-Lao1 , Lourdes Díaz-Rodríguez3 , Marta Legerén-Alvarez4 , Carmen Sánchez-Salado5 , Rosario Del-Moral-Avila6 and Manuel Arroyo-Morales	2013	RCT Protocol	Spain	17
17.	Telehealth System: A Randomized Controlled Trial Evaluating the Impact of an Internet-Based Exercise Intervention on Quality of Life, Pain, Muscle Strength, and Fatigue in Breast Cancer Survivors	Noelia Galiano-Castillo, PhD1,2; Irene Cantarero-Villanueva, PhD1,2,3; Carolina Fernandez-Lao, PhD 1,2,3; Angelica Ariza-Garc ıa, MSc2,4; Lourdes Dıaz-Rodrıguez, PhD1,3,5; Rosario Del-Moral-Avila, MD 6 ; and Manuel Arroyo-Morales, PhD	2016	RCT	Spain	18
18.	mPalliative Care Link: Examination of a Mobile Solution to Palliative Care Coordination Among Tanzanian Patients With Cancer	Mamsau Ngoma, MD1 ; Beatrice Mushi, MD2 ; Robert S. Morse, BS3 ; Twalib Ngoma, MD2 ; Habiba Mahuna, RN1 ; Kaley Lambden, MS4 ; Erin Quinn, MA4 ; Sarah B. Sagan, BA4 ; Yun Xian Ho, PhD4 ; F. Lee Lucas, PhD5 ; Joshua Mmari, BS1 ; and Susan Miesfeldt, MD5	2021	cross-sectional study	Tanzania	26
19.	How a Digital Case Management Platform Affects Community-Based Palliative Care of SubSaharan African Cancer Patients: Clinician-Users' Perspective	Yun Xian Ho, Robert S. Morse, Kaley Lambden, Beatrice P. Mushi, Mamsau Ngoma, Habiba Mahuna, Twalib Ngoma, and Susan Miesfeldt	2022	structured interactions	Tanzania	41
20.	Using information and communication technologies to improve the management of pain from advanced cancer in the community: Qualitative study of the experience of implementation for patients and health professionals in a tria	Julia Hackett University of Leeds, UK; University of York, UK Matthew J Allsop University of Leeds, UK Sally Taylor The Christie NHS Foundation Trust, UK Michael I Bennett Bridgette M Bewick	2020	RCT	UK	19
21.	Telephone interventions for symptom management in adults with cancer (Review)	Ream E, Hughes AE, Cox A, Skarparis K, Richardson A, Pedersen VH, Wiseman T, Forbes A, Bryant A	2020	Literature review	USA	36
22.	A Randomized Trial of Weekly Symptom Telemonitoring in Advanced Lung Cancer	Susan E. Yount, PhD, Nan Rothrock, PhD, Michael Bass, MS, Jennifer L. Beaumont, MS, Deborah Pach, RN, MSN, Thomas Lad, MD, Jyoti Patel, MD, Maria Corona, BA, Rebecca Weiland, BA, Katherine Del Ciello, MSW, and David Cella, PhD	2013	RCT	USA	56
23.	Automated Pain Intervention for Underserved Minority Women With Breast Cancer	Karen O. Anderson, PhD, MPH1 ; Guadalupe R. Palos, DrPH, LMSW, RN2 ; Tito R. Mendoza, PhD1 ; Charles S. Cleeland, PhD1 ; Kai-Ping Liao, PhD, MHA3 ; Michael J. Fisch, MD, MPH4; Araceli Garcia-Gonzalez, MD, DSc1 ; Alyssa G. Rieber, MD4; L. Arlene Nazario, MD4; Vicente Valero, MD5 ; Karin M. Hahn, MD, MPH6 ; Cheryl L. Person, MD7 ; and Richard Payne, MD8	2014	RCT	USA	46
24.	The electronic self report assessment and intervention for cancer: promoting patient verbal reporting of symptom and quality of life issues in a randomized controlled trial	Donna L Berry1,2*, Fangxin Hong3 , Barbara Halpenny2 , Anne Partridge4, Erica Fox2 , Jesse R Fann5,6, Seth Wolpin1 , William B Lober1 , Nigel Bush7, Upendra Parvathaneni8 , Dagmar Amtmann9 and Rosemary Ford6	2014	RCT	USA	47
25.	Web-Based Symptom Management for Women With Recurrent Ovarian Cancer: A Pilot Randomized Controlled Trial of the WRITE Symptoms Intervention	Heidi S. Donovan, PhD, RN, Sandra E. Ward, PhD, RN, FAAN, Susan M. Sereika, PhD, Judith E. Knapp, PhD, LCSW, Paula R. Sherwood, PhD, RN, CNRN, FAAN, Catherine M. Bender, PhD, RN, FAAN, Robert P. Edwards, MD, Margaret Fields, MSN, RN, and Renee Ingel, MSN, RN	2014	RCT	USA	34
26.	Web-Based Collaborative Care Intervention to Manage Cancer-Related Symptoms in the Palliative Care Setting	Jennifer L. Steel, PhD1,2,3; David A. Geller, MD2 ; Kevin H. Kim, PhD2 ; Lisa H. Butterfield, PhD5 ; Michael Spring, PhD6 ; Jonathan Grady, PhD6 ; Weiing Sun, MD7 ; Wallis Marsh, MD2 ; Michael Antoni, PhD8 ; Mary Amanda Dew, PhD4 ; Vicki Helgeson, PhD9 ; Richard Schulz, PhD3 ; and Allan Tsung, MD2	2015	RCT	USA	54
27.	Trajectories of change during a randomized controlled trial of internet-delivered psychological treatment for adolescent chronic pain: how does change in pain and function relate?	Tonya M. Palermoa,b,*, Emily F. Lawa,b, Chuan Zhoua,b, Amy Lewandowski Holleyc , Deirdre Logand , Gabrielle Tai Tamara J. Somers, PhD, Amy P. Abernethy, MD, PhD, Sara N. Edmond, MA, Sarah A. Kelleher, PhD, Anava A. Wren, MA, Greg P. Samsa, PhD, and Francis J. Keefe, PhD	2015	RCT	USA	51

Table IV: Selected article's characteristics

Publication Number	Title	Author	Year of Publication	Type of study	Country	Reference
28.	A Pilot Study of a Mobile Health Pain Coping Skills Training Protocol for Patients With Persistent Cancer Pain	Tamara J. Somers, PhD, Amy P. Abernethy, MD, PhD, Sara N. Edmond, MA, Sarah A. Kelleher, PhD, Anava A. Wren, MA, Greg P. Samsa, PhD, and Francis J. Keefe, PhD	2015	RCT	USA	27
29.	The Effect of Technology-Based Interventions on Pain, Depression, and Quality of Life in Patients With Cancer: A Systematic Review of Randomized Controlled Trials	Stephen O Agboola, MD, MPH, Woong Ju, MD,PhD, MPH, Aymen Elfiky, MA,MD,MPH, Joseph C Kvedar, MD, and Kamal Jethwani, MD	2015	Systematic review	USA	44
30.	Internet-delivered cognitive-behavioral treatment for adolescents with chronic pain and their parents: a randomized controlled multicenter trial	Tonya M. Palermoa,b,*, Emily F. Lawa,b, Jessica Falesc , Maggie H. Brombergb , Tricia Jessen-Fiddickb , Gabrielle Taib	2016	RCT	USA	52
31.	The rationale, design, and methods of a randomized, controlled trial to evaluate the effectiveness of collaborative telecare in preserving function among patients with late stage cancer and hematologic conditions	Andrea L. Cheville, Timothy Moynihan, Jeffrey R. Basford, John A. Nyman, Marty L. Tuma, Debra A. Macken, Terry Therneau, Daniel Satelel, Kurt Kroenke	2017	RCT	USA	14
32.	Challenges in a Technology-Based Cancer Pain Management Program Among Asian American Breast Cancer Survivors	Eun-Ok Im, PhD, MPH, FAAN, Xiaopeng Ji, PhD, Sangmi Kim, PhD, Eunice Chee, BSE, Ting Bao, MD, DABMA, MS, Jun J. Mao, MD, MSCE, Wonshik Chee, PhD	2018	Cohort study	USA	21
33.	Effect of Collaborative Telerehabilitation on Functional Impairment and Pain Among Patients With Advanced-Stage Cancer A Randomized Clinical Trial	Andrea L. Cheville, MD, MSCE; Timothy Moynihan, MD; Jeph Herrin, PhD; Charles Loprinzi, MD; Kurt Kroenke, MD	2019	RCT	USA	15
34.	"My Surgical Success": Effect of a Digital Behavioral Pain Medicine Intervention on Time to Opioid Cessation After Breast Cancer Surgery—A Pilot Randomized Controlled Clinical Trial	Beth D. Darnall, PhD,* Maisa S. Ziadni, PhD,* Parthasarathy Krishnamurthy, PhD,† Pamela Flood, MD,* Lauren Heathcote, PhD,* Ian G. Mackey,* Chloe Jean Taub, MA,‡ and Amanda Wheeler, MD§	2019	RCT	USA	58
35.	Cost-effectiveness of the Collaborative Care to Preserve Performance in Cancer (COPE) trial tele-rehabilitation interventions for patients with advanced cancers	Colleen F. Longacre1 | John A. Nyman1 | Sue L. Visscher2 | Bijan J. Borah2 | Andrea L. Cheville	2019	RCT	USA	35
36.	A Stepped-Wedge Randomized Controlled Trial: Effects of eHealth Interventions for Pain Control among Adults with Cancer in Hospice	Wilkie DJ, Yao Y, Ezenwa MO, Suarez ML, Dyal BW, Gill A, Hipp T, Shea R, Miller J, Frank K, Nardi N, Murray M, Glendenning J, Perez J, Carrasco JD, Shuey D, Angulo V, McCurry T, Martin J, Butler A, Wang ZJ, Molokie RE	2019	RCT	USA	55
37.	A pilot study of the preliminary efficacy of Pain Buddy: A novel intervention for the management of children's cancer-related pain	John F. Hunter1 Amanda M. Acevedo1 Sergio Gago-Masague2 Alexandra Kain3 Christine Yun4 Lilibeth Torno4,5 Brooke N. Jenkins3,6,7 Michelle A. Fortier	2020	RCT	USA	48
38.	Behavioral cancer pain intervention using videoconferencing and a mobile application for medically underserved patients: Rationale, design, and methods of a prospective multisite randomized controlled trial	Sarah A. Kelleher a , Joseph G. Winger a , Hannah M. Fisher a , Shannon N. Miller a , Shelby D. Reed b,c , Beverly E. Thorn d , Bonnie Spring e , Gregory P. Samsa f,g , Catherine M. Majestic a , Rebecca A. Shelby a , Linda M. Sutton h , Francis J. Keefe a , Tamara J. Somers a,*	2021	RCT	USA	24

Table V: General description of the 38 publications included in the review

Classification category	Subcategories	N (%)*	Reference
Country of research	Australia	5.26	1,2
	Canada	13.16	3-7
	China	5.26	8,9
	India	2.63	10
	Iran	5.26	11,12
	Italy	2.63	13
	Mexico	2.63	14
	Netherland	2.63	15
	Spain	5.26	16,17
	Tanzania	5.26	18,19
	United Kingdom (UK)	2.63	20
	United States of America (USA)	47.37	21-38
Research approach	Cohort	7.89	3,14,22
	Cross-sectional	5.26	13,18
	Literature review	2.63	21
	Randomised clinical trial (RCT)	57.89	1,4,5,6,15,16,20,23,24,25,26,27,28,29,30,31,32, 33,34,35,36,37
	Protocol of RCT	2.63	17
	Structured interaction	7.89	8,10,19
	Systematic review	15.79	2,7,9,11,12,39
Year of publication	2012	2.63	3
	2013	7.89	4,16,23
	2014	7.89	23,24,25
	2015	10.53	26,27,28,29
	2016	5.26	17,30
	2017	7.89	5,15,31
	2018	2.63	32
	2019	10.53	33,34,35,36
	2020	15.79	6,10,14,20,21,37
	2021	10.53	1,8,18,38
	2022	18.42	2,7,9,13,14,15,19

* percentages show the share of the total publications reviewed.

pain management were explored in this review. Regardless of the year, slow or limited Internet access, a lack of technological know-how among the healthcare team, and computer literacy were the most frequently reported.[12-28] A study in 2020 also elucidated a similar finding, and the researchers believed access to the Internet was critical for successful telehealth implementation.[29] Poor connections to networks and slow Internet connections adversely impact communication between healthcare workers and patients during telehealth consults. If the Internet connection is slow, it will also be challenging to perform a visual examination, which requires higher-resolution imaging and may create a space for medical error or misdiagnosis.[30]

Technological and Computer Literacy Barriers

'Lack of technological expertise among healthcare teams' was a challenge noticed in 2018, 2020, 2021, and 2022.[19,21,23,25,31] This finding is consistent with a study conducted in 2022, which indicated that any novel technology's efficacy and future development are significantly impacted by factors including user awareness and comprehension of the concept, implementation skills, and a work setting that fosters technology adoption.[32] Clinicians' inadequate understanding of telemedicine appears to have shaped how they perceive the technology. Consequently, giving healthcare workers additional knowledge about new innovations, like telemedicine, can aid in getting a more accurate depiction of their perspectives.[12]

In 2013, 2016, 2017, and 2019, the common challenge was 'computer literacy'.[14,18,22,28] A Philippine study found that after completing computer literacy training, their participants had a positive attitude towards computers and the internet. Their comfort with using a computer and their favourable opinion of the advantages of the internet largely influenced their behavioural intention to use telehealth. These results demonstrate the significance of computer literacy training as a crucial element of an effective telehealth programme.[33] Patients can efficiently learn how to utilise computers and the internet via proper computer literacy training, and they can also comprehend how important it is to support their interests in using telehealth.

Human Resource and Reimbursement Issues

Another food for thought that emerged from the review was the human resource-related challenges that involve telehealth. This includes reimbursement mechanisms for healthcare providers, concerns regarding malpractice-related issues, longer staff time, and a lack of formal organisational structures.[13,14,18,31,34,35,36,37] Among these, **reimbursement mechanisms for healthcare providers were recorded in most of the years (2019, 2020, and 2022).[31,35,36] Despite evidence from earlier studies elucidating that clinicians were generally in support of its utilisation, it would be challenging for them to afford to deliver the service without payment.[38] Payment rates should also be in line with the cost of the service to prevent paying too much if physicians can deliver more visits per session using telehealth. To prevent unintentionally

Table VI: Major challenge of telehealth-based intervention in cancer pain management identified in this review

Year	Types of challenges	References
2012	• Large variances between care delivery systems and a lack of standardization in home telehealth devices. • Questionable role of remote monitoring of vital signs. • Difficulty in operating the software/ app leads to frustration among patients.	37
2013	• Limited or slow Internet access. • Computer-illiteracy. • Excessive time needed for tele-consultation represents an overwhelming burden for some who are struggling to cope with advanced stage of cancer.	17,18,56
2014	• Contacting the patient for feedback and follow up was often a challenge. • Patients' complaint of "symptoms and quality-of-life" issues. • It took significantly longer than anticipated for participants to complete the consultation session with physician.	34,46,47
2015	• Patients showed only small improvements over the treatment period. • The routine utilization of telehealth is limited by persistent patient access barrier.	27,44,51,54
2016	• Longer staff time required. • Limited or slow Internet access. • Computer-illiteracy.	18,52
2017	• Excessive number of steps required to complete a function in telehealth-based intervention. • Difficulty in operating the software/ app leads to frustration among patients. • The constrained screen size of smartphones diminishes the capacity of patient to interact with the device. • High workload and burnout detected among healthcare workers. • Computer-illiteracy.	14,20,22
2018	• Lack of technological expertise among healthcare team. • Limited or slow Internet access	21
2019	• Lack of delivery models that match patients' challenges and needs. • Reduced engagement of patient due to time burden involved in telehealth intervention. • Patients receiving hospice care may be too ill to benefit from and utilize of telehealth intervention. • Reimbursement mechanisms for healthcare providers. • Computer-illiteracy	15,35,55,58
2020	• Questionable role of remote monitoring of vital signs. • Challenges multidisciplinary pain management. • Ethical challenges. • Policy issues. • Concerns regarding malpractice-related issues. • Lack of formal organizational structures. • Reimbursement mechanisms for healthcare providers. • Lack of technological expertise among healthcare team. • Poor interest from health care workers. • Social/cultural challenge. • Privacy issues. • Limited or slow Internet access. • Longer staff time required. • Difficult to motivate patients to adopt behaviour change.	13,16,19,36, 45,48
2021	• Limited or slow Internet access. • Lack of technological expertise among healthcare team. • Reduced engagement of patient due to time burden involved in telehealth intervention. • Data security. • Display of content in software/app lacks attractiveness. • Lack of electricity. • Limited availability and expense of maintaining a professional workforce to deliver telehealth.	24,25,26,50
2022	• Concerns regarding malpractice-related issues. • Lack of formal organizational structures. • Reimbursement mechanisms for healthcare providers. • Lack of technological expertise among healthcare team. • Poor interest from health care workers. • Social/cultural challenge. • Prescription issue. • The complexity of the technology used. • Data management challenges. • Large variances between care delivery systems and a lack of standardization in home telehealth devices. • High workload and burnout detected among healthcare workers.	23,31,40,41, 49,53,57

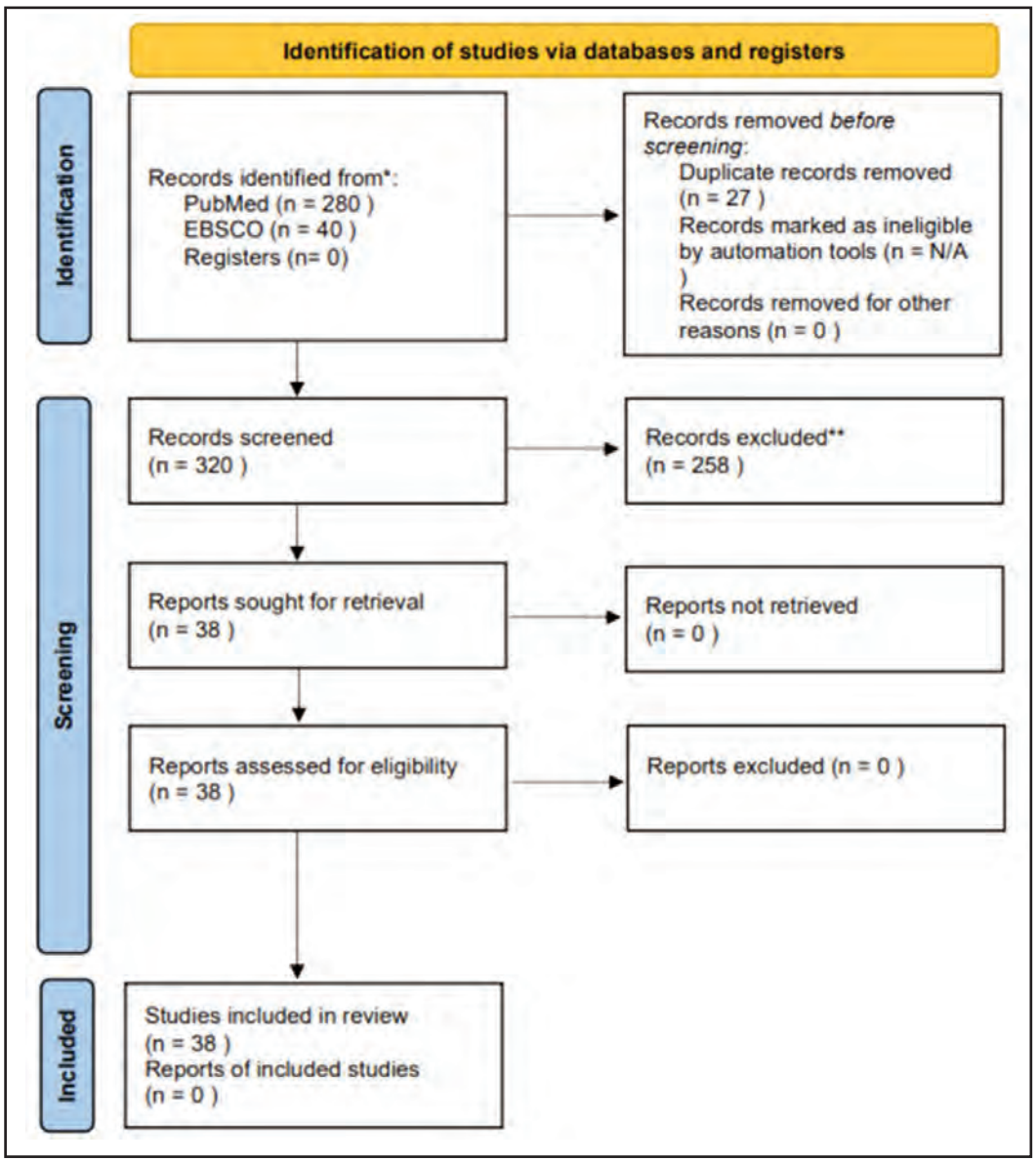

Fig. 1: Prisma flowchart diagram of the screening process

encouraging the use of telehealth interactions, the idea of payment equality is emerging. This payment parity is an important step because some clinics have made a significant change, raising the percentage of telehealth consultations from 10% prior to the pandemic to more than 90% during the pandemic.[39] After the pandemic, regulatory reform dictating payment parity will need to be maintained, and proper reimbursement for telemedicine will be a key element in ensuring widespread usage. Without these adjustments to reimbursement, fewer physical clinical visits may force some small practices, particularly those in rural regions, to run into financial difficulties.

Data Security and Privacy Concerns

Another interesting finding that was noticed in studies that were conducted after the COVID-19 pandemic (2021 and 2022) was data-related deterrents, including data security and data management.[25,40,41] To protect patients and increase public trust, a comprehensive policy framework is required to secure the privacy and security of data gathered by telehealth technologies. Lack of limits or controls on the collection, use, and disclosure of sensitive personal data is one of the privacy concerns of telehealth. Specifying the types of security threats that telehealth systems should be protected against is necessary when describing the security risks and suitable security controls.[42] There are several technical safeguards that can guard against these security threats. By using complex mathematics and encryption keys to electronically lock data, data encryption can assure that even if an attacker obtains access to the raw data, the data will be useless.[43]

Limitations of the Review

There are a few limitations in our review. The relative scarcity of studies from certain years, particularly 2012, 2016, and 2018, may limit the accuracy of estimating the magnitude of the problem during those periods. Selection bias was a key limitation, as the reviewed studies did not consistently account for patients with different cancer types and stages.[44-58]

Additionally, our review was restricted to English-language publications and studies indexed in a limited number of academic databases. This linguistic restriction may have led to the exclusion of relevant studies published in other languages, particularly those from non-English-speaking regions where telehealth adoption may differ. Consequently, this could have introduced a geographical bias and limited the generalizability of our findings. Future research should aim for a more inclusive approach by incorporating studies in multiple languages and broadening the database search strategy.

Another potential source of bias stems from the process of data extraction and study evaluation, which was primarily conducted by a single researcher. Although we mitigated this bias to some extent through verification by a second and third researcher, the risk of subjective interpretation remains. Despite our efforts to apply a rigorous and comprehensive search strategy, it is possible that some relevant studies were inadvertently overlooked, particularly those under consideration for publication or indexed in other databases.

CONCLUSION

The use of telehealth in clinical settings for managing chronic medical conditions, including cancer pain, is expanding rapidly, particularly in the wake of the COVID-19 pandemic. While this technology presents opportunities, its adoption remains hindered by multiple challenges. As telehealth continues to evolve, healthcare providers, researchers, and policymakers must consider strategies to optimize its implementation. To enhance telehealth adoption and overcome existing barriers, we recommend that healthcare policymakers establish clear guidelines and regulations to standardize telehealth-based interventions for cancer pain management. This includes addressing legal concerns, ensuring data security, and developing reimbursement models that incentivize telehealth services without imposing financial burdens on providers. Furthermore, efforts should be made to integrate telehealth training into healthcare education programs to improve technological literacy among medical professionals.

Telehealth developers should tailor their technologies to the specific needs and capacities of different populations, considering factors such as infrastructure limitations and digital literacy. The insights from this analysis can guide the design of more accessible and effective telehealth solutions. By proactively addressing these challenges, telehealth has the potential to significantly improve cancer pain management and patient outcomes. We hope that the findings from this review will contribute to shaping future research and policy discussions, ensuring that telehealth interventions are both effective and sustainable.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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Not relevant since this is a systematic review.

REGISTRATION OF PROTOCOL

This protocol was not registered.

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SYSTEMATIC / NARRATIVE REVIEW ARTICLE

Job satisfaction among public health and primary care physicians: A systematic review

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ABSTRACT

Introduction: Job satisfaction among physicians involved in public health services including public health physicians and primary care physicians is critical for their performance, motivation, and retention. These professionals address systemic health challenges and ensure effective health promotion at the population level. Despite their significance, they face challenges such as high workloads, administrative burdens, and insufficient resources, adversely affecting their satisfaction. This systematic review aims to examine the levels and determinants of job satisfaction among physicians engaged in public health roles.

Materials and Methods: This review followed PRISMA guidelines and was registered in PROSPERO (CRD42024613843). Articles were retrieved from PubMed, Scopus, and Web of Science databases. Fourteen eligible studies were selected based on strict criteria. Data synthesis employed an emerging clusters approach to identify factors influencing job satisfaction, categorised into four themes: job characteristics and role clarity, organisational support and leadership, work environment and culture, and rewards and career development.

Results: Data from 7313 physicians highlighted high workloads (60%) and administrative burdens (53%) as key sources of dissatisfaction. Approximately 44.7% reported high satisfaction, driven by autonomy in decision-making, supportive environments, doctor-patient relationships, and work-life balance. In contrast, 32% experienced moderate satisfaction, linked to manageable administrative tasks and fair remuneration. However, 20% reported low satisfaction, primarily due to excessive workloads, poor leadership support, financial insecurity, and limited career progression opportunities.

Conclusion: Job satisfaction among physicians in public health roles is moderate through a combination of high and low satisfaction factors. These professionals face demanding environments requiring them to balance administrative responsibilities, staff issues, community satisfaction, and resource allocations. Enhancing job satisfaction is essential for improving workforce morale and achieving effective public health outcomes. Implementing targeted interventions to address these challenges can foster long-term workforce stability and organisational success.

KEYWORDS:
Job satisfaction, public health physicians, primary care doctors, general practitioners, work environment, organisational leadership, career development

INTRODUCTION

The concept of job satisfaction has been defined in various ways since the early 20th century. Hoppock[1] described job satisfaction that it combines several factors such as physiological, psychological, and environmental situations. There were many different perspectives on job satisfaction.[2] Job satisfaction is a pivotal element influencing professionals' performance, motivation, and retention across various sectors, particularly in healthcare.

Physician dissatisfaction remains a significant concern that warrants attention. When physicians are dissatisfied with their practice conditions, they have two options.[3] Through Hirschman's classic formulation, physicians may either exit (abandon their current job or the profession) or voice their concerns by complaining individually or organising collectively.[4] Therefore, it would trigger some embarrassment in medical circles.[5]

Among all the physicians, physicians in public health play a crucial role in safeguarding the populations by addressing systemic health issues, managing disease prevention programs, and responding to emergencies.[6] Their work is inherently challenging, requiring medical expertise and skills in leadership, policy-making, and community engagement.[7] Given the complexity and responsibility of their roles, understanding their job satisfaction is essential to ensuring sustained excellence in public health services.

Job satisfaction among physicians in public health service is caused by many factors, including workplace environment, opportunities for professional growth, financial compensation, and the availability of resources to perform their duties effectively.[8] Equally important are intrinsic motivators, such as a sense of purpose and the impact of their work on improving community health. However, these professionals often face challenges like bureaucratic hurdles, high workload demands, and limited autonomy, which can hinder their satisfaction and lead to burnout or attrition where, to some extent, they have been diagnosed with mental disorders in Brazil.[9]

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Therefore, exploring the levels and determinants of job satisfaction in this workforce is crucial for their well-being and the broader healthcare system. When physicians are satisfied, they stay committed to their jobs and contribute to developing innovative and effective health interventions. On the other hand, dissatisfaction may lead to increased employee turnover, diminished productivity, and a potential compromise in public health outcomes.

Hence, this systematic review aims to examine the levels and determinants of job satisfaction among physicians engaged in public health services, including public health physicians, family medicine specialists, and general practitioners with postgraduate qualifications. This review synthesises evidence from multiple settings to identify key influencing factors and inform future strategies to improve workforce satisfaction and retention in public health.

For this review, the term "public health physicians" refers to all physicians who deliver population-level health services. This includes formally recognised public health specialists, as well as general practitioners and primary care doctors with relevant postgraduate training, who are actively involved in health promotion, disease prevention, and community-based care. In Malaysia, such roles are typically held by Family Medicine Specialists (FMS) or public health specialists working at the district (PKD) and state (JKN) levels. This broader functional definition was adopted to reflect the global diversity in job titles, qualifications, and roles associated with public health service delivery. In many high-income countries, general practitioners (GPs) are integrated within public health systems and undertake responsibilities similar to Family Medicine Specialists (FMS) or public-sector Medical Officers (MOs) in Malaysia. These roles typically include population-based functions such as disease prevention, screening, and health promotion. In contrast, GPs in Malaysia's private sector primarily focus on individual clinical care.

MATERIALS AND METHODS

The study adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework, ensuring transparency and reproducibility.[10] The protocol for this review was registered in PROSPERO (Registration No: CRD42024613843) to maintain methodological rigour.

Research Question Formulation

The PEO (population, exposure, outcome) concepts were the foundation for developing the review question. Aetiology and risk factor reviews benefit from applying the PEO concepts.[11] The PEO concept characterises the population as physicians working in public healthcare services worldwide, including general practitioners as they were specialised in some countries. Exposure is the factor affecting job satisfaction, and the outcome was levels of job satisfaction measured using quantitative, qualitative scales or mixed method approaches. Hence, the main research question was, what are the levels and determinants of job satisfaction among physicians working in public health and primary care settings?

Data Source and Search Strategy

As for data sources, the systematic review utilised a comprehensive search across multiple electronic databases to ensure the inclusion of diverse and relevant studies. The following databases used were PubMed Scopus, and Web of Science since they were highly recognised and widely used in universities. The search terms were developed strategically and cross-checked by the two authors. The search strategy was built around three key phrases: job satisfaction rate, factors influencing the rate, and public health physicians. The keywords used to search for related articles are provided in Table I. The search terms included a combination of keywords and Medical Subject Headings (MeSH) terms tailored to capture the core components of the research question. Boolean operators (AND, OR) were used to refine the search. The date for the search was on Nov 1 2024, with no language restriction.

Inclusion and Exclusion Criteria

The inclusion criteria for this systematic review were defined to ensure the selection of studies relevant to the research question. Studies were included if they (1) focused on public health physicians as the primary population, (2) examined factors influencing job satisfaction, such as workload, leadership, work environment, remuneration, or career development, and (3) employed quantitative, qualitative, or mixed-methods designs. The inclusion criteria for this systematic review did not impose restrictions on the publication date, allowing for the inclusion of studies published across various periods to ensure a comprehensive understanding of the topic. Exclusion criteria were applied to filter out studies that were: (1) focused on healthcare professionals other than public health physicians, (2) meta-analysis, descriptive reports, commentaries, or reviews without original data, (3) lacking clear outcomes related to job satisfaction, and (4) not accessible in full text. These criteria ensured that the review remained focused, rigorous, and relevant to the target population while minimising bias.

Study Selection

The study selection process was conducted in multiple stages to ensure a systematic and unbiased approach. All search results from the identified databases were initially imported into reference management software, where duplicates were removed. After eliminating duplicates, each reviewer rescreened the remaining papers. Two rounds of screening were conducted on articles before they were included in the review. In phase one, the authors will pre-screen study titles and abstracts against the eligibility criteria. In phase two, two authors will independently retrieve the full texts of studies identified as potentially relevant during the first screening and screen them again against the eligibility criteria. The third and fourth reviewers will discuss and, if necessary, resolve any uncertainties regarding study eligibility. The PRISMA-based flow diagram below in Figure 1 will illustrate the transparency of the study selection process at the different stages, including the excluded studies.

In phase one, 41 articles were removed due to the wrong population, unrelated articles, and systematic review. In phase two, eight (8) articles were removed due to the inability to extract the public health physician component from the

other healthcare workers. At the final stage, only 14 articles were selected after removing duplicate articles, primary screening, and secondary screening. All the selected articles were confirmed against the inclusion and exclusion criteria; some studies that required further reading were read more than once to ensure their suitability before inclusion. No additional clarification was required from the original study authors, as all necessary data were available within published manuscripts.

Data Extraction and Data Synthesis

Two authors extracted key information from all included studies and organised the relevant data into a data extraction form. The most significant results were selected and compiled into study characteristics shown in Table II. To ensure accuracy and completeness, another author cross-checked all data extractions. As a result, the data was extracted twice to minimise the risk of omitting any vital information.

The form requested information about the following: (1) Author; (2) Country; (3) Job Title; (4) Objective; (5) Participant; (6) Design; (7) Questionnaire; (8) Job Satisfaction Rate and (8) Themes or factors as shown in Table II. A narrative synthesis was carried out because of the study's variability.

Quality Assessment Tool

Using the Mixed Methods Appraisal Tool (MMAT), the authors evaluated the quality of each of the 14 studies.[12] This tool can assess the methodology quality of five different types of studies: mixed methods studies, quantitative randomised controlled trials, quantitative non-randomised studies, quantitative descriptive studies, and qualitative studies. Since this study has quantitative and qualitative studies, MMAT is the best tool for assessing this type of research.

The appraisal process began with two screening questions, followed by five criteria applied to each category to assess the study's quality. The MMAT evaluated various aspects, including the appropriateness of the study aim and design, participant recruitment, methodology adequacy, data collection, presentation of findings, data analysis, and the authors' discussions and conclusions. Each criterion carried equal weight; the final score was the sum of the five individual items.13 The MMAT results were reported using a rating system: 5***** (100% of quality criteria met), 4**** (80% met), 3*** (60% met), 2** (40% met), and 1* (20% met). To interpret the risk of bias, MMAT scores were mapped to risk categories: studies rated 5***** or 4**** were classified as having a low risk of bias, while those rated 3*** were considered moderate risk, and studies scoring 2** or below were considered high risk of bias. The quality assessment was conducted independently by two reviewers for each included article. No discrepancies were found between the reviewers regarding the quality assessment of the included studies.

Handling of Non-English Articles

Four non-English articles which were written in Spanish, Norwegian, and German were included in this review.[14–17] The full texts were translated into English using an AI-based language model (ChatGPT-4), a large language model developed by OpenAI. While expert linguistic validation was not performed due to resource limitations, the translated texts were reviewed carefully by the research team to ensure interpretive accuracy and contextual relevance. The use of ChatGPT for language translation in academic reviews has gained traction in recent literature. For example, Brewster et al.[18] demonstrated its utility in translating medical education material across multiple languages including Spanish and Norwegian, with satisfactory accuracy when cross-checked by bilingual reviewers. Similarly, the preprint by Jiao et al.[19] supports ChatGPT's capability to preserve core meaning in non-English texts during translation tasks in research settings. These precedents support the use of AI-assisted translation as a pragmatic approach in systematic reviews when professional translation services are unavailable.

Data Analysis

This review employed the emerging clusters approach to synthesise data from the included studies. The analysis was conducted in two stages: first, identifying all factors influencing job satisfaction among Public Health Physicians, and second, organising these factors into clusters under relevant themes. Given the study's objective of identifying job satisfaction determinants, the cluster mapping approach was deemed appropriate. The results were presented narratively and supplemented with tables highlighting the identified themes and clusters. The process involved iterative reading and interpretation of findings from eligible studies to ensure accuracy and consistency in factor categorisation.

Through this approach, the findings were structured into four primary themes: Job Characteristics and Role Clarity, Organisational Support, Work Environment and Culture, and Rewards and Career Development, with associated sub-domains for each theme, representing specific factors identified in the studies. Due to substantial heterogeneity in study designs, populations, measurement tools, and outcome reporting, a formal meta-analysis was not feasible. The use of varied instruments such as different job satisfaction scales alongside context-specific factors and inconsistent reporting of quantitative metrics across studies would have led to statistically non-meaningful results. Instead, a descriptive synthesis was adopted to retain the depth and contextual relevance of the findings, allowing for a more comprehensive understanding of job satisfaction patterns. For quantitative articles, trends in frequency, percentages, and reported satisfaction levels were summarised narratively. Additionally, the risk-of-bias ratings based on the MMAT were incorporated into Table II to reflect the quality and strength of the evidence.

RESULTS

Seventy-seven studies were found during the early search of the included databases. After removing duplicate articles and the primary and secondary screening process, 14 papers were considered for inclusion in this study (Figure 1). Nearly 80% of qualifying papers were guaranteed high quality, and all the articles were evaluated using the MMAT. No article was removed because none of the documents had a high-risk bias.

Table I: Search Strategy and Boolean Strings Used in Major Databases

Database	Search String
Scopus (Advanced Search), PubMed, WoS (Advanced Search)	(("Job Satisfaction" [MeSH] OR "career contentment" OR "occupational gratification" OR "employment happiness" OR "work fulfilment" OR "job enjoyment" OR "job happiness" OR "professional well-being" OR "vocational satisfaction" OR "workplace morale" OR "happiness at work" OR "job quality" OR "workforce inspiration")) AND (("Public Health" [MeSH] AND ("Physicians" [MeSH] OR "Doctors" [MeSH])) OR "public health physician" OR "public health doctor" OR "public health specialist" OR "Occupational doctor" OR "Occupational specialist" OR "general practitioner") AND (("Factors" [MeSH] OR "cause" OR "element" OR "circumstance" OR "component" OR "influence" OR "rate"))

Characteristics of included studies

The characteristics of the 14 studies included in this systematic review are presented in Table II. These characteristics include the year of publication, country of research, study design, job title, participant characteristics, questionnaire used in the study, and job satisfaction level. There is a wide choice of articles available from 1988 to 2024, as there is no restriction on the year of publication. Hence, the year of publication may be categorised into before the 20th century and after the 20th century. Only one article was published before the 20th century, [20] while the rest (92.8%) were published after the 20th century.[14–17,21–29] Out of 14 included studies, three were conducted in England and Germany (21.4%), and Denmark contributed two articles (14.2%). Most of these studies originate from high-income countries, as classified by Gross National Income (GNI)[30], except for one study from a lower-middle-income country which is Pakistan (7.1%).[8]

Next, only three articles use qualitative research methods (21.4%), while the rest are quantitative study designs, with the cross-sectional method being the most commonly used (81.8%). As per the participants, a total of 7313 public health physicians have been sampled in this review, with the majority job title of participants being General Practitioners with postgraduate qualifications (71.4%), while the rest have specific job titles as Public Health Residents or Family and Community Physicians.[15]

Only 11 articles have used questionnaires to measure job satisfaction among public health physicians, with seven articles using a similar questionnaire, the Warr-Cook-Wall Job Satisfaction Scale (WCW-JSS) (63.6%,) as shown in Table IV. The rest utilised different questionnaires, such as the Minnesota Satisfaction Questionnaire from a study by Kumar et al.[8], the Hospital Consultants' Job Stress & Satisfaction Questionnaire by Peter et al.[24], and a self-developed questionnaire from an exploratory qualitative study.[26] Only one study has measured depressive symptoms as an outcome of job satisfaction with Patient Health Questionnaire-9 (PHQ-9).[29] Only 10 articles documented satisfaction rates or scores among public health physicians, of which five articles documented satisfaction scores and three studies on satisfaction rates. The remaining two articles indirectly record statements on job satisfaction. Most studies documented moderate satisfaction (60%), followed by a low satisfaction level (30%), and only one study demonstrated a high satisfaction level.[25]

Quality Appraisal

According to the MMAT evaluation criteria, most studies score 5*****/100% and were therefore classified as having a low risk of bias. Three studies scored 3***/60% and were categorised as moderate risk of bias.[17,23,24] Nevertheless, all 14 articles met the quality appraisal and were included in this study, as shown in Table III.

This systematic review identified multiple factors influencing job satisfaction among healthcare professionals, categorised into four key domains, which were:

Job characteristics and role clarity

High satisfaction was strongly associated with autonomy, flexibility, and leadership roles. Autonomy in decision-making significantly enhanced satisfaction, scoring 5.11 out of 7 in findings.[20] Similarly, autonomy and role clarity contributed to 44.7% of participants' high satisfaction.[17,25] Flexibility was another factor; physicians with flexible work arrangements were more satisfied with their roles.[26] Leadership roles were also valued, with involvement in leadership enhancing satisfaction for many respondents.[16]

Moderate satisfaction arose from manageable administrative responsibilities. While administrative tasks were persistent, they were not overwhelming. Additionally, 56.6% of respondents experienced moderate satisfaction in managing these roles alongside clinical workloads.[22]

Low satisfaction was linked to excessive workloads, unclear roles, overwhelming administrative burdens, and time pressure. Unclear roles were typical, leading to stress and dissatisfaction.[23,24,27] High workloads were a high concern, identified as a primary source of dissatisfaction.[17,29] For example, 70% of public health professionals cited workload as their primary stressor.[8] Overwhelming administrative burdens were other key dissatisfiers, and one study led to scoring 2.8 out of 7.[17,28] Time pressure was also notable, with excessive time demands negatively affecting satisfaction.[8]

Table II: Result of data extraction from the included studies (n=14 articles)

No	Author/ Year	Country	Job title	Objective	Participant	Design	Questionnaire	Job satisfaction levels	Themes/ Factors	Risk of Bias (MMAT Score)
I.	Cedrone et al.[29]	Italy	Public Health Residents	To assess depression among Public Health Residents in Italy	N: 379 residents Mean age: 30 years	Quantitative study Cross-sectional	Patient Health Questionnaire-9 (PHQ-9)	Resident with depressive symptoms associated with poor job satisfaction (AOR=0.456, 95% CI=0.283–0.734). 61% experienced depressive symptoms; 26% had clinically relevant symptoms negatively impacting job satisfaction.	**Job Characteristics and Role Clarity** **Low** • High workload • Unclear role expectation **Work environment and culture** **Low** • Emotional exhaustion • Depressive symptoms	Low
II.	Götz et al.[14]*	Germany	GP	To analyse job satisfaction among GPs and its influencing factors.	N: 523 GPs Age: N/A	Quantitative Study Cross-sectional study	Warr-Cook-Wall (WCW) Scale 7 scale Likert	Mean: 5.58. • Highest: Colleagues and staff (6.00); • Lowest: - Income (4.33), - Work hours (4.49). - psychological workload	**Work environment and culture** **High** **Supportive colleagues and staff** **Rewards and Career Development** **Low** • The mismatch between effort and rewards. • Low pay • Limited career growth	Low
III.	Hall et al.[28]	England	Primary care physicians	To investigate strategies for enhancing GP well-being and mitigating burnout based on GPs' perspectives on workplace factors influencing their well-being and burnout levels.	N: 25 practicing GPs Age: The mean age of the sample is 42.15 years	Qualitative Study Focus group discussion	N/A	N/A	**Job Characteristics and Role Clarity** **Low** • High workload • Time pressure • Administrative work **Organisational Support and Leadership** **Low** • Lack of team support/ cohesion • poor communication **Work Environment and Culture** **High patient complaint** Negative portrayal of GP	Low

Table II: Result of data extraction from the included studies (n=14 articles)

No	Author/ Year	Country	Job title	Objective	Participant	Design	Questionnaire	Job satisfaction levels	Themes/ Factors	Risk of Bias (MMAT Score)
IV.	Huby et al.[27]	Scotland	GPs	To examine experiences of well-being and workplace distress, identify their perceptions of the causes and potential solutions, and outline implications for enhancing morale in general practice.	N: 63 GPs Age: N/A	Qualitative Study In-depth interview and Focus group discussion	N/A	N/A	**Job Characteristics and Role Clarity** **Low** • Undefined responsibilities within partnerships • No task delegation • There is no role clarity. • High Workload	Low
V.	Le Floch et al.[26]	France	GP	Identify which of these 31 factors are crucial and applicable for shaping future policies to enhance the attractiveness, recruitment, and retention of family medicine professionals in France.	N: 29 respondents among family medicine specialists (GP) Age: N/A	Quantitative study Delphi Consensus and Nominal Group Technique	31 job satisfaction factors questionnaire	N/A	**Job Characteristics and Role Clarity.** **High** • Flexibility • Autonomy in work • Independent decision-making **Work environment and culture** **High** • Patient-centred • Work-life balance • Good communication with the hospital **Rewards and Career Development** **High** • Career development opportunities and diversity (78%)	Low

Table II: Result of data extraction from the included studies (n=14 articles)

No	Author/ Year	Country	Job title	Objective	Participant	Design	Questionnaire	Job satisfaction levels	Themes/ Factors	Risk of Bias (MMAT Score)
VI.	Makin et al.[20]	England	GP	To determine aspects of the job GPs report as causing stress and job satisfaction	N: 101 GP Age: 25-64	Quantitative study Cross-sectional	Job satisfaction questionnaire -seven-point Likert-type scale.	Mean (SD) =5.11 (0.98) Overall job satisfaction was somewhat above the scale's mid-point, between moderately and very satisfied.	**Job characteristics and role clarity** **High** • Flexibility • Autonomy **Low** • Administrative workload **Work Environment and Culture** **Low** • High emotional involvement • Unpredictable interruptions • Long hours of work **Rewards and Career Development** **Low** • Low pay • Lack recognition	Low
VII.	Nørøxe et al.[25]	Denmark	GP	To investigate changes in mental well-being and job satisfaction among Danish GPs and examine potential associations with age, gender, and practice organisation	N: 1697 GP Age: no mean age <45: 501 46-59: 771 >60: 425	Quantitative study Cross-sectional	1) WCW-JSS- 7-point scale 2) Maslach Burnout Inventory (MBI) 3) WHO-5	**Low job satisfaction: 22.1% of participants** (score ≤3 on a 7-point scale). **Moderate job** satisfaction: 33.2% (scores 4–5). **High job satisfaction:** 44.7% (score ≥6).	**Organisational Support and Leadership** **Low** • Poor leadership **Work Environment and Culture** **Low** • High stress • No Work life balance **High** • Autonomy	Low
VIII.	Iglesias et al.[15]*	Spain	Family and Community Physicians	To explore factors influencing young family physicians' decisions to leave Family and Community Medicine practice and provide recommendations	N=13 young family physicians Age=N/A	Qualitative study	N/A	There is no rate, but qualitative findings indicate low satisfaction	**Work Environment and Culture** **Low** • No work-life balance • COVID-19 exacerbated the work culture **Rewards and Career Development** • Lack of recognition • Job insecurity	Low

Table II: Result of data extraction from the included studies (n=14 articles)

No	Author/ Year	Country	Job title	Objective	Participant	Design	Questionnaire	Job satisfaction levels	Themes/ Factors	Risk of Bias (MMAT Score)
IX.	Peter et al.[24]	Germany	GPs providing Palliative Care (PC)	To assess the impact of palliative care qualifications on the job stress factors experienced by GPs in palliative care settings	N=445 GPs Age: mean age 53.6 years	Quantitative Study Cross-sectional survey	Hospital Consultant Job Stress & Satisfaction Questionnaire (HCJSSQ)	N/A	**Job Characteristics and Role Clarity** **Low** • High levels of responsibility • Unclear job description **Organisational Support and Leadership** **Low** • Bureaucratic burdens • Lack of adequate support **Work Environment and Culture** **Low** • No work-life balance • Emotional with physical distress from patient care. **Rewards and Career Development** **Low** • Financial remuneration uncertainty • Lack of career progression opportunities.	Moderate
X.	Sibbald et al.[22]	England	GPs	To evaluate GP intentions to leave direct patient care, analyse changes between 1998 and 2001, and examine factors associated with this decision, with a particular focus on job satisfaction	N=1,949 GPs (790 in 1998, 1,159 in 2001) Age: Mean age:43.75 years in 1998, 44.35 years in 2001	Quantitative Study Cross-sectional survey	Job Satisfaction Scale A standardised instrument with a 7-point scale for job satisfaction (higher scores indicate greater satisfaction)	Mean job satisfaction scores: • 1998: 4.64 (out of 7) • 2001: 3.96 (declined significantly)	**Job Characteristics and Role Clarity** **Low** • Administrative workload • Unclear job descriptions. • High workload **Organisational Support and Leadership** • Bureaucratic burdens **Work Environment and Culture** **Low** • Long working hours	Moderate
XI.	Vedsted et al.[22]	Denmark	GP	To examine the relationship between practising as a GP in a walk-in open-access setting and the incidence of burnout among a sample of Danish GPs.	N=376 Age= mean age 51.8 (SD=6.7)	Quantitative study Cross-sectional	-Maslach Burnout Inventory Human Services Survey (MBI-HSS) -Job Satisfaction Scale by Warr, Cook, and Wall 7-point scale	20.5% reported high satisfaction (score ≥6/7), while the rest reported moderate or low satisfaction	**Job Characteristics and Role Clarity** **Low** **High workload** **Work Environment and Culture** **Low** • Long working hours	Low

Table II: Result of data extraction from the included studies (n=14 articles)

No	Author/ Year	Country	Job title	Objective	Participant	Design	Questionnaire	Job satisfaction levels	Themes/ Factors	Risk of Bias (MMAT Score)
XII.	Kumar et al.[8]	Pakistan	Public health professionals with postgraduate qualifications	To assess the level of job satisfaction and identify the factors influencing it among public health professionals in the public sector.	73 Age= NA	Quantitative study Cross-sectional	Minnesota Satisfaction Questionnaire	The overall satisfaction rate was reported at 41%, with 45% somewhat satisfied and 14% highly dissatisfied	**Job Characteristics and Role Clarity** **Low** • Irrelevant tasks • lack of autonomy • Unclear job and role • Time pressure **Organisational Support and Leadership** **Low** • Poor supervision • Insufficient professional support • Lack of cooperation within organisations **Work Environment and Culture** **Low** • Low support • Lack of resources in the public sector **Rewards and Career Development** **Low** • Low salaries • Lack of training opportunities, • Inadequate career progression pathways • No recognition	Low
XIII.	Nylenna & Aasland[16] *	Norway	GPs	To assess job satisfaction among Norwegian physicians and identify differences by speciality, work type, and demographics	n: 1,072 Norwegian physicians Age: N/A	Quantitative study Cross-sectional	Job Satisfaction Scale	Mean: 5.3 (on a 7-point scale). Private practitioners: 5.8; Hospital specialists: 5.1; Community medicine: 5.6.	**Job Characteristics and Role Clarity** **High** • Leadership role • Autonomy **Low** High workload **Work Environment and Culture** **Low** Long working hours	Low
XIV.	Löffler et al.[17] *	Germany	GPs	To examine the job satisfaction of GPs, identify the factors influencing it, and compare satisfaction levels over time	n: 568 GP Age: N/A	Quantitative study Cross-sectional	Job Satisfaction Scale	Mean: 4.1. High: Doctor-patient relationship (4.6): 48%. Low: Administrative tasks (2.8). : 20%	**Job Characteristics and Role Clarity** **High** • Autonomy • Task Variety **Low** • Administrative burdens • Workloads • Time pressure **Work Environment and Culture** **High** • Continuity of patient relationship • Trust for patient care **Rewards and Career Development** **Low** • Income stability in the rural area	Moderate

* Original article available in other language than English, where ChatGPT was used for the translation process N/A: not available, GP: General Practitioners

Table III: MMAT (Quality Appraisal)

Author and Year		SQ		1. Qualitative study					2. Quantitative study: Randomized Controlled Trials					3. Quantitative Non-Randomised					4. Quantitative Descriptive Only					5. Mixed Methods study					Bias
		S1	S2	1.1	1.2	1.3	1.4	1.5	2.1	2.2	2.3	2.4	2.5	3.1	3.2	3.3	3.4	3.5	4.1	4.2	4.3	4.4	4.5	5.1	5.2	5.3	5.4	5.5	
I.	Cedrone et al.[29]	✔	✔	-	-	-	-	-	-	-	-	-	-	✔	✔	✔	✔	✔	-	-	-	-	-	-	-	-	-	-	Low
II.	Götz et al.[14]	✔	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	✔	✔	✔	✔	-	-	-	-	-	Low
III.	Hall et al.[28]	✔	✔	✔	✔	✔	✔	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Low
IV.	Huby et al.[27]	✔	✔	✔	✔	✔	✔	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Low
V.	Le Floch et al.[26]	✔	✔	-	-	-	-	-	-	-	-	-	-	✔	✔	✔	✔	✔	-	-	-	-	-	-	-	-	-	-	Low
VI.	Makin et al.[20]	✔	✔	-	-	-	-	-	-	-	-	-	-	✔	✔	✔	✔	✔	-	-	-	-	-	-	-	-	-	-	Low
VII.	Nørøxe et al.25	✔	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	✔	✔	✔	✔	-	-	-	-	-	Low
VIII.	Iglesias et al.15	✔	✔	✔	✔	✔	✔	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Low
IX.	Peter et al.24	✔	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	✘	✔	✘	✔	-	-	-	-	-	Moderate
X.	Sibbald et al.[23]	✔	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	✘	✔	✘	✔	-	-	-	-	-	Moderate
XI.	Vedsted et al.[22]	✔	✔	-	-	-	-	-	-	-	-	-	-	✔	✔	✔	✔	✔	-	-	-	-	-	-	-	-	-	-	Low
Author and Year		**SQ**		**1. Qualitative study**					**2. Quantitative study: Randomized Controlled Trials**					**3. Quantitative Non-Randomised**					**4. Quantitative Descriptive Only**					**5. Mixed Methods study**					**Bias**
		S1	S2	1.1	1.2	1.3	1.4	1.5	2.1	2.2	2.3	2.4	2.5	3.1	3.2	3.3	3.4	3.5	4.1	4.2	4.3	4.4	4.5	5.1	5.2	5.3	5.4	5.5	
XII.	Ramesh Kumar et al.[21]	✔	✔	-	-	-	-	-	-	-	-	-	-	✔	✔	✔	✔	✔	-	-	-	-	-	-	-	-	-	-	Low
XIII.	Nylenna & Aasland[16]	✔	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	✔	✔	✔	✔	-	-	-	-	-	Low
XIV.	Löffler et al.[17]	✔	✔	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✔	X	✔	✔	✔	-	-	-	-	-	Moderate

Table IV: Job satisfaction level

Author (Year)	Questionnaire	Job satisfaction rate or score	Level
Cedrone et al.[29]	Patient Health Questionnaire-9 (PHQ-9) +	61% of residents experiencing clinically significant depressive symptoms reported lower job satisfaction levels	Low
Götz et al.[14]	Warr-Cook-Wall (WCW) Scale*	Mean= 5.58	Moderate
Hall et al.[28]	-#	-	-
Huby et al.[27]	-#	-	-
Le Floch et al.[26]	-#	-	-
Makin et al.[20]	Job satisfaction scale*	Mean =5.11	Moderate
Nørøxe et al.[25]	Warr-Cook-Wall Job Satisfaction Scale (WCW-JSS) *	44.7% highly,33.2% moderately and 22.1% low satisfaction	High
Iglesias et al.[15]	- +	There is no rate, but qualitative findings indicate low satisfaction	Low
Peter et al.[24]	-#	-	-
Sibbald et al.[23]	Job Satisfaction Scale *	Mean =3.96	Low
Vedsted et al.[22]	Job Satisfaction Scale by Warr, Cook, and Wall*	20.5% highly, 56.6% moderately, and 22.9% low satisfaction	Moderate
Ramesh Kumar et al.[21]	Minnesota Satisfaction Questionnaire	41% highly, 45% moderately, and 14% low satisfaction	Moderate
Nylenna & Aasland et al.[16]	Job Satisfaction Scale *	Mean= 5.3	Moderate
Löffler et al.[17]	Job Satisfaction Scale *	Mean= 4.1	Moderate

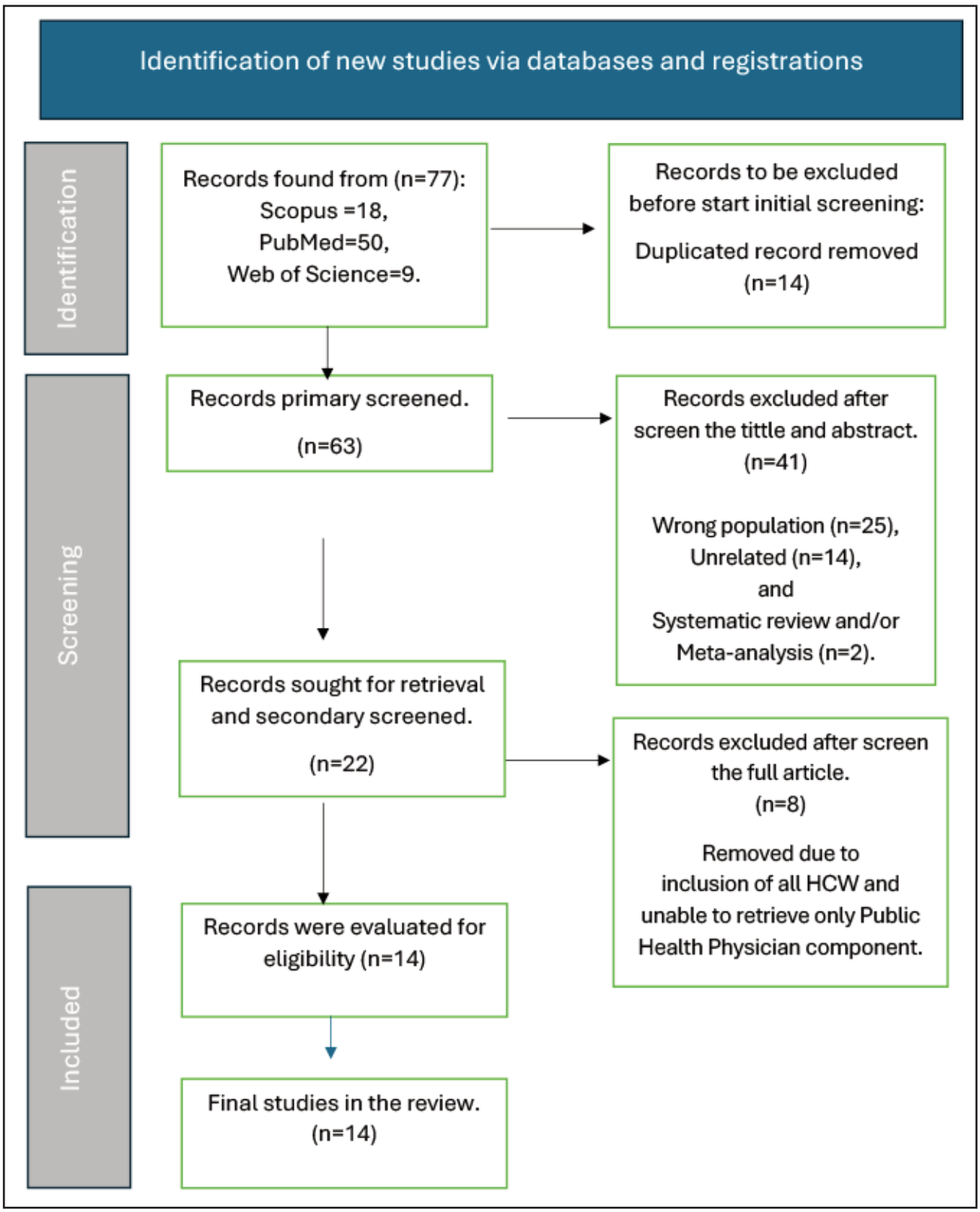

Fig. 1: PRISMA 2020 flow diagram for this study

Work Environment and Culture

High work environment and culture satisfaction were strongly linked to positive doctor-patient relationships, manageable work-life balance, and supportive workplace culture. Positive doctor-patient interactions were highly valued, contributing significantly to job satisfaction. For example, physicians reported high levels of fulfilment when engaging with patients meaningfully, with a rate of 4.6 from 7.[17] A manageable work-life balance was another key factor, with 78% of professionals noting that flexible schedules allowed them to maintain personal and professional responsibilities.[26] Supportive workplace culture also played a role, with professionals working in environments encouraging collaboration and inclusivity reporting higher satisfaction levels.[14,26]

Moderate satisfaction arose from environments with good team dynamics but high patient demands. While teamwork and cooperation among colleagues were seen as positive aspects, the heavy workload caused by high patient volumes occasionally dampened satisfaction. The interplay of these factors led to a moderate level of job satisfaction.[28]

Low satisfaction was linked to emotionally draining environments, high patient expectations, poor work-life balance, long working hours, and frequent interruptions. Emotionally taxing environments were a significant concern, as reported in several studies, where up to 61% of professionals cited burnout due to the intensity of their work.[20,24,29] High patient expectations added to this burden, particularly in demanding settings.[28] Poor work-life balance was another major issue, with dissatisfaction stemming from an inability to separate personal and professional responsibilities, leading to a job satisfaction rate of less than 3 out of 7.[15,25] Long working hours were a consistent source of frustration, with professionals frequently citing this as a primary driver of low satisfaction.[16,20,22,23] Interruptions during work also contributed to dissatisfaction, often disrupting clinical workflows and adding stress.[20]

Rewards and Career Development

Fair payment and opportunities for career advancements were key drivers of high satisfaction among healthcare professionals. In Le Floch et al.[26], 78% of professionals who perceived their salaries as fair and reflective of their responsibilities reported significantly higher satisfaction. Moderate satisfaction was observed among professionals who found their salaries adequate but not entirely competitive.[8,17]

Poor salaries, limited training opportunities, job insecurity, restricted career growth, and lack of recognition primarily drove low satisfaction. Poor salaries were a recurring issue across studies, with respondents citing dissatisfaction when wages did not match their responsibilities.[17,20,21] Limited access to training programs hindered professional development, as noted in 14% of professionals.[8] Job insecurity further exacerbated dissatisfaction, with Peter et al.[24] and Iglesias et al.[15] highlighting stress and uncertainty among professionals about long-term career prospects. Additionally, limited opportunities for career growth were a consistent theme.[8,14,24] Finally, lack of recognition for achievements significantly affected the morale of up to 62% of respondents, as observed in several studies.[8,14,15,20]

Organisational Support and Leadership

High satisfaction was linked to supportive leadership and cohesive team dynamics. According to Hall et al.[28], 70% of participants who experienced regular mentorship programs and team check-ins reported high satisfaction, as these practices significantly reduced burnout and improved morale.

Moderate satisfaction was associated with inconsistent leadership support and limited communication from management. Sibbald et al.[23] reported that 40% of respondents experienced moderate satisfaction, as some leadership involvement was present but lacked consistency. While guidance and mentorship were available sporadically, their absence in critical areas prevented higher satisfaction.

Inadequate leadership support, conflicting demands, and poor organisational governance predominantly drove low satisfaction. In Peter et al.[24], 64.25% of participants with low satisfaction reported stress from unclear priorities and insufficient leadership intervention. Additionally, rural physicians were disproportionately affected, with 53% identifying the lack of leadership support as a key dissatisfier contributing to their low job satisfaction.[24]

Overall, the results indicate that while some public health physicians experience satisfaction due to positive work environments and professional autonomy, many continue to face significant challenges, particularly in unclear roles, workload management, and career advancement opportunities.

DISCUSSION

Interest in job satisfaction grew significantly, driven by critical societal shifts, the economy, and organisations. The growth of industrialisation and the shift towards a knowledge-driven economy highlighted how crucial it is to prioritise employee well-being for boosting productivity and achieving success within organisations. Research in psychology began examining workplace behaviour, drawing on theories such as Maslow's hierarchy of needs and Herzberg's two-factor theory, which highlight the role of intrinsic and extrinsic motivators in job satisfaction.[31] Moreover, globalisation and technological progress have heightened competition, leading companies to focus on employee engagement and retention as vital resources.[32]

There has been a greater focus on studying job satisfaction in high-income countries, influenced by various factors. These nations often possess greater resources to dedicate to academic and organisational research, allowing for a more thorough understanding of workplace dynamics.[32] Moreover, wealthier countries enjoy greater economic stability, enabling businesses to move beyond survival and enhance employee engagement and performance. Additionally, having well-developed education systems and a strong corporate sector leads to a significant need for research that guides human resource practices, employee policies, and strategies for organisational growth, highlighting job satisfaction as an important area of focus.[33]

Importantly, the role of general practitioners (GPs) in these countries often differs from that in Malaysia. In countries such as the UK and Denmark, GPs are integrated into public health systems and perform population-level functions akin to Malaysia's Family Medicine Specialists (FMS) and public health specialists. In contrast, GPs in Malaysia's private sector primarily provide individual clinical care. This distinction is essential when comparing international findings on job satisfaction, as the expectations and responsibilities of GPs vary across healthcare systems. Contextualising these differences is crucial for accurate interpretation of the results.

Quantitative study designs are commonly utilised in job satisfaction research because they offer measurable, generalisable, and statistically reliable insight.[34] These designs help researchers gather extensive data from various groups of people, making it possible to spot patterns, trends, and connections between factors like salary, work environment, leadership style, and employee satisfaction.[35] The WCW-JSS is a popular tool for assessing job satisfaction, created to reflect employee's diverse feelings about their work.[36] Created by Peter Warr, John Cook, and Toby Wall, this scale evaluates satisfaction through various lenses, encompassing intrinsic elements like personal achievement and growth and extrinsic factors such as salary, work environment, and job stability.[37] The WCW-JSS usually employs a Likert scale format, allowing respondents to express their satisfaction with different aspects of their job. It helps create a well-rounded understanding of their workplace experience.

Job satisfaction among public health physicians is often moderate due to combining the four thematic areas of job characteristics and role clarity, organisational support and leadership, work environment and culture, and rewards and career development. Job characteristics and role clarity were identified as key factors influencing moderate job satisfaction among public health physicians, with high workloads, unclear roles, and administrative tasks consistently emerging as significant challenges. Streamlining administrative tasks and clearly defining roles are critical for alleviating stress and improving efficiency. For instance, Gustavsson et al.38 showed that reducing non-clinical duties improved satisfaction by fostering meaningful professional engagement. Integrating strategies to balance workload distribution and clarify job expectations can address a primary source of dissatisfaction across healthcare systems.[38]

The second factor is the work environment and culture in which work-life balance and inclusivity are critical to reducing stress and fostering job satisfaction. As Iglesias et al.[15] emphasised, resilient workplace environments can mitigate the impact of external stressors, including pandemic disruptions. Next, promoting an inclusive and supportive culture is essential for addressing these systemic challenges. Third, fair financial incentives and professional growth opportunities are crucial for retention and job satisfaction. Floch et al.[26] highlighted that 78% of healthcare professionals viewed fair remuneration as essential for job satisfaction, a finding consistent with this review. Career autonomy remains a key motivator, reinforcing the need for development pathways tailored to individual goals.16 Addressing financial inequities and establishing structured growth opportunities can improve workforce stability.[26]

Finally strong leadership and robust support systems were important in shaping morale and reducing burnout.[39,40] Findings align with Liu et al.[41], who demonstrated that integrated care models, supported by effective leadership, enhanced job satisfaction despite workload challenges. Strengthening leadership through targeted training and fostering collegial support can enhance organisational resilience, particularly during the pandemic.[15] Leadership alignment with organisational goals contributed to a sense of fulfilment and professional satisfaction among this high-satisfaction group.[28]

Implication and Future Directions

Most public health physicians exhibit modest satisfaction in their work, which may result in elevated turnover rates and reduced productivity, potentially leading to a decline in public health outcomes. Hence, healthcare organisations must prioritise administrative reforms, leadership development, and inclusive workplace policies to enhance job satisfaction. Addressing financial and professional inequities is crucial for retention.

Future research should investigate the long-term effects of these interventions and specifically examine underrepresented subgroups within the public health workforce such as subspecialty public health professionals like epidemiologists, and those working in rural or resource-constrained settings. These groups often face distinct challenges, including limited autonomy, unclear career progression, and mental health stressors, which are underexplored in current literature.

Among the included studies, Cedrone et al.[29] and Kumar et al.[8] specifically examined early-career public health residents and non-clinical public health professionals, respectively. Although no subgroup analysis was conducted, these studies highlighted unique satisfaction challenges such as limited autonomy, unclear career progression, and mental health stressors, suggesting the need for future research focusing on specific workforce subgroups.

This systematic review has notable strengths that enhance its credibility and relevance. First, the comprehensive search strategy included diverse studies across various healthcare settings, providing a broad understanding of job satisfaction determinants. The thematic analysis facilitated a detailed and nuanced synthesis of findings, capturing commonalities and unique insights. Additionally, the review spans pre-pandemic and pandemic contexts, offering valuable perspectives on how external crises influence job satisfaction.

However, several limitations are present. The dependence on cross-sectional studies limits the ability to link causal relationships between factors and job satisfaction. Furthermore, heterogeneity in sample sizes, study designs, and methodologies among included studies limits the generalizability of the findings. This review did not incorporate a meta-analysis due to the heterogeneity in study

designs, measurement tools, and outcome reporting, which restricted the feasibility of statistical aggregation. Finally, the absence of longitudinal data restricts insights into the long-term effects of interventions and job satisfaction trends over time. Despite these limitations, the consistency of themes across diverse studies strengthens the validity of the conclusions. These findings establish a strong foundation for future research to investigate targeted interventions and assess their long-term impact on improving job satisfaction among healthcare professionals.

CONCLUSION

Job satisfaction among public health physicians is moderate, influenced by a combination of high and low satisfaction factors. These professionals face demanding environments requiring them to balance administrative responsibilities, staff issues, community satisfaction, and resource allocations. Enhancing job satisfaction is essential for improving workforce morale and achieving effective public health outcomes. Implementing targeted interventions to address these challenges can foster long-term workforce stability and organisational success.

CONFLICT OF INTEREST

The authors confirm that they have no conflict of interest to declare.

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Patient satisfaction and experience for virtual consultation services in the Malaysian government health clinics: A review

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ABSTRACT

Introduction: Virtual consultation (VC) has emerged as a vital mode of healthcare delivery, particularly accelerated by the COVID-19 pandemic. The Ministry of Health (MOH) has progressively implemented VC services across government health clinics in Malaysia, guided by national digital health strategies. As VC becomes integral to primary care, evaluating patient satisfaction and experience becomes essential to ensure service quality. Despite the global availability of various tools, a lack of validated instruments remains in the context of Malaysian primary care, particularly in Malay. This narrative review aims to identify existing instruments used to assess patient satisfaction and experience with VC, evaluate their relevance and psychometric robustness, and highlight gaps in measurement, particularly for public primary care in Malaysia.

Materials and Methods: A systematic search was conducted using PubMed, employing a comprehensive search strategy combining MeSH terms and text words related to "patient satisfaction," "patient experience," "surveys and questionnaires," and "telemedicine." The search was restricted to English-language publications involving adult populations and returned 876 articles. After applying the free full-text filter, 397 articles were screened. Title and abstract screening yielded 83 potentially eligible studies, from which only eight were found to involve original development or adaptation of relevant instruments and were included for further analysis.

Results: Among the seven included studies, most questionnaires were focused primarily on domains related to usability and acceptability, such as interface ease, access, and convenience. However, few instruments addressed core components of clinical care quality, including communication, diagnostic confidence, care continuity, and coordination. Furthermore, none of the reviewed questionnaires underwent complete validation and reliability assessment within the context of Malaysian primary care. Four studies were conducted in Malaysia; however, these either lacked robust validation processes or focused solely on acceptability. Additionally, no tools were validated in Malay or tailored specifically to the cultural and healthcare delivery context of Malaysia's government clinics.

Conclusion: The findings reveal a significant methodological gap in assessing patient satisfaction and experience with VC in Malaysian primary care. Existing tools largely derive from models focused on technology usability or service acceptability, with limited attention to the clinical dimensions of virtual care. Instruments such as the Telemedicine Satisfaction Questionnaire (TSQ), the Telemedicine Usability Survey (TUS) and the Service User Technology Acceptability Questionnaire (SUTAQ) offer partial frameworks but lack comprehensive validation or contextual adaptation. In Malaysia, while efforts have been made to develop VC-related surveys, these are insufficiently validated and often lack specificity for primary care. Moreover, tools currently in use do not capture the broader service quality domains emphasised by frameworks like SERVQUAL or Picker's Patient Experience Principles.

As VC services expand in Malaysian public healthcare, there is an urgent need to develop and validate culturally appropriate, linguistically accessible, and psychometrically sound questionnaires to assess patient satisfaction and experience. These instruments must integrate both technological usability and the core clinical components of healthcare delivery. Such efforts are essential to guide quality improvement and ensure that VC services align with patients' needs and expectations in the primary care setting.

KEYWORDS:
Virtual Clinic, Virtual Consultation, Telemedicine, Patient Satisfaction, Patient Experience

INTRODUCTION

Background of Virtual Consultation

Virtual consultation (VC) is a method of delivering healthcare services through live and interactive clinical consultations and treatment planning between healthcare providers and clients.[1] This is a relatively new concept in healthcare which uses technology and multimedia to improve accessibility. It allows healthcare professionals to remotely evaluate, diagnose and provide treatment recommendations to patients. Patients can communicate with healthcare providers using devices such as smartphones, tablets, or personal computers, while providers can use their preferred devices for consultations.[2]

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In the 21st century, digital health advances and mobile applications have further integrated telemedicine and VCs into the healthcare system. Patients began receiving medical advice, diagnoses and treatment plans from home using smartphones and computers, enhancing access to care and enabling continuous medical monitoring.[3] The COVID-19 pandemic in 2020 accelerated the adoption of these technologies, reducing in-person contact and ensuring that medical care continued without risking exposure to the virus. This period highlights the critical role of telemedicine in public health emergencies, solidifying its importance in health.[3]

Malaysia has been at the forefront of adopting telemedicine, with the Ministry of Health Malaysia (MOH) launching a Telemedicine Blueprint in 1997. This ambitious initiative aimed to use technology and multimedia capabilities to improve medical services nationwide, laying the groundwork for future digital healthcare innovations.[4] In line with this vision, the Malaysian Strategic Plan on Digitalization for 2021-2025 included a crucial second strategy to expand access to virtual initiatives. This strategy highlights the government's dedication to improving healthcare accessibility through digital means, ensuring that more patients can benefit from virtual consultations and other telemedicine services.[5]

Virtual Consultation in the Government Health Clinics Of Malaysia

In 2021, the World Health Organization (WHO) released findings that reinforced the importance of virtual consultations as a key aspect of primary care, allowing medical professionals to offer remote and efficient consultation services.[6] This approach is implemented worldwide, including in Malaysia. The MOH has actively integrated telemedicine services into its healthcare delivery model. It recognises the potential of digital technology to enhance patient care. In 2019, five health clinics nationwide introduced a proof-of-concept for virtual consultations. This pilot project aimed to test the viability and effectiveness of VCs in the public healthcare system.[1] As the COVID-19 pandemic unfolded, the MOH expanded telemedicine to 35 additional clinics nationwide, adapting to the new normal and demonstrating the scalability of virtual health services in a crisis.[1] By 2022, the initiative had expanded significantly, with 230 health clinics offering telemedicine services (Table I). This represents a substantial increase in the infrastructure and resources supporting virtual healthcare, both in urban and rural settings.[1]

The number of people using VC services has increased significantly, showing that more people in Malaysia are trusting and relying on virtual health consultations. In 2019, there were 3,101 registered users of these services. By the end of December 2021, this number had surged to 29,311, indicating the Malaysian public's rapid and robust adoption of VCs.[7-8]

Furthermore, the range of services provided through VC has expanded since its introduction in 2019. The services offered include outpatient care for non-communicable diseases, such as stable diabetes mellitus (DM), as well as for communicable diseases like tuberculosis (TB) through directly observed treatment, short-course (DOTS). Additionally, laboratory findings are part of the services provided. Maternal and child health services encompass booking consultations, antenatal follow-ups, and family planning consultations that do not require physical examinations. Pharmacy services include smoking cessation counselling, medication adherence counselling, and various medication-related consultations. Other virtual services available include occupational therapy interventions that can be conducted online, individual or group physiotherapy sessions, dietetic consultations focused on food preparation, and specialised services for conditions such as gestational diabetes mellitus (GDM).[1]

Understanding the Importance of Patient Satisfaction and Experience in the Light of Expanding Virtual Consultation Services in Primary Care

As VC services expand, assessing patient satisfaction and experience is crucial, just as it is with all healthcare services. The Agency for Healthcare Research and Quality (AHRQ) defines patient experience as encompassing the full range of interactions within the healthcare system, including medical care and administrative services. It is a key element of healthcare quality, measured by aspects highly valued by patients, such as timely appointments, accessible information and effective communication with providers.[9] Evaluating patient experience fosters shared decision-making, enhances patient-doctor communication and identifies service gaps, ultimately leading to better-individualised care and improved health outcomes.[10]

On the other hand, patient satisfaction is a highly subjective measure closely linked to a patient's expectations and perceptions of their care experience. Factors such as personal beliefs and the information provided to them before and during care can influence satisfaction levels. Patient satisfaction is an individual reaction to the healthcare experience and can be influenced by various factors, such as the attitude of healthcare providers, the facility's environment and care outcomes. Due to its subjective nature, improving patient satisfaction can be more challenging.[9] Patient satisfaction is a vital component in healthcare, as it serves as a key indicator of quality, encompassing aspects such as communication with providers and efficiency of services. High satisfaction was associated with better adherence to treatment plans and improved clinical outcomes. Additionally, it can impact patient retention and referrals and reduce the risk of medical malpractice claims. For healthcare providers, patient satisfaction is a vital measure that affects health outcomes, as well as operational and relational aspects of care delivery.[11]

Furthermore, despite their interconnectedness, the AHRQ emphasises the differences between patient satisfaction and patient experience. Both are vital for healthcare providers to develop and implement quality improvement strategies. High-quality care delivery relies on assessing both factors, which inform service enhancements, patient care protocols, and strategic planning for organizations.[9]

Questionnaire as The Best Method to Assess Patient Satisfaction and Experience

Assessing and evaluating patient satisfaction and experience is a complex process due to the latent nature of satisfaction. It is an unobservable variable that cannot be directly measured with a single question. A multifaceted approach is necessary to capture the full scope of patient satisfaction and experience.[20] The evaluation encompasses several domains that interact and contribute to overall satisfaction and experience, as stated in Table II.

To obtain a comprehensive understanding of patient satisfaction and experience, questionnaires are often utilised. They are considered the most effective method for this purpose.[21] However, the creation of such questionnaires is not a straightforward task. It is important to adhere to a systematic and evidence-based process when developing, validating, and ensuring the reliability of these questionnaires. This involves measures such as providing content validity, testing the instrument's reliability, conducting pilot studies, and potentially utilising factor analysis to confirm the questionnaire's structure. By employing such a rigorous development process, healthcare providers can guarantee the acquisition of precise, reliable, and all-encompassing data on patient satisfaction and experience, which can then inform quality improvement initiatives within the healthcare system.[22]

Hence, this review evaluates the existing literature on patient satisfaction and experience concerning VC services, which is relevant to government health clinics in Malaysia. Specifically, it identifies gaps and limitations in currently available questionnaires, emphasising validity, reliability, and suitability for primary care.

MATERIALS AND METHODS

The literature search was conducted exclusively in the PubMed database to identify studies examining patient satisfaction in telemedicine using validated survey instruments. The search strategy incorporated Medical Subject Headings (MeSH) and text word terms to enhance both sensitivity and specificity. The search query included combinations of terms related to patient satisfaction—such as "Patient Satisfaction"[Mesh], "patient satisfaction", "Patient Experience", and "consumer satisfaction"—coupled with terminology indicative of measurement tools, including "Surveys and Questionnaires"[Mesh], "questionnaire*", "survey*", "questionnaire development", "instrument development", "scale development", and "instrument validation". These were further combined with terms reflecting telemedicine contexts, such as "Telemedicine"[Mesh], "Telehealth", "video consultation", "virtual consultation", "video visit", "virtual visit", and "teleconsultation". Filters were applied to restrict results to English-language studies involving adult populations. This targeted strategy included studies relevant to developing, validating or adapting survey instruments that assess patient satisfaction with VC services.

RESULTS

The systematic search initially yielded 876 articles from the PubMed database. After applying the free full-text filter, 397 articles were available for further assessment. Title and abstract screening of these records narrowed the pool to 83 studies that appeared to align with the inclusion criteria of addressing patient satisfaction in adult telemedicine contexts using survey or questionnaire-based instruments. Following a comprehensive full-text review, eight studies were identified as specifically reporting on the original development or adaptation of relevant instruments. These eight studies were subsequently included in the analysis for this narrative review. Table III presents a summary of the key points extracted from the papers.

DISCUSSION

Overview of Questionnaires and the Domains Related to Virtual Consultation Services

Studies have been conducted in foreign countries that may offer valuable insights into this research topic, despite the limited number of questionnaires used globally for VC services. Among these are six commonly employed questionnaires designed to evaluate patient satisfaction and experience in VC settings.[31]

The two most commonly utilised questionnaires in the field of Telemedicine are the Telemedicine Usability Survey (TUS) and the Telemedicine Satisfaction Questionnaire (TSQ). The TUS is designed to evaluate the usability experience of patients. While it claims to have content validation from previous studies, no published articles have been found to date that demonstrate the items have undergone psychometric analysis for construct validation.[32] On the other hand, the TSQ claimed to have been thoroughly validated through content, construct validation and reliability analysis. However, the exact values of the Content Validation Index (CVI) and Face Validation Index (FVI) were not reported, and there was no further breakdown of satisfaction domains.33 According to Gohari et al., the next is the Service User Technology Acceptability Questionnaire (SUTAQ), which was devised by Hirani et al. in 2016 to assess the patient acceptance of technological processes and devices across several domains, including enhanced care, increased accessibility, privacy and discomfort, care personnel concerns, substitution, and satisfaction. This questionnaire was developed systematically, and its reliability was analysed.[31]

Attkisson and Greenfield developed the Client Satisfaction Questionnaire (CSQ). This questionnaire was created in 1996 when VC services were still in their infancy and not widely accessible. Despite being among the top six questionnaires for VC services, the items were designed for general healthcare services. The CSQ consists of 8 items that have been validated and tested for reliability.[32] Gohari et al. also mentioned in their systematic review that another questionnaire was developed earlier in 1988 by Chin et al., with a broader scope related to telehealth services. The Questionnaire for User Interaction Satisfaction (QUIS) encompasses overall satisfaction, user satisfaction regarding the screen, terminology, and information, as well as learning

Table I: Summary of Number and Percentage of Government Health Clinics Providing Virtual Consultation Services According to State and Urban/Rural Status

State	Number of Health Clinics in Rural Areas Providing VC	Percentage of Clinics in in Rural Areas Providing VC	Number of Health Clinics in Urban Areas Providing VC	Percentage of Clinics in Urban Areas Providing VC	Overall Percentage of Health Clinics in the state Providing VC
Perlis	2	40%	1	13%	23%
Kedah	8	27%	11	33%	30%
Pulau Pinang	3	21%	6	29%	26%
Perak	2	8%	20	31%	25%
Selangor	2	8%	34	61%	45%
Wilayah Persekutuan	0	0	5	21%	21%
Negeri Sembilan	7	24%	6	29%	25%
Melaka	2	18%	12	55%	42%
Johor	13	16%	4	24%	17%
Pahang	1	2%	16	34%	19%
Terengganu	10	34%	10	43%	38%
Kelantan	14	15%	2	17%	16%
Sarawak	4	2%	13	32%	8%
Sabah	9	10%	13	59%	20%
MALAYSIA	77	12%	153	39&	22%

Table II: Summary of Differences between Patient Experience and Patient Satisfaction[12-19]

Aspects	Patient Experience	Patient Satisfaction
Definition	Objective measurement of healthcare interactions from the patient's perspective (what happened)	Subjective evaluation of care received based on patient expectations and perceptions (how patients feel about the care provided)
Measurement Approach	Objective: typically assesses the frequency and consistency of specific interactions or events	Subjective: typically assesses patients' perceptions and judgments against their expectations
Domains / Dimensions	- Communication (clarity, empathy) - Responsiveness (promptness) - Respect for patient preferences - Physical comfort and environment - Coordination and continuity of care - Emotional support - Access to care and information	- Fulfilment of expectations - Perceived quality of care - Overall contentment - Perceived value for cost - Likelihood to recommend services - Attitudes toward healthcare providers
Basis of Evaluation	Actual events and interactions	Personal values, expectations, and emotional reactions
Reliability and Validity	More reliable due to specific and measurable criteria	Less reliable due to subjective and personal variability
Influencing Factors	Provider-patient interactions, organisational processes, service delivery standards	Patient expectations, previous experiences, personal values, emotional state, cultural factors - SERVQUAL Model
Common Tools for Measurement	- CAHPS (Consumer Assessment of Healthcare Providers and Systems) - Picker Patient Experience Questionnaire (PPE-15) - NHS Patient Experience Framework	- Patient Satisfaction Questionnaire (PSQ-18) - Press Ganey Surveys
Utility in Quality Improvement	Directly identifies actionable areas for improving healthcare delivery	Reflective; identifies overall perceptions, less specific actionable feedback
Impact on Healthcare Outcomes	Strongly correlated with clinical outcomes, patient safety, and care continuity	Correlated with patient loyalty, compliance, and provider reputation

and system capabilities. This questionnaire has been validated, and its reliability has been tested.[31] Last but not least, the systematic review also touched on the System Usability Scale (SUS) questionnaire developed by Brooke et al. in 1986. This questionnaire aims to assess the patient usability of the general electronic systems, which do not focus on VC per se, as the service was still in its early stages when this questionnaire was developed. This questionnaire consisted of 10 items with no specific domains and underwent content and construct validation, followed by a reliability analysis.[31]

For instance, in Bangladesh, Hoque et al. conducted a study to assess the level of satisfaction among psychiatric patients who received VCs. The researchers utilised a questionnaire based on the e-Servqual and Technology Acceptance Model. Although the study reported reliability among the questions (Cronbach's alpha = 0.87), no validation processes were mentioned.[27] Furthermore, the intraclass consistency should also be reported to enhance the understanding of internal consistency within each questionnaire domain. On the other hand, in Saudi Arabia, Abdulwahab et al. researched patients who had experienced virtual services from Outpatient Departments (OPDs) and Pharmacies in a hospital. The researchers adapted the Patient Satisfaction Questionnaire (PSQ-18) and TSQ satisfaction questionnaires, presumably into Arabic, but did not carry out validation or reliability assessments.[28] Furthermore, Arrighi-Allisan et al. assessed patient satisfaction with VCs in the Otolaryngology Department of a United States hospital. The researchers modified the Press Ganey Survey for their study, but the modifications were not validated, raising concerns about the

Table III: Paper Related to the Development, Validation or Adaptation of Patient Satisfactionand/or Experience Questionnaire for Virtual Consultation Services

Country	Authors	Questionnaire Items	Study Population	Language	Validity & Reliability
Malaysia	Hassan et al.,[23]	Satisfaction	Patient using SLT (Virtual-Conventional-Hybrid)	Developed in English & Translated to BM	No validation or reliability outcome was reported
Malaysia	Othman et al.,[24]	Satisfaction	Mental Health patients using VC	English & Malay	No proper validation & reliability test reported
Malaysia	Tan et al.,[25]	Acceptability & Usability (UTAT)	Patient and caregiver attending Outpatient Geriatric Clinic HKL	English	Unsure of the Validation & Reliability process
Malaysia	Jusof et al.,[26]	Acceptability	VC patients in KK Percint 18, Putrajaya	Malay	No proper validation & reliability test reported
Bangladesh	Hoque et al.,[27]	Satisfaction	Psychiatric patients using VC	English	Originally developed. No Validation parameters reported
Saudi Arabia	Abdulwahab et al.,[28]	Satisfaction-adapted PSQ-18 and TSQ	The patient had experience with virtual services from OPD & Pharmacy	English	No validation & reliability parameters were reported
United Kingdom	Murthy et al.,[29]	Experience	Patient of VC for oral care services	English	No validation & reliability outcomes reported
USA	Arrighi-Allisan et al.,[30]	Satisfaction using Press Ganey Survey	Patient of VC Otolaryngology Department	English	Adaptation of the Press Ganey Survey was not validated

relevance of the findings. The original Press Ganey Survey was designed for traditional health services.[30]

Research Conducted on Patient Satisfaction and Experience for Virtual Consultation Related to Outpatient Services in Malaysia and the Issues Identified

All the above questionnaire versions in Malay were unavailable based on searches in PubMed and other open-access databases, indicating the high possibility that they were not translated into Malay or validated for the Malaysian population. However, the Technology Acceptance Model Questionnaire (TAM) was translated and validated by Husin et al. in 2022. However, this questionnaire is meant only for healthcare providers.[33]

Several studies have been conducted in Malaysia regarding VC services or telemedicine, and the findings can be accessed through free-text databases such as PubMed, ScienceDirect, and Web of Science. In 2023, Hassan et al. did a study to compare the satisfaction of recipients of conventional speech-language therapy (C-SLT), speech-language teletherapy (SLTT), and hybrid speech-language therapy (H-SLT) among the patients and caregivers using their services. A questionnaire was developed based on an existing questionnaire in English and validated by five language speech therapists. The content was adjusted and translated into Malay using the forward and backwards translation process. Experts commented on the high comparability between the languages, with a mean ($\bar{x}$) of 4.7 and a standard deviation (s) of 0.26. However, despite having five expert panels, no results on content and construct validation outcomes were mentioned.[23] They should also report the range of the difference for a better understanding of the comparability.

Othman et al. researched patient satisfaction with VC services for mental health for the Malaysian general population. They developed a questionnaire based on existing questionnaires to evaluate satisfaction based on four domains of satisfaction: communication and rapport, clinical assessment, convenience and equipment, and technical issues. The questionnaire was distributed to the public via the Google Forms online link. Unfortunately, validation and reliability tests were not reported.24 In contrast, Tan et al. focused their study on the acceptability and usability of telemedicine for outpatient geriatric clinic patients and caregivers. They created an English-language questionnaire and employed the Unified Theory of Acceptance and Use of Technology (UTAUT) for validation and reliability. However, the precise details of this process remain undisclosed.[25]

The most pertinent study on this topic was conducted by Jusof et al. in 2023. This study comprised patients who had enrolled in VC services at KK Percint 18, Putrajaya. The study's primary focus was on the acceptability of these services among patients. Three Family Medicine Specialists validated the content development. Validation and reliability testing parameters were not reported.[26]

Summary of the Gaps Identified in Current Questionnaires Related to Patient Satisfaction and Experience for Virtual Consultation Services

Currently, most validated and reliability-tested questionnaires available for assessing patient satisfaction and experience in primary care settings focus predominantly on conventional, face-to-face consultations. This limitation means that the currently used tools may not adequately capture the unique dimensions and expectations associated with VC services, potentially missing critical aspects influencing patient satisfaction in a digital context.

Furthermore, questionnaires designed for VC services still encounter significant challenges in meeting standard validation and reliability criteria. This is partly due to the rapidly evolving nature of telehealth technologies, the lack of established benchmarks and the variability in service delivery models. Consequently, many of these questionnaires lack robust psychometric validation, undermining their effectiveness in accurately reflecting patients' experiences and satisfaction.

On the other hand, reliable and validated questionnaires initially developed for outpatient hospital services have not been adequately adapted for primary care contexts, nor have they been sufficiently tested among the Malaysian population or translated and validated into Malay. This gap limits their applicability and relevance, as cultural nuances, linguistic differences and context-specific factors significantly influence patient perceptions and responses to healthcare surveys.

Finally, there is a notable lack of validated questionnaires that comprehensively address both the infrastructure aspects of VC services and the core components of services. Addressing these elements is crucial to gaining a holistic understanding of patient satisfaction and experience, which can drive meaningful improvements in virtual healthcare delivery. For further explanation on this point, it is important to understand that VC provides different dimensions of patient satisfaction and experience. It should not be based solely on theoretical frameworks for technology acceptance and usability, but also on the key or core component of the services.[34] While standard frameworks for patient satisfaction and experience, such as the Scale for Measuring Consumer Perceptions of Service Quality (SERVQUAL) and the Patient's Experience Framework by Picker's Institute Principles, were originally developed for physical services, there is a need to merge these two domains, the core services related to satisfaction and experience with technology usability and acceptance, into a more relevant framework of patient satisfaction and experience with VC services. Ojasalo explains this understanding and concept well in his manuscript on the E-SERVQUAL Model.[35] These are the aspects often neglected by most questionnaires, which tend to concentrate more on technological or infrastructure aspects when assessing satisfaction or experience with VC services.

Recommendation for Future Directions

Development of a Validated Questionnaire for the Malaysian Context

Developing a validated questionnaire tailored specifically to assess patient satisfaction and experience with VC services in Malaysian primary care settings requires a systematic approach. Initially, a comprehensive literature review should be conducted to identify existing validated instruments and theoretical frameworks such as SERVQUAL, the TAM and Picker's Principles, ensuring comprehensive coverage of patient satisfaction and experience domains. Following this, qualitative methods involving focus groups or interviews with stakeholders, including patients, healthcare providers, and administrators, should be utilised to ensure cultural appropriateness and context specificity. The questionnaire development process would benefit significantly from an expert panel review, comprising clinicians, public health specialists, telehealth experts, and psychometricians, to ensure robust content validity.

After developing the initial questionnaire, pilot testing among representative patient populations is critical for assessing clarity, comprehensiveness, and practical applicability. Statistical methods, including item-total correlation and exploratory factor analysis, should be conducted to evaluate item reliability and internal consistency. Subsequently, confirmatory factor analysis (CFA) must be performed to validate the questionnaire's underlying structure. Reliability tests such as Cronbach's alpha and test-retest reliability assessments will further establish the questionnaire's stability. Given Malaysia's multicultural context, a rigorous forward-and-backwards translation process to Malay and other prevalent local languages is essential to guarantee linguistic appropriateness and cross-cultural relevance.

Policy Implications for Enhancing Virtual Consultation Services

Implementing validated instruments for assessing patient satisfaction and experience carries significant policy implications. Firstly, the consistent use of validated tools supports the systematic identification and rectification of service quality gaps, facilitating targeted improvements and promoting patient-centred care. Policymakers can utilise data from these assessments for informed strategic planning, efficiently directing resources towards priority areas such as technology infrastructure, network stability, and digital skills training for healthcare providers.

Furthermore, standardised questionnaires enable benchmarking across clinics, thus encouraging the establishment of uniform service quality standards nationwide. This facilitates regulatory oversight and continuous monitoring, contributing to service accountability and transparency. Policy frameworks should also address ethical and regulatory considerations related to VCs, including patient privacy, data security, consent, digital equity, and literacy disparities.

Finally, validated patient feedback should guide continuous professional development programs. Health authorities should emphasise ongoing training for healthcare providers in effective digital communication, cultural competency, and technological proficiency, ensuring comprehensive and high-quality patient-provider interactions in virtual care settings.

CONCLUSION

The importance, relevance and demand for VC services have noticeably risen in recent years. The MOH in Malaysia has observed a rising trend in the establishment of health clinics that offer VC services, as well as an expansion of the services these clinics provide. Given the increasing use of VCs in primary healthcare, evaluating patient satisfaction and experience is essential to ensure that these services meet patients' needs and provide high-quality care. Despite the importance of evaluating patient satisfaction and

experience, there is a lack of rigorous research and validated instruments specifically designed to measure these aspects for VC services provided by government health clinics in Malaysia. In Malaysia, the development of a self-administered questionnaire must consider the unique cultural, linguistic and social dynamics that characterise the Malaysian population. A self-administered questionnaire is a valuable tool for collecting data efficiently and effectively, particularly in a diverse society where respondents may have varying literacy levels and familiarity with academic language. The design of such a questionnaire should prioritise simplicity and clarity, using layman's terms to ensure that all participants can understand and respond accurately.

The proposed comprehensive framework for assessing patient satisfaction and experience with VC services presents an influential opportunity to shape Malaysia's national digital health policy. Its robust, culturally sensitive approach provides systematic, patient-centred feedback crucial for evidence-based policymaking. By standardizing evaluation methods, Malaysian health authorities can establish clear quality benchmarks for clinics nationwide, enabling comparative performance analysis, transparency and targeted interventions. Significantly, this framework integrates critical clinical care dimensions—such as patient-provider communication, diagnostic confidence, continuity and coordination—alongside technological usability, ensuring telehealth services are both clinically effective and culturally responsive. Embedding this framework into healthcare provider training further enhances telehealth effectiveness and aligns with Malaysia's Digitalization Strategic Plan (2021–2025), promoting sustained improvements in patient outcomes and national healthcare quality standards.

Therefore, there is a pressing need to develop and validate comprehensive patient satisfaction and patient experience questionnaires customised for VC services for the Malaysian population.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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Changes in fundus by optical coherence tomography in patients with chronic obstructive pulmonary disease: A systematic review

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) exerts a negative impact on various tissues and organs throughout the body due to chronic hypoxia. The retina and choroid are implicated in this process, and the application of optical coherence tomography (OCT) enables the detection of potential changes in the fundus. This study aims to explore and discuss OCT-assisted fundus alterations in individuals with COPD by undertaking a systematic review.

Materials and Methods: A systematic review of the literature was conducted in adherence to the PRISMA checklist. Exclusion criteria encompassed articles published in non–peer-reviewed journals or unpublished literature. Consistent criteria were applied during both the title-and-abstract screening and full-text screening phases. Inclusion criteria comprised research conducted in the English language and published after 1993. Selection criteria were articulated in accordance with PICOS. Articles falling within the purview of meta-analyses, systematic reviews, guidelines, case reports, pilot studies, and non-human studies (e.g., laboratory research) were excluded from consideration.

Results: A total of 68 articles were initially identified, 10 reports met inclusion criteria and were included in qualitative analysis. In Turkey were conducted 8 studies and 2 studies in Egypt. All the studies included are case-control designed. Above-mentioned changes in retina were studied in 10 cases and found in 8 of them. In the same time changes in choroid were studied in 9 cases and found in 6 of them.

Conclusions: The findings of this systematic review indicate that, as observed through OCT, chronic hypoxia and systemic inflammation resulting from COPD predominantly impact the retina and choroid.

KEYWORDS:
OCT, COPD, hypoxia, retina, choroid

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the most important causes of morbidity and mortality today. COPD is projected to become the third leading cause of death worldwide by 2030.[1] This condition poses a substantial public health issue, significantly burdening healthcare systems worldwide.[2] COPD may affect up to 10% of the general population with some significant contrasting prevalence in men and women[3], where the former are most exposed due to high smoking prevalence, occupational exposures4 and late admission for care, especially in the developing countries. Some population-based studies estimate that only one in four COPD patients know of the condition and receive a timely diagnosis.[5] COPD is a progressive chronic condition and affects almost all organs, leading to dramatic decrease in health-related quality of life and colossal costs for healthcare. One of these target organs can be retina and other ocular structures.[6-13] The retina, a crucial part of the eye, shares its embryonic origins with the brain, forming from the diencephalon.[12] Eye, retinal, and choroidal cells exhibit structural and mechanistic similarities with central nervous system cells.[13]

Distinguishing features of retinal circulation include a greater difference in oxygen content between arteries and veins, lower arteriolar saturation, and almost double the oxygen extraction from arterial blood compared to most body tissues.[14-15] The retina receives blood from two sources: the inner six layers are nourished by branches of the central retinal artery (a branch of arteria ophthalmica), while the outer layers are supplied by the choriocapillary layer of the choroid. Branches of the central retinal artery and vein traverse the nerve fiber and ganglion cell layers, forming a capillary network, that is the most prominent in the posterior retina.[16-18] This network lies between the feeding artery and draining vein. Retinal capillaries arise from precapillaries in the nerve fiber layer, creating a network at the junction of the outer plexiform and inner nuclear layers. The walls of retinal capillaries, similar to those in the brain, consist of a basement membrane and a non-fenestrated epithelium.

Approximately 98% of eye's blood flow occurs in the choroid, with 85% in the choriocapillary layer, which supplies the retinal pigment epithelium and outer retina. Choroidal circulation is characterized by high velocity, low oxygen extraction, and low resistance, regulated by the sympathetic nervous system, making it more responsive to systemic vascular changes than retinal vessels. Hypoxia's negative impact can lead to damage in retinal and choroidal cells.[19-26] Given the retina's heightened sensitivity to chronic hypoxia, fundus examination proves relevant for diagnosing and

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tracking the progression of diseases like chronic obstructive pulmonary disease, diabetes, hypertensive retinopathy, among others.[27-36]

Routine fundus examination methods encompass direct and indirect ophthalmoscopy. For a more detailed assessment, especially in diseases necessitating early detection, optical coherence tomography (OCT) serves as a valuable tool. Since its introduction in 1993, OCT employs non-invasive, intravital infrared radiation to provide a layer-by-layer assessment of eye structures. Its extensive research potential extends beyond ophthalmology into general medicine, facilitating early disease identification and prevention of irreversible tissue and organ changes.[19,37]

Numerous studies have explored the association between OCT-assisted fundus findings and somatic diseases.[19,38-42] Although, there is a noticeable lack of a comprehensive review specifically examining the relationship between OCT findings and chronic hypoxia in individuals with COPD. This study aims to address this gap by conducting a systematic narrative review of OCT-assisted fundus changes in patients with COPD.

MATERIALS AND METHODS

Literature search strategy

A systematic review of the literature was meticulously conducted following the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[43] checklist (Figure 1). Prior to initiating the review, the authors established internal protocols outlining the search strategy, selection criteria, and procedures for data extraction. Two authors independently conducted searches on Pubmed and MEDLINE. The search strategy incorporated specific terms of interest, with the search string adapted to include database-specific filters and relevant search terms. The search strings employed were: ((OCT) AND (retina)) AND (COPD), ((OCT) AND (retina)) AND (chronic obstructive pulmonary disease), ((optical coherence tomography) AND (retina)) AND (COPD), ((optical coherence tomography) AND (retina)) AND (chronic obstructive pulmonary disease), ((OCT) AND (choroid)) AND (COPD), ((OCT) AND (choroid)) AND (chronic obstructive pulmonary disease), ((optical coherence tomography) AND (choroid)) AND (COPD), ((optical coherence tomography) AND (choroid)) AND (chronic obstructive pulmonary disease). The search results were last updated on May 10, 2022. Any discrepancies between reviewers were resolved through discussion.

Inclusion and exclusion criteria

Articles published in non–peer-reviewed journals or unpublished literature were systematically excluded from this review. Consistent criteria were applied during both the title-and-abstract and full-text screening phases. Research conducted in the English language and published after the year 1993 was considered for inclusion. The selection criteria were defined in accordance with Population, Intervention, Comparison, Outcome, Study Design.[44] Exclusion criteria involved evidence from meta-analyses, systematic reviews, guidelines, case reports, pilot studies, and non-human studies (e.g., laboratory research). The exclusion of studies was executed following a thorough review of abstracts. Subsequently, articles were manually examined to eliminate those associated with other methods of ophthalmological assessment, oncology, pediatric cases, studies involving healthy subjects, separate diseases, lifestyle-related studies not directly related to disease, and studies lacking measurements of hypoxia signs in the retina or choroid. Both prospective and retrospective studies were considered in the review. Unspecified information in the abstract regarding any of the criteria did not automatically lead to exclusion during the title-and-abstract phase. In such cases, the full text was scrutinized before making a determination on inclusion or exclusion.

Data extraction

The process of data extraction and quality assessment was conducted independently by two reviewers. The information extracted from each study encompassed bibliographic details (authors and year of publication), the number of eyes included, patients' age, gender distribution, concomitant pathology, and pathological changes observed in the retina and/or choroid. Studies lacking any of the aforementioned information were excluded from consideration.

RESULTS

Initially, 68 articles were identified, and after eliminating 46 duplicates, 22 publications remained. Subsequently, 7 articles were excluded during the screening process for the following reasons: study type (n=2), non-English language (n=1), studies unrelated to COPD (n=4). This left 15 publications for full-text review, and 5 of them were excluded for the following reasons: utilization of another assessment method (n=3), studies involving children (n=1), and non-English language (n=1). Ultimately, 10 reports met the inclusion criteria and were included in the qualitative analysis (Fig. 1). Quality assessment utilized checklists with responses of 'yes,' 'no,' or 'unclear' to eight questions, each signifying whether the study met specific quality criteria. All 10 studies clearly articulated their objectives. Among these, 8 studies were conducted in Turkey, and 2 studies were conducted in Egypt, all following a case-control design. The age range of participants was 43-80 years, with children defined as individuals under the age of 18. Gender information was absent in only one study. Five studies categorized patients based on the severity of COPD, while the remaining five did not consider COPD severity. Changes in the thickness of any quadrant of the retina and/or choroid were considered indicative of the effects of COPD. The fundamental characteristics of the included studies are summarized in Table I, with more detailed information available in Table II.

Overall, most included studies concluded that COPD patients exhibited changes in both retina and choroid compared to healthy controls, but these differences did not reach statistical significance in all studies. Thus, retinal changes were found in eight out of ten studies. In those eight studies, where statistically significant differences in COPD patients compared to controls were identified, seven studies consistently showed retina thinning, whereas the remaining study showed the opposite effect, with retinal thickening in COPD patients. The country of origin did not affect such

Table I: Characteristics of the included studies

Author	Country	Sample size	Age range	Gender (m/w)	Division to groups according to the severity of COPD**	Effects of COPD	
						Retina	Choroid
M. Ozcimen et al. (2015)[49]	Turkey	73 (50)*	57-73	45/28	No	Was indicated significant changes	Studied, without
E. Ugurlu et al. (2016)[50]	Turkey	43 (31)*	53-73	43/0	No	Was indicated significant changes	Studied, without
M. Gok et al. (2017)[7]	Turkey	79 (71)*	51-73	59/20	Yes	Was indicated	Studied, without significant changes
O. Kocamıs and D. Zorlu (2018)[52]	Turkey	60 (23)*	56-72	N/A	Yes	Studied, without significant changes	Was indicated
M. Gunduz et al. (2019)[51]	Turkey	30 (29)*	50-70	26/4	No	Was indicated	Not studied
Mai G. Abd El-Naser et al. (2019)[45]	Egypt	40 (20)*	52-62	33/7	Yes	Was indicated	Was indicated
N. Ogan et al. (2019)[46]	Turkey	48 (40)*	50-80	38/10	Yes	Was indicated	Was indicated
S. Alim et al. (2019)[53]	Turkey	26 (26)*	50-68	26/0	No	Studied, without significant changes	Was indicated
P. Ozer and N. Ogan (2020)[47]	Turkey	55 (48)*	56-78	39/16	No	Was indicated	Was indicated
Noha Othman Ahmed et al. (2021)[48]	Egypt	50 (50)*	43-60	42/8	Yes	Was indicated	Was indicated

*Control group
** COPD - Chronic obstructive pulmonary disease

Table II: COPD*-associated changes by OCT

Author	COPD-associated retinal changes	COPD-associated choroidal changes
M. Ozcimen et al. (2015)[49]	Average RNFL** thickness was significantly lower in COPD patients (p=0.044).	SFCT*** measurements of the COPD group were lower than the control group; but did not show any statistical significance (p = 0.111).
E. Ugurlu et al. (2016)[50]	Changes in all parts of the retina, but statistically significant changes only in the inferior quadrant (p=0.003). The inferior quadrant RNFL was significantly thinner in the COPD group.	The mean SFCT was found to be similar in both groups, COPD and control.
M. Gok et al. (2017)[7]	Statistically significant changes in the mean value of all RNFL quadrants (p = 0.023) and the nasal segment of RNFL (p = 0.027); separately, other RNFL quadrants did not show statistically significant results in comparison with the control group. RNFL thickness was lower in COPD group.	The macular choroidal thickness at all locations were somewhat lower in both patient subgroups compared with the control group, but statistical significance was not attained (p=0.536).
O. Kocamıs and D. Zorlu (2018)[52]	No statistically significant difference was present between the mean RNFL of the COPD patients and the control group.	SFCT of the COPD patients in both the exacerbation and stable groups was found to be statistically significantly thinner than the control group (p = 0.047 and p = 0.046, respectively).
M. Gunduz et al. (2019)[51]	The average and superior quadrant RNFL thickness parameters were found to be significantly thicker in COPD subjects compared to the control subjects (p<0.05).	Not studied.
Mai G. Abd El-Naser et al. (2019)[45]	RNFL was significantly thinner in the COPD groups than the control group in all quadrants (except the superior one) and in the average values (p<0.001). When comparing group 1a (mild to moderate COPD group) and group 1b (severe to very severe COPD group), was found a statistically significant thinning in the RNFL in inferior and temporal quadrants in group 1b (severe to very severe COPD group).	SFCT was significantly thinner in the COPD groups compared to the control group. The thinnest SFCT was observed in group 1b (severe to very severe COPD group) compared to control group and group 1a (mild to moderate COPD group). These differences were statistically highly significant (p<0.001).
N. Ogan et al. (2019)[46]	Statistically significant thinning of RNFL in the inferior (p<0.001) and temporal (p=0.009) quadrants.	Significant thinning in the thickness of the choroid (p < 0.001) in severe COPD patients compared with mild COPD and the control group.
S. Alim et al. (2019)[53]	There was no statistically significant difference between patients and control group regarding mean, superior, nasal, inferior, and temporal RNFL thicknesses.	SFCT measurements revealed a statistically significant lower results in COPD patients versus the control group (p<0.05).
P. Ozer and N. Ogan (2020)[47]	Inferior RNFL was lower than control during the initial and sixth month examination (p=0.002, p<0.001, respectively). Average RNFL was lower in COPD patients in sixth month examination (p=0.020).	Average SFCT was lower in COPD patients at the sixth month examination (p = 0.015).
Noha Othman Ahmed et al. (2021)[48]	The thickness of the superior, inferior, and temporal RNFL thickness was statistically decreased significantly in the patients with higher GOLD classification (p-value 0.001).	SFCT thinning showed a highly statistically significant thinning with the higher GOLD classification (p-value of 0.001)

* COPD - Chronic obstructive pulmonary disease
** RNFL – Retinal nerve fiber layer
*** SFCT - Subfoveal choroidal thickness

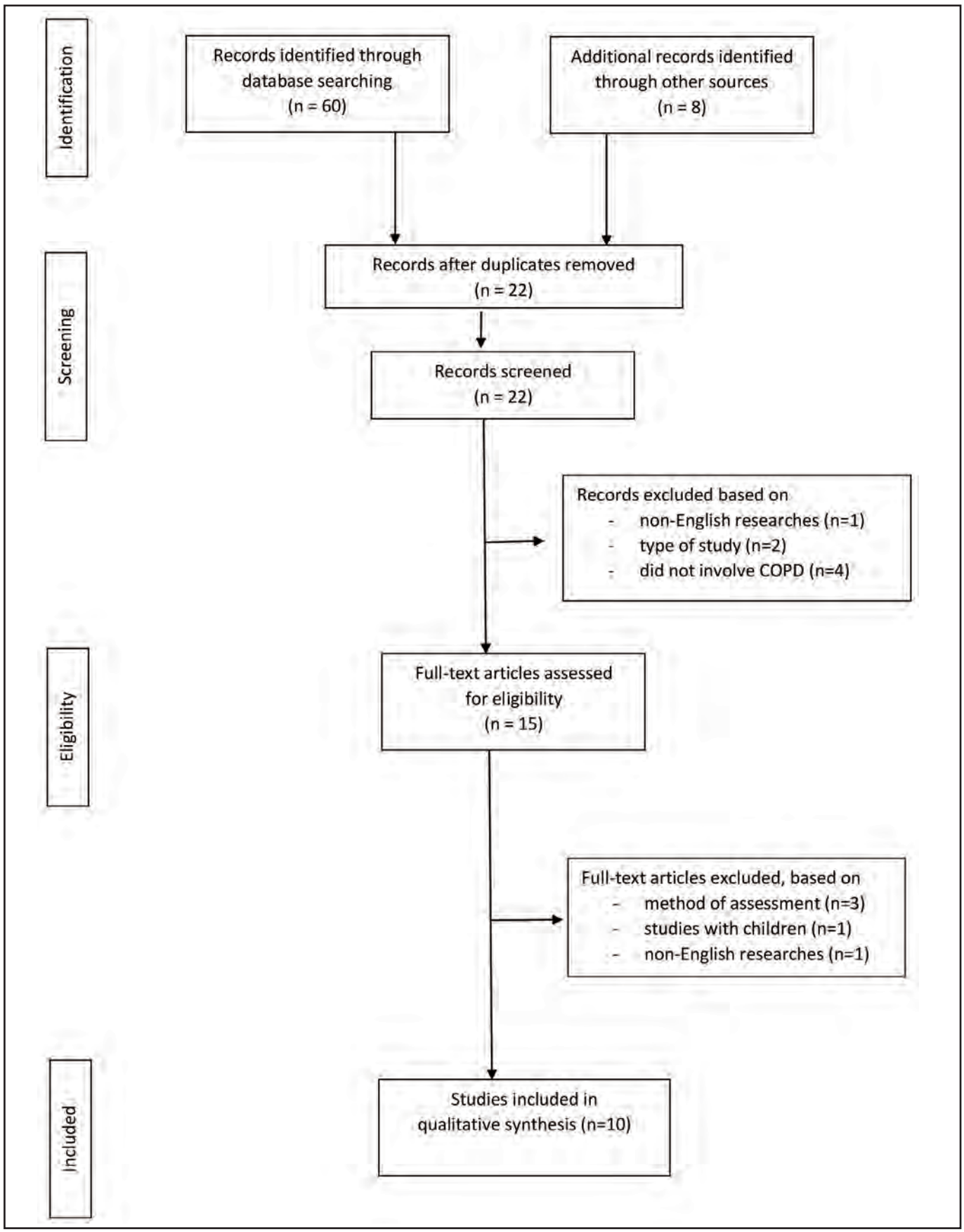

Fig. 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart of the process of study selection. Retrieved from Moher et al. (2009).

finding, because reports with consistently thinner retina in COPD patients were not only from Turkey, but from Egypt as well. Furthermore, location of such retina thinning could differ between studies. Finally, we found no differences in sample size, sex distribution or other attributes between studies showing thinner retina in COPD patients compared to those with thicker retina or no effect. We, therefore, conclude that some association between COPD and retina thinning is present.

With regard to choroid, all studies demonstrated either thinner choroid or no effect with no reports confirming the opposite effect. Thus, six studies out of nine with some choroid thickness data (66%), demonstrated thinner choroid in COPD patients, and in some studies the effect was also associated with COPD severity. Moreover, when studies showing a correlation between COPD and choroidal thickness were compared to those showing no correlation, we did not confirm differences in either sample size of the distribution. We thus conclude that some association between COPD and choroid thickness is likely.

DISCUSSION

The aim of this review was to elucidate the role of OCT in detecting changes in the retina and choroid attributed to COPD. To the best of our knowledge, this study represents the first systematic review on the application of OCT in assessing the fundus of patients with COPD. The qualitative analysis encompassed 10 studies, which utilized OCT to identify changes in the retina, choroid, or both. Four publications[45-48] reported statistically significant COPD-induced changes in both the retina and choroid. Changes in the retina alone were significant in four studies[7,49-51], while alterations in the choroid alone were observed in two manuscripts.[52-53]

The first metric we tested in our paper was retinal thickness. Retinal thickening was observed in one study[49], thinning in seven studies[7,45-50], and no changes in two studies.[52,53] The study by Gunduz et al. (2019)[51] attributed thickening to hypoxia/ischemia-induced retinal and optic disc edema, potentially masking peripapillary Retinal Nerve Fiber Layer (RNFL) loss associated with retinal ganglion cell death. Conversely, studies by Ozkan Kocamış and Duygu Zorlu (2018)[52] and S. Alim et al. (2019)[53] showed no changes in RNFL thickness, with sample sizes of 60 and 26 patients, respectively. The study by S. Alim et al. (2019)[53] did not include group divisions among COPD patients. In the other seven studies[7,45-50], thinning of RNFL in COPD patients was attributed to systemic inflammation and chronic hypoxia, with larger sample sizes (40 patients and above) and variations in the severity of COPD.

Choroidal thickness, the second metric under study in our analysis, was examined in six studies[45-48,52,53], and no changes were identified in three studies.[7,49,50] Thinning in six studies was explained by impaired choroidal vascular autoregulatory mechanisms or chronic hypoxia-induced increase in vascular resistance in COPD patients. The absence of changes in choroidal thickness in three studies might be attributed to small sample sizes and heterogeneity of COPD stages. Such findings need a deeper insight into the potential mechanism of the association, and the latter can be explained with the changes in blood flow, which develop gradually in COPD patients.

All included studies were published from only two countries, Turkey and Egypt, neglecting some potential association of COPD with eye pathology in other countries. The findings of our analysis should be interpreted with caution given that patients included did not have concomitant decompensated somatic pathologies, ophthalmological pathologies (a history of prior laser and intraocular surgeries, glaucoma, optic neuropathy, amblyopia, advanced cataracts, spherical equivalent refractive errors (RE) greater than ± 3.0 diopters, axial length (AL) over 25 mm, choroidal neovascularization or myopic degeneration, clinically significant opacities in the ocular media, and poor-quality images due to unstable fixation). Therefore, these findings cannot be generalized to the entire cohort of the world COPD population, which usually exhibits high heterogeneity in terms of comorbidities, COPD severity and compensation, as well as some interaction with other medications taken for the concomitant conditions. In addition, other confounders may affect the overall effect, including cigarette smoking, electronic cigarette use, secondhand smoke, leisure physical activity, occupational exposures, air pollution, and all these confounders may be hard to control and classify. Together with some unmeasured confounding usually present in epidemiological studies, these attributes may seriously bias the association, and we consider this a limitation of our analysis.

Cigarette smoking and electronic cigarette use deserves special attention in COPD patients and the associated changes in the eye fundus. From the current data, it is unclear whether the changes reflect the general smoking-related vascular pathology or, alternatively, COPD as a chronic condition. Smoking itself is a strong predictor of retinal vascular changes[54-55]; therefore, future studies should stratify all COPD patients based on their smoking status, and retinal abnormalities must be assessed separately in those who have never smoked and current daily smokers, including those amongst COPD patients.

Another limitation of our study is the overall small sample size. COPD is a prevalent disease, and millions of people in the world should be diagnosed with the condition; nevertheless, only very few COPD patients are included in the studies involving OCT, because eye involvement traditionally gets little attention in these patients. None of included studies enrolled more than 100 COPD patients, and this indeed necessitates larger studies with greater samples for greater statistical power. One more limitation in this analysis is heterogeneity between studies with regard to COPD severity and clinical attributes. COPD is a disease with contrasting clinical severity between patients, which may differ in the number of hospitalizations, severity of daily symptoms, use of medications, physical exercise tolerance, health-related quality of life, and even need for oxygen. Clear stratification into groups with varying clinical severity and even spirometry in these studies was challenging.

Future studies are needed to establish stronger, more consistent evidence in more homogenous groups of COPD

patients. Longitudinal studies with larger cohorts, standardized protocols for OCT imaging, and control for confounding variables (e.g., comorbidities, smoking status, medications use, etc.) will be critical to determine whether OCT can serve as a reliable marker of COPD severity. The future trajectory of OCT devices, including advancements like OCT angiography (OCTA) and Doppler OCT (FD OCT), holds promising potential for diverse clinical applications, transcending the realm of ophthalmology. This evolution is likely to open new frontiers in understanding and managing COPD and various diseases across medical disciplines.

CONCLUSION

This systematic review underscores that chronic hypoxia and systemic inflammation resulting from COPD likely impact the retina and choroid, with more pronounced changes observed in advanced stages of the disease. The widespread adoption of OCT devices extends beyond ophthalmology, enabling not only ophthalmologists but also specialists from diverse fields such as physicians, cardiologists, endocrinologists, and pulmonologists to confirm or monitor changes in the underlying disease.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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SYSTEMATIC / NARRATIVE REVIEW ARTICLE

Assessing male involvement in family planning: A scoping review of prevalence and its associated factors

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ABSTRACT

Introduction: Family planning (FP) is a key component of the Safe Motherhood Program, aimed at reducing maternal mortality and morbidity. Male involvement in FP is increasingly recognized as essential for improving reproductive health outcomes through shared decision-making and spousal collaboration. This scoping review aimed to assess the prevalence of male involvement in family planning and identify the factors that influence their participation.

Materials and Methods: A literature search was conducted in ProQuest, PubMed, and Scopus for peer-reviewed articles published between 2014 and 2024. Eligible studies reported on the prevalence and determinants of male involvement in FP. Two reviewers independently screened articles and extracted data. Findings were synthesised descriptively and thematically.

Results: Eight studies met the inclusion criteria. Reported male involvement in FP varied widely, ranging from 8.4% to 80%. Key influencing factors included education level, access to FP information, number of children, spousal communication, and attitudes towards contraception. Barriers included cultural norms, limited male-targeted services, and misconceptions about FP.

Conclusion: Male involvement in family planning remains inconsistent across regions. Targeted educational and community-based interventions are essential to enhance men's engagement in reproductive health and improve FP outcomes.

KEYWORDS:
Family planning, contraception, male, involvement, prevalence, factors, determinants, reproductive health

INTRODUCTION

Family planning (FP), or contraception, refers to the intentional prevention of pregnancy using various methods, including devices, medications, sexual practices, or surgical procedures. These methods are typically classified as modern or traditional.[1-2] According to the World Health Organization (WHO), family planning enables individuals and couples to achieve their reproductive goals and exercise their right to decide freely whether or not to have children.[2] FP is a cornerstone of the Safe Motherhood Program and plays a critical role in reducing maternal mortality and morbidity. It also helps prevent unplanned pregnancies, protects women's reproductive rights, and improves child health and nutrition through optimal birth spacing.[3]

Reproductive health is a shared responsibility between men and women. Increasing male involvement in family planning is essential for improving maternal health and achieving the Sustainable Development Goals (SDGs), particularly those related to reducing maternal mortality.[4] Male involvement in family planning refers to any organisational measures explicitly targeted at males to promote the acceptance and adoption of FP among either sex. It includes males engaging in decision-making, endorsing it, or encouraging their spouse to use FP.[5] Another definition of male involvement with family planning is defined as participation in at least one of the following activities: conversation or spousal communication, support, approval, and use of contraceptives by the husband.[6]

Malaysia's contraceptive utilisation is lower than that of several Southeast Asian counterparts, such as Singapore, the Philippines, Thailand, Indonesia, and Vietnam. In 2010, Malaysians had a birth control prevalence rate of 51.7%, which was relatively low when compared to Thailand, Singapore, and Vietnam, which had rates of more than 70.0% adoption.[3] It is important to note that countries like Myanmar and Malaysia report minimal usage of modern contraception, despite having low total fertility rates (TFRs). This discrepancy implies that TFR alone is an insufficient proxy for contraceptive access, underscoring the necessity of a more complex comprehension of reproductive health transitions in these societies.[7] According to the Confidential Enquiries into Maternal Deaths (CEMD) Malaysia Report 2001–2005, up to 70% of maternal deaths occurred without any form of family planning. A key but often overlooked issue in Malaysia's FP efforts is the lack of male engagement, gender awareness, and shared responsibility between partners.[8]

Male engagement in contraceptives increases spousal collaboration and decreases opposition, which enhances women's uptake and continuity of family planning techniques.4 Several studies in high- and middle-income

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countries have found a substantial link between male engagement and an increase in contraceptive adoption and use. According to FP studies, male engagement is strongly connected with access to media, especially television and radio, spouse work status, and average monthly income.[9] Few studies have identified barriers to male engagement in family planning. Still, most prior research has been conducted in urban settings, which differ from rural settings in socio-demographic and behavioural aspects.[4]

This scoping review was conducted to address a critical gap in understanding the role of men in family planning, particularly in low- and middle-income countries where male engagement remains limited and under-researched. Despite ongoing global and national efforts to improve reproductive health outcomes, male involvement has often been overlooked in both policy and practice. Malaysia, for example, reports relatively low modern contraceptive usage, and few studies have focused on men's participation in FP decision-making. Recognising that men often play a decisive role in reproductive choices, especially in patriarchal societies, this review was designed to map existing evidence on the prevalence of male involvement in family planning and to identify the key factors that influence such involvement. This work forms part of a broader initiative aimed at informing future interventions and health education programs that promote gender-equitable participation in reproductive health. By synthesising existing literature, the review aims to guide researchers, healthcare providers, and policymakers in developing targeted strategies to enhance male engagement in FP services and ultimately improve maternal and child health outcomes. Hence, this scoping review aimed to assess the prevalence of male involvement in FP activities and its associated factors.

MATERIALS AND METHODS

Data sources and searches

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist was used to complete the review. A comprehensive search was conducted in the ProQuest, PubMed, and Scopus databases on March 23, 2025, and was restricted to reviews published in English between December 31, 2014, and December 31, 2024. The search keywords were tailored to each database.

Search Terms and Strategy Used in This Scoping Review

The following generic search string was adapted for each database:

("male involvement" OR "male participation" OR "men participation") AND
("family planning" OR "contraceptive use" OR "reproductive health") AND
("prevalence" OR "factors" OR "determinants" OR "barriers")

Exclusion Criteria:

- Qualitative studies, systematic reviews, or mixed-methods studies without distinct quantitative prevalence data.
- Studies focused exclusively on women or couples where male-specific data could not be separated.
- Non-English publications or those without full-text access.

Study selection and data extraction

Duplicates were removed from the electronic search results after they were exported to Microsoft Excel. The primary reviewer determined which studies should be included. One reviewer extracted data from full-text reviews, with another independently evaluating 20% of these papers to assess eligibility and consistency. Any disagreements about study inclusion were settled with the help of a third reviewer.

Quality Appraisal

Although a formal, tool-based critical appraisal was not an a priori objective of this scoping review, we conducted a brief assessment of methodological rigour to provide context for interpreting the findings. Each included study was examined for: (i) clarity of aims and study design; (ii) sampling strategy and sample size justification; (iii) data collection instruments (e.g., pre-tested or validated questionnaires); and (iv) appropriateness of statistical analyses. All eight studies employed cross-sectional designs with structured or semi-structured questionnaires and reported their objectives, sampling frames, and analytic methods transparently.

RESULTS

In total, 1132 studies were identified through the electronic databases. ProQuest resulted in 593 studies, Scopus produced 242 studies, while PubMed produced 297 studies. After applying restrictions based on full-text availability (393 studies) and duplicates (57 studies), 682 studies were retrieved from the three databases. Then, 654 studies were further removed due to a lack of topical relevance. Twenty-eight studies were assessed for eligibility, of which twenty were excluded because the contents of the articles did not fulfil the inclusion criteria (ten are systematic reviews, seven are qualitative studies, and three are articles studying populations involving women or wives. Finally, eight reviews that fulfilled the eligibility criteria were included based on title and abstract screening.

A total of peer-reviewed articles conducted in several countries were included in this review, namely Malaysia (n=1), Ethiopia (n=4), Uganda (n=1), Malawi and Tanzania (n=1), and Myanmar (n=1). Research findings regarding prevalence and factors associated with male involvement in family planning were reported in Tables II. The prevalence of male participation in family planning varies significantly across different regions of the world, with reported rates ranging from as low as 8.4% in some areas to as high as 80% in others, highlighting the diverse cultural, social, and economic factors that influence men's engagement in reproductive health initiatives. Our reviewed articles indicate that male involvement in family planning is significantly associated with several factors, notably the educational status of married men, which enhances their understanding and engagement in reproductive health. Additionally, their knowledge about family planning plays a crucial role in determining their level of participation. Other important factors include the sources from which men obtain information about family planning, the number of children they currently have, and their overall attitudes towards family planning practices. These elements collectively shape men's involvement and influence the effectiveness of family planning initiatives within various communities.

Eligibility criteria

Table I: Inclusion Criteria

Study design	Quantitative studies using cross-sectional /longitudinal designs
Study population	Currently married men or male partners of women of reproductive age (15–49 years)
Outcomes	Studies reporting the prevalence of male involvement in family planning and its associated factors (e.g., knowledge, attitudes, education, spousal communication)
Geographic scope	No geographic restriction; studies from all regions were eligible
Language	English
Publication type	Peer-reviewed journal articles, reports
Publication date	Between January 2014 and December 2024

Table II: Summary of Included Studies on Male Involvement in Family Planning

Country	Author (Year)	Study Design	Sample Size	Prevalence of Male Involvement	Main Objective	Associated Factors
Ethiopia	Demissie et al. (2021)	Community-based cross-sectional	373	68.1%	To study the level and role of male involvement in FP and describe associated factors.	Education level, sources of FP information, spousal communication, desire to learn FP methods, approval and use of FP by men or their partners.
Ethiopia	Geltore & Lakew (2022)	Community-based cross-sectional	382	69.7%	To assess men's participation in modern FP among married couples in Durame Town.	Education, number of living children, sources of information, knowledge, and attitude.
Uganda	Omona & Mahoro (2023)	Cross-sectional	371	80.0%	To explore factors associated with male participation in postpartum FP in Kampala.	FP approval, FP knowledge, source of information.
Malaysia	Seng Fah et al. (2017)	Cross-sectional	167	39.2%	To identify men's involvement in FP discussions with spouses and associations with socio-economic characteristics.	Older age, higher education, higher income, longer marriage duration.
Malawi & Tanzania	Osuafor et al. (2023)	Cross-sectional using DHS data	10,996	53.0%	To assess male involvement in FP decisions and related determinants in household contexts.	Age 35–54, secondary/higher education, access to media, female-headed household.
Ethiopia (NW)	Kassa et al. (2014)	Semi-structured cross-sectional	524	8.4%	To assess male involvement in FP services and associated factors in Debre Markos.	Low involvement due to lack of information, service inaccessibility, and desire for more children.
Ethiopia (North)	Wondim et al. (2020)	Community-based cross-sectional	620	12.5%	To assess male involvement in FP use and its associated factors in rural communities.	Education (self and partner), positive FP attitude, spousal discussion, FP knowledge (positive), number of children (inverse relationship).
Myanmar	Myint et al. (2021)	Cross-sectional	388	40.7%	To determine male involvement in FP and its association with attitudes and behavioural factors using the Theory of Planned Behaviour.	Positive attitudes, subjective norms, and intention to engage in FP practices.

Despite setting no geographic restrictions in the search strategy, all eight included studies originated from Asia and sub-Saharan Africa. This outcome likely reflects two main factors. First, male involvement in family planning has been a more pressing and studied issue in these regions due to lower contraceptive uptake, higher fertility rates, and deeply rooted gender norms that impact reproductive decision-making. Second, there appears to be limited availability of region-specific quantitative research from high-income countries on this topic, possibly because male engagement in FP is less emphasized or more integrated into broader reproductive health systems in those settings.

Education Level

In this scoping review, five articles indicated a noteworthy correlation between men's participation in family planning initiatives and their educational attainment.[4,10-13] Specifically, the findings suggest that individuals with higher levels of

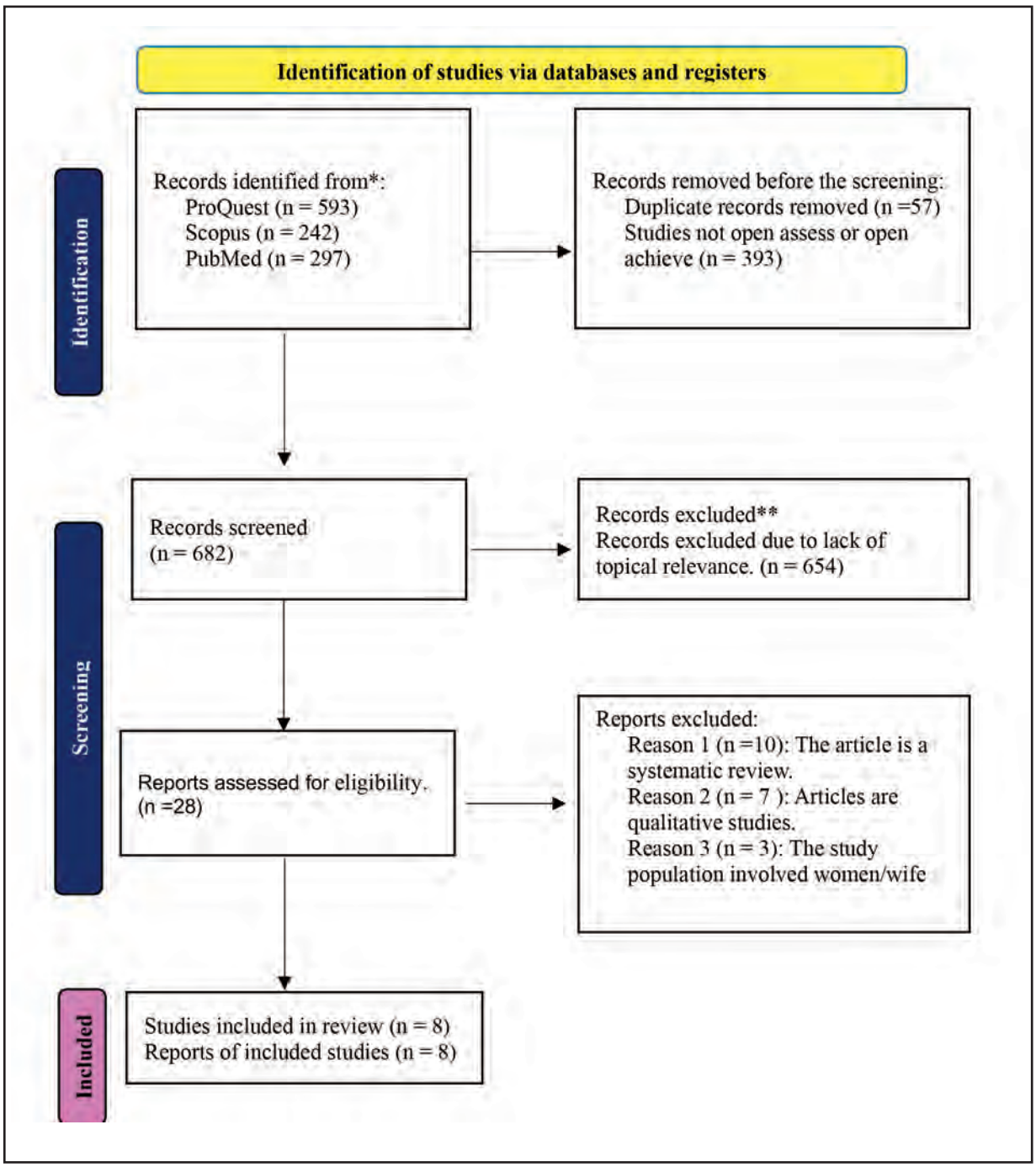

Fig. 1: Literature selection diagram

education are more likely to engage actively in family planning activities. This implies that as educational levels increase, so does the likelihood of men participating in discussions and decision-making processes related to family planning. Consequently, enhancing educational opportunities for men may serve as a crucial strategy for increasing their involvement in family planning, ultimately leading to more informed choices regarding reproductive health.[14-15]

Sources of Information About FP

Five quantitative studies examined sources of information about family planning as a factor for men's involvement in family planning.[10] The role of information sources in shaping men's participation in family planning is critical. Access to accurate and comprehensive information empowers men to engage more actively in reproductive health decisions, fostering better family planning practices. Research indicates that men's awareness of family planning options significantly influences their participation. Studies reveal

that men who receive information from healthcare providers, community programs, or educational campaigns are more likely to support and use family planning methods.

Various information sources, such as workshops, media campaigns, and peer discussions, are vital in informing men about family planning. Effective communication enhances understanding and acceptance of FP methods, thus promoting involvement.[9] Impact on Decision-Making: Male participation in family planning decisions often hinges on the quality and accessibility of information. When men are well-informed, they are more likely to participate in discussions about contraceptive choices, leading to higher usage rates.[16] In conclusion, accessible and reliable information sources are essential for increasing men's involvement in family planning.

Attitude Towards Family Planning

In this scoping review, the attitude of the respondents towards family planning was examined and discussed in three studies.[4,10,13] Research indicates a strong link between positive attitudes toward family planning and male involvement in postpartum family planning. When men actively support and engage in family planning discussions, it can enhance their partners' willingness to adopt contraceptive measures. This involvement is crucial as it not only promotes shared responsibility in reproductive health and empowers women, leading to higher contraceptive uptake.[17]

A positive perspective on family planning among men often translates to better communication and collaboration within couples. Such dynamics can alleviate concerns about contraceptive methods, making women feel more secure in their choices. Moreover, studies have shown that male involvement can significantly improve maternal and child health outcomes by ensuring mutual and well-informed family planning decisions.[18]

DISCUSSION

The primary aim of this paper is to conduct a comprehensive review of the existing literature concerning the prevalence of male involvement in family planning (FP) activities and explore the various factors associated with such involvement. This examination will not only highlight the extent to which men participate in FP initiatives. Still, it will also identify key determinants that influence their engagement, including socio-cultural, economic, and educational factors. By synthesising this information, the paper seeks to provide valuable insights into the role of men in family planning, thereby contributing to the broader discourse on reproductive health and gender dynamics.

This comprehensive review revealed a significant variance in the prevalence of male involvement in family planning across different countries, highlighting the disparities in participation rates and the scarcity of studies conducted in lower-middle-income countries. The variation observed between studies can largely be attributed to differences in research design, evaluation methodologies, and the sociocultural contexts of the studied populations. Among the countries examined, Ethiopia emerged as the most researched, with a robust body of literature, followed closely by Malaysia, Uganda, Malawi, Tanzania, and Myanmar. Notably, the findings indicate that Uganda boasts the highest level of male involvement in family planning, with an impressive participation rate of 80%. In stark contrast, the Northwest region of Ethiopia demonstrates the lowest prevalence, with only 8.4% of men actively participating in family planning initiatives. This striking contrast underscores the need for targeted interventions to enhance male engagement in family planning across various cultural contexts.

In Uganda, recent research indicates a significantly higher level of male involvement in postpartum family planning than the national average. This suggests a growing trend of active participation among men in supporting their partners during the critical period following childbirth.[19] This increase in engagement highlights a shift in societal attitudes towards shared responsibility in reproductive health. It reflects the positive outcomes of various health initiatives promoting collaborative decision-making regarding family planning. Furthermore, this trend signifies a shift in cultural attitudes towards male participation and highlights the positive impact of targeted health education initiatives to foster collaborative family planning efforts.[17] As such, the enhanced male involvement in postpartum family planning represents a crucial development for improving maternal and child health outcomes across the country.[20] However, the existing body of research concerning the prevalence of male involvement in family planning in Malaysia remains insufficient, highlighting a significant gap in understanding how men's participation influences reproductive health outcomes.[14]

In this study, men's involvement in family planning is influenced by various factors, including their education level, the number of children they currently have, the sources of information they rely on, their level of knowledge, and their attitudes towards family planning practices. Each of these elements plays a significant role in shaping men's engagement in reproductive health decisions. Research indicates that men with more children may adopt different perspectives towards family planning than those with fewer or no children. This correlation often arises from a sense of responsibility or the desire for family size control. Men with several children might be more motivated to participate in family planning discussions to avoid financial strain or to ensure better living conditions for their existing children.[12]

A man's knowledge about family planning methods and their benefits directly correlates with his willingness to engage. Increased knowledge empowers men to make informed decisions, dispelling myths surrounding contraceptive use. Studies show that men with comprehensive knowledge are more likely to support their partners in family planning initiatives.[5] Men's attitude towards family planning can either facilitate or hinder their involvement. Positive attitudes, often shaped by cultural, social, or personal beliefs, promote active participation. Men who view family planning as a shared responsibility are more inclined to engage. In contrast, negative perceptions,

often rooted in traditional gender roles, can lead to resistance.[21]

Understanding male partner influence in contraceptive decision-making is crucial not only for influencing individual behaviours but also for advancing broader public health goals.[22] Evidence consistently shows that male involvement in family planning contributes to better maternal and child health outcomes. These findings underscore the importance of adopting holistic approaches that view reproductive health as a shared responsibility between partners.[23] A shared decision-making model, where both partners actively engage in discussions and decisions about contraceptive use, fosters mutual respect, improves communication, and supports more informed and sustainable reproductive choices.[24] Promoting male engagement within this framework not only enhances the effectiveness of family planning programs but also empowers women by reinforcing their autonomy in reproductive health decisions.[25-26]

Several strengths were discovered during this review. First, this scoping review may give a complete overview of the current corpus of research, including a wide range of study designs, approaches, and settings. This is especially beneficial for countries and diverse areas with many distinct people and locations, whose healthcare delivery is influenced by various cultural, economic, and political challenges.

The findings of this review can help policymakers and healthcare providers understand the prevalence and factors associated with male involvement in family planning. This knowledge may lead to better-tailored policies and initiatives that are also more successful overall. Nevertheless, the insights derived from this review will likely enhance our understanding of the prevalence of male involvement in family planning initiatives and the various factors that influence such participation. By exploring these dynamics, we can better comprehend the barriers and facilitators that shape men's roles in reproductive health decisions. This knowledge is crucial for developing targeted interventions that promote greater engagement among men, ultimately contributing to improved family planning outcomes and healthier communities.

This review has several limitations that should be considered when interpreting the findings. First, only eight studies met the inclusion criteria, which limits the breadth and generalisability of the conclusions. The small number of studies may not capture the full diversity of male involvement in family planning across different cultural and socioeconomic settings. As a result, the patterns observed may reflect the specific contexts of the included studies rather than global trends. Second, the review included only articles published in English and indexed in three databases (PubMed, Scopus, and ProQuest), which may have led to the exclusion of relevant studies published in other languages or local journals. Although a supplementary search was performed using Google and Google Scholar, some relevant studies might have been missed, particularly from underrepresented regions. Third, most of the included studies used cross-sectional designs, which are limited in establishing cause-and-effect relationships. In addition, potential biases such as self-reporting, convenience sampling, and varying definitions of "male involvement" across studies could affect the reliability of the reported findings. Despite these limitations, the review provides valuable insights into the prevalence and influencing factors of male participation in family planning and highlights important gaps for future research.

CONCLUSION

In conclusion, the scoping review on male involvement in family planning highlights a critical gap in participation, particularly in various contexts such as Ethiopia and other regions. The prevalence of male involvement remains significantly low, despite the recognized benefits of active participation in reproductive health decisions. Factors influencing this involvement include men's knowledge of family planning options, their attitudes toward reproductive health, and the number of children they currently have.

To enhance male engagement in family planning, targeted educational interventions are essential. These should focus on dispelling myths, improving knowledge about contraceptive methods, and fostering supportive attitudes among men. Additionally, health programs must address the accessibility of information and services to encourage men to take a proactive role in family planning. By recognizing and addressing these factors, stakeholders can promote healthier family dynamics and improve overall community health outcomes.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

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Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios can only predict the severity of COVID-19 if the criteria for a biomarker are met

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We were interested to read the article by Wulandari et al. on a retrospective study on the value of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in predicting the severity of SARS-CoV-2 infection (SC2I) in critically ill patients.[1] In 221 patients diagnosed with severe SC2I infection between August 2021 and March 2022, severe SC2I patients were found to have high NLR and PLR values.[1] The highest NLR and PLR values were found in SC2I patients with renal failure.[1] It was concluded that elevated NLR and PLR levels could serve as potential prognostic markers for predicting disease severity in these patients, especially those with renal disease.[1] The study is encouraging, but some ambiguities should be clarified.

Firstly, the study design is unsuitable for assessing whether NLR and PLR can actually serve as prognostic factors in severely ill COVID-19 patients. The study was retrospective and had no control group.[1] Retrospective designs have several disadvantages: Some data may be missing, the accuracy of the data cannot be easily verified, desired missing or new data can no longer be generated, references to specific studies are often untraceable, and the design does not allow for follow-up studies. A control group is needed to provide a standard of comparison for the trial results. It makes it possible to study the effects of the independent variable alone without adding confounding conditions. During an experiment, a scientist must consider what their independent variable is and what is to be tested.

The second point is that NLR is a very non-specific parameter, as it can be elevated in numerous other diseases (e.g. cholangitis, post-surgery, ischemic stroke, thyroid cancer) and is considered a prognostic factor.[2] Therefore, NLR and PLR can only be considered as a prognostic factor for the severity of critically ill SC2I patients if all these other diseases have been excluded in each of the included patients.

The third point is that the severity of the infection depends not only on parameters reflecting the intensity of the infection, but also on other factors, such as the type and intensity of the immunological response, concomitant diseases and comedications, and genetic background. As far as the immunological response is concerned, the course of SC2I depends strongly on the type of antibodies produced in response to the SARS-CoV-2 virus. This variable immunological response may be responsible for the involvement of organs other than the lungs. These include the brain, heart, endocrine organs, kidneys and gastrointestinal tract. Therefore, we should know whether only patients with lung involvement or also patients with involvement of other organs were included. We should also know whether comorbidities were systematically recorded and to what extent they influenced the NLR and PLR figures.

In summary, it can be said that this interesting study has limitations that relativize the results and their interpretation. Removing these limitations could strengthen the conclusions and reinforce the message of the study. All unanswered questions need to be clarified before readers can uncritically accept the study's conclusions. Before NLR and PLR can be recommended as biomarkers of SC2I severity, their suitability as biomarkers needs to be confirmed by appropriately designed studies.

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