Histopathologic Finding of Esophageal Lesions a Five-Year Retrospective Descriptive Study at Tikur Anbesa Specialized Hospital from 2016 up to 2020.

Thesis submitted to Department of Pathology, Tikur Anbessa Specialized Hospital, School of Medicine, College of Health Sciences, Addis Ababa University for Partial Fulfillment of the Requirements for Post Graduate diploma in Pathology

Investigator - Dr. Fadil Nuredin (MD, Final Year Pathology Resident)

Advisor - Dr. Tufa Gemechu (MD, Associate professor of pathology)

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AACCR- Addis Ababa City Cancer Registry

ADC – Adenocarcinoma

CMV- Cytomegalovirus

EC – Esophageal carcinoma

EGD - Esophagogastroduodenoscopy

ESG - Ectopic sebaceous glands

GERD- Gastroesophageal reflex disease

Globocan –Global cancer observatory

HGM - Heterotopic gastric mucosa

HP - Hyperplasia polyp

HSV- Herpes simplex virus

SCC- Small cell carcinoma

SQC- Squamous cell carcinoma

TASH-Tikur Anbesa Specialized Hospital

UGE- Upper gastrointestinal endoscopy

WHO – World health organization

Abstract

Background: According to Globocan 2018 estimate esophageal cancer ranks the eighth and ninth as the leading cause of cancer mortality and morbidity respectively in Ethiopia. Although esophageal lesions particularly cancer is a public health problem in Ethiopia, there are limited data on the margin status, gross description of carcinoma, and proportion of nonneoplastic disease in the country.

Objectives: This study aims to assess the histologic type and anatomic location of esophageal lesions overall, and gross description, length of the involved segment, radial margin status, and pathologic stage group of esophageal carcinoma at Tikur Anbessa Specialized Hospital Addis Ababa, Ethiopia.

Methods: The study was carried out at Tikur Anbessa Specialized Hospital Addis Ababa, Ethiopia. The record of 518 patients who had histopathological diagnosis of esophageal lesions over a period of 4 years and 8 months between January 01, 2016, and August 30, 2020, were retrospectively analyzed. A structured data extraction tool was used to collect important variables. Descriptive statistics such as mean, median, frequency, and percentages, etc... were computed using SPSS computer software version 26.0.

Result: Out of 518 esophageal endoscopic and resection specimens studied 294(56.8%) were females and 224(43.2%) were males. An age range of 35 days up to 86 years was observed. There Were 475 (91.7%) malignant Cases, 34(6.56%) nonneoplastic cases, and 9(1.73%) precancerous cases. From malignant cases, 46.9% occurs in the distal third of the esophagus followed by 25.1% in the middle third. The mean and median tumor lengths were 4.23 and 4 cm respectively. The most common macroscopic (gross) finding was diffusely infiltrative or constricting 46(48.4%) followed by Fungating or ulcerative38(40.0%). There were 374(78.7%) squamous cell carcinoma and its variants, 94(19.8%) adenocarcinoma and its variants, 6(1.3%) adenosquamous cell carcinoma, and 1(0.2%) undifferentiated carcinoma. 42(44.7%) had positive radial margin status. The commonest histologic grade is G1 29 (48.3%) followed by G3 17 (28.3%) and G2 14 (23.3%). The most common pathologic stage group was stage III 49(54.5%) followed by stage II 27(30%), and stage I and IV each account for 7(7.8%).

Half of premalignant cases occur in the middle third and the other half in the distal third. The most common histologic type was high-grade squamous dysplasia 5(55.6%) followed by Barrett's esophagus with low-grade dysplasia 2(22.2%). 56.3% nonneoplastic cases occur in the distal third followed by two or more segments in 21.9%. Barrettes esophagus, Nonspecific esophagitis, and benign ulcers account for more than 60 % of the cases

Conclusion: The majority of esophageal lesions were malignant and are squamous cell carcinoma. Overall cancer of the esophagus mainly affects the distal 1/3 of the esophagus including GEJ. Most carcinomas are well-differentiated, in pathologic stage III, and have positive radial margin status.

Keywords: Non-Neoplastic, Precancerous, Esophageal Cancer, Histologic Type, Radial margin, Histologic grade, pathologic Stage group.

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1. Introduction

1.1. Background

The esophagus is among the simplest of organs: a hollow, muscular conduit lacking significant secretory or absorptive function that serves to connect the pharynx and stomach. The total length varies with the height of the individual but averages about 25 cm in adults. By common endoscopic measurement, this corresponds to an esophagus beginning at 15 to 18 cm from the incisor teeth and extending to approximately 40 cm (range 30 to 43 cm) [1]. The esophagus traverses three anatomic compartments: cervical, thoracic, and abdominal. The thoracic esophagus is divided arbitrarily into equal thirds: upper, middle, and lower. Cervical esophagus, upper thoracic esophagus, middle thoracic esophagus, lower thoracic esophagus measured from the incisors extend from 15 to <20 cm, 20 to <25 cm, 25 to <30 cm, 30 to 40 cm respectively [2]. Similar to the rest of the gastrointestinal tract, the esophagus is assembled from four microscopic layers: mucosa, submucosa, muscularis propria, and serosa or adventitia. For the most part the mucosa is stratified non keratinizing squamous epithelium which become simple columnar for distal 2 to 3cm of esophagus [1].

The junction between squamous and columnar mucosa represents the squamocolumnar junction or Z-line. The squamocolumnar junction does not necessarily coincide with the anatomic gastroesophageal junction (the site at which the tubular esophagus joins the first fold of the saccular stomach). Numerous studies have found that many adult patients have metaplastic cardiac-type mucosa in the distal esophagus (up to 2 to 3 cm proximal to the gastroesophageal junction) as a consequence of physiologic or pathologic gastroesophageal reflux [1].

The esophagus can be sited for a wide variety of infections, inflammatory disorders, vascular disorders, mechanical conditions, toxic and physical injury, including radiation injury and neoplasm [3]. Esophageal lesions can be classified in different ways; histologically depending on the involved layer into epithelial or subepithelial lesions, depending on histogenesis into neoplastic or non neoplastic, depending on behavior into benign or malignant, and endoscopically depending on endoscopic features such as flat, raised, or cystic lesions [4].

Esophageal benign lesions have a diverse spectrum of etiologies in terms of clinical course and underlying pathologic features. Benign esophageal tumors, while uncommon compared with esophageal carcinoma, can sometimes cause dysphagia but often have insignificant clinical outcomes. Benign esophageal tumors are rare, with a prevalence $\leq 0.5\%$, while benign tumors represent 20% of esophageal neoplasms on autopsy. Since many of these tumors are small and asymptomatic, few benign esophageal lesions attract clinical attention. Benign esophageal lesions could be detected more often with the widespread use of endoscopes, radiologic imaging, and increased awareness of the disease [4].

There are two main type of precursor (precancerous)lesion in esophagus: Barrett dysplasia and squamous dysplasia [5]. Barrett's esophagus is an epithelial metaplasia which replaces esophageal squamous epithelium for variable lengths from the lower esophageal sphincter region cephalad. It is a complication that occurs in approximately 12% of patients with prolonged gastroesophageal reflux. The importance of this disorder is that it is associated with an increased risk of adenocarcinoma of the esophagus [6]. Barrett's esophagus with dysplasia, especially high grade is considered to be a precursor lesion for adenocarcinoma [6]. In common with squamous dysplasias elsewhere e.g. the cervix, squamous dysplasia of the esophagus also appears to be a precancerous lesion. Thus, it is commonly found adjacent to invasive cancers, and follow-up studies of dysplasia have shown progression to cancer in many instances [6].

Esophageal cancer is one of the common malignancies worldwide, with clearly defined endemic regions [7]. Esophageal cancer incidence varies globally, with its highest across the "esophageal cancer belt" (Countries of the East and South Africa and Asia) [8]. There are two main histological subtypes of carcinoma of the esophagus; squamous cell carcinoma (SCC) and adenocarcinoma. For many years, squamous cell carcinoma has been the commonest subtype across the world. However, in the last four decades there has been a dramatic rise in the incidence of adenocarcinoma of the esophagus, especially in the western countries [7]. This has been attributed to certain risk factors including obesity, gastroesophageal reflux disease (GERD) and diet (7). Squamous cell carcinoma is more common in Central, Eastern, and Southern parts of Africa; with the African esophageal squamous cell carcinoma (ESCC) corridor stretching from the Southern part of Sudan to the Eastern Cape province of South Africa. Ethiopia is one of esophageal cancer belt countries [8].

1.2. Statement of the problem

The definitive diagnosis of upper gastrointestinal disorders rests on the histopathological confirmation and is one of the bases for planning proper treatment. The esophagus is one of the most common sites of endoscopic mucosal biopsy in the gastrointestinal tract. Most of these biopsies are performed to exclude esophagitis (usually secondary to gastroesophageal reflux disease) or to document the presence or absence of Barrett esophagus, with or without dysplasia. Other forms of infectious esophagitis include esophagitis secondary to Candida spp., cytomegalovirus, or herpes simplex virus. The esophagus is also the site of glandular and squamous dysplastic processes that predispose to adenocarcinoma and squamous cell carcinoma, respectively [3,9].

Study done in one of teaching hospital of India from November 2006 to July 2008 shows of the total 25 cases of esophageal biopsies, 56% constituted non neoplastic lesions and 44% had

neoplastic pathology. All of the neoplastic cases was SQC (squamous cell carcinoma) occurred most commonly (73%) in the middle one third of the esophagus [3]. Similarly, study was carried out in one of Indian Medical College Hospital and Research Centre, for a period of one year between March 2018 and February 2019 shows from a total of 22 esophageal biopsies received 16 (72%) of them showed non neoplastic lesions and the remaining 6 (28%) were neoplastic lesions. The study report showed that the common non neoplastic lesion was chronic nonspecific esophagitis, followed by esophageal ulcer. It was also observed that squamous cell carcinoma was the most frequently reported neoplastic lesion [10]. in contrary study done in one tertiary Care hospital of Kashmir over a period of 26 months from March 2011 To April 2013. Among 50 esophageal biopsies studied, 9/50 (18%) revealed non neoplastic pathology while 41/50 (82%) Were malignancies. The most common non neoplastic lesion was nonspecific esophagitis followed by hyperplastic polyp and squamous papilloma. All of malignant case were squamous cell carcinoma [11].

Based on 2018 Globocan estimate esophageal cancer is the seventh most common cancer globally, with an estimated 572,034 new cases (3.2% of the total), and the sixth most common cause of death from cancer with an estimated 508,585 deaths (5.3% of the total) [12]. The largest share occurs in eastern Asia 335,080 new cases with male to female ratio around 2.4:1 and 300,878 deaths. In eastern Africa there was 17,792 new cases with male to female ratio of 1.2:1 and 17564 deaths [12].

Ethiopia one of east African countries with a population of 115,145,696 as of July 2020 [13]. In Ethiopia Esophageal cancer ranks the eighth and ninth as the leading cause of cancer mortality and morbidity respectively according to Globocan 2018 estimate [12]. Study conducted in Ayder Referral Hospital Tigray, northern Ethiopia from 2011 up to 2015 there were a total 22 esophageal biopsies with histopathologic diagnosis 0f which majorities was neoplastic (72.7%). There were 10 cases of squamous Cell Cancer (45.5%), 4 cases of adenocarcinoma (18.2%), 1 case of Undifferentiated Malignant tumor (4.5%) and 1 case of esophageal Dysplasia (4.5%). The remaining 27.3% were non neoplastic 2 cases of acute esophagitis (9.1%), 2 cases of Glycogen Acanthosis (9.1%), 1 case of Barret's Esophagitis (4.1%, and 1 case of Normal (4.1%)., and 2 Inconclusive cases (8.3%) [14].

According to the Addis Ababa City Cancer Registry (AACCR), there were a total of 5701 newly diagnosed cancer cases over the period of three years (2011–2014). Majority of the cases occurred in female patients accounting for 67%(3820 cases) of total newly diagnosed cancer cases. Among cancers affecting females, esophageal cancer account for about 2% making esophageal cancer the ninth most common cancer in female [15].

There are few old study (more than a decade old) done in Tikur anbesa Specialized Hospital to assess prevalence of histopathologic patterns of neoplastic esophageal lesion. Although two

recent study on esophageal cancer talks about histologic pattern, staging and location of tumor [16,22]. There is no recent research on margin status and macroscopic pattern (gross appearance, length of involved segment) of neoplastic esophageal lesion, and there is limited study that asses the prevalence of non-neoplastic and premalignant esophageal lesion in Ethiopia particularly in this hospital. Hence, this study intended to provide evidence on demographic pattern, gross finding, histopathologic type, pathologic staging, quality of surgery (margin status), location of neoplastic esophageal lesions and demographic patterns, anatomic location, and histopathologic types of non neoplastic and premalignant esophageal lesions in TASH.

1.3. Significance of the study

Upper GI endoscopic biopsies are one of the common specimen submitted to Tikur anbesa specialized teaching Hospital(TASH) department of pathology. As mentioned earlier there is no recent research on margin status and macroscopic pattern (gross appearance, length of involved segment) of neoplastic esophageal lesion and there is limited study that asses the prevalence of non-neoplastic esophageal lesion in Ethiopia particularly in this hospital. The aim of this study is to fill this gap by inclusively assessing pathologic finding of both neoplastic and non-neoplastic esophageal lesions.

Although individual biopsy reports can act as feedback mechanism on margin status for the surgeon's, the result of this study will indicate the general quality of the surgery with regards to margin status.

Data from the literature shows differences in the relative frequencies of neoplastic and non neoplastic esophageal lesions. This research will also try to address the controversy on proportion of neoplastic and non neoplastic esophageal lesions.

2. Literature review

2.1. Epidemiology and histopathologic patterns of neoplastic Esophageal lesion

Between January 2008 and December 2011, a total of 106 cases of esophageal cancer were received in the department of pathology, BP Koirala Memorial Cancer Hospital (Nepal). Out of 106 cases, 57 (53.8) were males and 49 (46.2%) were females. The male to female ratio was 1.2:1. The esophageal cancer was most common in the age group of 61-70 years, comprising 34% of total cases. The esophageal cancer was uncommon in less than 30 years or more than 80 years of age. There were 68 (64.15%) cases of squamous cell carcinoma, 33 (31.13%) cases of adenocarcinoma including 6 cases of signet ring cell carcinoma, 4 (3.76%) cases of undifferentiated carcinoma and 1 (0.94%) case of Small cell carcinoma(SCC). Out of 68 cases of SQC, 25 (23.58%) were well differentiated, 37 (34.91%) were moderately differentiated and 6 (6.58%) cases were poorly differentiated SQC. Out of 33 cases of adenocarcinoma, 11 (10.35%) cases were well differentiated, 9 (8.47%) were moderately differentiated and 7 (6.58%) cases

were poorly differentiated. The gross findings in SQC were either exophytic or ulcerative lesion with deep irregular ulcers and adenocarcinoma in distal esophagus showed flat patches to nodular masses. Distal third of esophagus was the most common site for esophageal carcinoma, followed by middle esophagus and proximal esophagus. The maximum number of SQC was seen in middle esophagus (n=22) followed by distal (n=21) and proximal esophagus (n=14). Similarly, the maximum number of adenocarcinoma was seen in distal esophagus (n=27) followed by middle esophagus (n=2) [17].

Study done in Uganda over a period of 3 years between January 2009 and December 2011 shows that of the 71 results analyzed, the female to male ratio was 1:3 with mean age of 55.45 years ± SD 11.83. The common histopathological subtype of cancer of esophagus was squamous cell carcinoma of esophageal consisting of 66 patients (92.96%). The ratio of squamous cell carcinoma to adenocarcinoma was 13:1. The majority of the esophageal cancers were found in the middle third with 38 patients (53.52%), followed by lower third with 27 patients (38.03%) and the upper third which was only 6 patients (8.45%) [18].

Study done in two tertiary health institutions of Tanzania from March 2008 and February 2013, During the period of study, a total of 1,296 malignant gastrointestinal tract tumors were registered. Of these, 328 patients, representing 25.3% of all cases, were histopathologically confirmed cases of esophageal cancer and formed the study population. The age of patients at presentation ranged from 24 to 78 years with a median age of 47 years. The modal age group was 41 to 50 years; 158 (48.2%) patients were aged 50 years or below. There were 226 (68.9%) men and 102 (31.1%) women with a male to female ratio of 2.2:1. The difference in mean age between men and women at presentation was not statistically significant (P = 0.456). The middle third of the esophagus was the most frequent anatomical site for esophageal cancer in 58.5% of patients. This was followed by the lower third of the esophagus and upper third of the esophagus in 27.4% and 10.4% of patients, respectively. The anatomical site was not recorded in 3.7% of patients. On endoscopic examination, most of lesions were ulcerative (40.2%). The median tumor length according to endoscopy and barium swallow was 5 cm (range 4 to 7 cm). The tumor length was ≤5 cm in 40.2% of patients and >5 cm in 185 (52.4%) patients. The tumor length was not documented in 11 (3.4%) patients. Squamous cell carcinoma was the most common histopathological type, occurring in 315 (96.0%) patients. Of these, 34 (10.8%) tumors were in the upper third, 200 (63.5%) in the middle third and 81 (25.7%) in the lower third. Adenocarcinoma occurred in 13 (4.0%) patients, of which 9 (69.2%) were in the lower third and 4 (30.8%) in the middle third. Out of 13 patients with adenocarcinoma, 3 (23.1%) patients had evidence of Barrett's esophagus. TNM staging was documented in only 104 (31.7%) patients. Of these, 102 (98.1%) patients were diagnosed with advanced esophageal cancer (stages III and IV). According to tumor grading, most of tumors were moderately differentiated, accounting for 56.1% of cases. Distant metastasis was documented in 43.3% of patients [19].

A total of 448 EC patients visited National Cancer Institute at the University of Gezira (NCI-UG) in Sudan 1999-2012, and the annual number of EC cases increased steadily from 1999. The overall male-to-female ratio for EC was 1:1.8, but the ratio was tumor type-dependent, being 1:2 for SQC and 2:1 for ADC. The age distribution of the patients shows an increase in the number of EC cases with increasing age, peaking around 60-69years of age and then decreasing at older ages. The median patient age was 60 years, and patients aged 35 years or younger(n=27) constituted 6.0% of the total number of patients, with similar proportions among females (5%) and males (8%). Squamous cell carcinoma (SQC) was the predominant EC tumor type (90%), and adenocarcinoma (ADC) was reported in 9.4%. SCC was also the most common tumor type (diagnosed in 96.3% of cases) among the patients aged 35 years or younger at diagnosis [20].

A cross-sectional descriptive study carried out at Kenya, Kenyatta National Hospital (KNH) Endoscopy Unit and Surgical outpatient clinics from March 2014 to December 2014. A total of 74 patients were recruited in the study. The majority (78.4%) were male with male female ration of 3.6:1. The youngest patient was 34 years old and the oldest patient was 88 years old. The mean age was 57.72 (SD +/- 11.76) years. There were 14 (18.9%) adenocarcinoma and 60 (81.1%) squamous cell carcinoma [7].

A ten-year histopathologic review of solid malignant tumors in TASH from 1st January 2003 to 31th December 2012 shows out of 15,685 histopathologic diagnoses 483 (3.08%) were esophageal malignancy. Which makes esophageal malignancy the 7th most common solid malignant tumor [21].

A total of 349 esophageal cancer patients diagnosed from 2010 to 2016 in Tikur Anbessa Specialized Hospital (TASH). Out of this 143 (49%) were males and 206 (51%) were females. the male to female ratio was 0.69:1. The overall mean age was 51 years (18-95) with SD of 11.9 years, the mean age for female patients was 50.5 years (+_10.9 SD) whereas the mean age for male patients was 52.7years (+_ 13.1SD), minimum age of 18 years and maximum age of 95 years. Majority (32.4%) of esophageal cancer patients were in the age range of 50 -59 years (n=113). Majority (56.9%) of esophageal cancer patients came from Oromia at the time of diagnosis. Only 318 out of 349 esophageal cancer patients have documented histologic type and only 57 patients have document about histologic grades. In this study the commonest histologic type of cancer found was squamous cell carcinoma 90.3% (n=287), the second most common type was adenocarcinoma 9.4%(n=30) and adenosquamous cell carcinoma account for 0.3% (n=1). One hundred eight six (54.1%) of the cases had the cancer at the lower third of esophagus whereas 105 cases (30.5%) had the cancer at the middle third. 269 (77.1%) of patients who had document concerning stage at diagnosis, 188(69.9%) were diagnosed as stage four followed by 51(19.0%) as stage three [16].

A retrospective document review from ten referral hospitals which are located in seven regional states and one city administration of Ethiopia; Amhara, Oromia, Southern Nations Nationality People Region (SNNPR), Tigray, Afar, Harari, Somali and Dire Dawa from 2012- 2017. Over

the period of six years, a total of 777 esophageal cancer cases were identified and the median age of these patients was 55 years with interquartile range (IQR) of 19. More than half 428 (55.1%) of the cases were males and majority of them were reported from Oromia and Somali regional states with 388 (49.9%) and 202 (25.9%) respectively. The highest number of esophageal cancer cases were recorded in 2016 with a total number of 185 (23.8%) while the lowest 98 (12.6%) was in 2012. Eighty percent of esophageal cancer cases were diagnosed at late stage of the disease. More than one fourth 210 (27.0%) of patients were operated with the majority 156 (74.3%) to insert a feeding tube followed by trans-hiatal esophagostomy 23 (10.9%). Of the 118 results analysed, squamous cell carcinoma and adenocarcinoma were the predominant histologic type with 67(56.7%), and 43(36.4%) respectively. One fourth 194 (25.0%) of the patients were alive and more than two third 557 (71.7%) patients' current status was unknown at the time of the review. two third of the patients 209 (66.1%) site of mass was located. Of the patients underwent endoscopy, Of the site of mass located, esophageal cancers were found in the middle thoracic in 98(31%), followed by lower thoracic with 75(23.7%) patients. From the total 123 patients whose cancer stage was recorded, 98(80%) of them were at the stage III and IV during their first presentation [8].

A case control Study published in 2019 on prevalence of HPV and H.pylori in esophagus and GEJ cancer biopsies done in collaboration between two private endoscopy clinic in Addis Ababa and TASH shows from 62 esophageal and GEJ cases 34% occurs in distal third,31% in middle third,18% in GEJ, and 6% in proximal third of esophagus. The most common histologic type is squamous cell carcinoma accounting for 74% of the cases and 18% cases were adenocarcinoma [22].

2.2. Epidemiology and histopathologic patterns of non neoplastic esophageal lesions

In one 2015 article published in Taiwan on endoscopic and pathological features of esophageal benign lesions. Out of 2997 endoscopic examinations retrospectively reviewed there were a total of 149 benign esophageal lesions of which 108 were non neoplastic and the remaining 41 were neoplastic benign esophageal lesions. Glycogenic acanthosis was demonstrated as nodules involving otherwise normal esophageal mucosa in 66 patients (42 men and 24 women; mean age: 52 years, range: 45-79 years). 21 patients had histologically proven heterotopic gastric mucosa (HGM) (12 men, 9 women; mean age: 48 years, range: 25-69 years). Most patients have no symptom but some patients present with pharyngeal globus sensation, heartburn, acid regurgitation, or dysphagia because HGM produces mucin and acid. 18 patients had histologically proved hyperplasia polyp (HP) (12 men, 6 women; mean age: 36 years, range: 18-69 years). HPs were most common in the region of the esophagocardiac junction (67%), followed by the distal esophagus (27%) and mid-esophagus (6%). Three patients with Ectopic sebaceous glands(ESG) (one man and two women; mean age: 52 years, range: 45-69 years). EGD revealed variable numbers from single to > 100 yellowish plaques measuring 1-2 mm in diameter in the middle and lower esophagus and one a 62-year-old male patient with esophageal xanthomas localized in the lower esophagus [4].

Study conducted in India for a period of one year between March 2018 and February 2019 on spectrum of histomorphological patterns on endoscopic biopsy in patients with upper gastrointestinal tract disorders. Among the 22 esophageal biopsies received 16 (72%) of them showed non neoplastic lesions and the remaining 6 (28%) were neoplastic lesions with over all male to female ratio of 14/8. The commonest non-neoplastic lesion was chronic non-specific esophagitis, followed by esophageal ulcer. There were 9 cases of chronic non-specific esophagitis (40.9%), 3 cases of esophageal ulcer (13.63%), 1 case of esophageal candidiasis (4.54%) and 3 cases of barrettes esophagus (13.63%) [10].

Study conducted in Ayder Referral Hospital Tigray, northern Ethiopia from 2011 up to 2015 there were a total 22 esophageal biopsies with histopathologic diagnosis 0f which majorities was neoplastic (72.7%). The remaining 27.3% were non neoplastic 2 cases of acute esophagitis (9.1%), 2 cases of Glycogen Acanthosis (9.1%), 1 case of Barret's Esophagitis (4.55%), and 1 case of Normal (4.55%) [14].

3. Objective

3.1. General objective

- To determine pathologic finding of esophageal lesions.

3.2. Specific objective

- To describe the relationship of different esophageal lesions with age and sex of individuals.
- To determine prevalence of non neoplastic, premalignant and malignant esophageal lesions.
- To assess different esophageal lesion with regards to different parts of esophagus (proximal, middle or distal third).
- To determine distribution of histologic type of nonneoplastic, premalignant and neoplastic esophageal lesions.
- To describe the length of involved segment and gross patterns of neoplastic esophageal lesions.
- To assess quality of surgery with regards to radial margins status.
- To establish patterns of grade and stage of malignant esophageal lesions.

4. Material and method

4.1. Study area

Ethiopia is a country located in the Eastern Horn of Africa, has a population of more than 110 million. The Black Lion Hospital in Addis Ababa is the university teaching hospital of the Addis Ababa University and the largest referral hospital in the country. The Hospital is located in Addis Ababa at Lideta sub-city opposite to Immigration office Ethiopia. In pathology department there are about 12 pathologists, 22 residents, about 10 histotechnologist, 1 secretary, 2 typists and 6 supporting stuffs. Histopathology, cytopathology, hematopathology and neonatal autopsy are day to day working areas in which diagnosis of the abnormalities as well as teaching learning processes accomplished. Pathology department receives about 10,000 biopsy specimens annually. Endoscopic esophageal biopsies and esophagectomy specimen account for significant number of them.

4.2. Study Design and period

The study will apply retrospective cross-sectional descriptive method to review all histopathology reports of endoscopic and resection specimen of esophageal lesions submitted to pathology department of Black Lion specializes teaching Hospital from January 01, 2016 to August 30, 2020.

4.3. Source population

All patients whose biopsy specimens were submitted to the department of pathology.

4.4. Study population

All patients who had endoscopic or resection specimen of esophageal lesions submitted to pathology department of Black Lion specializes teaching Hospital during the study period.

4.5. Inclusion and exclusion criteria(Eligibility)

4.5.1. Inclusion criteria

- All patients with esophageal lesion who underwent endoscopic biopsies or esophagectomy.

4.5.2. Exclusion criteria

- Esophageal specimen with no primary or secondary pathology.

- Esophageal lesions with descriptive diagnosis or non diagnostic result.
- Esophageal lesions without original biopsy request form.
- Endoscopic biopsies of esophageal lesion which also have resection specimen.
- Those patients with two or more missing variables.

4.6. Sample size estimation

All patients fulfilling the criteria during the study period will be included.

4.7. Sampling procedure

All the hard copy histopathology reports with corresponding requests paper of esophageal lesions from January 01, 2016 to August 30, 2020 will be reviewed from the archive of pathology department.

4.8. Data collection tools and procedures

Demographic data, anatomic site of lesion, gross (macroscopic) finding, histopathology diagnoses, margin status and stages of cancers will be extracted from the hard copy using data extraction sheet.

4.9. Operational definitions

Histopathologic pattern: In this study histopathologic pattern is defined as non-neoplastic or neoplastic

Non neoplastic - Nonspecific esophagitis, eosinophilic esophagitis, infectious esophagitis (fungi, CMV, HSV), Achalasia, GERD, barrettes esophagus without dysplasia and others(name).

Neoplastic – barrettes esophagus with dysplasia, squamous dysplasia, Squamous cell carcinoma, adenocarcinoma, undifferentiated carcinoma and others(name).

Location of lesion: in this study location of lesion is defined as Distal third including GEJ neoplasm with epicenter proximal to 2cm of cardia of stomach, middle third and proximal third of esophagus.

Length of involved esophagus: in this study length of involved segment is defined as < 2cm, 2-5cm and >5cm.

Radial margin status: in this study radial margin status is defined as positive when the tumor is ≤ 1mm from inked surface or negative when the tumor is > 1mm from inked surface.

Macroscopic pattern: in this study macroscopic pattern is defined as flat or plaque, ulcerative, fungating, constrictive, diffusely infiltrative and mixed.

Staging: Tumor staged as esophageal if a tumor involves the EGJ and its epicenter is ≤2 cm into the proximal stomach (i.e, ≤2 cm distal to the EGJ) and staged as stomach if the tumors involving the EGJ with their epicenter >2 cm into the proximal stomach (i.e., >2 cm distal to the EGJ).

4.10. Study variables

In the study, the variables included for analysis and interpretation are depicted as the following.

- Age of patient at diagnosis
- Sex of patient
- Histopathologic type
- Anatomic site of the lesion
- Macroscopic description
- Length of involved segment
- Radial margin status
- Histologic grade of cancer
- Stage of cancer at diagnosis

4.11. Data analysis

The data sheets will be coded and data entry, cleaning and analysis will be done using the Statistical Package for the Social Sciences (IBM SPSS 26.0).

4.12. Ethical consideration

Ethical permission will be sought from the Department of Pathology, College of Health Sciences, Addis Ababa University, and ethics committee at Tikur Anbesa Specialized Hospital.

Names of patients or their chart numbers will not be mentioned in the study to keep the confidentiality of the patients.

5. Result

5.1. General.

A total of 648 esophageal specimens were submitted to the pathology department of TASH from January 01, 2016, to August 30, 2020. Out of this136 were resection and 512 were endoscopic specimens. 130 cases were excluded from the study due to99of endoscopic biopsies had no definitive diagnosis (signed as non diagnostic, suggestive, suspicious, or with description and comment),11 had no primary or secondary pathology (normal histology) and 20 had repeated biopsies and/or followed by resection. Therefor finally a total of 518 biopsies (136 resections and 382 endoscopic) were analyzed. Out of 136 resection specimens, 135 were neoplastic and the remaining 1 was non neoplastic. Out of 382 endoscopic biopsies, 33 were nonneoplastic,9 premalignant and the remaining 340 were malignant (Table 1, Figure 1).

Table 1: Distribution of all the lesions

		Count (n = 518)	%
Specimen type	Endoscopic	383	73.9%
	Resection	135	26.1%
Nature of lesion	Malignant	475	91.7%
	premalignant	9	1.7%
	Non neoplastic	34	6.6%

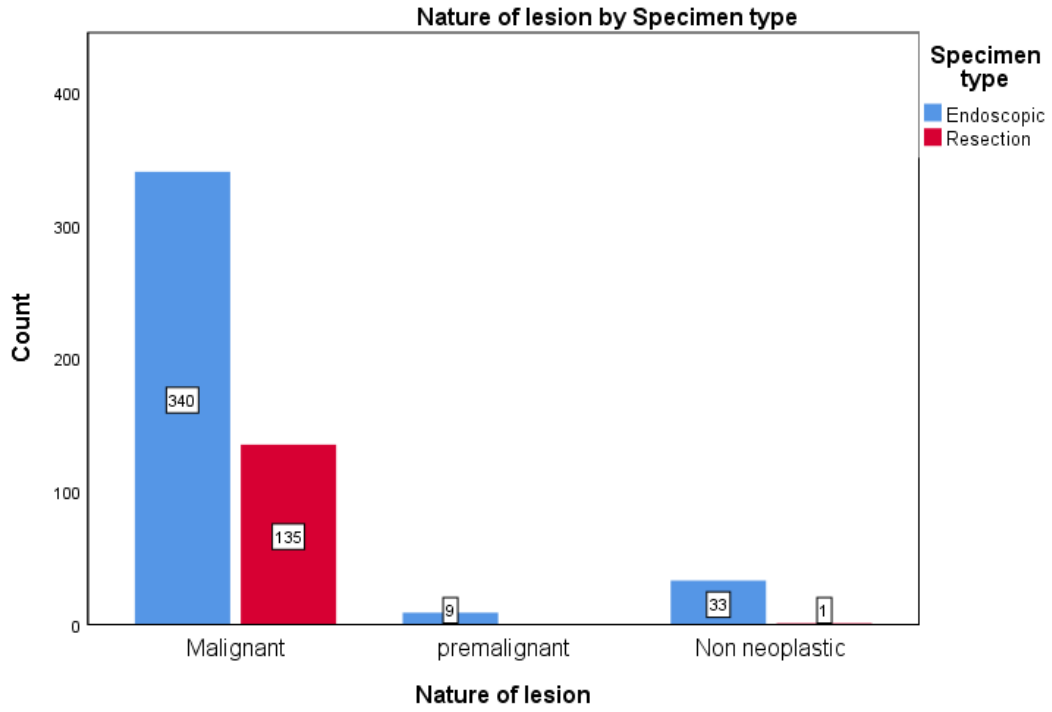

Figure 1 Cluster bar graph of all esophageal lesions by specimen type.

5.2. Description of age and gender characteristics of esophageal lesions.

From a total of 518 esophageal lesions, 56.8%occurs in female and 43.2% occurs in male. The female to male ratio was 1.3:1. The mean and median age was 52.5and 54 years respectively with a SD of 12.9years, the mean age for female patients was 50.6 years (±12 SD) whereas the mean age for male patients was 55 years (±13.7SD), minimum age of 35 days, and maximum age of 86 years. The majority (31.1%) of esophageal lesions occur in the age range of 50 -59 years (n=161) followed by the age range of 60 -69 years 24.1% (n=125) (Table 2).

From a total of 475 esophageal malignant lesions, 56.8% were in females and 43.2% were in males. The mean age was 53.2years (±12.02 SD), the mean age for female patients was 51years (±11.25 SD) whereas the mean age for male patients was 56 years (±12.44SD), minimum age of 15 years, and maximum age of 86 years. The majority (31%) of esophageal malignant lesions occurs in the age range of 50 -59 years (n=147) followed by 24.6% in the age range of 60 -69 years(n=117) (Table 3).

From a total of 9 precancerous esophageal lesions 77.8 % occurs in females and 22.2% occurs in males. The female to male ratio was 3.4:1. The mean age was 54 years (±11.15 SD), the mean age for female patients was 51.7 years (±11.5 SD) whereas the mean age for male patients was 62 years (±5.65SD), minimum age of 29 years and maximum age of 66 years. The majority (44.4%) of precancerous esophageal lesions occur in the age range of 50 - 59 years (n=4) (Table 4).

From a total of 34 nonneoplastic esophageal lesions 50% occurs in females and 50% occurs in males. The female to male ratio was 1:1. The mean and median age was 42.9and 48years respectively with a SD of 19.8 years, the mean age for female patients was 43.7years (± 19.45SD) whereas the mean age for male patients was 42years (±20.76SD), minimum age of 35 days, and maximum age of 75 years. The majority (29.4%) of nonneoplastic esophageal lesions occur in the age range of 50 -59 years (n=10) (Table 5).

Table 2: Age and sex distribution of all esophageal lesions

		Count(n=518)	%
Gender	Male	224	43.2%
	Female	294	56.8%
Group age	0-9	2	0.4%
	10-19	4	0.8%
	20-29	12	2.3%
	30-39	51	9.8%
	40-49	109	21.0%
	50-59	161	31.1%
	60-69	125	24.1%
	70-79	49	9.5%
	80-90	5	1.0%

Table 3: Age and sex distribution of malignant esophageal lesions.

		Count (n=475)	%
Gender	Male	205	43.2%
	Female	270	56.8%
Group age	10-19	1	0.2%
	20-29	6	1.3%
	30-39	49	10.3%
	40-49	103	21.7%
	50-59	147	30.9%
	60-69	117	24.6%
	70-79	47	9.9%
	80-90	5	1.1%

Table 4: Age and sex distribution of premalignant esophageal lesions.

		Count (n=9)	%
Gender	Male	2	22.2%
	Female	7	77.8%
Group Age	20-29	1	11.1%
	40-49	2	22.2%
	50-59	4	44.4%
	60-69	2	22.2%

Table 5: Age and sex distribution of non neoplastic esophageal lesions.

		Count (n=34)	%
Gender	Male	17	50.0%
	Female	17	50.0%
Age Group	0-9	2	5.9%
	10-19	3	8.8%
	20-29	5	14.7%
	30-39	2	5.9%
	40-49	5	14.7%
	50-59	10	29.4%
	60-69	5	14.7%
	70-79	2	5.9%
	80-89	0	0.0%

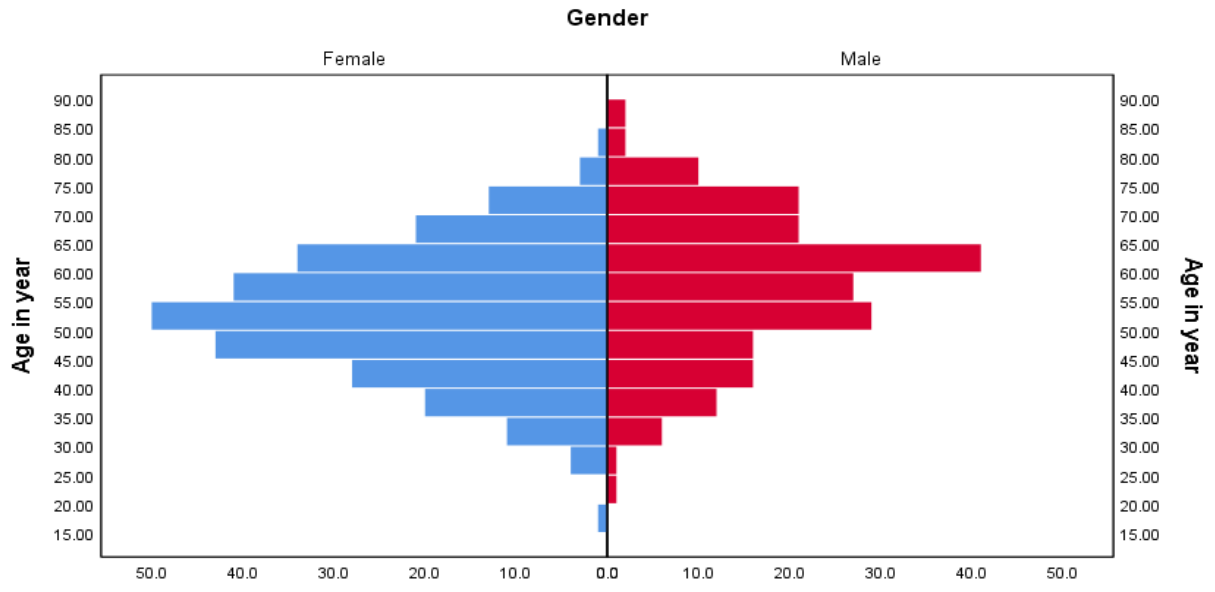

Figure 2: Age pyramid of malignant esophageal lesions.

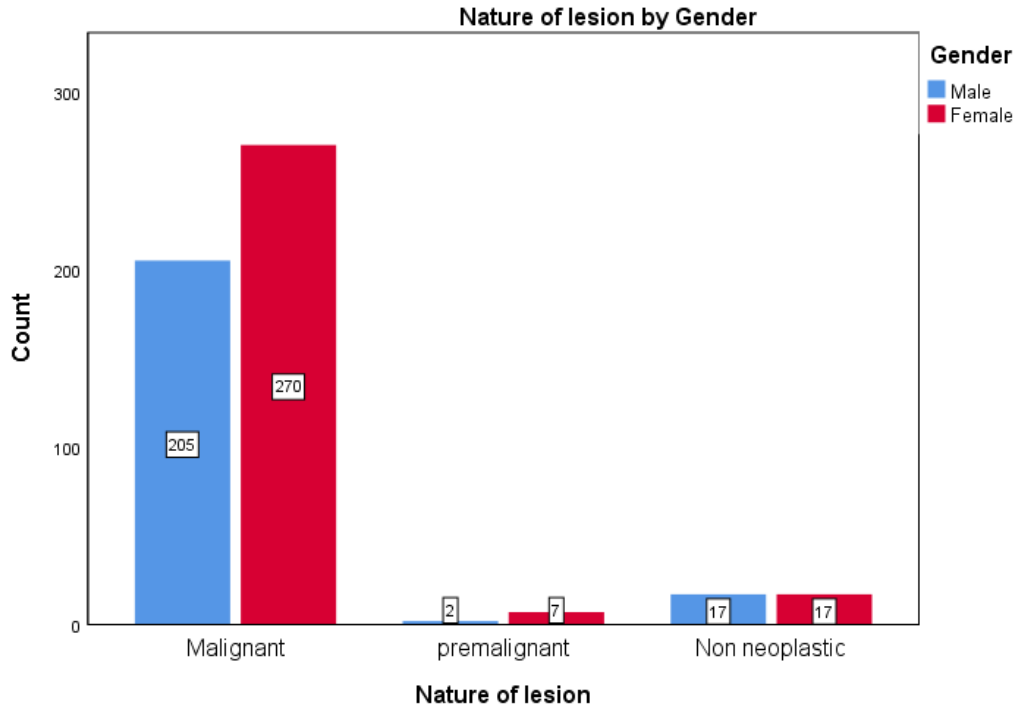

Figure 3: Cluster bar graph of all esophageal lesions with regards to gender.

5.3. Trends of Esophageal lesions based on years of diagnosis in TASH.

When we look at the year-to-year difference in terms of diagnosis 170(32.8%) of esophageal lesions were diagnosed in the year 2018 followed by130(25.1%) in the year 2019. The list number of diagnoses 53(10.2%) cases occurs in the year 2020 (Figure 4).

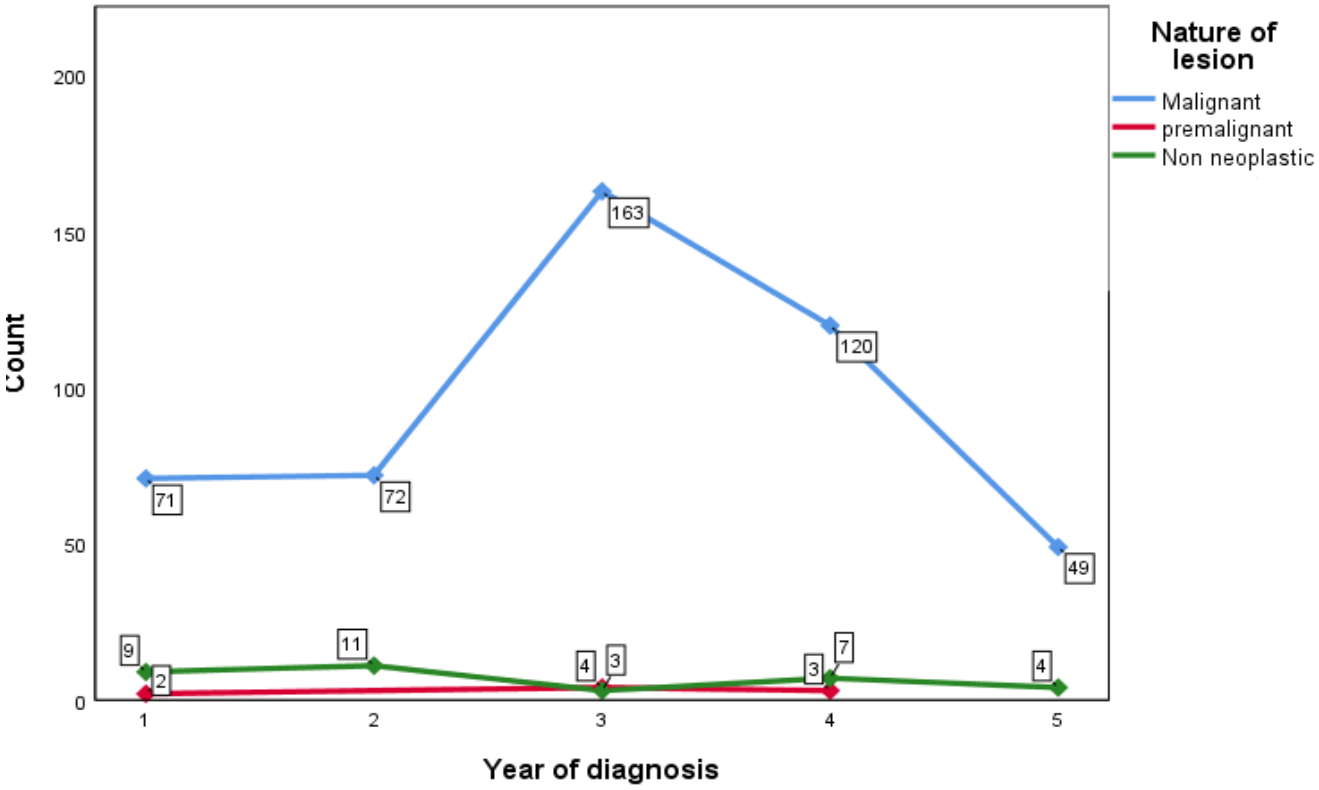

Figure 4: Frequency polygon of different esophageal lesions with regards to years of diagnosis (1= 2016, 2= 2017, 3= 2018, 4= 2019, and 5=2020).

5.4. Macroscopic and microscopic finding of malignant esophageal lesions.

Out of 454 malignant cases had described anatomic location 46.9% occurs in the distal esophagus followed by 25.1%, 14.8%, and 11.5% occurs in middle, GEJ, and proximal esophagus, respectively. The remaining 1.8%of cases involve more than one segment. The location of the tumor varies with the histological type. Squamous cell carcinoma is commonly found in the distal third in 47.5%, middle third in 31.6%, proximal third in 14.4%, GEJ in 5.1%, and two or more segments in 1.4% of the esophagus while adenocarcinoma is more commonly located in GEJ in 51%, distal third in 44.7%, in both GEJ and distal third in 3.2%, and middle

third in 1.1%. 131 of 135 malignant resection cases had described tumor length of the esophagus which is involved by carcinoma. The mean and median tumor lengths are 4.23 and 4 cm respectively. length was <2 cm in 4 (3%), 2-5cm in 76(56.3%) and >5cm in 51(37.8%). The tumor length was not documented in 4 (3%). 95(70.4%) of malignant resection cases had documented gross description. The most common macroscopic (gross) finding was diffusely infiltrative or constricting 46(48.4%) followed by Fungating or ulcerative38(40.0%). There were 4(4.2%) cases of mixed gross patterns all of them was ulcerative and constricting. There were 374(78.7%) squamous cell carcinoma its variants, 94(19.8%) adenocarcinoma and its variants, 6(1.3%) adenosquamous cell carcinoma, and 1(0.2%) undifferentiated carcinoma. Only 60 (12.6%) of malignant cases (20 endoscopic and 40 resections) had documented histologic grade and the commonest histologic grade is G1 29(48.3%) followed by G3 17(28.3%) and G2 14(23.3%).50 (54.3%) in pathologic stage group of III, 28(30.5%) in II, 7(7.6%) in IV, and 7(7.6%) in I. A total of 90 (67.6%) of resection specimens had the TNM stage which can be converted to a complete pathologic stage group. The most common stage group was stage III 49(54.5%) followed by stage II 27(30%), and stage I and IV each account for 7(7.8%) (Table 6, Table 7).

Table 6: Macroscopic finding of malignant esophageal lesions.

		Count (n=475)	%
Anatomic location (n=454)	Proximal third	52	11.5%
	Middle third	114	25.1%
	Distal third	213	46.9%
	GEJ	67	14.8%
	Two or more segment	8	1.8%
Group length (n=131)	<2	4	3.1%
	2-5	76	58.0%
	>5	51	38.9%
Macroscopic tumor type (n=95)	Flat or plaque	2	2.1%
	Polypoid or exophytic	5	5.3%
	Fungating or ulcerative	38	40.0%
	Diffusely infiltrative or constricting	46	48.4%
	Mixed	4	4.2%

Table 7: Microscopic finding of malignant esophageal lesions.		Count	%
Histologic type(n=475)	Squamous cell carcinoma	82	17.3%
	Keratinizing squamous cell carcinoma	223	46.9%
	Non keratinizing squamous cell carcinoma	68	14.3%
	Sarcomatoid squamous cell carcinoma	1	0.2%
	Adenosquamous cell carcinoma	6	1.3%
	Adenocarcinoma	80	16.8%
	Signet ring carcinoma	8	1.7%
	Mucinous adenocarcinoma	5	1.1%
	Papillary adenocarcinoma	1	0.2%
	Undifferentiated carcinoma	1	0.2%
Radial margin status (n=94)	Positive	42	44.7%
	Negative	52	55.3%
Histologic grade (n=60)	G1	29	48.3%
	G2	14	23.3%
	G3	17	28.3%
Pathologic stage group (n=92)	IB	6	6.5%
	IC	1	1.1%
	IIA	17	18.5%
	IIB	11	12.0%
	IIIA	5	5.4%
	IIIB	45	48.9%
	IVA	6	6.5%
	IVB	1	1.1%

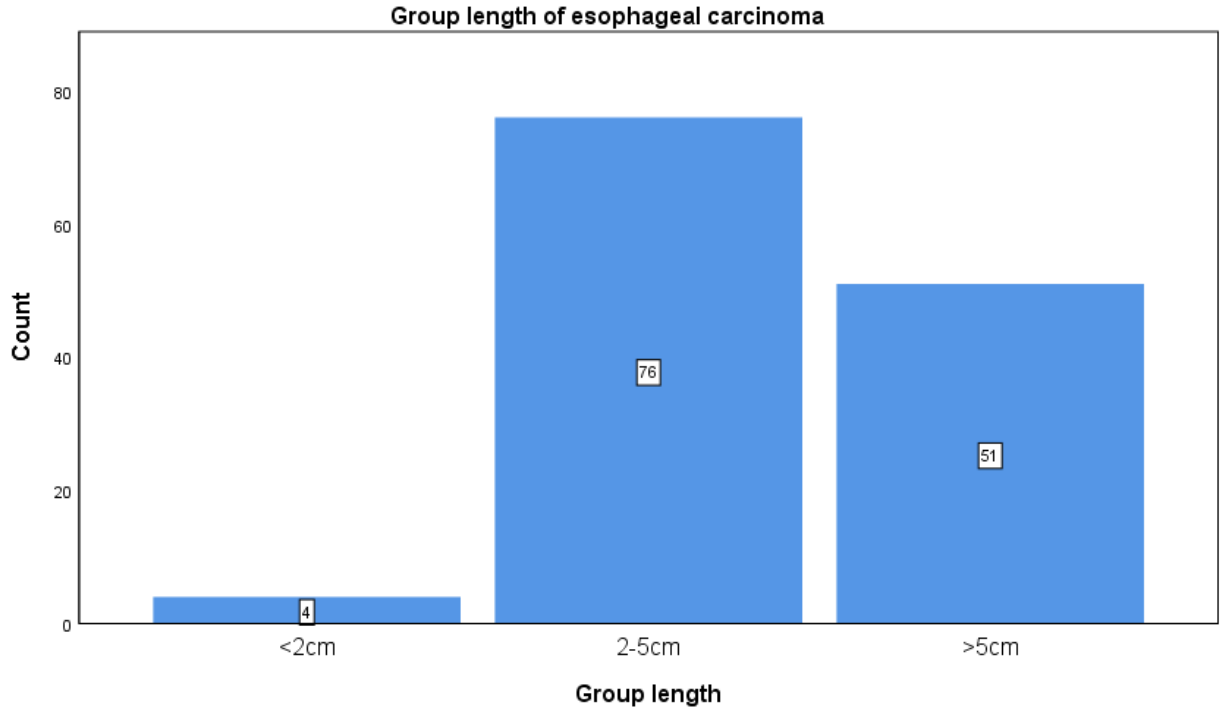

Figure 5: Tumor length of malignant esophageal lesions (carcinoma).

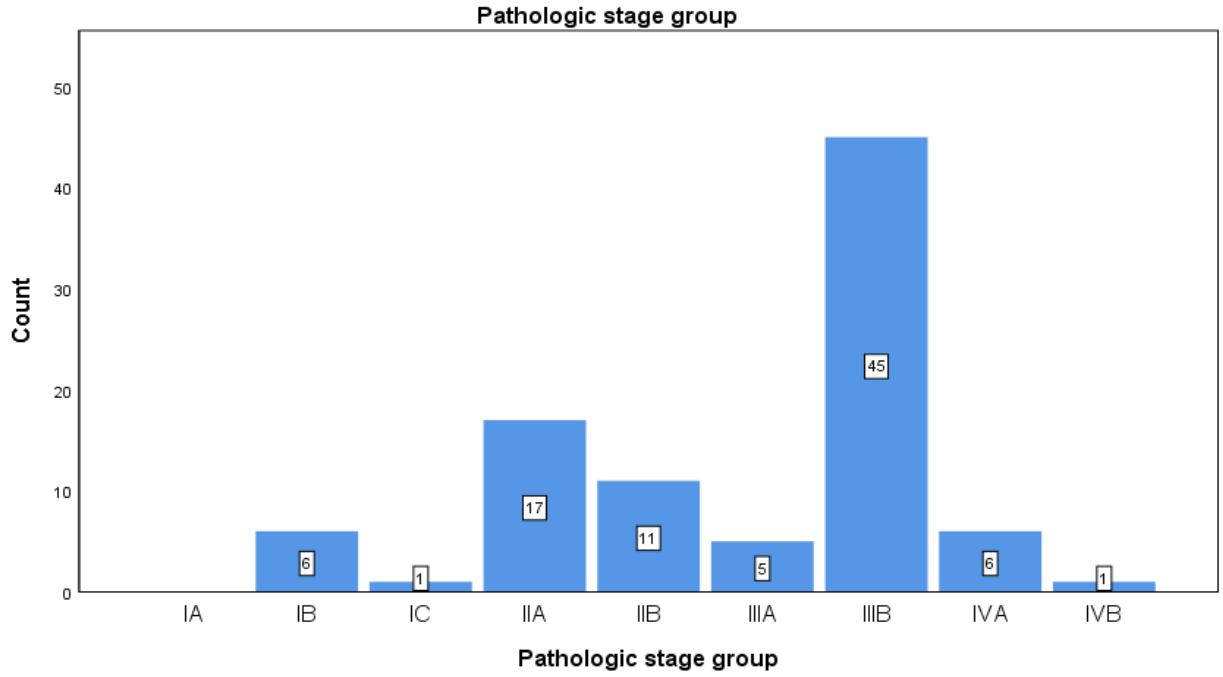

Figure 6: Pathologic stage group of malignant esophageal lesions (carcinoma).

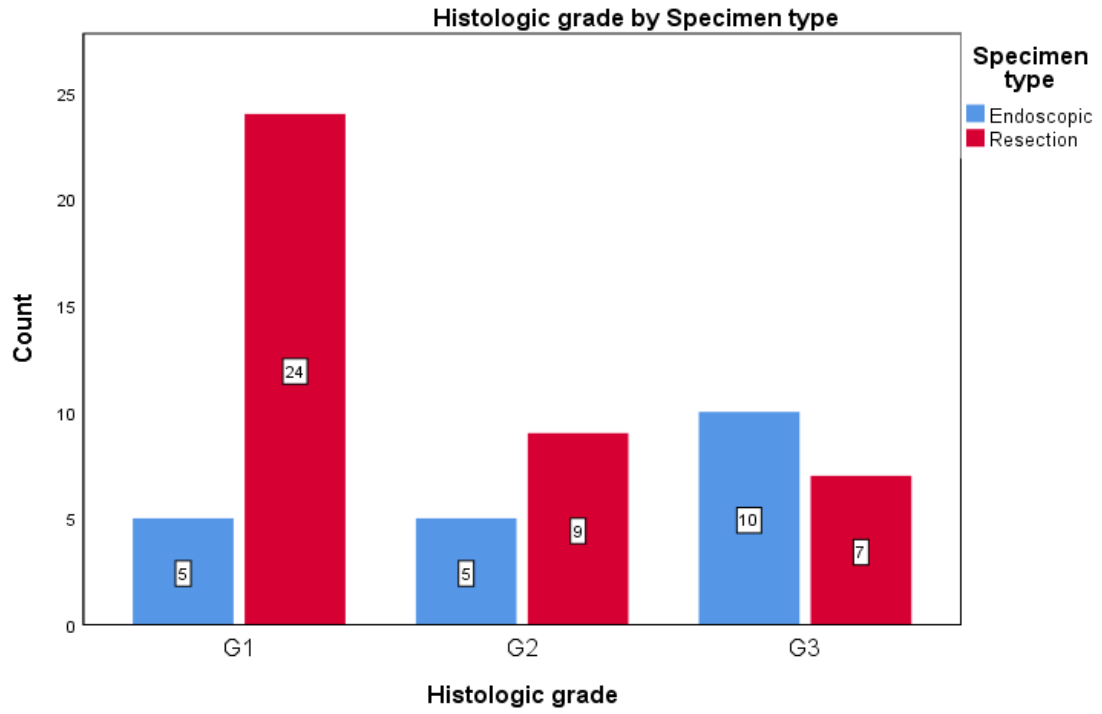

Figure 7: Histologic grade of malignant esophageal lesions by specimen type.

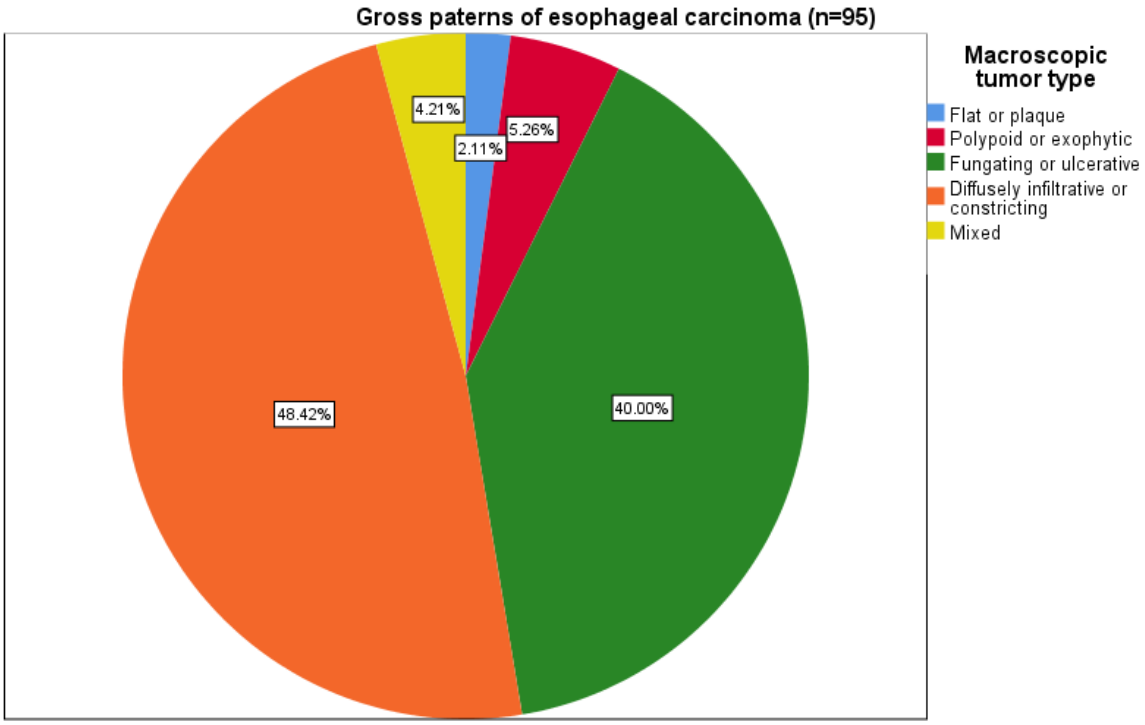

Figure 8: Gross pattern of malignant esophageal lesions (carcinoma).

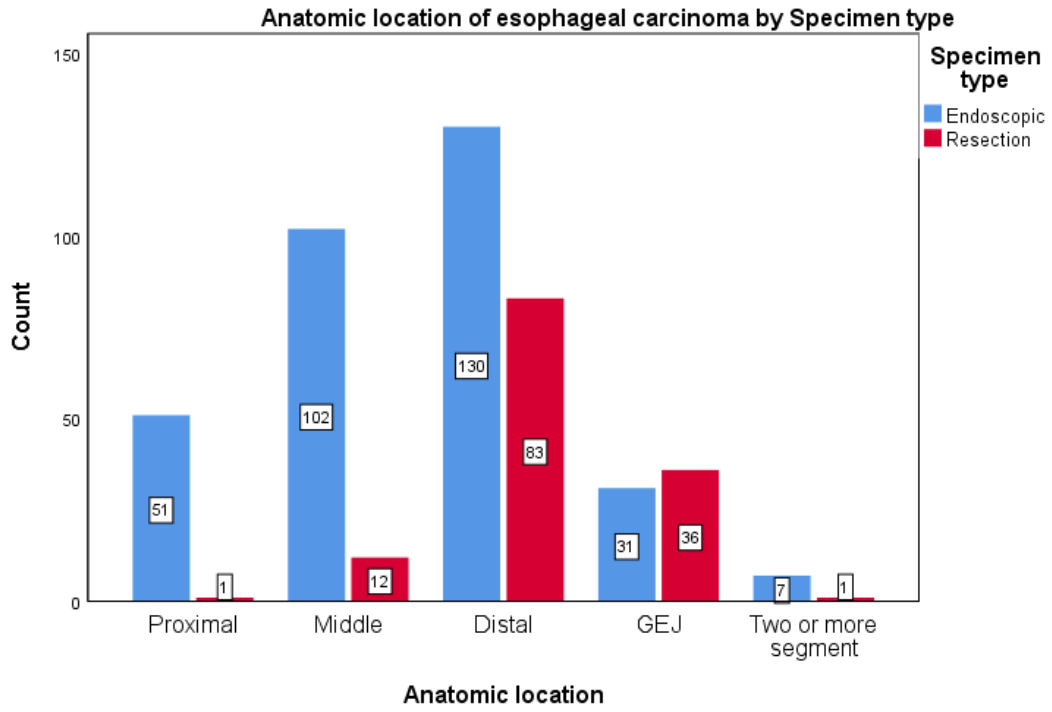

Figure 9: Anatomic location of malignant esophageal lesions by specimen type.

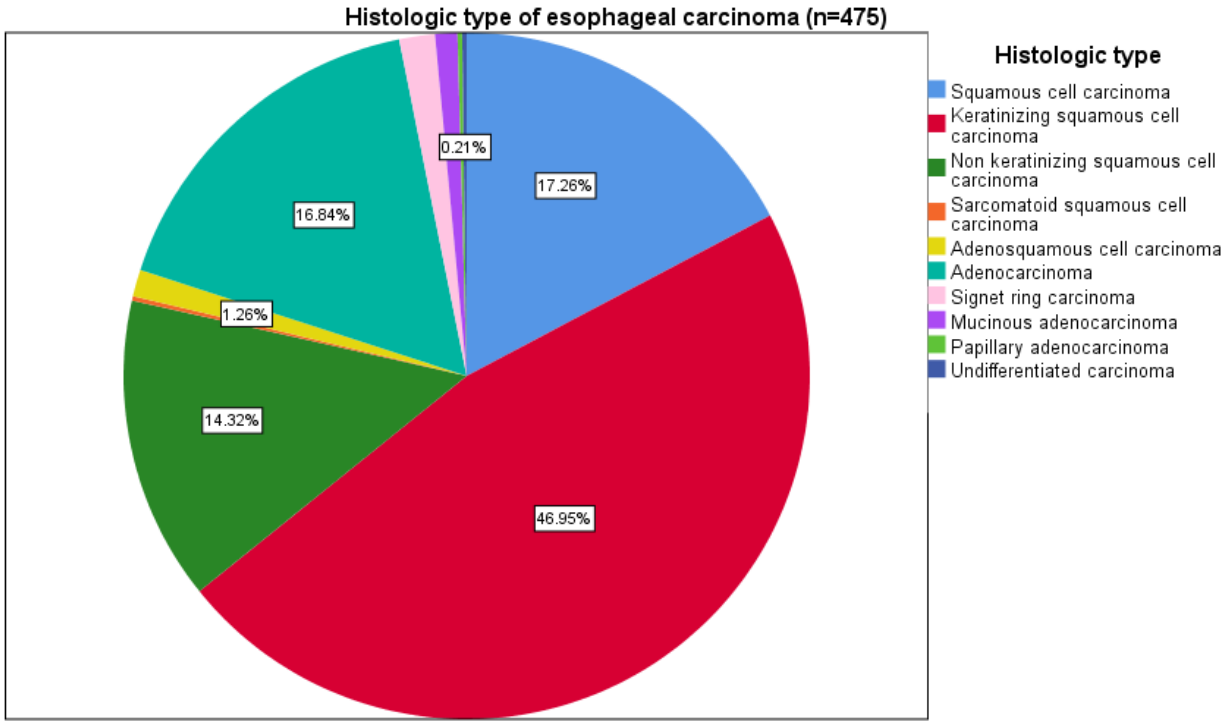

Figure 10: Histologic type of malignant esophageal lesions (carcinoma).

5.5. Description of radial margin status of malignant esophageal lesions.

Out of 135 resections specimens for carcinoma, only 94(69.6%) had documented radial margin status and 52(55.3%) had negative radial margins and the remaining 42(44.7%) had positive radial margins.

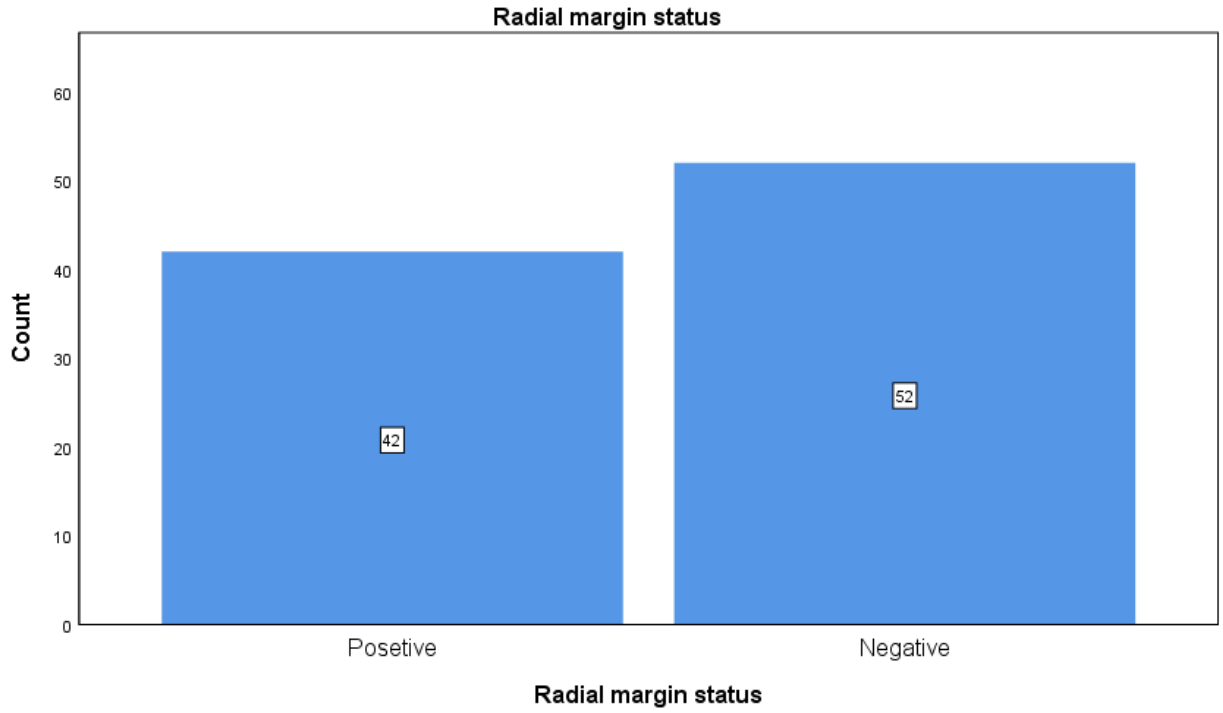

Figure 11: Radial margin status of malignant esophageal lesions (carcinoma.)

5.6. Histologic type of premalignant esophageal lesions

There were 9 premalignant cases account for 1.73% of esophageal lesions. The most common histologic type was high-grade squamous dysplasia 5(55.6%) followed by Barrett's esophagus with low-grade dysplasia 2(22.2%). Low-grade squamous dysplasia and Barrett's esophagus with high-grade dysplasia each account for the remaining 1(11.1%). With regards to anatomic location, 4(50%) occurs in the middle third, and 4(50%) in the distal third. The location was not documented for one of the cases (Table 8).

Table 8: Anatomic locations and histologic type of premalignant esophageal lesions.

	Count (n=9)	%

Anatomic location	Proximal third	0	0.0%
	Middle third	4	50.0%
	Distal third	4	50.0%
Histopathologic diagnosis	High grade squamous dysplasia	5	55.6%
	Low grade squamous dysplasia	1	11.1%
	Barrett's with high grade dysplasia	1	11.1%
	Barrett's with low grade dysplasia	2	22.2%

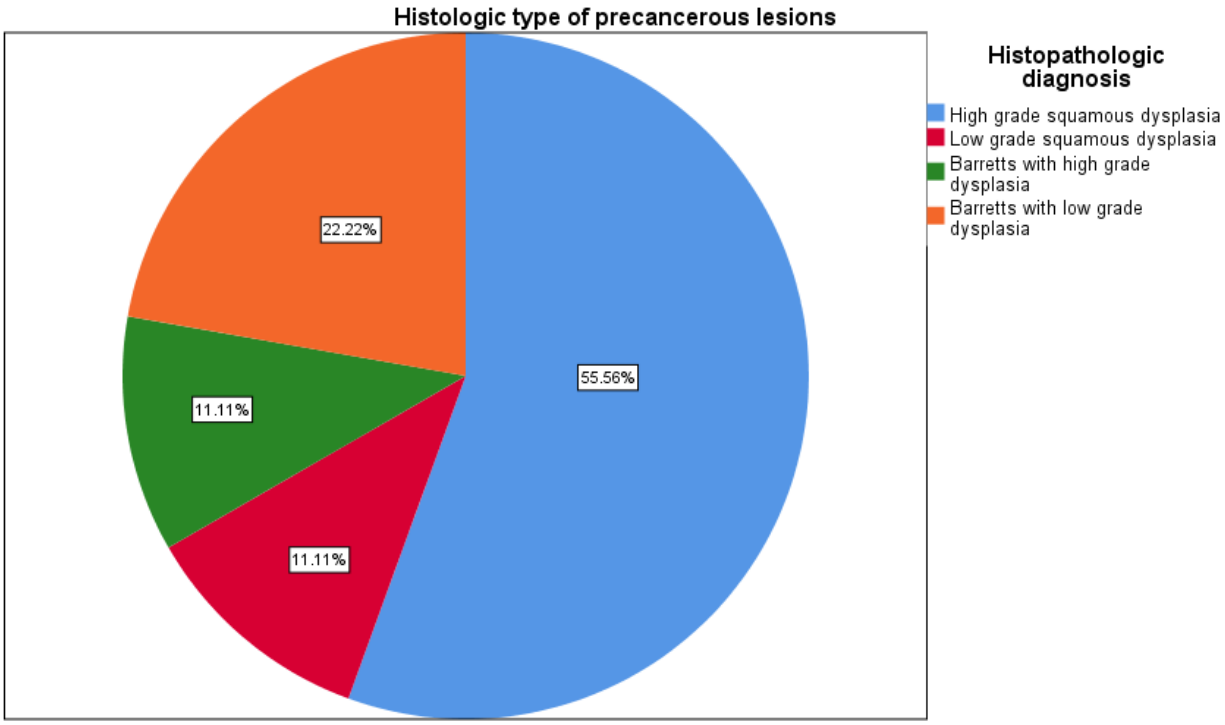

Figure 12: Histologic types of premalignant esophageal lesions.

5.7. Histologic type of non neoplastic esophageal lesions

There were a total of 34 esophageal biopsies with a nonneoplastic diagnosis. Out of this, there were 10(29.4%) barrettes esophagus,6(17.6%) nonspecific esophagitis, 5(14.7%) benign ulcers, 3(8.8%)cases of gastric epithelial metaplasia, 2(5.88%) cases of duplication cysts, squamous papilloma, and basal cell hyperplasia each, 1(2.94%) case of heterotopic gastric mucosa, GERD, achalasia, and herpes esophagitis each. The most common anatomic site is the distal third in 56.3%, followed by two or more segments in 21.9%, middle and proximal segments are affected in 12.5% and 9.4% respectively (Table 9).

Table 9: Anatomic location and histologic types of non neoplastic esophageal lesions.

		Count (n=34)	%
Anatomic location of lesion (n=32)	Proximal	3	9.4%
	Middle	4	12.5%
	Distal	18	56.3%
	Two or more segments	7	21.9%
Histopathologic diagnosis (n=34)	Benign ulcer	5	14.7%
	Nonspecific esophagitis	6	17.6%
	Herpes esophagitis	1	2.9%
	Achalasia	1	2.9%
	Duplication cyst	2	5.9%
	Heterotopic gastric mucosa	1	2.9%
	Squamous papilloma	2	5.9%
	Basal cell hyperplasia	2	5.9%
	GERD	1	2.9%
	Barretts esophagus	10	29.4%
	Gastric epithelial metaplasia	3	8.8%

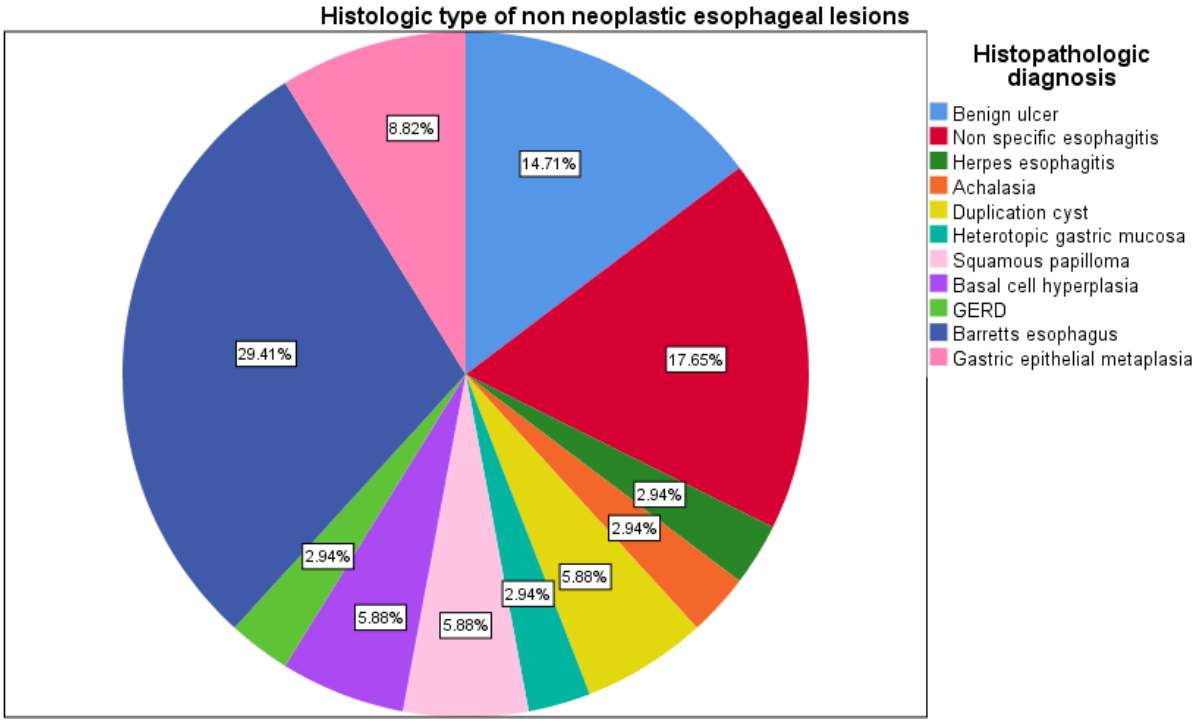

Figure 13: Histologic type of non neoplastic esophageal lesions.

6. Discussion

In the present retrospective cross-sectional descriptive study on esophageal endoscopic and resection specimen submitted to the pathology department of TASH Addis Ababa, Ethiopia from January 01, 2016, up to August 30, 2020, a total of 518 cases which fulfill the inclusion criteria were analyzed for the macroscopic (gross) type, length of the involved segment, radial margin status, histologic type, grade and stage of malignant esophageal lesions and histologic type, and location of premalignant and nonneoplastic esophageal lesions.

Concerning malignant esophageal lesions in terms of age, this study showed that the mean age was 53.2year (± 12.01 SD). This is almost similar to the mean age of 52.9 in a retrospective document review of ten referral hospitals in different regions of Ethiopia [8], the mean age of 51.4 years in a cross-sectional study conducted in TASH [16], and (57.8 ± 11.7SD) year in a retrospective study carried out in Ghana [23]. The mean age of esophageal cancer patients was 55.5 years(n=71) and 57.72 (SD +/- 11.76) (n=74) years in Uganda and in Kenya respectively [17,6].In a contrary study conducted in Iran showed The mean (± SD) age of patients were

68.91±10.06 years [25].In this study majority of esophageal cancer patients was in the age group of 50-59 years which is similar to the finding of a cross-sectional study conducted in TASH majority is in similar age range and a systematic review of esophageal cancer in sub-Saharan Africa, in which esophageal cancer was prevalent among the age group of 45-64 years in both sexes [16, 24]. But studies from Sudan and Nepal show the most common age group is in the range of 60-69 years [20,21].

In terms of sex, malignant esophageal lesions are more common in a female with F:M of 1.3:1 which is identical to the finding of a retrospective document review of ten referral hospitals in different regions of Ethiopia [8], a study was done in Iran, Sudan, and TASH reveled F:M of 1.1:1, 1.8:1, and 1.6:1 respectively[25, 20, 16].In opposite to these findings, a study conducted in India, Tanzania, Kenya, Ghana, and Uganda showed that F:M of 1:1.8, 1:2.2, 1 :3.6, 1:4, and 1:3 respectively [26,19,7, 23,18]. The difference could be in most countries the risk factor for esophageal cancer is tobacco smoking and alcohol. While the prevalence of cigarette smoking and alcohol consumption was low among esophageal cancer patients in Ethiopia with 5% and 2% respectively [27].

In this study, in the majority of cases 454 (95.6%) anatomic location of mass was mentioned. Of which, the most common anatomical sites of esophageal cancer occurred in the distal esophagus including GEJ 280(61.7%), followed by the middle third of esophagus 114 (25.1%), which is consistent with the results of a study in TASH, 186(54.1%) and 105(30.5%) in the distal and middle third of esophagus respectively [16], and 54% distal third, 30.3% middle third of study done in Nepal [17]. Besides, a retrospective study done in Ghana shows the most common anatomical location was the distal third 84.9%, middle third 11.8%, and the upper third 3.3% [23]. In contrary studies done in Sudan, Kenya, and Uganda shows that lesion is more common in the middle third [20,7,18].

95(70.4%) of malignant resection cases had documented gross description. The most common macroscopic (gross) finding was diffusely infiltrative or constricting 46(48.4%) followed by fungating or ulcerative 38(40.0%). On the contrary, a Tanzania study showed most lesions were ulcerative (40.2%) followed by infiltrating and stricture 32.3% and 3.7% respectively [19].

The mean and median tumor length was 4.2 cm and 4 cm respectively (range 0.5 to 12 cm). The tumor length was ≤5 cm in 80 (59.3%) and >5 cm in 51 (37.8%) patients. The tumor length was not documented in 4 (3%) cases. In a contrary study done in Tanzania shows the median tumor length was 5 cm (range 4 to 7 cm). The tumor length was ≤5 cm in 40.2% of patients and >5 cm in 185 (52.4%) patients. The tumor length was not documented in 11 (3.4%) patients [19].

In this study out of 475 malignant cases with regards to histologic type 374 (78.7%) were squamous cell carcinoma, 94 (19.8%) were adenocarcinoma, 6 (1.3%) were adenosquamous cell carcinoma, and 1 (0.2%) was undifferentiated carcinoma. This is almost similar to the Study done in Ghana showed Squamous cell carcinoma accounted for 78.7% and adenocarcinoma 21.3%, study was done in Kenya There were 60 (81.1%) squamous cell carcinoma and 14 (18.9%) adenocarcinoma, and a study was done in TASH 46(74%) were squamous cell carcinoma,11 (18%) were adenocarcinoma and,3 (3%) were mixed [7,23,22]. In a retrospective

document review of ten referral hospitals in different regions of Ethiopia of the 118 results analyzed for histopathological subtype, squamous cell carcinoma accounts for 67(56.7%), followed by adenocarcinoma with 43(36.4%) and finding of a study done in Nepal was 68 (64.15%) cases of squamous cell carcinoma, 33 (31.13%) cases of adenocarcinoma including signet ring cell carcinoma, 4 (3.76%) cases of undifferentiated carcinoma and 1 (0.94%) case of small cell carcinoma [8,17]. Also, a study was done in Sudan, another study in TASH, Uganda, and Tanzania showed Squamous cell carcinoma account for more than 90% of esophageal carcinoma [10, 16, 18, 19]. In a contrary study done in Iran in terms of tumor pathology, the more common histologic type was adenocarcinoma, 47(49 %), and the SCC 43 (44.8 %) and other (6 %) [25].

In this study, only 60 (12.6%) of malignant cases had documented histologic grade. 29 of them (48.3%) was well-differentiated(G1), 17(28.3%) was poorly differentiated (G3) and the remaining 14 (23.4%) was moderately differentiated (G2). Similarly, a study done in TASH shows out of 57 cases 66.7% cases were well-differentiated(G1), 17.7% moderately differentiated (G2), 10.5% poorly differentiated(G3), and 5.3% undifferentiated [16]. In a contrary study done in Kenya, Tanzania, and Nepal shows moderately differentiated (G2) carcinoma was the most common tumor grade followed by well-differentiated (G1) [7,19,17].

In this study, there were 9 premalignant cases account for 1.73% of esophageal lesions. Relatively larger proportion reported in India, in private, and public sector of South Africa 20%(n=6), 22.2%(n=136), and 6.54%(n=31) respectively [28, 29]. The most common histologic type was high-grade squamous dysplasia 5(55.6%) followed by Barrett's esophagus with low-grade dysplasia 2(22.2%). Similarly, in a study in India, there were 3 cases (50%) of high-grade squamous dysplasia, 2 cases (33.3%) of low-grade dysplasia, 1 case (16.7%) of dysplasia associated with Barret's esophagus [28].

In this study, there were a total of 34 esophageal biopsies with nonneoplastic diagnoses accounting for 6.56% of esophageal lesions. Comparable with this, a study was done in Ayder Referral Hospital Tigray, northern Ethiopia, and India that shows nonneoplastic lesions account for 16.7% (n=5) and 27.3% (n=6) respectively [14, 28]. In contrary other study done in India and Nepal showed non neoplastic lesions account for 72.7% (n=16) and 80% (n=12) respectively [10, 30]. This discrepancy in part explained by TASH is the largest referral hospital with the only cancer treatment center in the country so a large number of patients with carcinoma are referred for surgical and medical management and by a relatively larger number of cases in this study.

With regards to histologic type, the most common histologic types in this study were barrettes esophagus, nonspecific esophagitis, and benign ulcers accounting for more than 60 % of nonneoplastic lesions. Similarly, a study conducted in India revealed chronic non-specific esophagitis, esophageal ulcer, and barrette esophagus account for 68% of nonneoplastic esophageal lesions [10]. A study conducted in Ayder Referral Hospital Tigray, northern Ethiopia showed that the most common histologic type was acute esophagitis and Glycogen Acanthosis 2(33.3%) each, followed by Barret's Esophagitis 1(16.7%) [14]. A study was done in Nepal and Another study in India that showed Chronic non-specific esophagitis, Benign esophageal ulcer, Barret's esophagus account for all 100% of the cases [30, 28] (Table 10).

Table 10: Comparisons of distribution of histologic type of non neoplastic esophageal lesions.

Study	Current study (n=518)	Ganga H et al (n=30) [28]	KebedeY et al (n=22) [14]	Hirachand S et al (n=15) [30]	Margaret TJ et al (n=22) [10]
Proportion of non neoplastic lesions	6.56%(n=34)	16.7%(n=5)	27.3%(n=6)	80% (n=12)	72.7% (n=16)
Histologic type					
Esophagitis	17.6% (n=6)	60%(n=3)	33.3%(n=2)	66.7 % (n=8)	56.25% (n=9)
Barret's esophagus	29.4% (n=10)	40% (n=2)	16.7%(n=1)	8.3%(n=1)	18.75% (n=3)
Benign esophageal ulcer	14.7% (n=5)		-	25 % (n=3)	18.75%(n=3)
Glycogen Acanthosis			33.3%(n=2)		
Normal			16.7%(n=1)		
Esophageal candidiasis					6.25%(n=1)
Gastric epithelial metaplasia	8.8% (n=3)				
Duplication cysts, squamous papilloma, and basal cell hyperplasia	5.9% (n=2) each				
Heterotopic gastric mucosa, GERD, achalasia, and herpes esophagitis	2.9% (n=1) each				
Total	100%	100%	100%	100%	100%

7. Strength and limitation of the study

7.1. Strength of the study

Compared to other similar studies, this study is done with a relatively large sample size which increases the power of the study.

7.2. Limitation of the study

Since data were collected from the request paper, some variables were missed and difficult to collect.

Three of precancerous lesions (high grade squamous dysplasia) had mass endoscopically and may represent under sampled carcinoma.

8. Conclusion

The majority of esophageal lesions were malignant accounting for 91.7% of all esophageal lesions. More females were affected than males and majorities occur in the 6th decade of life. Overall cancer of the esophagus mainly affects the distal 1/3 of the esophagus including GEJ. The location of the tumor varies with the histological type. Squamous cell carcinoma is commonly found in the distal third followed by a middle third while adenocarcinoma is more commonly located in GEJ followed by the distal third of the esophagus. More than half of the lesions have tumor length in the range of 2-5cm. The most common macroscopic (gross) finding was diffusely infiltrative or constricting followed by fungating or ulcerative. Squamous cell carcinoma is the most common histologic type. More than 2/5 of carcinomas have positive radial margin status. Most carcinomas are well-differentiated and in pathologic stage group of III.

Premalignant lesions account for 1.73% of esophageal lesions. More females are affected than males and majorities are in the 6th decade of life. The most common histologic type was high-grade squamous dysplasia followed by Barrett's esophagus with low-grade dysplasia. Half of the lesions occur in the middle third and the remaining half in the distal third.

Nonneoplastic lesions account for 6.56% of the lesions. Females and males are affected equally and the majority occurs in the 6th decade of life. Barrettes esophagus, nonspecific esophagitis, and benign ulcers account for more than 60% of the cases. Most of the lesions occur in the distal third of the esophagus followed by lesions involving two or more segments.

9. Recommendation

The following recommendations are made from this study.

For FMOH

A significant number of carcinoma are diagnosed at an advanced stage. Therefore, awareness creation about esophageal carcinoma and easy access to medical service should be made.

For TASH

Clinician side

A considerable number of the request form does not mention the site of lesion and endoscopic description does not follow standard classification. This should be corrected.

A significant number of cases are nonrepresentative of the actual lesions so leads to in nondiagnostic result and repeated biopsies. This in part can be tackled by taking multiple samples at a different place at the time of initial biopsies.

Pathology side

Most of signed out cases doesn't mention about radial margin status and/or grade of carcinoma which should be corrected.

Gross (macroscopic type) description doesn't follow standard classifications we should adopt a standard classification system like the Japan esophageal society macroscopic classification of esophageal and gastric carcinoma.

Data archives of the department should be improved.

For researchers

There is limited study on the nonneoplastic esophageal lesion in our country and in Africa overall. Further studies are recommended.

10. Reference

1. Sternberg's Diagnostic Surgical Pathology 6th Ed, 2015 section VIII, chapter 31, Normal anatomy of esophagus (page 2873).

2. AJCC Cancer Staging Manual Eighth Edition,2018. https://t.me/MBS_MedicalBooksStore.

3. Rashmi k et al. (2013) 'A STUDY ON HISTOPATHOLOGICAL SPECTRUM OF UPPER GASTROINTESTINALTRACT ENDOSCOPIC BIOPSIES.'International Journal of Medical Research & Health Sciences,2(3) pp. 418- 424.

4. Shu-Jung Tsai, Ching-Chung Lin, Chen-Wang Chang, Chien-Yuan Hung, Tze-Yu Shieh, Horng-Yuan Wang, Shou-Chuan Shih, Ming-Jen Chen. (2015) 'Benign esophageal lesions: Endoscopic and pathologic features.' World J Gastroenterol,21(4): pp. 1091-1098.

5. WHO classification tumor of gastrointestinal system,5th edition ,2019.

6. J Lewin K. (1992) 'Malignant and Premalignant Lesions of the Esophagus Department of Pathology and Medicine, UCLA School of Medicine, Los Angeles, CA, USA,' Keio J Med 41 (3): pp 177-183.

7. Ojuka D,Dindi K, and Awori M. (2017) 'Prevalence of Esophageal Adenocarcinoma; School of Medicine, University of Nairobi.' The ANNALS of AFRICAN SURGERY, 14(2) pp. 82-85.

8. Wondimagegnehu. A, Hirpa . S, Wakuma . S, Gizaw . M, et al.; 'Oesophageal Cancer Magnitude and Presentation in Ethiopia.' pp. 1-18. NB: Preprint: Please note that this article has not completed peer review.

9. Juan Rosai: ROSAI AND ACKERMAN'S SURGICAL PATHOLOGY, Eleventh Edition edn. Philadelphia: Elsevier; 2018.

10. Margaret TJ et al.(2020) 'Evaluating the spectrum of histomorphological patterns on endoscopic biopsy in patients with upper gastrointestinal tract disorders.'6(1) pp. 1-9.

11. A Sheikh B, M Hamdani S and Malik R. (2015)'Histopathological Spectrum of lesions of upper gastrointestinal tract –A study of endoscopic biopsies.'GLOBAL JOURNAL OF MEDICINE AND PUBLIC HEALTH, 4(4) pp. 1-8.

12. Global cancer statistics 2018. GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. 2018 Visited July 27, 2020.

13. Ethiopia Population (2020) – Worldometer, July 28, 2020, based on the latest United Nations data. WWW.Worldometer.info/worldpopulation/ethiopian

14. Kebede Y, Tsegay B, and Abreha H. (2017)‘ endoscopic and histopathological correlation of gastrointestinal diseases in Ayder referal hospital, MEKELLE UNIVERSITY, NORTHERN ETHIOPIA.’ Ethiop Med J, 55(4) pp. 285 – 291.

15. Ethiopia – Addis Ababa city cancer registry; October 2014.

16. Ahmed M. (2018) ‘Histologic Types, Treatment Pattern, Outcome and Factors associated with Treatment outcome of Esophageal Cancer Patient treated at TikurAnbessa Specialized Hospital Addis Ababa, Ethiopia 2010-2016: A Cross-Sectional Study.’pp.1-48.

17. Pun CB et al. (2012) ‘Histological pattern of esophageal cancer at BP Koirala memorial cancer hospital in Nepal: athree-year retrospective study.’Journal of Pathology of Nepal, 2pp 277-281.

18. Alema ON and Iva B. (2014) ‘Cancer of the esophagus: histopathological sub-types in northern Uganda.’ Article in African Health Sciences, 14(1) pp.17-21. https://www.researchgate.net/publication/272455932

19. Mchembe M et al.(2013) ‘Endoscopic and clinicopathological patterns of esophageal cancer in Tanzania: experiences from two tertiary health institutions.’ World Journal of Surgical Oncology, 11(257) pp. 1-7.

20. Gasmelseed N, Abudris D, Elhaj A, Eltayeb EA, Elmadani A, Elhassan MM, et al. (2015)‘Patterns of esophageal cancer in the National Cancer Institute at the University of Gezira, inGezira State, Sudan, in 1999-2012.’ Asian Pacific J Cancer Prev.;16(15): PP. 6481–90.

21. Gemechu T, Lako W, and Deyessa N. (2018)‘the relative frequency and patterns of solid malignant tumor in TASH: A10 year histopathologic review.’ Scholar journal of applied medical sciences (SJAMS), 6(1D) pp.278-288.

22. Leon M et al. (2019) 'Prevalence of human papillomavirus and Helicobacter pylori in esophageal and gastroesophageal junction cancer biopsies from a case control study in Ethiopia.' Leon et.al infectious agents and cancer, 14(19) pp.1-10. https//dol.org/10.1186/s13027-019-0233-x.

23. Tettey M, Edwin F, Aniteye E, Sereboe L, Tamatey M, Ofosu-Appiah E, et al. (2012) 'The changing epidemiology of esophageal cancer in sub-Saharan Africa - the case of Ghana.' The Pan African medical journal.;13:6

24. Kachala R. (2010) 'Systematic review: epidemiology of Oesophageal Cancer in SubSaharan Africa.' Malawi Medical Journal;22(3).

25. Ghanadi K et al. (2018) 'Correlation between Histopathological Findings and Endoscopy in Esophageal Cance: Results in Khorramabad, Iran, Western Iran: Bangladesh Journal of Medical Science, 17(04) pp. 619-624.

26. Gupta V, Bhardwaj S, and Kumar O. (2017) 'Pattern of esophageal cancer in tertiary care hospital in North India: a clinicopathological study.' International Journal of Research in Medical Sciences, 5(4) pp.1405-1409.

27. Shewaye AB, and Seme A. (2016)'Risk factors associated with oesophagel malignancy amongethiopian patients: A case control study.' East Cent. Afri.J.Surg, 21(2) pp.33-39.

28. Dr. Ganga H and Dr. Indudhara PB. (2018) 'Histopathological spectrum of lesions of upper gastrointestinal tract: A study of endoscopic biopsies.' International Journal of Clinical and Diagnostic Pathology. 1(2)pp. 21-25.DOI: https://doi.org/10.33545/pathol.2018.v1.i2a.06.

29. Lutakwa A et al.(2019) 'A comparison of esophageal cancerbetween the public and private sectors in KwaZulu-Natal'.SAJS 57(2) pp. 16 -19.

30. Hirachand S et al. (2018)'Histopathological spectrum of upper gastrointestinal endoscopic biopsies.'JBPKIHS, 1(1)pp. 67-74.