

# Esophageal cancer epidemiology, diagnosis, and management in Sudan - A review

**Idriss Hussein Musa, MD<sup>1,2</sup>, Taha Hussein Musa, PhD<sup>2</sup>, Hassan Hussein Musa, PhD<sup>2,3</sup>, Mohamed Elmakki Ahmed, MD<sup>4</sup>**

<sup>1</sup>Sudanese Medical Specialization Board, General Surgery, Khartoum, Sudan, <sup>2</sup>Biomedical Research Institute, Darfur University College, Nyala, Sudan, <sup>3</sup>Faculty of Medical Laboratory Sciences, University of Khartoum, Sudan, <sup>4</sup>Department of Surgery, Faculty of Medicine, University of Khartoum, Sudan

## ABSTRACT

**Introduction:** In Sudan, cancer a common health challenge, is the leading cause of death after malaria and viral pneumonia. The aim of the review is to determine the risk factors associated with esophageal cancer (EC) among Sudanese population.

**Methods:** All published online data concerning EC epidemiology, diagnosis, and management in Sudan were studied.

**Results:** The prevalence of EC in Sudan is ranked fourth among cancer types in males and fifth in females. The squamous cell carcinoma is more predominant than adenocarcinoma. The dietary, dysplasia and teeth loss, cigarette smoking, age, sex, GERD, genetic and environmental interactions remain a risk for developing EC in clinical practice. A significant challenge for treatment is that most of EC patients were often diagnosed in advanced stages due to the lack of early clinical symptoms. Management of EC depends on patient fitness and tumor stage, endoscopic removal was used for early tumors, while chemotherapy, chemo-radiotherapy, surgical resection, or combinations of these were used for advanced tumors. Despite improvements in the management and treatment of EC patients, the general outcome remains very poor. Furthermore, using molecular techniques to better understand the etiology of EC, it may assist in identifying complicated and critical issues and improve therapy towards a new treatment strategy.

**Conclusion:** The remarkable factors associated with EC among Sudanese are geographical variation, environmental factors, ethnic differences, dietary and social habits.

## KEYWORDS:

*Esophageal cancer, epidemiology, diagnosis, management, Sudan*

## INTRODUCTION

Esophagus cancer (EC) is ranked sixth in causing cancer death worldwide.<sup>1</sup> Squamous cell carcinoma and adenocarcinoma are the two histological subtypes, varying in geographical and racial distribution.<sup>2</sup> Etiologically adenocarcinoma is primarily associated with gastric reflux, and Barrett's esophagus is a more common cancer type in developed countries that increased significantly to the global

health burden.<sup>3</sup> In contrast, squamous cell carcinoma was associated with red meat consumption, low intake of fresh fruit and vegetables, drinking hot tea, smoking, alcohol consumption, poor oral health, is more prevalent in a lower socioeconomic group and among those in developing countries.<sup>4</sup>

In our previous study we found that EC was associated with many risk factors such as age, sex, alcohol smoking, tobacco use, red meat, poor oral health, low intake of fresh food, and socioeconomic status. The study demonstrated that the literature on EC was continuously growing, in the field of squamous cell, carcinoma and adenocarcinoma. Research in EC was supported by China and United States of America (USA) funding agencies. Therefore, China, USA and Japan are the top productive countries on EC research.<sup>5</sup>

EC is a fatal disease among Sudanese populations and sub-Saharan Africa concerning prognosis and mortality rate.<sup>6</sup> It is the most reported gastrointestinal cancer,<sup>7</sup> with approximately 5.8 per 100000 cases in the general Sudanese population.<sup>7</sup> EC cases were relatively increased since 1993, with an estimated rate of 4.6% among Sudanese<sup>7</sup> to 5.4% in the year 2006.<sup>7</sup> In 2000, cancer was the third leading cause of death after malaria and viral pneumonia, accounting for 5% of all deaths.<sup>7</sup> EC ranks the 4th among Sudanese males and 5th cancer among females.<sup>8</sup> The incidence of adenocarcinoma was increased by 11% from 1986 to 1991<sup>7</sup> to 44.5% in 2010.<sup>9</sup> The remarkable factors associated with EC among Sudanese are geographical variation, environmental factors, ethnic differences, dietary and social habits, in addition, genetic factors.<sup>10,11</sup>

## Cancer registry in Sudan

Sudan is like other developing countries where the primary health system focuses against infectious diseases with less attention given to non-communicable diseases owing to an increase in EC cases.<sup>2</sup> The first national cancer registry was started in 1967, supported with a grant from the International Union against Cancer (IUAC) in cooperation with University of Khartoum, Stack Medical Research Laboratory, and the Ministry of Health, Sudan.<sup>2</sup> Recently, the primary cancer data are obtained from the hospital-based cases at only two oncology centers.<sup>6</sup> The first is the "Radiation and Isotope Center in Khartoum State, and the second is "National Cancer Institute in Gezira State established in 1992 by the University of Gezira. These centers were still facing

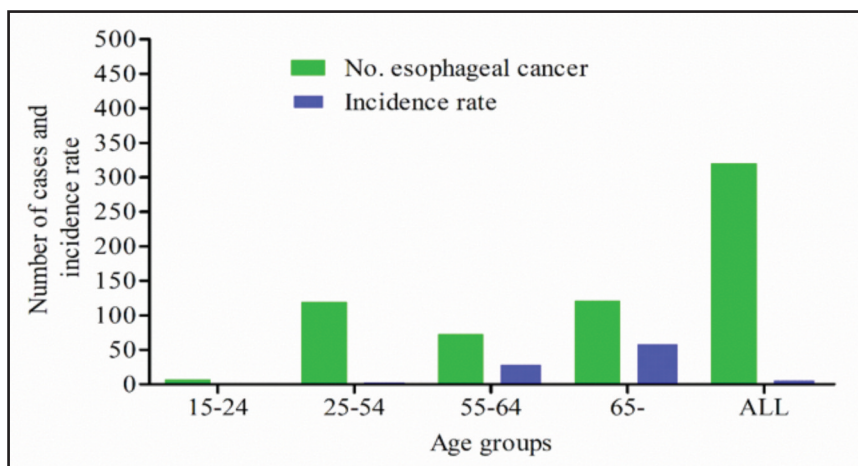
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*Corresponding Author: Dr. Idriss H Musa*

*Email: trsoo18@gmail.com*

**Table I: Gender ratio and age distribution of esophageal cancer patients in Sudan**

Gender	Male: Female ratio	Country	References
	1:3.3	Sudan	Mohammed et al., 2012
	1.3:1.0	Sudan	Mahmoud et al., 2014
	0.7:1.5	Sudan	Elhadi et al., 2016
	2:1	African Sub-Sahara region	Kachala, 2010
Age (year)	Range	Country	References
	52-66	Sudan	Mohammed et al., 2012
	45-64	Sudan	Mohammed et al., 2014
	50-80	Sudan	Ali and Ibrahim, 2014
	31-93	Sudan	Elhadi et al., 2016



**Fig. 1:** Age-wise distribution of esophageal cancer incidence among the top 10 cancer reported during the year 2009-2010 Saeed et al.<sup>8</sup>

many problems, such as lack of running cost and research activities, budget to support professional medical care staff, the fund for expansion of cancer registration at the state level, qualified oncologist, the fund for carryout health awareness, week health information system, insufficient cancer diagnostic facilities, lack of a national population-based cancer registry and standardized pathological reporting.<sup>12</sup>

**Geographical distribution of esophageal cancer**

Sudan is a large country with diversity in the population and the environment.<sup>13</sup> The change face EC presents a vast challenge in the management and control. The incidence of EC in Western Sudan was 38.9%, Khartoum state 30.5%, White Nile 18.1%, Eastern Sudan 5.5%, Northern Sudan 4.5%, and Blue Nile state 2.8%.<sup>11</sup> In the Gadarif State in Eastern Sudan, the EC cases are slightly higher among people living in town compared with the rural area, and the reason is that urban area has better health services and diagnostic tools.<sup>14</sup> Ali and Ibrahim<sup>15</sup> indicated that Khartoum and North Kordofan were the most geographical areas in Sudan affected by cancer. The population of the Southern and Eastern African Sub-Regions had ten times higher age-gender incidence and prevalence rates compared with the Western African Sub-Region.<sup>16</sup>

**The incidence of esophageal cancer in Sudan**

The incidence of EC was 1.4% in early 1977. Recently, 9.6% of patients referred for endoscopy units in Gezira state were proved to have EC.<sup>17</sup> Incidence data derive from population-

based cancer registries reported as 5.8 per 100000 in the general Sudanese population and 8.9 per 100000 in adults more than 15 years were at risk with EC.<sup>8</sup> The highest incidence was reported in the Northern region than in South Sudan.<sup>8</sup> In Sudan, the prevalence of the EC is generally higher among males.<sup>17</sup> The incidence of EC is high at the age of more than 15 years.<sup>7</sup> A recent study showed the incidence rate was higher in adults at 65 years (Figure 1).<sup>8</sup> The mortality rate of 10% indicated a remarkable improvement compared with the previous reports back to fifteen years ago.<sup>7</sup>

**Clinical presentation of the esophageal cancer**

In Sudan, the most common clinical presentation was dysphagia, followed by loss of body weight.<sup>18</sup> A few patients presented with epigastric pain and back pain,<sup>11</sup> pressure or burning, worsening indigestion or heartburn, and coughing or hoarseness.<sup>18</sup> The mean duration of dysphagia was 120 days.<sup>11</sup>

Squamous cell carcinoma was the common type of EC 92.5% compared to adenocarcinoma 4.7%.<sup>11,19</sup> In contrast, Elhadi et al.<sup>18</sup> reported 80.6% were adenocarcinoma, and 19.4% were squamous cell carcinoma. Adenocarcinoma was more frequent in males 75%, compared with females 25%, whereas Squamous cell carcinoma was more frequent in females 63.6%, compared to males 36.4%.<sup>2</sup>

The well-differentiated tumors were most common among the patients with Squamous cell carcinoma, in both males, 42.9%, and females 51.8%.<sup>11</sup> Whereas, poorly differentiated

tumors were predominant among the patients with Adenocarcinoma, representing 32.1% and 42.8% of the Adenocarcinoma in male and female patients, respectively.<sup>11</sup>

In general, the site of the tumour was located in the middle and lower third of the esophagus.<sup>18,19</sup> Gasmeseed et al.<sup>11</sup> indicated that squamous cell carcinoma cases were located in the middle and lower third of the esophagus, while most adenocarcinomas were located in the lower third.<sup>10</sup>

#### **Risk factors associated with esophageal cancer**

EC and gastrointestinal malignancies are the most common cancer, caused risk for up to 25.3% of people.<sup>20</sup> The rich diet in red and processed meat, saturated fats, and low intake fruits and vegetables, dysplasia, and teeth loss remain a risk for developing esophageal adenocarcinoma in clinical practice.<sup>18,21</sup> The incidence of esophageal carcinoma is rare in young people, and increases with age, reach the peak in 70 to 80 years of age.<sup>22</sup> GERD, cigarette smoking, and sex are also associated with esophageal adenocarcinoma.<sup>22,23</sup>

#### **Gender**

EC ranks fourth in Sudanese males, and the fifth in females<sup>7</sup>, it was more predominant in females.<sup>2,15,18-20</sup> The male-to-female ratio was 1:2 for squamous cell carcinoma and 2:1 for adenocarcinoma.<sup>11</sup> A minor female predominance was reported in Uganda in East Africa and Guinea in West Africa.<sup>13</sup> In contrast, Mahmoud et al.<sup>24</sup> indicated that EC is more prevalent in males (Table I). In African countries, the male-to-female ratio for EC was closer to 2:1 Tanzania,<sup>25</sup> Kenya,<sup>26</sup> and South Africa.<sup>27</sup> The reason for male-dominant is that smoking and alcohol drinking were more prevalent among males.<sup>28</sup> In addition, the inhibitory effect of estrogen in the growth of EC cells was reported. However, there is no documented role of estrogen in human EC etiology.<sup>29</sup> On the other hand, women with EC tend to have a better prognosis than men.<sup>30</sup>

#### **Age**

The maximum incidence of EC was in the 6th and 7th decades.<sup>10</sup> Previous studies have shown that the average age of females was 52.75 ± 11.66 years, and that of males was 66.11 ± 9.52,<sup>19</sup> while the average age for both male and female was 62.57±15.1years,<sup>18</sup> and 47.3% of women were in the age between 50 and 80 years old.<sup>15</sup> A recent study has shown that the peak was in the age 65 -69 years 40%, followed by 50 -54 years 27%, and over 70 years old 8.1%.<sup>2</sup>

#### **Nutrition**

Several studies reported a positive association between EC and alcohol and tobacco consumption,<sup>31</sup> low intake of fresh fruit and vegetables,<sup>4</sup> exposed to the hot drinks and food,<sup>14</sup> achalasia, lime, and caustic fluids ingestion.<sup>19</sup> Poor nutritional status, low fruits and vegetables intake are suggested to be partially responsible for EC. The nutritional status of EC patients was associated with surgical resectability, response to chemotherapy, length of hospital stays, and survival rate.<sup>32</sup> Patients on jejunostomy catheter feeding were considered optimized to receive neo-adjuvant therapy based on clinical assessment. A recent study revealed that feeding jejunostomy catheter combined with a locally prepared feeding formula was provided a reliable nutritional option for esophageal cancer patients in developing countries.<sup>9</sup>

#### **Smoking and Alcohol consumption**

Smoking is a risk factor, especially for people living in Western countries, and the risk increases by three-fold to sevenfold for smokers compared with non-smokers people.<sup>33</sup> However, smoking on EC is considerably higher among Asian populations compared with Western populations. In China, poor oral health, cigarettes, and hookah smoking, and smoking were not significantly associated with the risk of EC in the long-term.<sup>4</sup>

The incidence of tobacco smoking use among urban adult males is increasing in Sudan.<sup>7</sup> Among the male EC patients, the manual laborers had the highest percentage of ever tobacco use and alcohol consumption 66.1%, followed by the office workers 50% and farmers 37.3%.<sup>11</sup> Ever tobacco use was most common among patients who come from the Nilotic, Nubian, and Guhaina tribal backgrounds.<sup>11</sup> Ever tobacco use was frequently reported by males with adenocarcinoma 57.1% and squamous cell carcinoma 47.7%.<sup>11</sup> Alcohol is a risk for developing upper aero-digestive tract cancer.<sup>34</sup>

#### **Socioeconomic status**

The socioeconomic status of the population was associated with a higher risk of EC in both developed and developing countries.<sup>35</sup> In Sudan the daily diet components intake by people are poor, only few people have access to fruits and vegetables, which may have suggested to be partially responsible for EC. In Gezira State, EC patients who had occupations typically associated with the low socioeconomic status was associated with a higher risk of EC incidence.<sup>11</sup> In China, low socioeconomic status and obesity were associated with a higher risk of esophageal squamous cell carcinoma.<sup>4</sup> In addition, people's lifestyles, environmental and socioeconomic factors, such as reproductive and access to medical and health care services, were associated with EC.<sup>36</sup> Both body mass index and abdominal obesity were associated with the risk of cancer.<sup>37</sup> Obesity is a major public-related disease in developed countries.<sup>38</sup> Tooth loss was positively associated with squamous dysplasia of the esophagus, while good oral hygiene was negatively associated.<sup>39</sup>

#### **Gastro-esophageal reflux disease**

Gastro-esophageal reflux disease is the main esophagus adenocarcinoma risk factors.<sup>18,24</sup> Weekly GERD symptoms increase the odds of esophagus adenocarcinoma five-fold, and daily symptoms increased the odds seven-fold compared with those with less frequent episodes.<sup>40</sup> In Sudan, gastrointestinal malignancies are the most common cancer; 25.3% is EC.<sup>10</sup> Gastro-esophageal reflux disease (GERD) and Barrett's esophagus are associated mainly with adenocarcinoma.<sup>3,19</sup> Other studies also indicated that GERD is more common in patients with adenocarcinoma than squamous cell carcinoma, representing 5.5% for squamous cell carcinoma and 34.7% for adenocarcinoma.<sup>41</sup> GERD can cause and exacerbate mental complications in patients. Mental factors (anxiety and depression) play important roles in the development of GERD, especially non-erosive esophagitis.<sup>42</sup> In addition, anxiety and depression levels were significantly higher in subjects with GERD than in controls.<sup>43</sup>

#### **Infectious pathogens**

*Helicobacter pylori* infection was negatively associated with esophageal adenocarcinoma. The infection confers a

protective effect for esophageal adenocarcinoma.<sup>24</sup> *H. pylori* infection leads to atrophic gastritis and decreased gastric acid production, neutralizes the acid through the production of ammonia, decreased acid exposure of the distal esophagus, which reduces the chances of esophagitis and esophageal adenocarcinoma.<sup>44</sup> Xie et al.<sup>45</sup> indicated that *H. pylori* infection decrease the risk of esophageal adenocarcinoma by 41% through gastric atrophy, which leads to acid reduction.

In patients with GERD, the prevalence of *H. pylori* infection was higher among patients with than without peptic ulcers.<sup>46</sup> Early studies revealed that *H. pylori* eradication was positively associated with reflux esophagitis or GERD symptoms in patients with gastric and duodenal ulcer diseases.<sup>46</sup> A recent meta-analysis demonstrated that eradication therapy of *H. pylori* was related to a higher risk of developing de novo GERD in Asian studies.<sup>47</sup>

Human papillomavirus (HPV) is one of many factors contributing to EC.<sup>48</sup> HPV16 and HPV18 are the most detected types associated with cancers.<sup>49</sup> These serotypes have a strong association with vulva, anus, penis, and oropharynx cancers.<sup>49</sup> The wide range in HPV positivity could reflect, in part, differences in the sensitivity of the various detection methods used (PCR, In-situ hybridization, Southern blot hybridization, and Immunohistochemistry), and also differences in the incidence of HPV in the tumour samples examined.<sup>62</sup> There is no study to confirm the association of HPV with cancer in the Sudanese population.<sup>6</sup>

Epstein Barr Virus (EBV) infection and exposure to Plasmodium falciparum are cofactors in the pathogenesis of Burkitt's lymphoma, the most common pediatric cancer in equatorial Africa.<sup>51</sup> Furthermore, immunocompromised hosts and EBV have associated nasopharyngeal carcinoma and B cell lymphoma in the Sudanese population.<sup>6</sup> The etiological effects of EBV might cause EC in Sudan.<sup>52</sup>

Human immunodeficiency virus (HIV) related immunosuppression is a strong risk factor for Kaposi's sarcoma, associated with its specific herpesvirus, and non-Hodgkin lymphoma, associated with Epstein Barr virus.<sup>53</sup> HPV-associated cervical carcinoma is also considered an AIDS-defining malignancy.<sup>53,54</sup> AIDS-defining malignancies were reported in Zimbabwe, Zambia, Uganda, Rwanda, and South Africa.<sup>55</sup>

Schistosomiasis is endemic in Sudan, Schistosoma haematobium was associated with bladder cancer.<sup>56</sup> Recently a case of sigmoid colonic adenocarcinoma coexisting with schistosomiasis was reported.<sup>57</sup> Schistosoma mansoni ova were seen in the tumor tissue.<sup>57</sup> An astomotic esophageal leak due to Taenia saginata following esophagectomy for esophageal cancer in a 50-year-old female with squamous cell carcinoma at the lower third site was reported.<sup>58</sup>

### Genetic factors

Genetic and environmental interactions play a role in the incidence of EC progression.<sup>59</sup> Host genetics contribute up to one-third of the risk for sporadic Barretts esophagus and esophageal adenocarcinoma development, and 7% of Barretts esophagus and esophageal adenocarcinoma cases

are familial.<sup>60</sup> In the USA, the incidence rate was greatest for each stratification in males, blacks, distant disease, and adenocarcinoma.<sup>61</sup> Familial aggregation of esophageal carcinoma in northern regions of China was reported.<sup>62</sup> Ethnic and genetic factors are stand towards an increase the cancer cases in Sudan and Africa region.<sup>36,63</sup> There was an association between family history and EC.<sup>14</sup> Guhaina was the most prevalent tribal origin for cancer in Sudan 42.2%, followed by Jaali 23.9%, Beja 11.2% and Darfurian 5.6%.<sup>11</sup>

Tylosis, an autosomal dominant disease, was related to esophageal squamous carcinoma.<sup>53</sup> Somatic mutations in TP 53 and other tumor suppressor genes were reported in esophageal squamous cell carcinomas.<sup>63</sup> There is a mutational profile of EC that closely resembles those of squamous cell carcinomas.<sup>64</sup>

The p53 arg/pro polymorphism has a different pattern of frequency in various types of cancer in Sudanese patients, indicating different etiology and biology of these tumors.<sup>65</sup> Overexpression of TP53 protein and mutation in exon 4 and 8 were associated with EC in Sudanese patients.<sup>63</sup>

Genome-wide association studies (GWAS) identified loci linked to esophageal embryonic development (FOXF1, BARX1), host immune response (MHC locus 16.24), and cellular proliferation and transformation (CRTC1 (19p13)).<sup>66</sup> Epigenetic was associated with the development of esophageal adenocarcinoma.<sup>67</sup> Identification of susceptible genes and biomarkers will predict the treatment response of patients and improve their survival rates.<sup>68</sup>

### Environmental factors

There is evidence of the association between environmental and occupational exposures and specific cancer types.<sup>69</sup> In Sudan it is difficult to assess the possible role of air pollution in the disease. Air pollution in rural areas is low to moderate, and in the urbanized areas is moderate to high.<sup>6</sup> In general, air pollution was derived from industries, oil-producing facilities, and traffic. Whereas, in Sudan and other African countries, fires lit for cooking within poorly ventilated mud huts and the habit of burning trash were main factors.<sup>6</sup> Active pesticide ingredients used to control mosquito, pests of cotton, and other rotation crops were risks for cancer.<sup>6</sup>

Common hazardous substances in the workplace include acids, caustic substances, disinfectants, heavy metals, including mercury, lead, cadmium and aluminum, paint, pesticides, petroleum products and solvents. Health effects depend on the type of hazardous substance and the level of exposure (concentration and duration). Occupational exposures such as polycyclic aromatic hydrocarbons, silica, and mixed dusts have been consistently shown to increase risk of esophageal cancer, while the risk has decreased among education employees and technical workers.<sup>70</sup> In contrast, specific airborne occupational exposures do not seem to be of major importance in the aetiology of EC.<sup>71</sup>

### Diagnosis of Esophageal cancer

Delay in the diagnosis of EC caused a potentially life-threatening condition and increased mortality. The poor diagnosis of EC highlights the need to improve detection and prediction methods. A challenge facing proper diagnosis is

the lack or availability of reagents of poor quality, which effect diagnosis and later improper treatment of cancer.<sup>13</sup> Very few specialist doctors are working on EC and they are only in Khartoum, the Capital of Sudan, so those in other cities are facing poor diagnosis problems. The local training for clinical oncologists is started in the late 1990s, provided trained staff committed to work in the country.<sup>13</sup> EC is often diagnosed in its advanced stages due to the lack of early clinical symptoms.<sup>68</sup> Patients with the same clinical features and treatments may have different clinical outcomes, indicating that genetic variants may effect EC prognosis.<sup>34</sup> Squamous cell carcinoma of the esophagus presents as asymptomatic, lead to late diagnosis with a poor prognosis.<sup>62</sup>

### Management of esophageal cancer

EC is a fatal malignant worldwide, increased dramatically in the Western world.<sup>68</sup> Despite improvements in the management and treatment of EC patients, the general outcome remains very poor for over 5-year survival rates 10% and 5-year post-esophagectomy survival rates 15-40%.<sup>68</sup> Primary prevention of EC includes tobacco avoidance and alcohol intake, maintenance of a healthy weight, increasing fresh fruit and vegetable intake, and reduction in red meat consumption.<sup>1</sup>

Management of EC depends on patient fitness and tumor stage. Early tumors may be suitable for endoscopic removal, and locally advanced cancers are treated with chemotherapy, chemo-radiotherapy, surgical resection, or combinations of these.<sup>1</sup> Patients with EC that are not suitable for operative management are treated with systemic chemotherapy.<sup>1</sup> In Sudan, patients often have advanced disease at presentation, they are dehydrated and malnourished, making rehydration and feeding an emergency initial step in the management.<sup>8</sup>

### Treatment of esophageal cancer

The crucial point of EC management is the time from the initiation of symptoms to admission to primary health care centers or hospitals. In Sudan, Radiation and Isotope Center in Khartoum, established in 1959, and National Cancer Institute, established in 1999, were provide chemotherapy and radiation treatment for cancer patients.<sup>11</sup> The early detection of cancer requires early diagnosis for symptomatic patients and screening of asymptomatic patients at risk.<sup>7</sup> A significant challenge to the treatment of cancer is that most patients present with advanced-stage disease. In Sudan, 78% of patients seek first medical treatment at stage III or IV of disease. In these stages, treatment involves multiple modalities, including surgery, radiotherapy, chemotherapy, and hormone therapy.<sup>15</sup> Patients with advanced or metastatic EC are treated with cytotoxic chemotherapy; those who are HER2 positive may also benefit from trastuzumab treatment.<sup>1</sup> Immuno-oncology therapies have promising early results in squamous cell carcinoma and adenocarcinoma.<sup>1</sup> Neo-adjuvant concurrent chemo-radiotherapy has been increasingly administered to treat EC.<sup>72</sup>

Clinic-based cohort studies have shown a significant association between treatment with proton-pump inhibitors and a decreased risk of high-grade dysplasia and adenocarcinoma in patients with Barrett's esophagus.<sup>24</sup> Cervical esophageal squamous cell cancers are treated with chemotherapy and radiation therapy. Mid and lower

esophagus and gastric cardia were treated with induction therapy and esophageal resection.<sup>3</sup> Endoscopic therapies, including radiofrequency ablation, endoscopic mucosal resection, and endoscopic sub-mucosal dissection, have become the standard treatment modality for Barrett's esophagus and early carcinoma.<sup>3</sup> Observational studies with a large number of patients showed that the use of non-steroidal anti-inflammatory drugs, proton pump inhibitors, and statins in patients with Barrett's esophagus, reduced the progression to adenocarcinoma.<sup>79</sup> Minimally invasive esophagectomy by thoracotomy is gaining acceptance due to advantages in short-term outcomes.<sup>73</sup>

Radiation therapy in Sudan was started in Khartoum Teaching Hospital in 1959, with a superficial x-ray machine and deep x-ray machine. In 1967, the work was started in a new oncology hospital in Khartoum. Brachytherapy using radium-226 was first used in the same hospital. Later in the 1990s, the old name of the hospital was changed to Radiation and Isotopes Center of Khartoum (RICK). In 1999 radiation therapy was started in the Institute of Nuclear Medicine and Molecular Biology, the University of Gazira in Madani. Since then, radiation therapy Divisions have been established in the College of Medical Radiologic Sciences, Sudan University of Science and Technology, and cancer centers all over Sudan.<sup>69</sup>

### CONCLUSIONS

As a result of increasing EC cases in Sudan, there is an urgent need for early detection programs for patients to attend the cancer center for treatment and make the EC treatment more effective, less costly and invasive, and conduct rapid confirmed and appropriate therapy for patient diagnoses with EC. Furthermore, understanding the etiology of EC using molecular techniques may assist in the management and identifying complicated and critical issues and improve therapy towards a new treatment strategy. Understand a significant impact of changes in community dietary behaviors, eco-environmental effects, ethnic, dietary, and cultural, and other factors associated with increased EC incidence.

### CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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