



CLINICAL PROFILE AND EVALUATION OF PATIENTS OF CARCINOMA ESOPHAGUS AT AVBRH

Akshay Bora^{1*}, Meenakshi Yeola², Chandrashekhar Mahakalkar³, Tanu Pradhan⁴, Aniket Khadatkar⁵,
Anunay Kumar⁶ and Pratik Abhishek⁷

¹Resident, Department of Surgery, AVBRH, Sawangi (Meghe), Wardha.

^{2,3}Professor, Department of Surgery, AVBRH, Sawangi (Meghe), Wardha.

^{4,5,6,7}Resident, Department of Surgery, AVBRH, Sawangi (Meghe), Wardha.

***Corresponding Author: Akshay Bora**

Resident, Department of Surgery, AVBRH, Sawangi (Meghe), Wardha.

Article Received on 11/10/2017

Article Revised on 01/10/2017

Article Accepted on 22/11/2017

ABSTRACT

Introduction - Esophageal carcinoma is a malignant disease seriously threatening human health and lives. In 2012, it was estimated that 455,800 new cases and 400,200 deaths from esophageal cancer occurred in the whole world, which ranked the eighth in incidence and the sixth in mortality of cancers.^[1] In India, according to data from the National Cancer Registry, esophageal and gastric carcinomas are the most common carcinomas found in men, while esophageal cancer ranks third in women after carcinoma of breast and cervix. **Aim and objectives** - To study the clinico-pathological co-relation of patients of carcinoma esophagus. To study the demographic profile of patients of carcinoma esophagus admitted at AVBRH. To study the mode of presentation. To study the etiological factors. To study the endoscopic findings. To study the co-relation with the histo-pathology. **Methods** - This is a prospective observational study of patients diagnosed as carcinoma esophagus at Acharya Vinoba Bhave Rural Hospital, Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha, a 1280 bedded tertiary, rural, university affiliated teaching hospital in central India, from July 2015 to October 2017 with a sample size of 50 patients. **Results** - The study demonstrated that esophageal cancer was found mostly in females (56%) rather than males (44%). Dysphagia was the most common presenting complaint followed by weight loss. Squamous cell carcinoma was far more common than adenocarcinoma. The incidence of metastasis was 30% in the study. **Conclusion** - Carcinoma esophagus is a fatal malignancy owing to high rate of metastasis at the time of diagnosis of the condition. Any patient presenting above age of 50 years with symptoms of progressive dysphagia should undergo flexible endoscopy of upper gastrointestinal tract. In case of suspected lesions biopsy from the lesion should be taken and patient needs to be subjected for further radiological evaluation like CT Thorax.

KEYWORDS: To study the co-relation with the histo-pathology.

INTRODUCTION

Carcinoma esophagus, is a disease with a wide range of global variation in its incidence.^[1] Carcinoma esophagus is common in the developing countries of the world. There are two geographical esophageal belts in the world. The 'Asian cancer esophageal belt' comprises of Mongolia, China, and Kashmir and Iran, Turkmenistan, and Quetta in Pakistan.^[3] The incidence of esophageal carcinoma is as high as 100/100,000 cases in some parts of the globe, including parts of Iran, China and USSR.

Esophageal cancer including squamous cell carcinoma (SCC) and adenocarcinoma is considered as a fatal malignancy concerning its prognosis and a fatal outcome in the vast majority of cases.^[4,5] Esophageal cancer exhibits epidemiologic pattern distinct from all other different types of cancers.^[6,7] The main pathological types of esophageal cancer comprise of SCC,

adenocarcinoma and neuroendocrine carcinoma. In the western countries and the US, approximately 50% of esophageal carcinomas are adenocarcinoma;^[8] while in Asian countries, about 90% are SCC and incidence is increasing.^[9,10] In general, the overall survival of esophageal cancer is as low as about 20%.^[11]

It is not surprising, that the etiology of esophageal cancer has been investigated for over a century. Based on the clinical observations, Craver in 1932 and Watson in 1939 had listed that the excessive consumption of alcohol and tobacco, low socioeconomic status, poor oral hygiene, and consumption of hot drinks as risk factors for esophageal cancer.^[12,13] Etiology of esophageal cancer differs by histology. Esophageal cancer can be histologically classified into two main types: squamous cell carcinoma (SCC) and adenocarcinoma. These two types of cancer differ not only histologically, but also

differ concerning their incidence trends, populations that they affect, and risk factors associated with them. One could call adenocarcinoma “an emerging disease” Until the 1970s, SCC constituted the vast majority (over 90%) of all esophageal cancer cases in all parts of the world. Since then, however, the incidence of adenocarcinoma has steeply increased in many parts of the Western World,^[14-18] so that this cancer type now constitutes approximately half of all esophageal cancer cases in some Western countries. In contrast, SCC continues to be the dominant type in the rest of the world. Most etiological studies conducted before the 1980s did not distinguish between SCC and adenocarcinoma, but their results were mainly relevant to SCC because adenocarcinoma was uncommon before then. Also, results of the more recent studies from Asia, South America, or Africa that do not report histology are mainly applicable to SCC because adenocarcinoma is still relatively uncommon in these areas.^[19-21] Extensive investigations into the etiology of adenocarcinoma started only in the 1990s, mainly in Western countries, where larger numbers of this carcinoma began to be diagnosed.

The middle 1/3rd of the esophagus is the commonest site for SCC, and the lower 1/3rd is the commonest site for adenocarcinoma.^[22,23,24] Most patients present with progressive dysphagia and weight loss with dysphagia being the most important and the first symptom. As most of the patients present at an advanced stage, mortality is very high and even with operable tumors, postoperative mortality is about 50%.^[25] The symptoms of esophageal carcinoma usually appear 3 to 4 months before the diagnosis and such symptoms vary depending on the segment of the esophagus initially involved.

Dysphagia is the most common presenting symptom occurring in more than 90% of cases while weight loss of over 5 to 10% of body weight occurs in the majority of patients and is associated with a worse prognosis.^[26] Less common symptoms, such as hoarseness, cough and progressive lesions with invasion to other organs resulting in symptoms such as hematemesis, hemoptysis, dyspnea and cough secondary to broncho-esophageal and trachea-esophageal fistula.^[25,26]

The clinical stage of the disease at the time of presentation is important for the outcome of the patient with esophageal cancer. However, the results of treatment of esophageal cancer in our environment have been poor because of the majority of patients presenting late to the hospital with an advanced disease, and only palliative treatment is possible. This is partly because of the paucity of published local data regarding this disease and the lack of community awareness on the importance of early reporting to the hospital for early diagnosis and treatment.

The diagnosis of esophageal carcinoma is established with flexible endoscopy with biopsy.^[27] Traditionally

barium swallow was used as a diagnostic tool in esophageal cancer detection, a so-called “road map” before endoscopy. Polypoid tumors, strictures with mucosal irregularity, and an “apple core” deformity are characteristic findings on barium swallow studies for cancer. The barium swallow studies may also provide with information that can help with surgical planning. This includes the location of the tumor, the axis of the esophagus at the level of the tumor (angulation can add to the difficulty in resection of tumor) and the presence of other pathology (such as hiatal hernia or diverticulum). At more experienced centers, however, features such as the location and size of the tumor can be more accurately assessed with the help of endoscopy than by barium swallow studies.^[28] There has been debate about the value of barium swallow studies as an initial diagnostic test.^[29,30] One situation where a barium swallow study is essential is when there is suspicion of a tracheoesophageal fistula.^[31] Barium swallow studies may provide additional data in the differentiation of gastroesophageal junction (GEJ) tumors from gastric tumors^[32] in situations where large tumors are seen on retroflexion.

The modern work-up for esophageal disorders is therefore mainly focused on the upper gastrointestinal tract endoscopy, which is an essential component for any patient suspected of having an esophageal tumor. Endoscopy can provide with a complete visual description of the gross tumor characteristics including length, location relative to the GEJ, and the description and the length of any extension into the gastric cardia. Presence, length, and location of any areas of metaplasia within the esophagus should be noted as well. Biopsy from the suspected area must be taken at the time of endoscopy; several biopsies will increase the diagnostic accuracy of the test. The diagnostic yield approaches to 100% when six or more samples are obtained using a standard endoscopic biopsy protocol.^[33,34] In situations where standard biopsies or brushings do not yield a diagnosis in cases with high suspicion, endoscopic ultrasonography (EUS) should be considered.^[35]

The treatment of esophageal cancer should be stage-specific for better clinical results. Recent treatment strategies tend to evolve into a multimodality approach to the management, which includes surgical resection and preoperative or definitive chemoradiation.^[36] Consequently, precise pretreatment staging of esophageal carcinoma is integral for assessing operability, determining a suitable treatment plan, and minimizing inappropriate treatment of the patient.^[37]

The internationally used staging system for esophageal carcinoma is the TNM classification system maintained by the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC). It includes depth of local invasion by the primary tumor (T), the extent of regional lymph nodal involvement (N), the presence or absence of distant metastasis (M) and

provides a stage grouping on the basis of T, N, and M.^[38] The staging system for carcinoma of the esophagus and esophagogastric junction has been revised in the seventh edition, published in 2009. Currently, a multimodality-assessed preoperative staging of esophageal carcinoma is advocated to determine a treatment plan and this includes the use of computed tomography (CT), endoscopic ultrasonography (US), and positron emission tomography (PET)/CT with fluorodeoxyglucose (FDG).^[39]

In this study, we are going to discuss the clinical profile and the evaluation of patient of carcinoma esophagus.

AIM

To study the clinico-pathological co-relation of patients of carcinoma esophagus.

OBJECTIVES

To study the demographic profile of patients of carcinoma esophagus admitted at AVBRH. To study the mode of presentation. To study the etiological factors. To study the endoscopic findings. To study the co-relation with the histo-pathology.

MATERIAL AND METHODS

Setting

This is a prospective observational study of patients diagnosed as carcinoma esophagus at Acharya Vinoba Bhave Rural Hospital, Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha, a 1280 bedded tertiary, rural, university affiliated teaching hospital in central India, from July 2015 to October 2017.

Sample size

50 patients

Inclusion Criteria

1. All patients admitted as diagnosed cases of Carcinoma Esophagus.

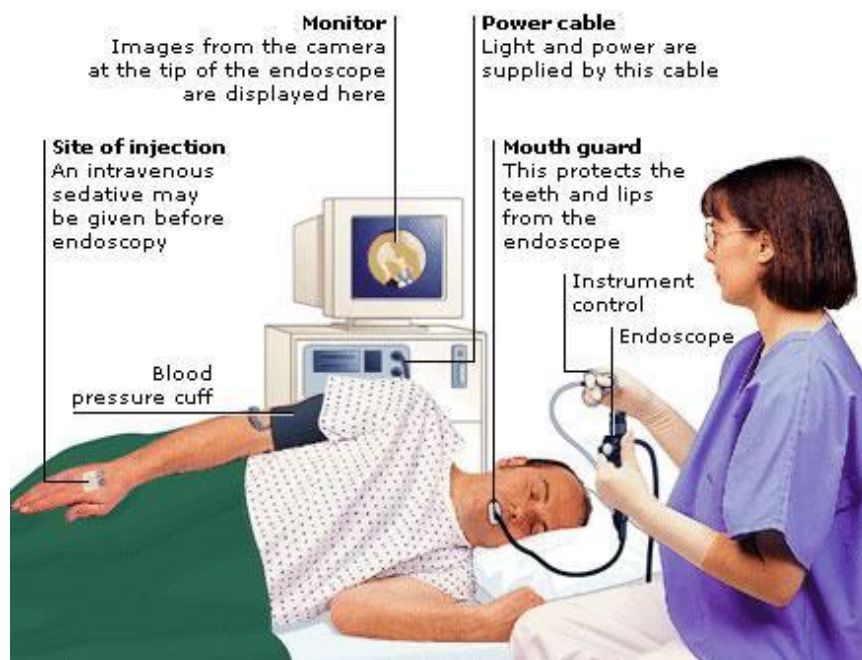
Exclusion Criteria

1. Patients whose upper GI endoscopy/biopsy could not be done.
2. Patients whose biopsy is negative for carcinoma.
3. Patient with complain of dysphagia but not diagnosed as carcinoma.

Study Design

We enrolled patients presenting to the inpatient departments of Surgery, Medicine, ENT in this study. All the patients diagnosed as carcinoma esophagus have been enrolled in my study. We obtained their informed consent and performed their Upper GI Endoscopy. Endoscopy was done by trained professors in the department with more than 10 years of experience. Every patient enrolled in the study underwent endoscopy. Endoscopists were blind to the patient's history and physical examination. Endoscopic guided biopsy was taken and patients were subjected to radiological evaluation. The study protocol was approved by ethics committee of the institute.

After history and clinical examination, patient was subjected to Upper GI Endoscopic evaluation which was done by consultants having endoscopic expertise and biopsy was taken whenever was necessary. Biopsy from the growth was taken and sent for histopathological examination. Patients were then also subjected to radiological investigation like CT thorax for further evaluation. The consultants were blind to the history and clinical examination findings. The endoscopy was performed by Fujinon Upper GI Endoscopy Unit as follows:



The biopsies taken from doubtful lesions were sent to Department of Pathology for Histological examination. Patient were also sent for CT in the Department of Radiology.

OBSERVATIONS AND RESULTS

Table 1: Distribution of cases according to age.

Age distribution	No. of patients	Percentage
31 – 40	4	8%
41 – 50	13	26%
51 -60	15	30%
61 - 70	16	32%
71 - 80	2	4%
Total	50	100.00%

Table 1 provides the distribution of cases according to age. Maximum i.e. 16 (32%) cases belonged to the age group 61 - 70 years, followed by 15 (30%) cases in the age group of 51 - 60 years, while 13 (26%) cases belonged to age group of 41 - 50 years. The mean age was 56.82 with standard deviation of 9.82 years (± 9.82 SD) while median age group was 55.5. The minimum

age was 35 years and maximum age was 80 years. A bar chart representation of age distribution is shown in Figure 1.

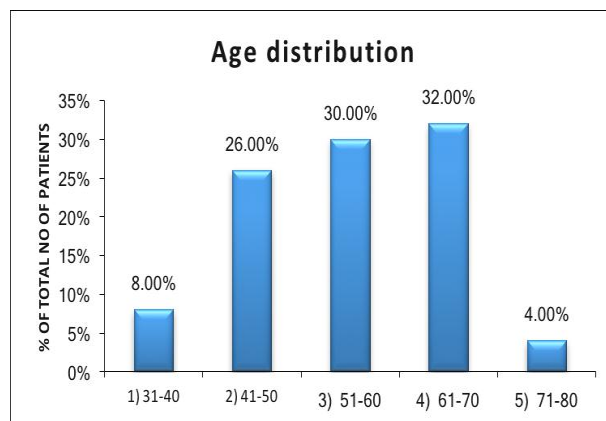


Figure 1: Bar chart showing the distribution of cases as per age.

Table 2: Distribution of cases according to age and biopsy report.

		Biopsy report		Total
		Squamous cell carcinoma	Adenocarcinoma	
Age distribution	1) 31-40	4 (100.00%)	0 (0.00%)	4 (100.00%)
	2) 41-50	11 (84.62%)	2 (15.38%)	13 (100.00%)
	3) 51-60	15 (100.00%)	0 (0.00%)	15 (100.00%)
	4) 61-70	14 (87.50%)	2 (12.50%)	16 (100.00%)
	5) 71-80	2 (100.00%)	0 (0.00%)	2 (100.00%)
Total		46 (92.00%)	4 (8.00%)	50 (100.00%)

Table 2 represents distribution of cases according to age and biopsy report. Maximum cases of squamous cell carcinoma cases i.e 15 were seen in age group of 51 – 60 years, followed by 14 cases in the age group of 61 - 70 years while 11 were seen in age group of 41 – 50 years. In case of adenocarcinoma 2 cases each were in age group of 41 – 50 years 61 – 70 years. A bar chart representation of distribution of cases according to age and malignant lesions is shown in Figure 2.

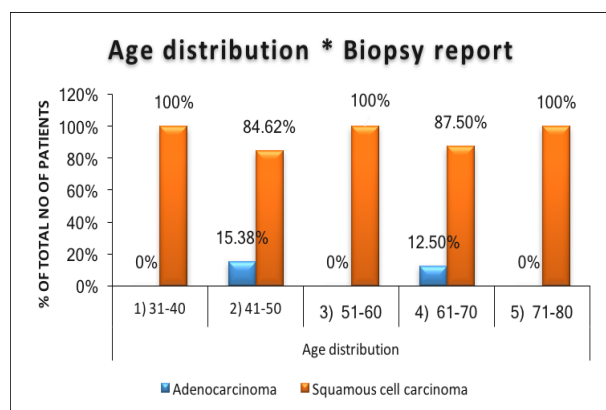


Figure 2: Bar chart showing distribution of cases according to age and biopsy report.

Table 3: Distribution of cases according to gender.

Gender	No.	Percentage
Male	22	44.00%
Female	28	56.00%
Total	50	100.00%

Table 3 shows distribution of cases according to gender. Male cases were 22 (44%) and female cases were 28 (56%). The pie chart representation of the distribution of cases according to gender is shown in Figure 3. The female: male ratio is 1.3:1. A pie diagram shows us the distribution of cases according to gender in Figure 3.

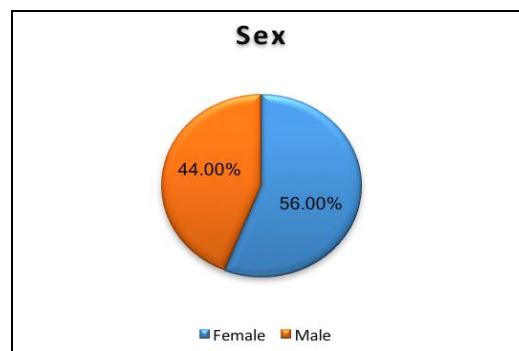
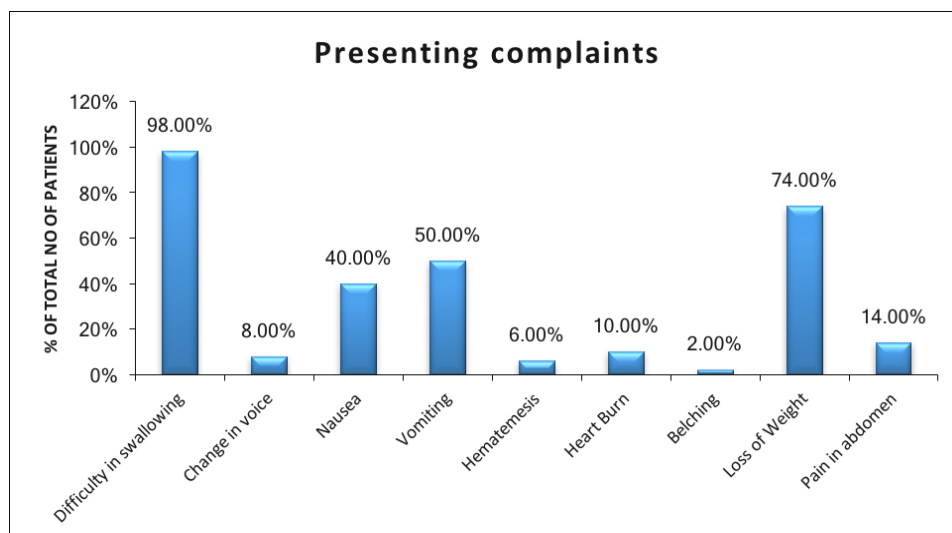


Figure 3: Pie chart showing distribution of cases according to gender.

Table 4: Distribution of cases according to presenting complaints of patients.

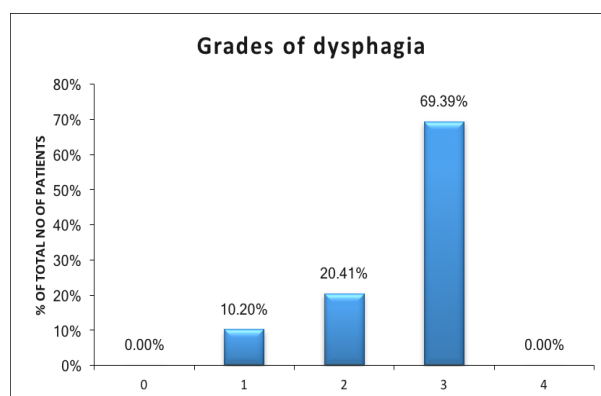
Presenting complaint	No.	Percentage
Difficulty in deglutition	49	98.00%
Change in Voice	4	8.00%
Nausea	20	40.00%
Vomiting	25	50.00%
Hematemesis	3	6.00%
Heart Burn	5	10.00%
Belching	1	2.00%
Loss of weight	37	74.00%
Pain in abdomen	7	14.00%

Table 4 shows distribution of cases according to presenting complaints of patients. The most common presenting complaint was dysphagia present in 49 (98%) cases, followed by loss of weight present in 37 (74%) cases, followed by vomiting present in 25 (50%) cases and nausea was present in 20 (40%) cases. 1 case who didn't had dysphagia had regurgitation. A bar graph representing distribution of cases according to presenting complaints of patients in Figure 4.

**Figure 4: Bar chart showing distribution of cases according to presenting complaints.****Table 5: Distribution of cases with dysphagia according to grades of dysphagia.**

Grade	No.	Percentage
0	0	0
1	5	10.00%
2	10	20.00%
3	34	68.00%
4	0	0
Total	49	98.00%

Table 5 shows distribution of cases with dysphagia according to grades of dysphagia. The cases who presented with grade 3 dysphagia were 34 (68%), followed by grade 2 dysphagia which were 10 (20%) cases and remaining 5 (10%) cases had grade 1 dysphagia. The bar graph shows us the distribution of cases with dysphagia according to grades of dysphagia in figure 5.

**Figure 5: Bar chart showing distribution of cases with dysphagia according to grades of dysphagia.****Table 6: Distribution of cases according to habit according to gender**

Habit		Male	Female	P value
	Yes	18	6	0.001
	No	4	22	
	Total	22	28	

Table 6 shows distribution of cases according to habit according to gender. In male habit was present in 18 (81.82%) cases and in females it was present in 6

(21.43%) cases. The p value is 0.001 (<0.05) which is significant. A bar diagram showing distribution of cases according to habit according to gender is shown in Figure 6.

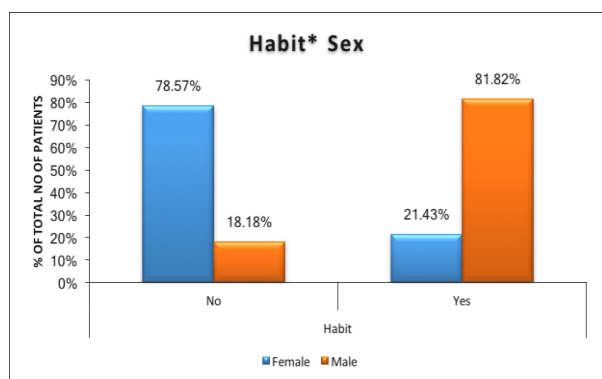


Figure 6: Bar chart showing distribution of cases according to habit and gender.

Table 7: Distribution of cases according to type of habit.

Type of habit	No	Percentage
Tobacco	22	44.00%
Smoking	10	20.00%
Alcohol	11	22.00%

Table 7 shows distribution of cases according to type of habit. Tobacco chewing was present in 22 (44%) cases, smoking was present in 10 (20%) cases while alcohol drinking was present in 11 (22%) cases. A bar graph showing distribution of cases according to type of habit is shown in Figure 7.

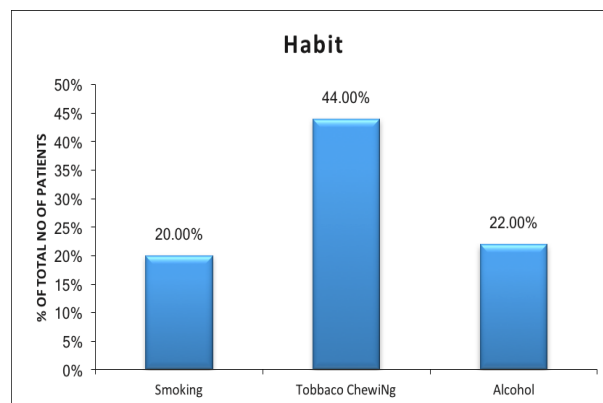


Figure 7: Bar chart showing distribution of cases according to type of habit.

Table 8: Distribution of cases according to type of habit and gender.

		Sex		Total	P value
		Male	Female		
Tobacco chewing	Yes	16 (72.73%)	6 (21.43%)	22 (44.00%)	0.0003
	No	6 (27.27%)	22 (78.57%)	28 (56.00%)	
Alcohol	Yes	11 (50.00%)	0 (0.00%)	11 (22.00%)	0.0001
	No	11 (50.00%)	28 (100.00%)	39 (78.00%)	
Smoking	Yes	10 (45.45%)	0 (0.00%)	10 (20.00%)	0.0001
	No	12 (54.55%)	28 (100.00%)	40 (80.00%)	

Table 8 shows distribution of cases according to type of habit and gender. In males tobacco chewing was present in 16 (72.73%) cases, alcohol drinking was present in 11 (50%) cases while smoking was present in 10 (45.45%) cases. In females tobacco chewing was present in 6 (21.43%) cases, alcohol drinking and smoking was

absent. The p value for tobacco chewing was 0.0003 (<0.05) and for smoking and alcohol drinking was 0.0001 (<0.05). A bar graph of distribution of cases according to type of habit and gender is shown in Figure 8.

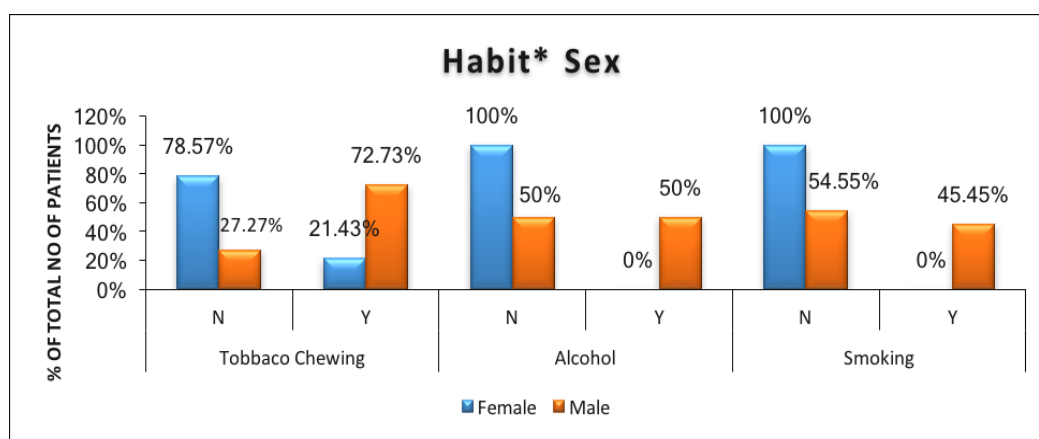


Figure 8: A bar chart showing distribution of cases according to type of habit and gender.

Table 9: Distribution of cases according to type of diet.

	No.	Percentage
Non Veg	32	64.00%
Veg	18	36.00%
Total	50	100.00%

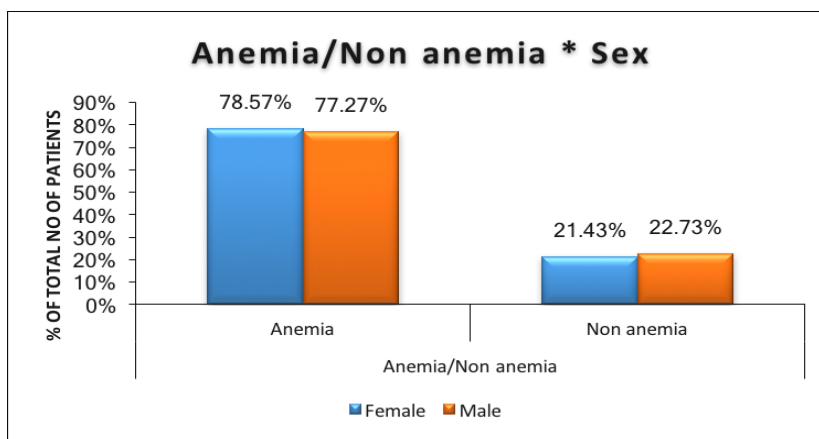
Table 9 shows distribution of cases according to type of diet. 32 (64%) cases were taking non-vegetarian diet while remaining 18 (36%) cases were taking vegetarian diet. A pie diagram showing distribution of cases according to type of diet is shown in Figure 9.

**Figure 9: Pie chart showing distribution of cases according to type of diet.****Table 10: Distribution of cases according to presence of anemia and gender.**

		Gender		
		Female	Male	Total
Anemia/ Non anemia	Anemia	22 (78.57%)	17 (77.27%)	39 (78.00%)
	Non anemia	6 (21.43%)	5 (22.73%)	11 (22.00%)
Total		28 (100.00%)	22 (100.00%)	50 (100.00%)

Table 10 shows distribution of cases according to presence of anemia and gender. 17 (77.27%) males had anemia while 22 (78.57%) females had anemia. According to World Health Organisation defines anemia as Hemoglobin < 13g/dl in men and <12g/dl in women.

The mean Hb levels were 11.13 (± 1.7 SD) while median was 10.95. Minimum Hb level was 6.8 and maximum was 15.1. A bar diagram shows distribution of cases according to presence of anemia and gender in Figure 10.

**Figure 10: Bar chart showing distribution of cases according to presence of anemia and gender.****Table 11: Distribution of cases according to albumin levels and gender.**

		Gender		
		Female	Male	Total
Albumin levels	Deranged	8 (28.57%)	5 (22.73%)	13 (26.00%)
	Normal	20 (71.43%)	17 (77.27%)	37 (74.00%)
Total		28 (100.00%)	22 (100.00%)	50 (100.00%)

Table 11 shows distribution of cases according to albumin levels and gender. 5 (22.73%) males had hypoalbuminemia while 8 (28.57%) females had presence of hypoalbuminemia. Normal albumin levels in human blood ranges from 3.5 – 5.5 g/dl. The mean

albumin levels were 3.78 (± 0.58 SD), median was 3.8. Lowest levels were 2.2 and highest levels were 4.9. A bar diagram showing distribution of cases according to presence of hypoalbuminemia and gender in Figure 11.

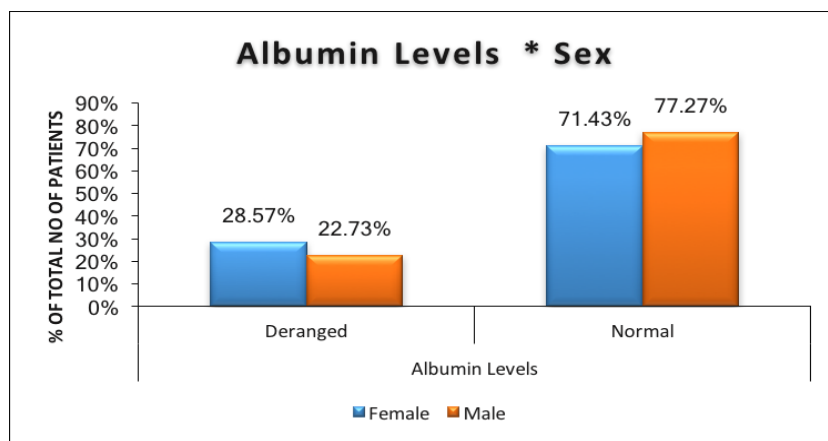


Figure 11: Bar chart showing distribution of cases according to albumin levels and gender

Table 12: Distribution of cases according to type of growth on endoscopy.

Type of growth	No.	Percentage
Narrowing/stricture	3	6.00%
Nodular	1	2.00%
Proliferative growth	3	6.00%
Ulcerated growth	6	12.00%
Ulceroproliferative growth	37	74.00%
Total	50	100.00%

Table 12 shows distribution of cases according to type of growth on endoscopy. Most cases had ulceroproliferative growth on endoscopy i.e 37 (74%), followed by 6 (12%) cases who had ulcerated growth, followed by 3 (6%) cases who had proliferative growth and narrowing/stricture each and followed by 1 (2%) case who had nodular growth. A bar graph showing distribution of cases according to type of growth on endoscopy is shown in Figure 12.

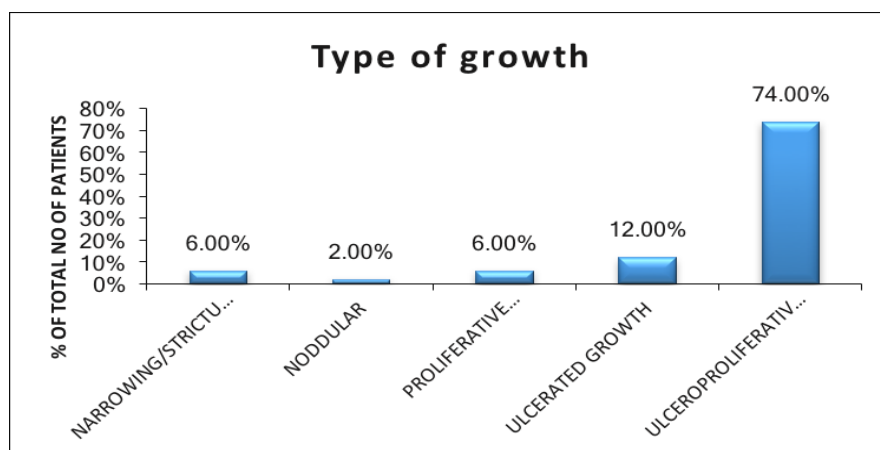


Figure 12: Bar chart showing distribution of cases according to type of growth on endoscopy.

Table 13: Distribution of cases according to level of growth.

Level Of Growth	No.	Percentage
Upper	5	10.00%
Middle	30	60.00%
Lower	15	30.00%

Table 13 shows distribution of cases according to level of growth. In 30 (60%) cases growth was present in middle 1/3rd part of esophagus, followed by 15 (30%) cases were growth was present in lower 1/3rd part of esophagus while in 5 (10%) cases growth was present in upper 1/3rd part of esophagus. Out of 50 cases, only in 9 cases, the scope was negotiable beyond growth. In rest 41 cases scope could not be negotiated beyond the growth. A pie diagram showing the distribution of cases according to level of growth is shown in Figure 13.

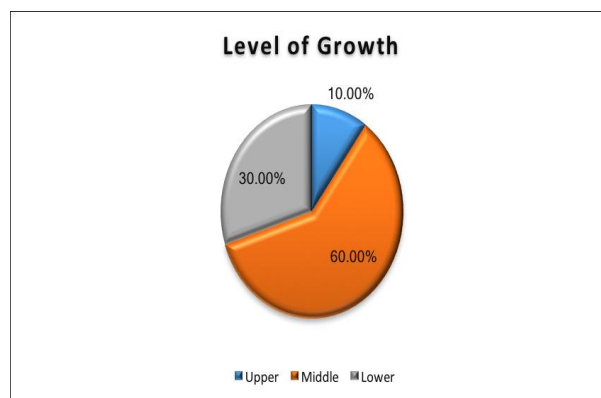


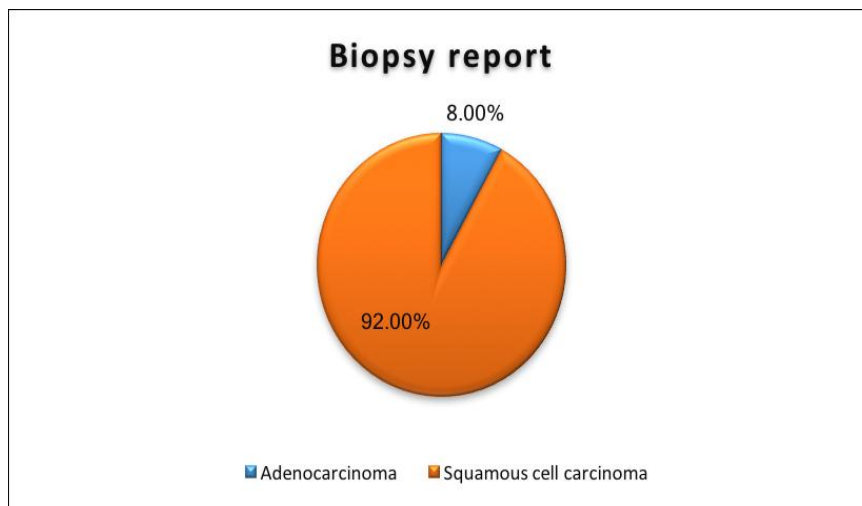
Figure 13: Pie chart showing distribution of cases according to level of growth.

Table 14: Distribution of cases according to histological type of carcinoma.

Histological Type	No.	Percentage
SQUAMOUS CELL CARCINOMA	46	92.00%
ADENOCARCINOMA	4	8.00%
Total	50	100.00%

Table 14 shows distribution of cases according to histological type of carcinoma. Squamous cell carcinoma was present in 46 (92%) cases while adenocarcinoma

was present in 4 (8%) cases. A pie diagram showing distribution of cases according to histological type of carcinoma is shown in Figure 14.

**Figure 14: Pie chart showing distribution of cases according to histological type of carcinoma.****Table 15: Distribution of cases according to histopathological grading of squamous cell carcinoma.**

Histopathological grading	No.	Percentage
WELL DIFFERENTIATED SQUAMOUS CELL CARCINOMA	17	36.96%
MODERATELY DIFFERENTIATED SQUAMOUS CELL CARCINOMA	15	32.61%
POORLY DIFFERENTIATED SQUAMOUS CELL CARCINOMA	14	30.43%

Table 15 shows distribution of cases according to histopathological grading of squamous cell carcinoma. Well Differentiated Squamous Cell Carcinoma was present in 17 (36.96%) cases, followed by moderately differentiated squamous cell carcinoma present in 15

(32.61%) cases and poorly differentiated squamous cell carcinoma was present in 14 (30.43%) cases. A pie diagram showing distribution of cases according to histopathological grading of squamous cell carcinoma is shown in figure 15.

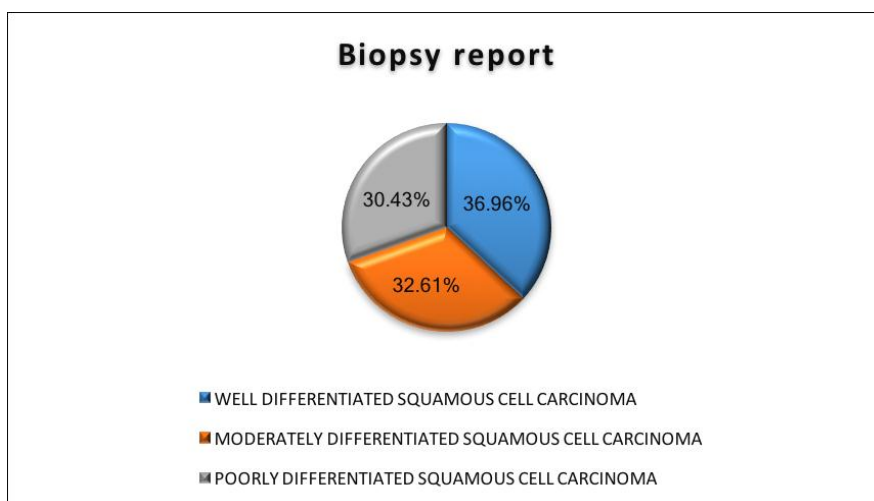
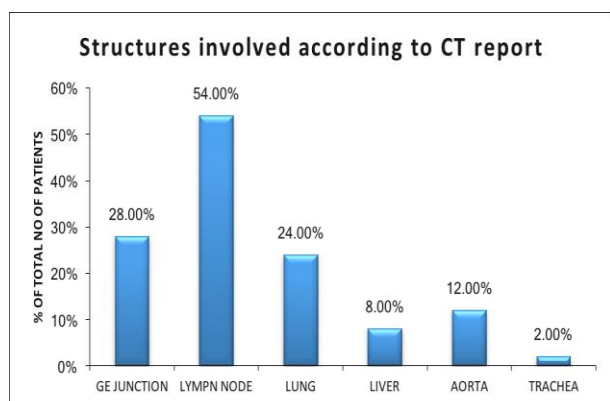
**Figure 15: A pie chart showing distribution of cases according to histopathological grading of squamous cell carcinoma.**

Table 16: Distribution of cases according to structures involved according to CT report.

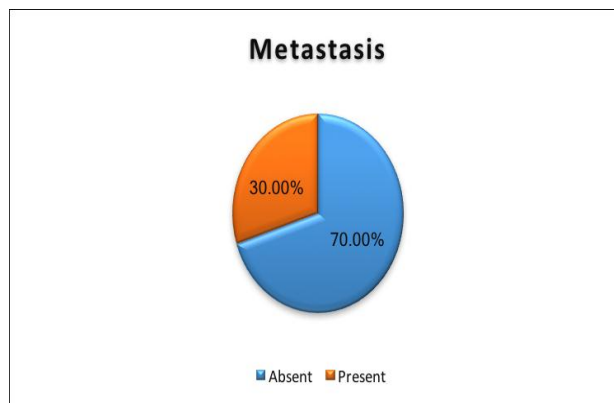
	No.	Percentage
GE JUNCTION	14	28.00%
LYMPH NODE	27	54.00%
LUNG	12	24.00%
LIVER	4	8.00%
AORTA	6	12.00%
TRACHEA	1	2.00%

Table 16 shows distribution of cases according to structures involved according to CT report. GE junction was involved in 14 (28%) cases, lymph node spread was present in 27 (54%) cases, lung metastasis was present in 12 (24%) cases, liver metastasis was present in 4 (8%) cases, involvement of aorta was present in 6 (12%) cases whereas tracheal involvement was present in 1 (2%) case. A bar diagram showing distribution of cases according to structures involved according to CT report is shown in Figure 16.

**Figure 16: A bar chart showing distribution of cases according to structures involved according to CT report.****Table 17: Distribution of cases according to presence of distant metastasis.**

	No.	Percentage
Present	15	30.00%
Absent	35	70.00%
Total	50	100.00%

Table 17 distribution of cases according to presence of distant metastasis. It was present in 15 (30%) cases. In particular lung metastasis was present in 12 (24%) cases and liver metastasis was present in 4 (8%) cases. In a case both liver and lung metastasis was present. A pie diagram showing distribution of cases according to presence of distant metastasis is shown in Figure 17.

**Figure 17: Pie chart showing distribution of cases according to presence of distant metastasis.**

DISCUSSION

In our study we will study the etiological factors and clinic-pathological correlation of esophageal carcinoma.

Age Significance

In our study, maximum number of cases of esophageal carcinoma i.e 16 (32%) cases were in 7th decade of life followed by 15 (30%) cases in 6th decade. The mean age was 56.82 with standard deviation of 9.82 years (± 9.82 SD) while median age group was 55.5. SCC was mostly common in 6th decade of life followed by 7th decade while adenocarcinoma was present in 5th and 7th decade of life in our study. The mean age for SCC is 56.21 years (± 10.16 SD) adenocarcinoma is 57 years (± 8.25 SD). The incidence of esophageal carcinoma increases with increase in age. SCC was seen more in elderly population while adenocarcinoma was seen in a younger age group as compared to SCC.

In a study done by Wong et al^[40] and El-Serag et al,^[41] it was found that a significant increase in incidence of esophageal adenocarcinoma among the 45–65 years of age group.

Shil BC et al^[43] observed that oesophageal carcinoma was seen in 6th (51–60yrs) decade of life followed by 7th and 5th decades. Population based data reveal that the esophageal cancer incidence peaks in the sixth decade as in most parts of the world.

In a study done by Zhang Y^[44] in 2013, for different types of esophageal cancer, the risk increases with age, with a mean age at diagnosis of 67 years.

In a study done by Samarasam et al^[42], showed that the mean age was 52 years.

Tercioti-Junior et al,^[45] investigated 103 patients with adenocarcinoma and found a mean age of 56.98 ± 10.28 . Our findings were consistent with the literature.

Gender

In our study we found that females (28) were affected more than males (22). The female:male ratio is 1.3:1.

In study done by **Henry MACA et al**,^[46] it was observed that there was a high incidence of esophageal cancer in male individuals. Many earlier studies have stated that esophageal cancer is four times more common and slightly more lethal in men than in women. (**Hwang JJ, May 01, 2014, Cancer Management, Esophageal Cancer**).^[47] **Puhakka & Aitsalo, Malik et al, Afidi SP et al** and **Salih M et al** reported a high ratio of males for this cancer as compared to females^[48,49,50,51]

But literature also suggests that the incidence of esophageal carcinoma is more in females than males. Study done by **Bukhari et al**^[52] suggests that a high frequency of cancer was seen in females with a total of 90 (57%) cases as compared to 68 (43%) males with female to male ratio of 1.3:1.

Study conducted by **Bhurgri et al**^[53] also showed that the cancer esophagus, predominantly squamous cell carcinoma was seen to be marginally higher in the females. **Celik S et al**^[54] also in their study, found esophageal tumors to be 2 times more common in females than males in contrast to the literature.

Grades of Dysphagia

Dysphagia grading system^[58]

Dysphagia	Symptom
Grade 0	Able to swallow all solid foods without difficulty
Grade 1	Able to swallow solid foods with some difficulty
Grade 2	Able to swallow soft or semi solid foods only
Grade 3	Able to swallow liquefied foods and liquids only
Grade 4	Unable to swallow liquids/saliva

In our study, around 34 (68%) patients had grade III dysphagia, followed by 10 (20%) patients with grade II dysphagia and remaining 5 (10%) patients with grade I dysphagia. None patients in our study had grade IV and grade V dysphagia.

Mchembe et al^[56] in his study found that 15 (4.6%) had grade 2 dysphagia, 49 (14.9%) had grade 3 dysphagia, 141 (43%) had grade 4 dysphagia and remaining 123 (37.5%) had grade 5 dysphagia.

Habit

In our study it was found that in males 16 (72.73%) had history of tobacco chewing, 11 (50%) had history of alcohol consumption while 10 (45.45%) had history of smoking while in females 6 (21.43%) had history of tobacco chewing and none had history of alcohol drinking and smoking. The p value for tobacco chewing was 0.0003 (<0.05) and for smoking and alcohol drinking was 0.0001 (<0.05). It was significant in all the three variables. This shows that there is a association between habit and esophageal carcinoma.

Kamangar et al^[59] had mentioned in his study that cigarette smoking is more strongly associated with esophageal squamous cell carcinoma than with

Presenting complaints

In our study it was seen that maximum patients presented with complain of dysphagia (98%) and 2nd most common presenting complaint was weight loss (74%). 50% patients presented with symptoms of regurgitation i.e nausea and vomiting while 5 (10%) patients had heart burn or retrosternal pain. The findings are consistent with the literature.

Hussain et al^[55] also found out that dysphagia was most common symptom which was followed by weight loss.

Mchembe et al^[56] also stated that all the patients in his study presented with progressive dysphagia and weight loss (100%). This was followed by 249 patients (75.9%) presented with regurgitation, and 102 (31.1%), 45 (13.7%) and 12 (3.7%) patients presented with retrosternal pain, odynophagia and hematemesis, respectively.

Vaishnav et al^[57] also found that dysphasia (100%) is the most common symptom followed by weight loss (45%).

esophageal adenocarcinoma. The risk of developing esophageal squamous cell carcinoma risk is increased by approximately 3–7-fold in current smokers. The association between cigarette smoking and esophageal adenocarcinoma in almost all of cases have found to have an increased risk of nearly 2-fold.

Zhang Y et al^[44] has also stated that tobacco consumption, alcohol drinking and smoking are risk factors for development of esophageal cancer.

M. P. Salaspuro et al^[60] has stated that the relative risk (RR) for oesophageal cancer is 5.8 among those having six or more drinks per day. There seems to be a synergistic effect in the presence of excessive alcohol consumption, which increases the risk notably. Individuals drinking > 1.5 bottles of wine and smoking 10 to 30 cigarettes daily have about a 150-fold increased risk of oesophageal cancer. Simultaneous exposure to the same moderate amounts of alcohol and smoking increases the risk 12- to 19-fold in men and women respectively.

As mentioned in the **Guidelines for the management of gastroenterological diseases (Ministry of Health & Family Welfare Govt. of India)**, esophageal cancers

have been associated with alcohol consumption, obesity and smoking counselling about avoiding these risk factors might be useful.

Type of Diet

In our study, out of 50 patients, 32 (64%) were non-vegetarians while 18 (36%) were vegetarians.

Kamangar et al^[59] has stated that high intake of fresh fruit and vegetables reduces the risk of oesophageal squamous cell carcinoma; it has been estimated such a diet decreases the risk by about 20% per 50 g of fruit or vegetable intake per day.

Anaemia

In our study, anaemia was present in 17 (77.27%) males and 22 (78.57%) females.

Zhang F et al^[61] the incidence of anaemia was 29.1%. The main reason for the high incidence of anaemia in our study is due to poor nutritional status of the Indian population. Anaemia is more prevalent in females in India and in our study the presence of anaemia is more in females than males.

Hypoalbuminemia

In our study, hypoalbuminemia was present in 5 (22.73%) males and 8 (28.57%) females.

Yang et al^[62] in his study reported that hypoalbuminemia was present in 10% cases.

The main reason for the high incidence of hypoalbuminemia in our study is due to poor nutritional status of the Indian population.

Type of growth

In our study, the most common growth seen on endoscopy was ulceroproliferative growth seen in 37 (74%) patients. This was followed by 6 (12%) patients with ulcerated growth. Proliferative growth and narrowing/stricture was seen in 3 (6%) patients each while only 1 patient had nodular growth.

Krishnappa Rashmi et al^[63] in his study showed that squamous cell carcinoma of esophagus endoscopically presented as proliferative and ulceroproliferative lesions with four cases (36%) each, while ulcerative with two cases (18%) and stenosis/stricture as one case (9%).

Aledavood et al^[64] in his study found that on endoscopy, 51.3% of lesions were polypoid while 48.7% were ulcerative, infiltrative.

Level of growth

In our study, maximum lesions i.e 30 (60%) were found in middle 1/3rd of esophagus, followed by 15 (30%) lesions in lower 1/3rd and 5 (10%) were present in upper 1/3rd of esophagus.

Abilash SC et al^[65] observed that the level of growth in esophageal carcinoma was middle third esophagus to be the commonest affected site with 12 cases (75%) followed by lower third and upper third esophagus constituting 12.5% each. Similar findings were seen in the study done by **Rumana et al**^[66]

Krishnappa Rashmi et al^[63] found that the growth was most commonly seen in the middle third in which accounted for eight patients (73%). The next most common site was lower third with two patients (18%) and one patient had it in the upper third.

Incidence of Squamous cell carcinoma versus Adenocarcinoma

In our study, maximum cases i.e 46 (92%) were of SCC while 4 (8%) cases were of adenocarcinoma. We didn't find any other histological type in our study.

Bukhari et al^[52] found that out of 215 esophageal biopsies, 158 (73%) cases were diagnosed as cancers. The common malignancy was squamous cell carcinoma with a frequency of 150 (95%) followed by five (3%) cases of adenocarcinoma & three (2%) cases of undifferentiated carcinoma.

Krishnappa Rashmi et al^[63] in his study found that all the 11 cases of esophageal neoplastic lesions malignant and were squamous cell carcinoma type (100%)

Cherian et al^[67] **Mchembe et al**^[56] also found that SCC was more common type of histological esophageal malignancy followed by adenocarcinoma.

Histological grading

In our study, histological grading of SCC was done. In this, well differentiated type was seen in 17 (36.96%) patients, followed by 15 (32.61%) patients of moderately differentiated type and 14 (30.43%) had poorly differentiated type.

Hussain et al^[55] found that out of 37 esophageal biopsies, 33 were having SCC of which 10 had well differentiated squamous cell carcinoma, 20 had moderately differentiated squamous cell carcinoma and 9 had poorly differentiated squamous cell carcinoma.

Krishnappa Rashmi et al^[63] in his study showed that of all the 11 cases of esophageal carcinoma, eight cases (73%) were moderately differentiated; two cases (18%) were well differentiated squamous cell carcinoma, and one case was diagnosed as poorly differentiated squamous cell carcinoma.

Metastasis (local and distant)

In our study, metastasis was found in 15 cases. Local spread to aorta was present in 6 cases and to trachea was present in 1 case. Distant metastasis to lung was present in 12 cases and to liver in 4 cases.

Mchembe et al^[56] study revealed that distant metastasis was documented in 43.3% of patients.

Yang et al^[62] found distant metastasis in 27 patients (23%)

The high number of metastasis is due late reporting of patients to hospital leading to diagnosis of disease at an advanced stage due to which this disease carries a poor prognosis.

CONCLUSION

Carcinoma esophagus is a fatal malignancy owing to high rate of metastasis at the time of diagnosis of the condition. Any patient presenting above age of 50 years with symptoms of progressive dysphagia should undergo flexible endoscopy of upper gastrointestinal tract. In case of suspected lesions biopsy from the lesion should be taken and patient needs to be subjected for further radiological evaluation like CT Thorax. Most of the patient presenting with progressive dysphagia may also have weight loss symptom due to which patient's nutritional status is poor. In developing countries like India, the incidence of SCC is significantly more than that of adenocarcinoma as compared to western countries where incidence of adenocarcinoma is raising. Anaemia and low albumin levels can also be presented in patients of esophageal carcinoma. Addiction in the form of tobacco chewing, alcohol drinking and smoking increases the risk of an individual for development of esophageal carcinoma. Non-vegetarian diet with low consumption of fruits and vegetables is also a risk factor for development of esophageal carcinoma.

Owing to high incidence of metastasis in patients of esophageal carcinoma, a clinician should always bear in mind a suspicion of esophageal carcinoma in patients above 50 years of age and complaining of dysphagia by performing a flexible endoscopy of upper gastrointestinal tract coupled with multiple biopsies from suspected lesion.

REFERENCES

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA: a cancer journal for clinicians*, 2015; 65(2): 87±108. Epub 2015/02/06. <https://doi.org/10.3322/caac.21262> PMID: 25651787.
2. National Cancer Registry Programme. First All India Report 2001-2002. Vol. 1. Indian Council of Medical Research Bangalore, India. April 2004.
3. Bhurgri Y, Faridi N, Kazi LAG, Ali SK, Bhurgri H, Usman A, et al. Cancer esophagus Karachi 1995-2002: Epidemiology, risk factors and trends. *J Pak Med Assoc*, 2004; 54: 345-8.
4. Retraction: The candidate tumor suppressor gene ECRG4 inhibits cancer cells migration and invasion in esophageal carcinoma. *J Exp Clin Cancer Res*, 2011; 30: 19 [PMID: 21324197 DOI: 10.1186/1756-9966-30-19]
5. Esophageal cancer: epidemiology, pathogenesis and prevention. *Nat Clin Pract Gastroenterol Hepatol*, 2008; 5: 517-526. [PMID: 18679388 DOI: 10.1038/ncpgasthep1223].
6. Engel LS, Chow WH, Vaughan TL, Gammon MD, Risch HA, Stanford JL, Schoenberg JB, Mayne ST, Dubrow R, Rotterdam H, West AB, Blaser M, Blot WJ, Gail MH, Fraumeni JF. Population attributable risks of esophageal and gastric cancers. *J Natl Cancer Inst*, 2003; 95: 1404-1413 [PMID: 13130116].
7. Blot WJ, McLaughlin JK. The changing epidemiology of esophageal cancer. *Semin Oncol*, 1999; 26: 2-8 [PMID: 10566604].
8. Vizcaino AP, Moreno V, Lambert R, Parkin DM. Time trends incidence of both major histologic types of esophageal carcinomas in selected countries, 1973±1995. *International journal of cancer*, 2002; 99(6): 860±8. Epub 2002/07/13. <https://doi.org/10.1002/ijc.10427> PMID: 12115489.
9. Tran GD, Sun XD, Abnet CC, Fan JH, Dawsey SM, Dong ZW, et al. Prospective study of risk factors for esophageal and gastric cancers in the Linxian general population trial cohort in China. *International journal of cancer*, 2005; 113(3): 456±63. Epub 2004/09/30. <https://doi.org/10.1002/ijc.20616> PMID: 15455378.
10. Lu CL, Lang HC, Luo JC, Liu CC, Lin HC, Chang FY, et al. Increasing trend of the incidence of esophageal squamous cell carcinoma, but not adenocarcinoma, in Taiwan. *Cancer causes & control: CCC*, 2010; 21(2): 269±74. Epub 2009/10/30. <https://doi.org/10.1007/s10552-009-9458-0> PMID: 19866363.
11. Rustgi AK, El-Serag HB. Esophageal carcinoma. *The New England journal of medicine*, 2014; 371(26): 2499±509. Epub 2014/12/30. <https://doi.org/10.1056/NEJMra1314530> PMID: 25539106.
12. Craver LF. Clinical study of etiology of gastric and esophageal carcinoma. *Am J Cancer*, 1932; 16(1): 68-102.
13. Watson WL. Cancer of the esophagus: some etiological considerations. *Am J Roentgenol*, 1939; 41(3): 420-4.
14. Blot WJ, Devesa SS, Kneller RW, et al. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA*, 1991; 265(10): 1287-9. [PubMed: 1995976].
15. Brown LM, Devesa SS, Chow WH. Incidence of Adenocarcinoma of the Esophagus Among White Americans by Sex, Stage, and Age. *J Natl Cancer Inst*, 2008; 1184-7. [PubMed: 18695138].
16. Botterweck AA, Schouten LJ, Volovics A, et al. Trends in incidence of adenocarcinoma of the oesophagus and gastric cardia in ten European countries. *Int J Epidemiol*, 2000; 29(4): 645-54. [PubMed: 10922340].

17. Vizcaino AP, Moreno V, Lambert R, et al. Time trends incidence of both major histologic types of esophageal carcinomas in selected countries, 1973–1995. *Int J Cancer*, 2002; 99(6): 860–8. [PubMed: 12115489].
18. van Blankenstein M, Looman CW, Siersema PD, et al. Trends in the incidence of adenocarcinoma of the oesophagus and cardia in the Netherlands 1989–2003. *Br J Cancer*, 2007; 96(11): 1767–71. [PubMed: 17505507].
19. Corley DA, Buffler PA. Oesophageal and gastric cardia adenocarcinomas: analysis of regional variation using the Cancer Incidence in Five Continents database. *Int J Epidemiol*, 2001; 30(6): 1415–25. [PubMed: 11821356].
20. Islami F, Kamangar F, Aghcheli K, et al. Epidemiologic features of upper gastrointestinal tract cancer in northeastern Iran. *Br J Cancer*, 2004; 90(7): 1402–6. [PubMed: 15054463].
21. Tran GD, Sun XD, Abnet CC, et al. Prospective study of risk factors for esophageal and gastric cancers in the Linxian general population trial cohort in China. *Int J Cancer*, 2005; 113(3): 456–63. [PubMed: 15455378].
22. Schlansky B, Dimarino AJ Jr, Loren D, Infantolino A, Kowalski T, Cohen S: A survey of esophageal cancer: pathology, stage and clinical presentation. *Alimen Pharmacol Ther*, 2006; 23: 587–593.
23. Pindiga HU, Akang EE, Thomas JO, Aghadiuno PU: Carcinoma of the oesophagus in Ibadan. *East Afr Med J*, 1997; 74: 307–310.
24. Ali A, Ersumo T, Johnson O: Oesophageal carcinoma in Tikur Anbessa Hospital, Addis Ababa. *East Afr Med J* 1998; 75:590–593.
25. Obajimi MO, Ogunseyinde AO, Brimmo IA, Adebo AO: Trans-hiatal oesophagectomy as palliative treatment for carcinoma of the oesophagus. *East Afr Med J*, 2002; 79: 311–316.
26. Czito BG, Albers D, Christopher G, Willeett R: Esophageal cancer. In Perez and Brady's, Principles and practice of radiation oncology. 5th edition. Edited by C.halprin E, A.Ferez C, lutherw. Brady. Philadelphia: Lippincott Williams and Wilkins, 2008; 1131–1151.
27. Glaws WR, Etzkorn KP, Wenig BL, et al. Comparison of rigid and flexible esophagoscopy in the diagnosis of esophageal disease: diagnostic accuracy, complications and cost. *Ann Otol Rhinol Laryngol*, 1996; 105: 262–6.
28. Dooley CP, Larson AW, Stace NH, et al. Double-contrast barium meal and upper gastrointestinal endoscopy. A comparative study. *Ann Intern Med*, 1984; 101: 538–45.
29. Esfandyari T, Potter JW, Vaezi MF. Dysphagia: a cost analysis of the diagnostic approach. *Am J Gastroenterol*, 2002; 97: 2733–7.
30. Spechler SJ. AGA technical review on treatment of patients with dysphagia caused by benign disorders of the distal esophagus. *Gastroenterology*, 1999; 117: 233–54.
31. Burt M. Management of malignant esophagorespiratory fistula. *Chest Surg Clin North Am*, 1996; 6: 765–76.
32. Siewert JR, Stein HJ. Classification of adenocarcinoma of the oesophagogastric junction. *Br J Surg*, 1998; 85: 1457–9.
33. Graham DY, Schwartz JT, Cain GD, et al. Prospective evaluation of biopsy number in the diagnosis of esophageal and gastric carcinoma. *Gastroenterology*, 1982; 82: 228–31.
34. Lal N, Bhasin DK, Malik AK, et al. Optimal number of biopsy specimens in the diagnosis of carcinoma of the oesophagus. *Gut*, 1992; 33: 724–6.
35. Faigel DO, Deveney C, Phillips D, Fennerty MB. Biopsynegative malignant esophageal stricture: diagnosis by endoscopic ultrasound. *Am J Gastroenterol*, 1998; 93: 2257–60.
36. Korst RJ, Altorki NK. Imaging for esophageal tumors. *Thorac Surg Clin*, 2004; 14(1): 61–69.
37. Talsma K, Van Hagen P, Grotenhuis BA, et al. Comparison of the 6th and 7th editions of the UICC-AJCC TNM classification for esophageal cancer. *Ann Surg Oncol*, 2012; 19(7): 2142–2148.
38. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol*, 2010; 17(6): 1471–1474.
39. Kim TJ, Kim HY, Lee KW, Kim MS. Multimodality assessment of esophageal cancer: preoperative staging and monitoring of response to therapy. *RadioGraphics*, 2009; 29(2): 403–421.
40. Wong A, Fitzgerald RC. Epidemiologic risk factors for Barrett's esophagus and associated adenocarcinoma. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc*, 2005 Jan; 3(1): 1–10.
41. El-Serag HB, Mason AC, Petersen N, Key CR. Epidemiological differences between adenocarcinoma of the oesophagus and adenocarcinoma of the gastric cardia in the USA. *Gut*, 2002; 50(3): 368–372.
42. Samarasinghe I. Esophageal cancer in India: Current status and future perspectives. *Int J Adv Med Health Res*, 2017; 4: 5–10.
43. Shil BC, Islam MA, Nath NC, Ahmed. Oesophageal carcinoma: trends and risk Factors in rural Bangladesh. *J Dhaka Med. Coll*, 2010; 19(1): 29–32.
44. Zhang Y. Epidemiology of esophageal cancer. *World J Gastroenterol*, 2013; 19(34): 5598–5606 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v19/i34/5598.htm>DOI:<http://dx.doi.org/10.3748/wjg.v19.i34.5598>.
45. Terciotti-Junior Valdir, Lopes Luiz Roberto, Coelho-Neto João de Souza, Carvalheira José Barreto Campelo, Andreollo Nelson Adami. Esophagogastric junction adenocarcinoma: multivariate analyses of surgical morbi-mortality and adjuvant therapy. *ABCD, arq. bras. cir. dig.* [Internet]. 2012 Dec [cited 2017 Oct 01]; 25(4): 229–234. Available from:

- http://www.scielo.br/scielo.php?script=sci_arttext&pid=S010267202012000400004&lng=en. <http://dx.doi.org/10.1590/S010267202012000400004>.
46. Henry MAC de A, Lerco MM, Ribeiro PW, Rodrigues MAM. Epidemiological features of esophageal cancer. Squamous cell carcinoma versus adenocarcinoma. *Acta Cir Bras*, 2014 Jun; 29(6): 389–93.
 47. Jimmy J. Hwang, Rajesh V. Iyer, Michael Mulligan. Cancer Management, Esophageal Cancer, Cancer Network home of the journal ONCOLOGY, May 01, 2014.
 48. Puhakka HJ, Aitsalo K. Oesophageal carcinoma: Endoscopic and clinical findings in 258 patients. *J Laryngo & Otology*, 1988; 102: 1137–41.
 49. Malik IA, Khan WA, Khan ZK. Pattern of malignant tumours observed in a University Hospital; A retrospective analysis. *J Pak Med Assoc*, 1998; 48(5): 120–122.
 50. Afridi SP, Khan A, Waheed I. High risk factors in patient with carcinoma esophagus. *J Coll Physicians Surg Pak*, 2000; 10(10): 368–70.
 51. Salih M, Abid S, Hamid SS, Ali SH, Abbas Z, Jafri MW. Carcinoma of the esophagus: Are we different? *J Coll Physicians Surg Pak*, 2005; 15(5): 313–14.
 52. Bukhari U, Siyal R, Memon FA, Memon JH. Oesophageal carcinoma: A review of endoscopic biopsies. *Pak J Med Sci*, 2009; 25(5): 845–848.
 53. Bhurgri Y, Bhurgri A, Nishter S, Ahmed A, Usman A, Pervez S, et al. Pakistan--country profile of cancer and cancer control 1995–2004. *JPMA J Pak Med Assoc*, 2006 Mar; 56(3): 124–30.
 54. Celik S, Yilmaz EM, Özden F, Kotan C, Okut H. The Relationship between Eating and Lifestyle Habits and Cancer in Van Lake Region: Another Endemic Region for Esophageal and Gastric Cancers. *J Cancer Epidemiol*, 2015; 2015: 254823.
 55. Hussain SI, Reshi R, Akhter G, Beigh A. Clinico histopathological study of upper gastrointestinal tract endoscopic biopsies. *Int J Cur Res Rev*, 2015 Aug; 7(16): 78–85.
 56. Mchembe et al.: Endoscopic and clinicopathological patterns of esophageal cancer in Tanzania: experiences from two tertiary health institutions. *World Journal of Surgical Oncology*, 2013; 11: 257.
 57. Vaishnav KU, Vaishnav UG, Patel SB, Bhatt CJ, Shah DS, Shah MS. Role of CT Scan In Staging of Carcinoma of Esophagus – A Study of 100 Cases. *GUJARAT Med J*, 2014 Mar; 69(1): 87–92.
 58. Coia LR, Myerson RJ, Tepper JE. Late effects of radiation therapy on the gastrointestinal tract. *Int J Radiat Oncol Biol Phys* 1995; 31:1213. *Int J Radiat Oncol Biol Phys*, 1995 Mar 30; 31(5): 1213–36.
 59. Kamangar F, Chow W-H, C. Abnet C, M. Dawsey S. Environmental Causes of Esophageal Cancer. *Gastroenterol Clin North Am*, 2009 Mar; 38(1): 27–57.
 60. Salaspuro MP. Alcohol consumption and cancer of the gastrointestinal tract. *Best Pract Res Clin Gastroenterol*, 2003 Aug; 17(4): 679–94.
 61. Zhang F, Cheng F, Cao L, Wang S, Zhou W, Ma W. A retrospective study: the prevalence and prognostic value of anemia in patients undergoing radiotherapy for esophageal squamous cell carcinoma. *World Journal of Surgical Oncology*, 2014; 12: 244. doi:10.1186/1477-7819-12-244.
 62. Yang Y, Jia J, Sun Z, Du F, Yu J, Liu C, et al. Prognosis impact of clinical characteristics in patients with inoperable esophageal squamous cell carcinoma. *PLoS ONE*, 2017; 12(8): e0182660. <https://doi.org/10.1371/journal.pone.0182660>.
 63. Krishnappa R, Horakerappa M, Ali K, Gouri M. A study on histopathological spectrum of upper gastrointestinal tract endoscopic biopsies. *Int J Med Res Health Sci*, 2013; 2(3): 418.
 64. Aledavood A, Anvari K, Sabouri G. Esophageal Cancer in Northeast of Iran. *Iran J Cancer Prev*, 2011; 4(3): 125–9.
 65. Abilash S, Kolakkada H, MM G, S S, S B. Histopathologic Spectrum of Upper Gastrointestinal Tract Mucosal Biopsies: A Retrospective Study. *Sch J Appl Med Sci SJAMS*, 2016 May; 4(5E): 1807–13.
 66. Rumana M, Khan AR, Khurshid N; The changing pattern of oesophago-gastric cancer in Kashmir. *JK-Practitioner*, 2005; 12(4): 189–192.
 67. Cherian JV, Sivaraman R, Muthusamy AK, Jayanthi V. Carcinoma of the esophagus in Tamil Nadu (South India): 16-year trends from a tertiary center. *J Gastrointest Liver Dis JGLD*, 2007 Sep; 16(3): 245–9.