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Original Article

Clinical, Pathologic, and Endoscopic Characteristics of Esophageal Cancer Patients at St. Paul´s Hospital Millennium Medical College (SPHMMC), Addis Ababa, Ethiopia: A Five-Year Retrospective Review

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Abstract

Background*: Esophageal cancer is the eighth leading cancer and the top sixth cause of cancer mortality worldwide. According to Globocan 2012 estimate, in Ethiopia, esophageal cancer ranks the seventh and eighth as the leading cause of cancer mortality and morbidity respectively.*

Methods: *A retrospective cross-sectional study using record review was employed at Gastroenterology and Hepatology Unit and Department of Pathology of SPHMMC with the aim to assess the clinical, pathological and endoscopic characteristics of esophageal cancer patient attending at St Paul Hospital Millennium Medical College (SPHMMC) from January, 2015 to December, 2019 in Addis Ababa, Ethiopia. . All newly confirmed esophageal cancer patients (n=255) who were registered at SPHMMC from January 2015 to December 2019 were included in this study. Patients chart, Endoscopy report and Histology data were reviewed . Finally, basic descriptive statistics (frequency, mean, median), bivariate and multivariable analysis were performed.*

Result: *A total of 255 esophageal cancer patients' charts were reviewed. and 222 patients have confirmed Histology report of esophageal cancer. There were 173 (77.9%) cases of squamous cell carcinoma. The mean age at diagnosis was 57 years with comparable male to female ratio. The Upper , middle . lower esophagus are involved in 10.4%,38.4%, and 48.6% of the patients respectively. Most patients 220(86.6%) seek esophagogastrduodenoscopy for dysphagia and only 15(6.8%) of patients have staging work up and majority presented at stage (80%).*

Conclusion*: Squamous cell carcinoma was the most predominant histologic type followed by adenocarcinoma affecting males and females equally. Most of the esophageal cancer patients were diagnosed in advanced stages affecting the treatment outcome of esophageal patients.*

Keywords: *Esophageal cancer; histology; endoscopic site; Ethiopia*
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Introduction

Esophageal carcinoma (EC) is the eighth most common cancer worldwide and the sixth leading cause of cancer-related mortality. Unfortunately, it is often associated with a poor prognosis, with a 5-year survival ranging from 4 to 40% depending on stage and an 18% overall 5-year survival(1; 2).

The epidemiology of EC presents many unusual features. Even over short distances, the incidence of EC varies considerably, usually more marked among females than males. The incidence is rising rapidly in some communities, often those that might be regarded as suffering from particularly modern forms of deprivation. Esophageal cancer has the fastest-growing incidence of any cancer in the United States, with an increase of 50% in the past two decades (1; 2; 3).

Histologically, EC can be squamous cell carcinoma (ESCC) or adenocarcinoma (EAC). Both types are more common in males than females. ESCC is more commonly encountered in individuals from low-resource regions like Africa and East Asia, while EAC is more prevalent in more developed countries

like the United States (4). Ethiopia is among the most pervasive countries in the East African region, “the so -called East African Esophageal Cancer Corridor,” which stretches from Sudan to South Africa. Multiple studies showed a tendency to increase EAC worldwide, including in Africa. In a recent Kenyan study, the prevalence of EAC among esophageal tumors was 18.9%, which is significantly higher than the 1978 study, which found the EAC to represent 1.1%, and a recent Ethiopian study showed EAC contributed to 13% of the total esophageal cancer patients (5; 6; 7; 8; 9).Risk factors, screening programs, and some management differ for the different types of histology of esophageal cancer and tumor sites. Hence, this study aims to analyze the prevalence and characteristics of esophageal cancer among SPHMMC patients sent for endoscopy examination in the last five years. This study will provide clinicians, policymakers, and society with valuable evidence to tackle this deadly cancer.

Methods

Study Area and Period

The study was conducted from May 15, 2020, to June 15, 2020at St. Paul Hospital Millennium Medical College (SPHMMC) in Addis Ababa, Ethiopia. SPHMMC is a teaching and tertiary referral hospital. It is the largest public hospital and was built in the early 1960s. SPHMMC is the only transplant center in Ethiopia and one of the two tertiary hospitals that provide sub-specialty training.

Study Design

A health facility-based, retrospective cross-sectional study using record review was conducted.

Study Population

The study included all endoscopically diagnosed esophageal cancer patients registeredatSPHMMC between January 2015 and December 2019 who fulfilled the eligibility criteria.

Inclusion and Exclusion Criteria

Patients diagnosed with esophageal cancer and registered with complete information, including age, sex, diagnosis, region of esophagus involved, and biopsy result, in the registration book or the chart were considered eligible for the study.All patients with incomplete Endoscopy reportswere excluded from the study.

Variables of Study

This study included variables such as the histology of esophageal cancer, the site of the cancer, the hemoglobin level, the MCV level, clinical symptoms, and background variables, including age, sex, and place of residence.

Operational Definition

Patient with esophageal cancer: Any patient diagnosed as having an esophageal mass lesion that was considered esophageal cancer by the gastroenterologist and confirmed to be cancer by the pathologist.

Upper Esophageal Cancer: Esophageal cancer that involves up to 19.9 cm from the mid-incisorand/or is reported by endoscopy-performing gastroenterologists as upper esophageal cancer.

Middle Esophageal Cancer: Esophageal cancer involving the distance between 20 cm and 34.9 cm from the mid-incisorand/or reported by endoscopy-performing gastroenterologists as middle esophageal cancer.

Lower Esophagus: Any esophagus cancer patient involving the esophagus starting from 35 cm from the mid incisor up to the cardia or reported by endoscopy -performing gastroenterologists as having lower esophagus cancer.

Squamous cell carcinoma: any esophageal biopsy sample reported as squamous cell carcinoma by a pathologist.

Adenocarcinoma: Any esophageal biopsy sample reported to be adenocarcinoma by a pathologist.

Undifferentiated: Any esophageal biopsy witha malignant character, but it is challenging to differentiate between adenocarcinoma and squamous cell carcinoma.

No Malignancy: Any esophageal biopsy sample considered by a gastroenterologist doing an endoscopy as an esophageal mass but whose histology result was benign.

Data Collection Tools and Procedures

Before the actual data collection started, the principal investigator assessed the patients' charts for relevant variables, and based on that, data extraction tools were prepared. Then, trained nurses working in endoscopy clinics extracted and collected the data.Before collecting the data, the patients' charts were identified by their medical record number, and the investigator extracted and reviewed them.

Data Analysis

Basic descriptive statistics (frequency, mean, and median) are used for data analysis.

Results

Sociodemographic characteristics

From January 2015 to December 2019, 4337 patients underwent EGD at SPHMMC. Among these, 255 patients were diagnosed with esophageal cancer by gastroenterologists working at SPHMMC. Of the patients diagnosed, males make up about 47.5%, and females make up 52.5%. The minimum and maximum age of patients at diagnosis were 22 and 92 years, respectively, with the mean age being 57 years old.

Most patients came from the Oromia region, 147 (57.6%), followed by the SNNP region, 44 (17.3%). Addis Ababa residents contributed about 34 (14.3%), and the Amhara region contributed 26 (10.3%). Other parts of the country contributed only 4 (1.5%) (see Table 1).

Table 1: Background characteristics and indications for EGD in esophageal cancer patients who underwent EGD at St. Paul Hospital Millennium Medical College (Ethiopia) from January 2015 up to December 2019

Gender	Frequency	Percent
Male	123	48.1
Female	132	51.9
Age (in years)		
20 -40	36	14.1
41-60	115	45.1
61-80	82	32.2
>80	22	8.6
Indications for EGD		
Dysphagia	220	86.3
Vomiting	27	10.6
weight loss	2	0.8
epigastric pain	3	1.1
Anaemia	3	1.1
Residence		
Oromia	147	57.6
Addis Ababa	34	13.3
Amhara	26	10.3
SNNP	44	17.3
Other Region	4	1.5

Histologic types, anatomic sites, and stage of esophageal cancer

Thirty-three of the 255 patients had no histologic report attached to their chart. Two hundred twenty-two patients had histological diagnosis results, of which 173 (77.9%) had squamous cell carcinoma, 45 (20.3%) had adenocarcinoma, 3 (1.2%) had undifferentiated malignancy, and one (0.4%) had a benign lesion. The distribution data for the number of patients and different types of esophageal cancer diagnosed is presented in Table 2 below.

Based on the site of esophageal involvement, 25 (10.1%) have upper esophageal involvement, 98 (39.7%) have middle esophageal involvement, and 124 (48.6%) have lower esophageal involvement. The distribution data for the number of esophageal cancer patients based on endoscopic site for mass is presented in Table 2 below

Thereare twenty-two cases of upper esophageal cancer, including one adenocarcinoma and twenty-one squamous cell carcinomas. However, eighty-four squamous cell carcinomas and three adenocarcinomas exist in the middle esophagus. The lower esophagus has sixty squamous cell carcinomas and forty-oneadenocarcinomas, as shown in Figure 1 below.

Table 2: Site, histology, hemoglobin, MCV, and stage of esophageal cancer patients who underwent EGD at St. Paul Hospital Millennium Medical College (Ethiopia) from January 2015 to December 2019.

Study Variables	Frequency	Percent
Site of esophageal cancer		
Upper	25	10.1
Middle	98	39.7
Lower	124	50.2
Histology		
Squamous	173	77.9
Adenocarcinoma	45	20.3
Undifferentiated	4	1.8
Haemoglobin		
Male		
>14	26	56.5
<13.9	20	43.5
Female		
>12	32	69.4
<11.9	14	30.6
MCV		
>100	4	4.8
80-1100	69	83.2
<80	10	12
Stage of Esophageal Cancer		
Stage I	0	0
Stage II	1	6.7
Stage III	2	13.3
Stage IV	12	80.0

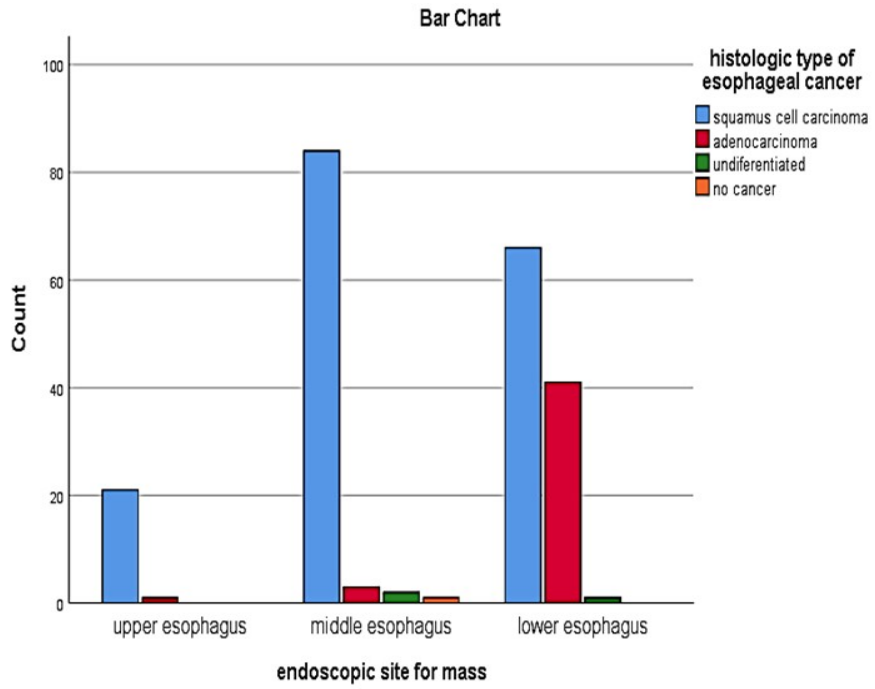

Figure 1: Comparison of different types of esophageal cancer histology with the endoscopic site of the esophageal cancer patients seen at SPHMMC from December 2015 to December 2019

Though only 15 (6.8%) patients have clinical staging workups, 93.3% of those who have workupsreached a very late stage.This small number with staging might be due to a lack of esophageal cancer treatment centers at SPHMMC, and patients are referred to other centers where treatment is available and staging is performed.

Indications for the EGD, hemoglobin, and MCV levels of the patients.

In terms of the presenting clinical symptoms, 220 (86.6%) have dysphagia, 27 (10.6%) have vomiting, 3 (1.2%) have epigastric pain, 2 (0.8%) have weight loss, and 2 (0.8%) have anemia as a primary symptom. Among the forty-six male patients with hemoglobin levels reported, 26 (56.5%) had hemoglobin levels less than 14 g/dl, which is in the anemic range for males. Among the forty-six female patients with hemoglobin determined, 14 (30.4%) had a hemoglobin below 12 g/dl, anemic for females.

Most patients (83.2%) have a normal MCV value between 80 and 100 fl, but 12% have a low MCV, and 4.8% are above one hundred fl (see Table 1).

Discussion

Among 4375 people who underwent esophagogastroduodenoscopy at the SPHMMC gastroenterology unit from January 1, 2015, to December 31, 2019, 255 werediagnosed with esophageal cancer by endoscopy, and 222 were confirmed with biopsy.

Female patients make up 51.9% of the total cases, and males make up 48.1%, which is different from other countries, where males are predominant in the studies from the USA, Europe, and South Africa.(1). A survey from neighboring Uganda showed that the male and female proportions were 74% and 26%, respectively. However, this is consistent with the previous Ethiopian studies, which showed females and males made 59%, 41%, 55%, and 45%, respectively, with a tendency for female predominance (10-12). Other data showed that the incidence rate of esophageal cancer is higher in females compared to males (3.3 vs. 2.2 cases per year per 100,000 people) (4), and in our cases, females made slightly higher. This might be due to less prevalent traditional risk factors, like cigarette smoking, among Ethiopian patients but more exposure of females to indoor pollution during cooking.

When we see the age distribution, there is a patient as young as 22 years and as old as 92 years, making the range 70 years. The mean age was 57, consistent with previous Ethiopian and other African studies.(7; 11; 13). This age is around ten years younger than the average in the Western world(14).

Most of our patients are from the Oromia region, 147 (57.6%). Previous studies done in other hospitals show the high prevalence of Oromia(10; 11; 15). This needs to be studied prospectively. Studies done in Iran, West Kenya, and Brazil showed that tea-drinking behavior (temperature, number of cups per day) and exposure to PAH are significantly associated with ESCC (16; 17; 18; 19).

Only fifteen (6.8%) patients have a CT scan for staging, which is very low to conclude. However, among these patients, twelve were in stage 4 disease, 80%, and 2 (13.3%) patients were in stage 3. This is consistent with another study done in Addis Ababa at another site, where stages 1, 2, 3, and 4 contributed 1.1%, 10%, 19%, and 69.9%, respectively (20).

Among all esophageal cancer diagnoses made by EGD in this period, 25 (10.1%) involved the upper esophagus, the middle esophagus was involved in 98 (39.7%), and 124 (48.6%) involved the lower esophagus. This is consistent with cases in the other hospitals based in Addis Ababa, which were 54.1%, 30.5%, and 15.4% in the lower, middle, and upper esophagus, respectively. However, another previous study from Addis Ababa and neighboring Uganda reported that the commonest site is the middle esophagus (10; 11). The discrepancy between middle and lower esophageal involvement might be due to interobserver differences (21).

The dominant type of histology was squamous cell carcinoma, which contributed 173 (77.9%), adenocarcinoma in 45 (20.3%), and undifferentiated carcinoma in 3 (1.4% of patients). The dominant type of histology was shown to be squamous cell carcinoma in Ethiopia. The results from previous publications reported squamous cells at 88% and adenocarcinoma at 12% (11). Another paper reported squamous cell carcinoma and adenocarcinoma as 90.3% and 9.4%, respectively, showing the majority being squamous cell carcinoma, which aligns with our study (10). Squamous cell carcinoma is the dominant histology type worldwide, making up 75% of the world's esophageal cancer histology (1). Studies in Kenya and Uganda also showed that squamous cell carcinoma is the dominant type, reporting 81.1% and 93% of squamous cell histology, which aligns with our study (7; 10). Adenocarcinoma is the dominant type of histology in North America (USA and Canada) (1). There is an increasing proportion of adenocarcinoma worldwide, including in this study, which is 20.3%, more significant than any previous reports from Ethiopia. This trend has been observed in Kenya, where the proportion of adenocarcinoma grew from 1.1% in 1978 to 18.9% in 2017, consistent with our observation and another Ethiopian study (7; 9).

When we compare esophageal region involvement and histology type by region involved, among the twenty-two cases in the upper esophagus, 21 (95.5%) were squamous cell carcinoma. In contrast, only 1 (4.5%) casewas adenocarcinoma. Among the eighty-nine cases with middle esophageal involvement and histology reports, 84 (94.4%) had squamous cell carcinoma, 3 (3.4%) had adenocarcinoma, and 2 (2.2%) had undifferentiated malignancy. One hundred seven patients have histology and EGD reports in the lower esophagus. Among these, 66 (61.7%) were squamous cell carcinomas, and 41 (38.3%) were adenocarcinoma. This is consistent with the Ugandan study, which showed the adenocarcinoma contribution of the upper, middle, and lower esophagus was 0%, 20%, and 80%, respectively (2).

The prevalence of anemia in our patients is higher than the national-level report. The prevalenceof anemia in males and females in our study is 56.5% and 30.4%, respectively, which is higher than the national prevalence for males, which is 18%, and females, which is 30.4% (22; 23; 24).

Since this is a retrospective study, there are many incomplete/partially filled data, which makes some conclusions difficult. Despite that, it has contributed significant information about the characteristics of esophageal cancer patients at SPHMMC and Ethiopia.

Conclusion

Esophageal cancer affects females in a slightly higher proportion than males, with the mean age being 57 years in Ethiopia, which is a productive age group affecting the economy. Though squamous cell carcinomas are the dominant histology, our data shows an increasing trend in adenocarcinoma. Most patients are from the Oromia region, which needs further prospective study to identify the cause and make public health interventions.

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Ethical Considerations: This research is approved by the SPHMMC Institutional Review Board.

Authors' contribution

Mifta Dellil Hamid is involved in literature preparation, manuscript writing, and editing.
All the authors are involved in manuscript writing and editing.
All the authors have read and approved the final manuscript.

Conflict of interest: **The authors declare no competing interests.**

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