

# Vitamin D status and its association with asthma control and severity in children

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## ABSTRACT

**Introduction:** Vitamin D has an immunomodulatory effect on innate and adaptive immunity within the body, which partially explains its links to inflammation-induced epithelial changes seen in asthma. Various evidence suggest a potential link between vitamin D deficiency and asthma control and severity. This study aimed to determine the vitamin D levels in asthmatic children and their association with asthma severity and control.

**Materials and Methods:** A cross-sectional prospective study was conducted on 72 children with persistent asthma aged 5 to 18 years old in a tertiary hospital in Kelantan. Asthma severity was assessed using the Global Initiative for Asthma (GINA) guidelines based on treatment given. Asthma control was evaluated using both parent/patient self-administered Asthma Control Test (ACT) or Children's Asthma Control Test (c-ACT) scores accordingly to their age and asthma control GINA classification. Serum 25-hydroxyvitamin D [25(OH)D] levels were measured, with <52 nmol/L defined as deficient and 52-73 nmol/L as insufficient.

**Results:** Of the 72 children with persistent asthma, 40.3% had vitamin D deficient and 38.9% had vitamin D insufficient with a mean 25(OH)D level of 58.74 nmol/L. Being female, older age group and higher body mass index (BMI) were associated with vitamin D deficiency ( $p = <0.05$ ). Lower vitamin D levels were significantly associated with increased asthma severity ( $p = 0.020$ ). There was no significant association between vitamin D levels and asthma control based on GINA classification ( $p = 0.470$ ) and c-ACT/ACT scores ( $p = 0.052$ ).

**Conclusion:** High prevalence of vitamin D deficient and insufficient was found among children with persistent asthma. Vitamin D deficiency was significantly associated with increased asthma severity. This group of children needs further evaluation for intervention. We recommend routine assessments of vitamin D levels among children with moderate to severe asthma.

## KEYWORDS:

*Asthma control, asthma severity, children, 25-hydroxyvitamin D, vitamin D*

## INTRODUCTION

According to the World Health Organization (WHO), approximately about 339 million people suffered from

asthma globally and the prevalence continues to rise, particularly among children.<sup>1</sup> Despite advancements in asthma management, achieving optimal control and preventing exacerbations remain ongoing challenges.<sup>2</sup> The global burden of asthma has increased significantly over the past 40 years, particularly among children.<sup>3</sup> This rise in asthma prevalence and severity poses a major public health challenge, necessitating the identification of new risk factors and the development of more effective management strategies. In the Asia-Pacific region, the Asthma Insights and Reality in Asia Pacific (AIRIAP) Phase II study reported that 53.4% of patients under 16 years old had uncontrolled asthma.<sup>4</sup> This high prevalence of uncontrolled asthma highlights the urgent need for improved asthma management approaches in this region. Uncontrolled asthma can lead to frequent exacerbations, hospitalizations, and a decreased quality of life for affected children and their families.<sup>5</sup>

Vitamin D plays a pivotal role in the inflammation pathway by regulating the production of inflammatory cytokines and modulating the activity of various immune cells.<sup>6</sup> This regulatory function is particularly relevant in the pathogenesis of inflammatory diseases, including asthma.<sup>6</sup> Research has shown that children with vitamin D deficiency are at a significantly higher risk for asthma, with one study indicating a 6.3-fold increase in risk compared to those with sufficient vitamin D levels.<sup>7</sup> Vitamin D not only serves as a potential predictor for the development of asthma but also influences its severity and control.<sup>8,9,10</sup> Vitamin D is synthesized in the skin upon exposure to ultraviolet B (UVB) radiation from sunlight and can also be obtained from dietary sources such as fish oils, fish, liver, egg yolks and supplements.<sup>10</sup> Vitamin D status was most accurately determined by measuring 25-hydroxyvitamin D since it is the highest of all metabolites and has half-life of approximately three weeks.<sup>10</sup> Vitamin D deficiency is prevalent globally, even in regions with ample sunlight, due to factors such as limited sun exposure, dietary insufficiency, and cultural practices.<sup>10</sup>

The prevalence of vitamin D deficiency and insufficiency among asthmatic children is alarmingly high.<sup>8-10</sup> A study among urban American youth found that 86% of children with persistent asthma had insufficient or deficient vitamin D levels.<sup>9</sup> Similarly, high prevalence rates have been reported in tropical countries, where adequate sunlight exposure would theoretically prevent vitamin D deficiency.<sup>11</sup> This paradox highlights the need for further investigation into underlying

*This article was accepted: 23 June 2025*

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factors contributing to vitamin D deficiency in these populations.

Deficiency in vitamin D has been associated with increased asthma exacerbations, heightened airway inflammation, decreased lung function, and poor asthma control in children.<sup>12</sup> Additionally, studies have shown that children with moderate to severe persistent asthma have significantly lower vitamin D levels compared to those with intermittent asthma.<sup>13</sup> The beneficial effects of vitamin D on asthma may be explained by its role in enhancing glucocorticoid responsiveness, promoting regulatory immune cell phenotypes, reducing infection rates, mitigating airway remodelling, and lowering eosinophilia and IgE levels.<sup>14</sup> However, some studies have reported conflicting results, showing either no effect or adverse effects of vitamin D on asthma incidence and severity.<sup>10-12</sup> This inconsistency makes the relationship between vitamin D levels and asthma unclear.

Surprisingly, vitamin D deficiency is prevalent even in tropical countries with abundant sunlight. In Malaysia, for example, a study among adults in Kuala Lumpur found that 67.4% had vitamin D deficiency, with Indian participants showing the highest prevalence.<sup>15</sup> Similar findings were shown among children and adolescents. A significant study involving 1361 adolescents aged 12 to 13 years old in Perak, Selangor, and Kuala Lumpur found that 78.9% had vitamin D deficiency, with only 7.4% had adequate levels of vitamin D.<sup>16</sup> The South-East Asian Nutrition Survey (SEANUTS) also reported that 47.5% of children aged four to twelve years had low vitamin D levels, with a higher prevalence among girls (54.1%) compared to boys (41.1%).<sup>17</sup>

To date there is no local data available on the association between vitamin D deficient/insufficient with asthma severity and asthma control in Malaysian children. It is important to identify asthmatic children with vitamin D deficient/insufficient as supplementation of vitamin D as an adjunct treatment may help to improve the control of asthma.

## MATERIALS AND METHODS

The study protocol received approval from the Medical Research & Ethics Committee Kementerian Kesihatan Malaysia (NMRR ID-22-02416-RVC (IIR)) and Research Ethics Committee Universiti Kebangsaan Malaysia (JEP-2022-694). All participants or their guardians provided informed consent and assent.

### Study design and participants

This cross-sectional prospective study was conducted at Paediatric clinic Hospital Raja Perempuan Zainab II (HRPZII), Kota Bharu, Kelantan from December 2022 to December 2023. The inclusion criteria included children with persistent asthma, aged 5 to 18 years, on preventer medications for at least 3 months duration. Exclusion criteria comprised children who were taking vitamin D supplements or had other chronic conditions such as other respiratory disease, congenital heart disease with heart failure, malabsorption, malignancy, chronic haematological disease,

immunological disease, chronic kidney disease, or liver disease.

We recorded the demographic data of the study population, including age, gender, Centers for Disease Control (CDC) body mass index (BMI) for age percentile, parents' education level, and household income. Factors affecting vitamin D levels, such as weekly sunlight exposure, duration of physical activity, and weekly dietary intake of vitamin D-enriched foods, were also noted via direct interview using a questionnaire. Vitamin D-enriched foods include eggs, oily fish, cheese and mushrooms.

Asthma severity was determined from the level of treatment required to control symptoms and exacerbations based on the Global Initiative for Asthma (GINA) asthma treatment strategy 2023.<sup>18</sup> Data on current medication required to control symptoms and exacerbations were recorded and the severity of asthma was assessed by the attending clinician. Participants were categorised into mild persistent, moderate persistent and severe persistent asthma.

Asthma control was determined by both GINA classification criteria via direct interview the researcher and parents/patient self-administered Asthma Control Test (ACT) questionnaire<sup>19</sup> for children more than 12 years old, or Childhood Asthma Control Test (c-ACT) questionnaire<sup>20</sup> for children aged 4-11 years old. The questionnaire was based on the symptoms over the last 4 weeks. Additionally, the number of hospitalisations and Emergency Department visits due to asthma in the past 12 months was recorded. Asthma control was classified into well-controlled, partly controlled, and uncontrolled asthma.

Blood samples were obtained to measure serum 25-hydroxyvitamin D [25(OH)D] levels and bone profile parameters, including serum calcium (Ca), phosphate (PO<sub>4</sub>), alkaline phosphatase (ALP), and magnesium (Mg). Since the Pathology Laboratory at HRPZ II couldn't process the 25(OH)D levels, the samples were stored at 2-8°C and transported to the Pathology Laboratory at Hospital Putrajaya for analysis twice a week. The results were then uploaded into the Patient Management System (SPPv3) application. Vitamin D status was classified as deficient (<52 nmol/L), insufficient (52-73 nmol/L), or sufficient (74-250 nmol/L).<sup>21</sup>

Those with sun exposure during 10 a.m. to 3 p.m. of at least 6 hours per week in the previous month were considered as having adequate sun exposure.<sup>22</sup> Physical activity of at least 1 hour daily in the previous month were considered as adequate.<sup>22</sup>

### Statistical analysis

All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) version 29.0. Means and standard deviations or median and interquartile range (IQR) were reported for continuous variables (e.g., age, serum 25(OH)D levels). Frequencies and percentages were reported for categorical variables (e.g., gender, vitamin D status categories). Different characteristics between the groups of the level of asthma control and asthma severity were assessed

**Table I Demographic and clinical data of the study population**

		Subjects (n=72)
Age in years, median (IQR)		8.0 (5)
Gender, n (%)	Male	40 (55.6)
	Female	32 (44.4)
BMI for age percentiles, n (%)	Underweight	14 (19.4)
	Healthy	41 (56.9)
	Overweight	7 (9.7)
	Obese	10 (13.9)
Parents education level, n (%)	Primary	1 (1.4)
	Secondary	33 (45.8)
	Tertiary	38 (52.8)
Household income, n (%)	<RM4000/month	46 (63.9)
	>RM 4000	26 (36.1)
Sun exposure per week, n (%)	<6 hours	65 (90.3)
	>6 hours	7 (9.7)
Physical activity per day, n (%)	<1 hour/day	39 (54.2)
	>1 hour/day	33 (45.8)
Enriched vitamin D containing food, times/week, mean (SD)		2.94 (1.91)
GINA classification of asthma severity, n (%)	Mild persistent	16 (22.2)
	Moderate persistent	44 (61.1)
	Severe persistent	12 (16.7)
Medications used for asthma, n (%)	ICS alone	33 (45.8)
	ICS + LABA	14 (19.4)
	ICS + LTRA	13 (18.1)
	ICS + LABA + LTRA	8 (11.1)
	ICS + LABA + LTRA +Biologics	4 (5.6)
GINA classification of asthma control, n (%)	Well controlled	51 (70.8)
	Partly controlled	18 (25)
	Uncontrolled	3 (4.2)
ACT/c-ACT score asthma control, n (%)	Well controlled	60 (83.3)
	Partly controlled	10 (13.9)
	Uncontrolled	2 (2.8)
Hospitalisations in past 12 months, n (%)	0 time/year	54 (75)
	1 time/year	18 (25)
ED visits past 12 months, n (%)	0 time/year	35 (48.6)
	1 time/year	29 (40.3)
	>2 times/year	8 (11.1)
Vitamin D status, n (%)	Deficient	29 (40.3)
	Insufficient	28 (38.9)
	Sufficient	15 (20.8)

n, numbers; SD, standard deviation; IQR, interquartile range; RM, ringgit Malaysia; BMI, body mass index; ED, emergency department; ICS, inhaled corticosteroids; LABA, long-acting Beta agonist; LTRA, leukotriene receptor agonists.

**Table II: Risk factors of vitamin D deficiency**

Factors	Category	Total	Vitamin D status			p
			Deficient n (%)	Insufficient n (%)	Sufficient n (%)	
Gender	Male	40	10 (25)	17 (42.5)	13 (32.5)	0.002*
	Female	32	19 (59.4)	11 (34.4)	2 (6.3)	
Age in years		72	11 (5)#	8 (3)#	6 (2)#	0.001*
BMI-for-age percentile	Underweight	14	3 (21.4)	9 (64.3)	2 (14.3)	0.010*
	Healthy	41	13 (31.7)	16 (39)	12 (29.3)	
	Overweight	7	6 (85.7)	0 (0)	1 (14.3)	
	Obese	10	7 (70)	3 (30)	0 (0)	
Enriched vitamin D containing food, times/week		72	3(1)#	3(3.5)#	3(2)#	0.626
Parents education level	Primary	1	0 (0)	0 (0)	1 (100)	0.488
	Secondary	33	13 (39.4)	14 (42.4)	6 (18.2)	
	Tertiary	38	16 (42.1)	14 (36.8)	8 (21.1)	
Household income per month	<RM2000	31	11 (35.5)	11 (35.5)	9 (29)	0.682
	RM2000-4000	15	7 (46.7)	6 (40)	2 (13.3)	
	>RM4000	26	11 (42.3)	11 (42.3)	4 (15.4)	
Sun exposure per week	<6 hours	65	26 (40)	24 (36.9)	15 (23.1)	0.160
	>6 hours	7	3 (42.9)	4 (57.1)	0 (0)	
Physical activity per day	<1 hour	39	16 (41)	17 (43.6)	6 (15.4)	0.425
	>1 hour	33	13 (39.4)	11 (33.3)	9 (27.3)	

\*Significant, p<0.05

#median (IQR)

**Table III: Association vitamin D status and asthma severity/control**

Factors	Category	Total	Vitamin D status			P
			Deficient n (%)	Insufficient n (%)	Sufficient n (%)	
GINA classification of asthma severity	Mild persistent	16	3 (18.8)	5 (31.3)	8 (50)	0.020*
	Moderate persistent	44	19 (43.2)	20 (45.5)	5 (11.4)	
	Severe persistent	12	7 (58.3)	3 (25)	2 (16.7)	
GINA classification of asthma control	Well controlled	51	19 (37.3)	19 (37.3)	13 (25.5)	0.470
	Partly controlled	18	8 (44.4)	8 (44.4)	2 (11.1)	
	Uncontrolled	3	2 (66.7)	1 (33.3)	0 (0)	
ACT/c-ACT score asthma control	Well controlled	60	23 (38.3)	22 (36.7)	15 (25)	0.052
	Partly controlled	10	4 (40)	6 (60)	0 (0)	
	Uncontrolled	2	2 (100)	0 (0)	0 (0)	
Hospitalisations in past 12 months	0 time	54	22 (40.7)	21 (38.9)	11 (20.4)	0.983
	1 time	18	7 (38.9)	7 (38.9)	4 (22.2)	
ED visits past 12 months	0 time	35	14 (40)	13 (37.1)	8 (22.9)	0.955
	1 time	29	11 (37.9)	12 (41.4)	6 (20.7)	
	>2 times	8	4 (50)	3 (37.5)	1 (12.5)	

\*Significant, p<0.05

by the Kruskal-Wallis test (for non-parametric data), and the chi-square test (for descriptive analysis). Pearson’s correlations were used to determine the relationship between two continuous variables. A p-value of <0.05 was considered statistically significant.

Based on previous study by Turkeli et al.<sup>23</sup>, a total of 72 study subjects were required to achieve 80% power of the study and a significance level of 0.05, taking into consideration of 20% dropout rate.

**RESULTS**

A total of 75 Malay children were recruited for the study. However, 3 blood samples with serum 25-hydroxyvitamin D levels were rejected, thus were excluded from the study. This was due to the unavailability of reagents for measuring serum 25- hydroxyvitamin D in the Pathology Laboratory at Hospital Putrajaya at the end of the study recruitment period. Hence, the final total number of participants in this study was 72 children.

**Demographic and Characteristics of Participants**

The median age was 8 years (IQR: 5), with a slight male predominance. Most of the parents (98.6%) had either secondary or tertiary education. About two-thirds of the study population had a total household income of less than RM4000. Many of the children had less than 6 hours of sun exposure per week (90.3%) and less than 1 hour of physical activity per day (54.2%). Half of the children had normal BMI for age percentiles. Over 60% of the children had moderate persistent asthma, with the majority of patients having well-controlled asthma based on both GINA classification and ACT/c-ACT scores, 70.3% and 83.3% respectively. Despite a high proportion of children with well-controlled asthma, 25% of the children experienced asthma-related hospitalizations and 51.4% of them had at least one emergency department visit in the past 1 year. Four patients received biologics as part of their asthma treatment, which includes Dupilumab and Omalizumab. A high percentage of vitamin D deficient (40.3%) and vitamin D insufficient (38.9%) were noted. These are presented in Table I.

**Risk Factors of Vitamin D Deficiency**

Asthmatic female children were found to be vitamin D deficient (59.4%) compared to males (p =0.002). There was a statistically significant difference in age and overall BMI across vitamin D status (p =<0.05). Underweight children had lower rates of vitamin D deficiency compared to overweight and obese children. Children with asthma in the deficient group have a significantly higher median age (11 years, IQR: 5) compared to those in the insufficient (8 years, IQR: 3) and sufficient groups (6 years, IQR: 2). Other factors were not statistically significant. (Table II)

Vitamin D levels were found to be negatively correlated with age (r = -0.336), weight (r = -0.410) and BMI (r = -0.392) among the study participants (Figure 1). The median serum vitamin D levels of mild persistent, moderate persistent and severe persistent groups were 73.72, 55.98 and 48.59ng/mL, respectively (Figure 2). Children with severe persistent asthma have significantly lower median vitamin D levels compared to those with mild asthma (p = <0.05). The plasma levels of calcium, phosphate, magnesium, and alkaline phosphatase were within normal range in all groups of vitamin D status.

**Vitamin D and asthma control/severity**

Vitamin D deficiency was significantly associated with increased severity of asthma (p = <0.05). The majority of the children with moderate persistent asthma were either vitamin D deficient or insufficient (n = 39). However, there was no statistically significant association between vitamin D status and asthma control when evaluated by both ACT/c-ACT score (p=0.052) and GINA classification symptoms (p=0.470). Additionally, no significant association between vitamin D status and the number of hospitalisations and ED visits was found. (Table III)

**DISCUSSION**

Our results showed a high percentage (79.2%) of vitamin D deficiency and insufficiency among Malaysian children with asthma. These findings are consistent with previous research in the neighbouring country, Thailand, which showed 64%

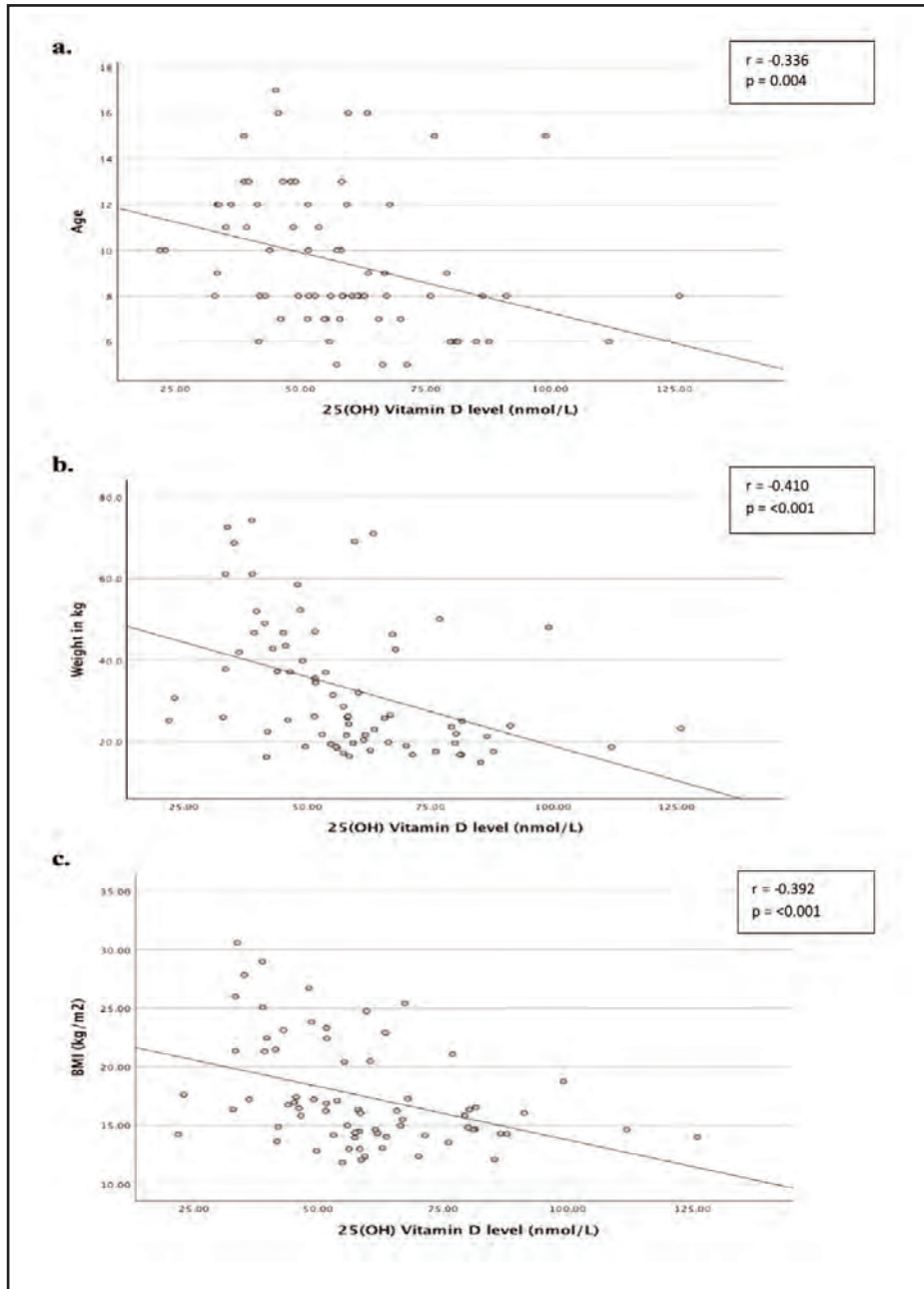


Fig. 1: Correlation plots between vitamin d level and age (a), weight (b) and BMI (c)

children with asthma had vitamin D deficient/insufficient.<sup>11</sup> Higher prevalence was also found in Western country among American asthmatic children (86%).<sup>9</sup> Our study found that the mean level of vitamin D among asthmatic children was 58.7 nmol/L. Similar findings were found by Turkeli et al. which showed the mean of serum hydroxyvitamin D among asthmatic children was 55nmol/L compared to children without asthma (80nmol/L).<sup>23</sup> There was no local data on the prevalence of vitamin D among asthmatic children in Malaysia. However, a high prevalence of vitamin D deficiency was found among school aged Malaysian children in the previous study not related to asthma.<sup>16</sup> Taken together, it is implied that vitamin D deficient or insufficient is a serious problem in Malaysia as a tropical country with

abundant sun exposure. The inadequate sun exposure, limited physical activity and lack of vitamin D rich food intake data among the study participants may contribute to the high prevalence of vitamin D deficient/insufficient in this study. Our hot and humid weather also render Malaysian children to avoid outdoor activities during the day.

We found that vitamin D deficiency was associated with female gender, older age and higher BMI in children. Research on vitamin D levels suggests that females are at higher risk of vitamin D deficiency due to various factors.<sup>15,17</sup> These include biological differences such as hormonal influences, lifestyle behaviours like limited sun exposure, and cultural practices, with their clothing habits, especially

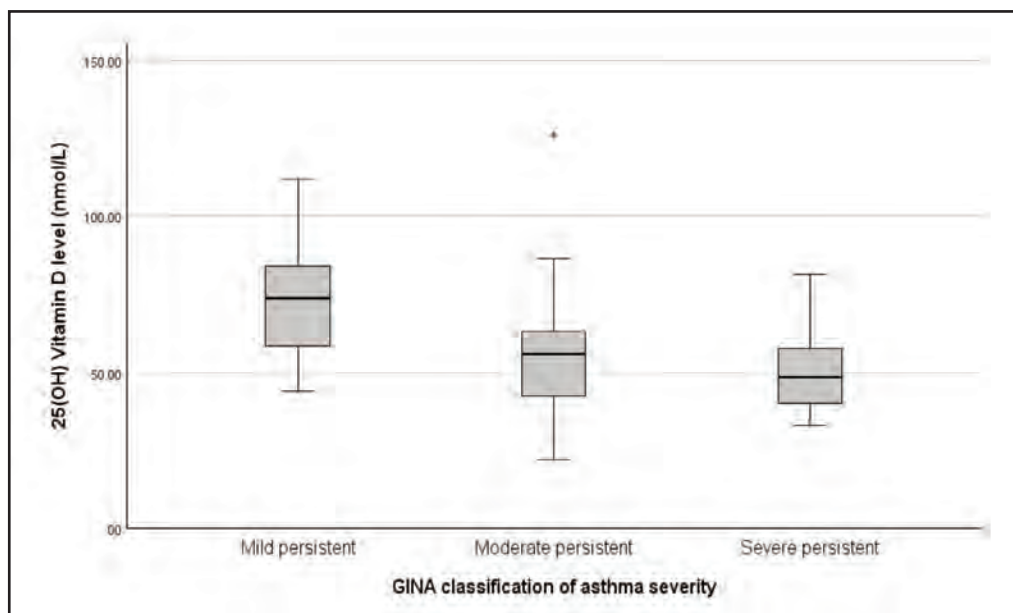


Fig. 2: The boxplot of serum vitamin D level in mild, moderate, and severe persistent asthma

among Muslims in Malaysia.<sup>15-17,24</sup> These practices can significantly reduce skin exposure to sunlight, thereby limiting the natural synthesis of vitamin D. Quah et al. found that being female, ethnicity of Malay and Indian, and consistently wearing long sleeves were associated with a higher likelihood of vitamin D deficiency.<sup>24</sup> Meanwhile, Anouti et al. from UAE demonstrated that over 80% of female migrants from Arab and South Asian countries were vitamin D deficient.<sup>25</sup>

Our study found that older children, particularly those in the adolescent age group have lower vitamin D levels. This observation aligns with a study by Al Sadat et al., which demonstrated a high prevalence of vitamin D deficiency among Malaysian adolescents, with 78.9% of those aged 12-13 years found to be deficient.<sup>16</sup> This finding could be linked to being adolescents often spend more time indoors due to academic commitments, increased use of electronic devices, and social activities which would limit their exposure to natural sunlight. Similarly, a study in Germany among children and adolescents found serum 25(OH)D levels generally decrease with age, starting high in younger age groups.<sup>26</sup> Additionally, hormonal changes during puberty in this age group, could also contribute to vitamin D deficiency, as these changes affect the body's metabolism and utilization of vitamin D.<sup>27</sup>

Those with higher BMI are found to have vitamin D deficiency, most likely due to lower physical activity and dietary intake affecting vitamin D metabolism.<sup>21,27</sup> A study conducted in Kuala Lumpur found a significant inverse association between vitamin D status and BMI-for-age among primary aged school children.<sup>28</sup> Similarly, a retrospective analysis among multi-ethnic Dutch children and adolescents found that vitamin D deficiency/insufficiency was highly prevalent among obese children.<sup>29</sup> This may be explained by the characteristics of

vitamin D itself as a fat-soluble vitamin; thus higher body fat reduces the availability of circulating serum 25(OH)D.<sup>21,27</sup>

The result of this study showed that vitamin D deficiency was significantly associated with increased asthma severity based on the GINA classification. Children with moderate and severe persistent asthma were more likely to have vitamin D deficiency than children with mild persistent asthma. The mean 25(OH)D level among our participants was 58.74 nmol/L, with lower levels correlating with higher asthma severity ( $p = 0.02$ ). This aligns with previous studies, by Sharif et al. which found that severe asthma cases in Iran had significantly lower vitamin D levels (53.4 nmol/L) compared to non-severe cases (70 nmol/L).<sup>30</sup> In another study by Al-Zayadneh et al., among 98 asthmatic children, they found children with severe persistent asthma to have significantly lower vitamin D levels than those with intermittent asthma.<sup>13</sup> They also found deficient vitamin D group used significantly higher usage of systemic corticosteroids to treat asthma exacerbation within a year.<sup>13</sup> In a case control study in Turkey by Ozkars et al., the vitamin D levels in the mild and moderate persistent asthma groups were significantly lower than the non-asthmatic children.<sup>31</sup>

Vitamin D deficiency has been significantly associated with increased markers of asthma severity.<sup>32</sup> A study in Saudi by Aldubi et al. found that lower levels of vitamin D are linked to higher asthma prevalence and correlated with various inflammatory markers (interleukin-10, tumor necrosis factor-alpha, and platelet derived growth factor) and atopy markers (total IgE and eosinophil count).<sup>32</sup> Vitamin D has been shown to influence both innate and adaptive immune systems as well as airway cells, where its deficiency increases inflammation.<sup>10,33</sup> Studies indicate that its deficiency is associated with higher asthma risks, increased symptoms, more frequent exacerbations, and reduced lung function in those already suffering from asthma.<sup>10</sup> Furthermore, analyses

from birth cohorts showed that low maternal vitamin D intake and levels during pregnancy were linked to increased likelihood of wheezing in children at ages 3 and 5.<sup>33</sup> Unfortunately, we did not study the biomarkers of asthma severity among the children, and future research using these biomarkers is encouraged.

Our findings did not show the association between vitamin D levels and asthma control based on both assessment tools; ACT/c-ACT score and GINA classifications. This lack of statistically significant results was most likely due to asthma control could be influenced by many other confounding factors such as compliance to medications, environmental exposures, uncontrolled comorbid conditions, inhaled corticosteroid dosages and inhaler technique. Furthermore, our study population involved a small sample size in the uncontrolled group, as the majority of them (70.8 – 83.3%) had controlled asthma. Despite that, the trend of better asthma outcomes with sufficient vitamin D levels was seen, indicating that further investigation with larger sample sizes and diverse populations is needed to confirm these observations.

A case control study from Italy and Turkey found that lower vitamin D levels are associated with worse asthma control and poorer pulmonary function.<sup>23,34</sup> The other study, Esfandiari et al. however did not find an association between vitamin D deficiency and asthma control similar to our result.<sup>7</sup> Chinellato et al. otherwise found higher serum vitamin D levels moderately correlated with better asthma control, as indicated by c-ACT scores but not in the GINA group.<sup>34</sup> This variability in findings may be attributed to differences in study populations, sample sizes and methodologies. More comprehensive research is needed to establish a definitive association and understand the potential mechanisms through which vitamin D might influence asthma control.

Supplementation of vitamin D has been shown to improve asthma severity, enhance asthma control, and reduce exacerbations, suggesting its potential role as a potent immunomodulator in children with asthma.<sup>10,14,33</sup> A meta-analysis of 14 randomized controlled trials found that vitamin D supplementation was associated with a reduction in asthma exacerbation rates, reduced the risk of severe asthmatic symptoms and improved pulmonary function.<sup>35</sup> Additionally, a study among Japanese children with asthma demonstrated that low-dose vitamin D supplementation for two months significantly improved asthma control based on GINA classification and c-ACT scores.<sup>36</sup> This findings further highlight its potential benefit in asthma management.

The strength of our study was a sufficient sample size, which enhances the reliability and generalizability of the findings. However, our study has several limitations. Firstly, it is crucial to utilize objective methods to assess confounding factors related to vitamin D deficiency, such as sun exposure, dietary intake, and physical activity. A major challenge is that the existing research lacks clear definitions for adequate levels of these factors, which are significant determinants of vitamin D status. Objective tools, such as personal UV dosimeters to measure body sun exposure, accelerometers or pedometers to

track physical activity, particularly the time spent outdoors, could provide more accurate assessments. These devices otherwise could be costly and pose compliance challenges, particularly among the paediatric population. Furthermore, in our study, we were unable to quantify dietary intake of vitamin D, which represents a limitation to accurately assessing the contribution of diet to overall vitamin D levels. Future studies utilizing detailed dietary assessment questionnaires would provide a more comprehensive understanding of vitamin D intake and its impact on deficiency. Additionally, the study was conducted at a single centre, with all participants being Malay ethnicity, which may not be representative of the broader population of children with asthma, particularly those from diverse geographical or ethnic backgrounds.

## CONCLUSION

Our study highlights a high percentage of vitamin D deficiency and insufficiency among children with persistent asthma. There was a significant association between vitamin D deficiency and increased asthma severity. However, there was no significant association with asthma control. Factors associated with vitamin D deficiency are female, older age and higher BMI. Based on these study findings, we recommend routine assessments of vitamin D levels among children with moderate to severe asthma. This proactive approach may enable timely supplementation, potentially reducing asthma severity, improving control, lowering morbidity, and enhancing quality of life.

## ACKNOWLEDGEMENTS

We would like to thank the Director General of the Ministry of Health for the permission to publish this paper. We would like to extend our appreciation to the Department of Paediatrics, Hospital Raja Perempuan Zainab II, Kota Bharu, for their cooperation and support in carrying out this study and assisting with data collection. Finally, to all the parents and children at the Pediatric Clinic whom we had the great pleasure of meeting during my tenure there, we wish you all a blessed and happy life.

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