

ORIGINAL ARTICLE

Histopathological Spectrum of Premalignant and Malignant Lesions of Esophagus in the Population of Karachi

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ABSTRACT

Background: Squamous cell carcinoma (SCC) and adenocarcinoma are the most common esophageal cancers. Barrett's esophagus is the change of esophageal stratified squamous epithelium to columnar cells which if remain undiagnosed follows the dysplasia – carcinoma sequence. The last two decades show a change in the histologic pattern of esophageal carcinoma. Adenocarcinoma is at majority rate than SCC in the West, however, in Asia, SCC is still the commonest cancer of esophagus. In this study, we aim to define a spectrum of premalignant and malignant neoplasms of esophagus in our region.

Methods: This study was done at Dow Diagnostic Research and Reference Laboratory (DDRRL). All the cases of preneoplastic and neoplastic lesions of esophagus received during the period of 7 years (2009-2015) were reviewed. The data obtained were subjected to descriptive statistical analysis using SPSS version 21.

Results: Out of 94 premalignant cases, 70 (74.5%) were diagnosed as Barrett's esophagus, 23 (24.5%) as dysplasia and 1 (1.1%) as adenoma. From the total of 450 malignant cases, 395 (87.7%) were SCC, 54 (12%) were adenocarcinoma and a single case of leiomyoma was diagnosed. Grade II SCC was found to be most the common lesion.

Conclusion: Barrett's esophagus was more than dysplasia and showed male preponderance. SCC was the predominant esophageal cancer, which is similar to the other studies in our country. SCC was found more common in females than males and vice versa for adenocarcinoma. Majority of all the cases belonged to 41-60 years of age group.

Keywords: Squamous Cell Carcinoma; Adenocarcinoma; Precancerous; Leiomyoma.

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INTRODUCTION

Cancer is one of the leading causes of high mortality worldwide. Epidemiology of esophageal cancer is one of the neglected disciplines, which is least studied, though being a very aggressive disease having poor prognosis. Worldwide, esophageal cancer is the 7th most common cancer and 6th leading cause of mortality¹. According to GLOB-

OCCAN 2018, Eastern Asia shows highest incidence (males=17.9, females=6.8) whereas, South East Asia region appears to have low incidence (males = 3.3, females = 0.7)¹. GLOBOCAN 2012 quoted that Pakistan shows esophageal cancer as 9th most common cancer in males and 5th most common cancer in females². According to Shaikat Khanum Memorial Cancer Hospital and Research Centre (SKMCHRC) (2017), it ranks 6th most common

cancer³. Previously, Karachi Cancer Registry (KCR) also observed high incidence of esophageal cancer in Quetta as compared to Karachi⁴.

Esophageal cancers are broadly divided into benign and malignant tumors. The commonest are squamous cell carcinoma (SCC) and adenocarcinoma (AC) which arise from epithelium. Esophageal squamous cell carcinoma occurs in upper one third or middle of the esophagus and esophageal adenocarcinoma usually arises from gastroesophageal junction or lower one third of the esophagus. The other rare malignant tumors are classified as endocrine and mesenchymal tumors, which include carcinoid tumor, lymphoma, melanoma and sarcoma⁵. Benign tumors comprise approximately only 1% of esophageal neoplasms amongst which leiomyoma is the most common and the other unusual tumors are adenomas, lipomas, neurofibromas, hemangiomas and lymphangiomias⁵.

Adenocarcinoma: Squamous cell carcinoma ratio is observed to be higher in countries with higher socioeconomic status. Literature shows that over last decade the incidence of adenocarcinoma exceeds than squamous cell carcinoma in Western world⁶⁻⁸. Although the incidence of squamous cell carcinoma is decreasing in Asia too, but it still appears to predominate in this region^{9,10}. Declining use of tobacco and alcohol consumption might have added to the decreasing trend of squamous cell carcinoma in Asian countries¹¹. However, low poverty and poor hygiene is still a major concern for esophageal squamous cell carcinoma burden in developing nations including Pakistan.

A very high rate of esophageal cancer is seen in the 'esophageal cancer belt', which has been labeled as 'African' and 'Asian' belts. The countries under these regions present with high risk towards esophageal squamous cell carcinoma. This high risk belt extends from Central Asia, Northern Iran and Eastern Africa^{12,13}. However, a changing trend is observed recently where incidence of esophageal adenocarcinoma is found to be highest in Iran among Central Asian countries¹⁴. Diet poor in fruits and vegetables, obesity, smoking and gastroesophageal reflux disease (GERD) are the major risk factors of esophageal adenocarcinoma (AC) whereas tobacco, alcohol, poor hygiene and consumption of hot beverages contribute towards esophageal squamous cell carcinoma (SCC).

Increasing incidence of gastroesophageal reflux disease (GERD) and obesity is known to promote development of Barrett's esophagus¹⁵. It is identified as preneoplastic condition of esophageal adenocarcinoma⁵. Most of the individuals with Barrett's esophagus are asymptomatic and remain undiagnosed. Western studies observed association of Barrett's esophagus with certain risk factors such as

old age, male gender, GERD, hiatus hernia, obesity, erosive esophagitis, metabolic syndrome, high consumption of fatty food and smoking. Approximately a 6-fold higher prevalence of Barrett's esophagus was observed in patients suffering from erosive esophagitis than with non-erosive esophagitis. In Asia, the common risk factors noted for Barrett's esophagus are hiatus hernia, smoking and male sex¹⁶. Whereas, studies from both, Western and Asian countries reported that *Helicobacter pylori* infection has a protective role against Barrett's esophagus¹⁶. Modifiable risk factors should be possibly controlled to prevent the disease.

Increasing prevalence of Barrett's esophagus in West is contributing towards increasing trend of adenocarcinoma¹⁶. Recently, a similar pattern is being noted in Asian countries, but it remains to be explored. Limited data are available regarding Barrett's esophagus from Asian countries which reported its prevalence with a range of 0.06% - 43%¹⁷⁻¹⁹. However, a review and meta-analysis conducted by Shiota et al., suggested that the prevalence of Barrett's esophagus was highest in South Central Asia then tracked by South Eastern, Western and East Asian countries¹⁶.

Only 1.9 publications per year is the average number of publications regarding esophageal cancer from Pakistan since last 40 years¹³. There are no national cancer registries in Pakistan, but few regional registries reported esophageal cancer as one of the commonest cancer in Pakistan. Moreover, up to our knowledge there are negligible data available related to Barrett's esophagus? Hence, it is extremely important to frequently present the regional status of this important pathology, which might contribute in future to establish a national scale cancer registry. In this study, we aim to know the spectrum of preneoplastic and neoplastic lesions of esophagus on the experiential status at Dow Diagnostic Research and Reference Laboratory (DDRRL) for 7 years (2009-2015).

METHODS

Descriptive study was conducted at Dow Diagnostic Research and Reference Laboratory (DDRRL) from January 2009 to December 2015. Approval was taken for ethical consideration by institutional review board of Dow University of Health Sciences (Ref no. IRB-459/DUHS/-14). All the registers for these 7 years were studied. Histologically diagnosed cases of preneoplastic and neoplastic lesions of esophagus entered in the registers during this period were taken into account. All the biopsy as well as resection specimens were included in the study. The inclusion criteria were all the biopsy proven preneoplastic and neoplastic lesions of esophagus with relevant information regarding age, gender, histopathology number, laboratory number, specimen and diagnosis, whereas, cases with inadequate

data were excluded. Data was entered and subjected to descriptive analysis using SPSS version^{20, 21}. Furthermore, association of diagnosis with age and gender was done using Chi square/Fishers exact test. p -value < 0.05 was considered as significant.

RESULTS

A total of 544 cases of premalignant and malignant

lesions from esophageal biopsies were received at Dow Diagnostic Research and Referral Laboratory during 2009-2015. Of these, 94 were diagnosed as premalignant and 450 as malignant lesions. Although there was no significant association seen between premalignant and malignant lesions with age, majority of the cases belonged to age group between 41-60 years.

Table 1: Distribution of premalignant lesions of esophagus according to gender and site of lesion.

Variables	Barrett's	Dysplasia	Adenoma	Total
Gender				
Male	43 (81.1%)	10 (18.8%)	0	53
Female	27 (65.8%)	13 (31.0%)	1 (2.4%)	41
Site of Lesion				
Esophagus other than gastroesophageal junction	63 (90%)	22 (95.6%)	1 (100%)	86
Gastroesophageal junction	7 (10%)	1 (4.3%)	0	8
Total	70	23	1	94

* p -value = 0.167

Chi-square (significant at p -value = < 0.05)

From the total of 94 premalignant cases, 70 (74.5%) were diagnosed as Barrett's esophagus, 23 (24.5%) as dysplasia and 1 (1.1%) as adenoma. No significant association was seen between premalignant lesions and gender of the patients. However, Barrett's showed a male preponderance and dysplasia was more common in females (Table 1). From the total of 450 malignant cases, 395 (87.7%) were squamous cell carcinoma (SCC), 54 (12%) were adenocarcinoma and a single case of

leiomyoma was diagnosed. Grade II squamous cell carcinoma was found to be most common lesion. Significant association was seen between malignant lesions and gender ($p=0.026$). Squamous cell carcinoma was more common in females as compared to males (female $n=216$ and male $n= 179$), whereas adenocarcinoma was found to be more frequent in males than in females (male $n= 33$ and female $n= 21$) (Table 2) (Figure 1).

Table 2: Distribution of malignant lesions of esophagus in both genders.

Gender	Grade I SCC	Grade II SCC	Grade III SCC	Grade I AC	Grade II AC	Grade III AC	Leiomyoma	Total
Male	29 (13.6%)	133 (62.7%)	17 (8.0%)	8 (3.7%)	19 (8.9%)	6 (2.8%)	0	212
Female	19 (7.9%)	178 (74.7%)	19 (7.9%)	8 (3.3%)	7 (2.9%)	6 (2.5%)	1 (0.4%)	238

* p -value = 0.026

Chi-square (significant at p -value = < 0.05)

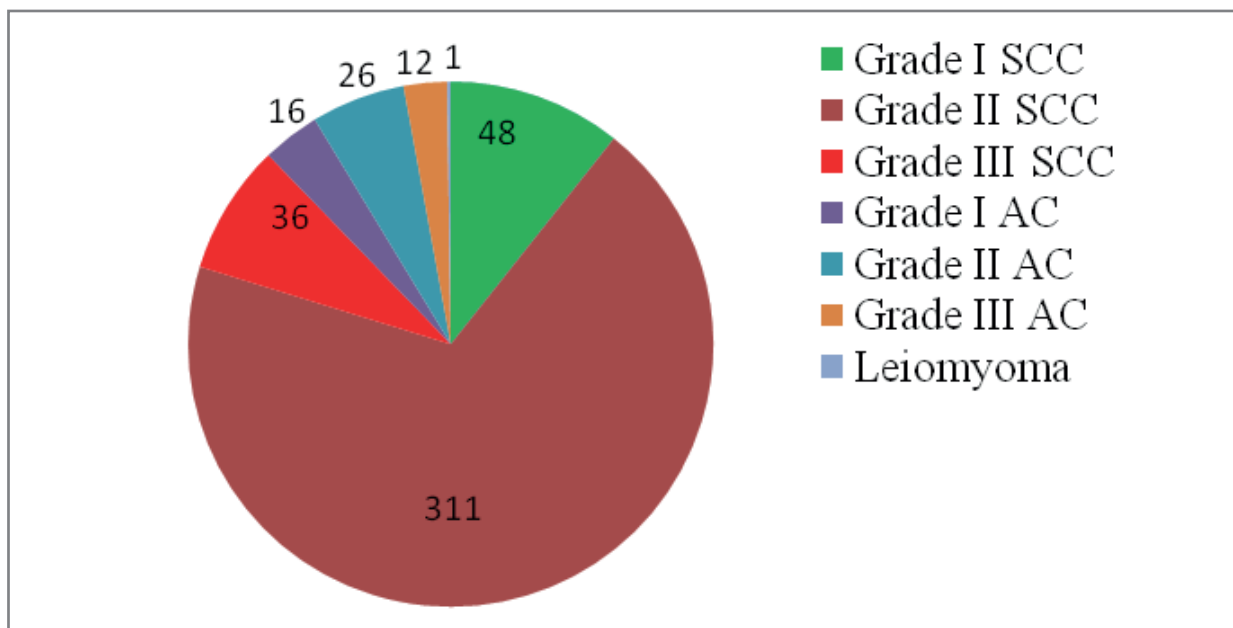


Figure 1: Frequency of esophageal malignancies.

*SCC = Squamous cell carcinoma

*AC = Adenocarcinoma

DISCUSSION

As the data pertaining Barrett's esophagus is not widely studied, the epidemiological data published for Barrett's esophagus can only be the approximation of its true prevalence²⁰. Risk factors of Barrett's esophagus including gastroesophageal reflux disease (GERD), obesity and smoking appears to be same in Western and Asian countries. Barrett's esophagus appears to have potential risk for esophageal adenocarcinoma in both Western and Asian countries. It was seen in 2% of adult population and in 5% of patients suffering from gastroesophageal reflux disease (GERD) in West but the prevalence and trend is still unclear in Asia²¹. However, the limited data available from Asian countries show higher rates of Barrett's esophagus in males with old age, which is similar to the data in West¹⁶. In accordance with other studies, we also found Barrett's esophagus predominantly in males than females and most common in the age group between 41 to 60 years of age.

A wide variation was observed in the demography as well as incidence of esophageal cancers. Over the last decade, western world showed higher rates of adenocarcinoma than squamous cell carcinoma^{6,7}. However, in Asia, squamous cell carcinoma remains the commonest cancer of esophagus⁹. Our study, showed similar pattern of esophageal cancer as rest of the Asian countries where squamous cell carcinoma cases were more than adenocarcinoma. Karachi Cancer Registry (KCR) reported that Quetta shows higher incidence of squamous cell carcinomas compared to Karachi, which might be owing to the habit of residing

people using kahwa, exposure to food rich in dietary amines and use of naswar as risk factors²².

Globally, decreasing trend of squamous cell carcinoma in men and increasing trend in females is being observed in some countries²³. Our results are also in accordance with global pattern of squamous cell carcinoma being more frequent in females than males and also agrees with regional studies done in past by Bhurgri et al., and Bukhari et al^{22,24}. Varying prevalence of tobacco and alcohol use might contribute to this drift. Our study is also in agreement with other studies where esophageal carcinoma is more common between 41- 60 years of age group^{22,24}.

We have attempted to highlight the frequency of this important malignancy in our region. One of the limitations is that it is a single center study, which cannot be the representative of the entire region. Further multicenter studies are needed to quote not only the frequency but also to look at the trend of notable risk factors associated with esophageal cancer. Moreover, esophageal cancer being a fatal disease it is highly imperative to know the incidence of premalignant lesions of esophagus, which can further help to restrict the disease progression. Similarly, screening, awareness and early diagnosis could together assist in achieving a better prognosis.

CONCLUSION

The diagnosed cases of Barrett's esophagus were more than dysplasia and showed male preponderance with age range between 41-60 years. Squa-

mous cell carcinoma was the predominant esophageal cancer in our series, which is similar to the other studies in our country. Squamous cell carcinoma was found more common in females than males and vice versa for adenocarcinoma. The age range for both subtypes was 41-60 years.

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CONFLICT OF INTEREST

There was no conflict of interest among the authors.

ETHICS APPROVAL

The study approval was sort from the Dow University Ethics Review Committee (Ref no. IRB-459/DUHS/-14).

PATIENTS CONSENT

The data was collected from the medical records.

AUTHOR'S CONTRIBUTION

TM, MAQ and AS conceived the idea of the research. AS and NK helped in the data collection. While, AS wrote the manuscript. MAQ and TM did the critical review. All the authors approved the manuscript.

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