

Frequency of different histopathological types of esophageal cancer patients at oncology department of a tertiary care hospital in Karachi

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ABSTRACT

Background: Around the globe, the carcinoma of the esophagus is the eight most prevalent cancer with an incidence of 456,000 cases per year and is the sixth cause of cancer mortality. There are two major histological subtypes of carcinoma of the esophagus, esophageal squamous cell carcinoma and adenocarcinoma. The aim of current study is to evaluate the frequency of different histopathological types of esophageal cancer in patients presenting at tertiary care hospital of Karachi.

Patients and methods: It was a cross-sectional study conducted at the Department of Clinical Oncology, Jinnah Postgraduate Medical Center, Karachi from March 2017 till March 2019. Two hundred and one histologically proven cases of esophageal cancer of in patients of either gender and between 15-80 years of age were included. Patients were interviewed and data regarding age, gender, education, marital status, employment status, addictions like cigarette or huqqa smoking, consumption of pan, betel nut, naswar, or gutka were recorded. Endoscopy and histology and computed tomography scan were performed. Stage, site, grade and type of tumor were noted. SPSS version 23 was used to analyze data. Mean and SD were calculated for quantitative variables. Frequency and percentage were calculated for qualitative variables. Chi-square test was used to assess the significance between age and gender with type of EC. A $p\text{-value} \leq 0.05$ was taken as significant.

Results: Mean age of the patients was 47.84. Majority of the patients had stage 2 of cancer (42.8%) and lower tumor site (62.2%). Squamous cell carcinoma was the most common histopathological type in 137 patients out 201 (68%). The age, gender, smoking, consumption of pan, grade, site and stage of tumor showed statistical significant difference when compared with esophageal squamous cell carcinoma and esophageal adenocarcinoma.

Conclusion: The burden of esophageal squamous cell carcinoma is dramatically increasing in Pakistani population and squamous cell carcinoma was the most common histopathological types.

Keywords:

Esophageal cancer, Etiology, Histopathological types, Frequency

INTRODUCTION

Around the globe, the carcinoma of the esophagus is the eight most prevalent cancer with an incidence of 456,000 cases per year and is the sixth cause of cancer mortality.¹⁻³ In 2019, with 16,080 deaths, approximately 17,650 new cases of esophagus carcinoma (EC) are estimated to be diagnosed in the US.⁴ The high incidence of EC as 800/100,000 population has been reported in some regions of Southern Russia, Northern Iran and Northern China.⁵ There are two major histological subtypes of EC, esophageal squamous cell carcinoma (ESCC) and adenocarcinoma (EA).⁶ ESCC is the most well-known type of EC in East Asia while

esophageal adenocarcinoma (EA) is leading Western nations.^{7,8} The epidemiology of ESCC and EA patients have various features which are highly associated with society, economy, lifestyle, culture, hereditary profile, dietary habits and environment.⁹ According to a local study in 2014, EC was reported as the 4th most frequent cancer in Pakistan with overall prevalence of 7%, was more common in women and squamous cell cancer had been the most common histological type.¹⁰ Another previous study from Karachi reported the elder age group (>50 years) at higher risk of ESCC.¹¹ In North West area of Pakistan, the ESCC is the predominant type of EC as compared to EA and ESCC is frequent among females whereas EA is common in males.¹² During recent years, the occurrence of esophagus is reportedly rising and there is lack of recent statistics available for Pakistani population. International data may not be much applicable in local population due to varied environmental factors, geographical area, dietary

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habits and genetic makeup. This study aims to observe the frequency of different histopathological types of esophageal cancer in patients presenting at tertiary care hospital of Karachi. This study would be helpful in reducing the burden of disease by taking initiative for early diagnosis and changing lifestyle.

PATIENTS AND METHODS

It was a cross-sectional study conducted at the Department of Clinical Oncology, Jinnah Postgraduate Medical Center, Karachi from March 2017 till March 2019 after approval by institutional ethics review board. The sample size of 201 was calculated by using OpenEpi online sample size calculator, based on frequency of adenocarcinoma as 32.7%, margin of error as 6.5% and 95% confidence level.¹² All histologically proven cases of EC of 15-80 years of age of either gender were included. Patients who had undergone chemotherapy, patients with infiltration of the tracheobronchial tree and patients who received salvage surgery were excluded.

Patients were interviewed and data regarding age, gender, education, marital status, employment status, addictions like smoking/huqqa, consumption of pan, betel nut, naswar, and gutka and symptoms at presentation. CT scans along with endoscopy and histological analysis was performed in all the patients and stage, site, grade and type of tumor was noted. The final stage was established according to the AJCC classification.¹ The esophagus is divided into three regions i.e. upper thoracic, midthoracic, and lower thoracic. The upper thoracic esophagus begins at the thoracic inlet and ends at the level of the tracheal bifurcation (approximately 24 cm from the incisors). The midthoracic esophagus is the proximal portion of the esophagus between the tracheal bifurcation and the esophagogastric junction, with a lower level that is approximately 32 cm from the incisors. The lower thoracic esophagus is the approximately 8 cm of distal esophagus and includes the intraabdominal portion and the esophagogastric junction (approximately 40 cm from the incisors).

Data was analyzed using SPSS version 23. Mean and SD were calculated for quantitative variables. Frequency and percentage were calculated for qualitative variables. Chi-square test was used to assess the significance between age and gender with type of EC. A p-value of ≤ 0.05 was taken as significant.

RESULTS

Total of 201 patients were evaluated. Mean age was 47.84 ± 14.20 years ranging from 15-80 years. Majority

of patients (53.7%) were of 50 years age or more. Females were predominant (57.7%) and most of them were married (69.2%). About 79 (39.3%) of the patients had education till intermediate and 61.2% were unemployed (n=123). Out of 201 cases, 74 patients were smokers, 43 were pan consumers and 21 were betel nut consumers. Rest of the findings are depicted in Table 1.

ESCC was the most common histopathological type seen in 137 patients (68%) followed by EA seen in rest 64 (32%) patients. Total 127 (63.2%) of tumors were moderately differentiated. Majority of the patients had stage 2 of cancer (42.8%) and lower tumor site (62.2%) (Table 2). The histological types were stratified with respect to socio-demographic and pathological features. The age, gender, smoking, consumption of pan, grade, site and stage of tumor showed statistical significant difference when compared with ESCC and EA ($p < 0.05$) (Table 3).

Table 1. Socio-demographic features

Characteristics	n	%
Age groups		
<50 years	93	46.3
≥50 years	108	53.7
Mean ± SD	47.84±14.20	
Gender		
Male	85	42.3
Female	116	57.7
Marital status		
Married	139	69.2
Unmarried	62	30.8
Education		
Illiterate	21	10.4
Matric	45	22.4
Intermediate	79	39.3
Graduate	52	25.9
Postgraduate	4	2
Employment status		
Unemployed	123	61.2
Employed	78	38.8
Addiction		
Smoking	103	51.2
Pan	43	21.4
Huqqa	13	6.5
Betel Nut	21	10.4
Gutka	17	8.5
Naswar	7	3.5

Table 2. Pathological characteristics

Characteristics	n	%
Tumor grade		
Well differentiated	36	17.9
Poorly differentiated	38	18.9
Moderately differentiated	127	63.2
Stage of cancer		
1	17	8.5
2	86	42.8
3	55	27.4
4	43	21.4
Site of tumor		
Upper	15	7.5
Middle	61	30.3
Lower	125	62.2

Table 3. Stratification of histological types of esophageal carcinoma with epidemiological and tumor variables

Variables	Squamous cell carcinoma	Adenocarcinoma	p-value
Age groups			
<50 years	50	43	0.001
≥50 years	87	21	
Gender			
Male	48	37	0.002
Female	89	27	
Education			
Illiterate	16	5	0.220
Matric	25	20	
Intermediate	59	20	
Graduate	34	18	
Postgraduate	3	1	
Marital status			
Married	99	40	0.163
Unmarried	38	24	
Employment status			
Unemployed	86	37	0.501
Employed	51	27	
Addiction			
Smoking	62	41	0.013
Pan	35	8	0.036
Huqqa	9	4	0.934
Betal nut	14	7	0.877
Gutka	11	6	0.749
Naswar	7	0	0.066
Grade of tumor			
Poorly differentiated	30	8	0.001
Moderately differentiated	93	34	
Well differentiated	14	22	
Site of tumor			
Upper	10	5	0.048
Middle	49	12	
Lower	78	47	
Stage			
1	12	5	0.024
2	51	35	
3	46	9	
4	28	15	

DISCUSSION

Worldwide, cancer of esophagus (EC) is the 8th most frequent and 6th most fatal malignancy.¹⁻³ The high incidence of EC has been reported in Eastern and Southern Africa, Asia and France.¹³ About more than seventy five percent of EC cases occurred in Asia, due to “Asian belt of EC”.¹⁴ In Pakistan EC is the 6th most frequent malignancy among women and 7th most frequent among men with SCC as dominant histological type.¹⁰ This study evaluated the frequency of different histological types of EC in patients presenting at tertiary care hospital of Karachi. Majority of the patients had SCC histopathological type (68%) whereas adenocarcinoma was reported in 32% of the EC patients. One previous local study reported hundred patients of EC and found ESCC more frequent than EA (84% vs 16%).¹⁵ In 2010 similar results were observed in another local study conducted with ESCC

in 84.26% and EA in 15.74%.¹⁶ In 2014, a study was conducted among Yemen populace which also showed the high prevalence of ESCC (50.2%) as compared to EA (48.6%).⁶ Similar findings was observed in the study from North West area of Pakistan; ESCC in 67.3% and EA in 32.7%.¹² An earlier study from Karachi reported ESCC in 97% and EA in 2.3% of the EC patients.¹⁰ Schlansky and coauthors found high prevalence of EA as compared ESCC (81% vs 17%).¹⁷ In Europe and North America, EA is most frequent type of EC, whereas in China ESCC is the most common histological subtype and contributes 90% of the EC cases.¹³ There is divergence in local and international studies when comparing the histological subtypes of EC, this might be due to screening approach, geographical, cultural and environmental variations. In the present study, the mean age of the EC patients was reported as 47.84 years ranging from 15-80 years and majority of the patients were greater than and equal to 50 years of age (53.7%). This range is similar to earlier local studies.^{12,16} The prevalence of ESCC also rise with increase in age and peaks have been seen in 7th decade of life (18). In the present study, ESCC was frequent among patients of age ≥50 years (53.7%) and significant statistical difference was observed in the types of EC with respect age ($p < 0.05$). The study conducted by Henry and colleagues found no statistical significant difference between ESCC and EA when compared to age and majority of the EC patients were of age more than 50 years.¹⁹ Ali and coauthors in their study found mean age of EA patients higher as compared to SCC patients.² The cancer of esophagus is four times more prevalent in males as compared to females in many countries.²¹ The ESCC and EA both subtypes of EC are dominant in males.²² EC male to female was reported as 8.5 in North America and 1.7 in sub-Saharan Africa.²³ Most of the white men are presented with EA in USA, whereas in Iran the incidence of EA is comparable among men and women.²⁴ One previous report found 63% of the women and 37% of the men had ESCC.¹² In the present research, majority of the patients with EC were females (57.7%) and most of those females had ESCC histological subtype. When gender was compared between ESCC and EA subtypes, significant statistical difference was found. However, contrary results were observed in the study by Henry and associates, the frequency of males was higher as compared to females with EC, and no statistically significant difference between ESCC and EA was found when compared to gender ($p > 0.05$), moreover, majority of the male EC patients had SCC subtype¹⁹ In another

research by Al-Samawi and group reported 109 female EC patients had ESCC histological type whereas 111 male EC patients had EA histological type and the relationship of gender and types of EC was statistically significant.⁶ Smoking, naswar (oral snuff), pan and betel nut consumption are the potential risk factors for EC.^{15,25,26} The cigarette and huqqa smoking and use of smokeless tobacco (areca nut, betel quid, gutkha, pan and naswar) are very common among Pakistani populace owing to its simple accessibility, low price, peer pressure and misconception that it relieves headache, toothache and stomach pain.²⁷ In the present study smoking and pan consumption showed significant relationship with types of EC and majority of them had ESCC histological subtype. In the study, author found positive relationship between risk of ESCC and smoking among males. Somewhat different results were observed in the research by Sun and colleagues who found no association between odds of EC and smokers.²⁸ One local study found majority of oral snuff (naswar) users had ESCC type of EC and only one patient had EA, this showed significant statistical difference between both types.¹⁵ Chitra and coworkers from India showed the odds of EC was 2.5 times more for tobacco consumers and 2.8 times more for both smokers and betel nut consumers and concluded them as the major risk factors for EC in Southern India.²⁹ Akhtar and associates found in a multivariate analysis that risk of ESCC was significantly higher among individuals who consumed areca nut (adjusted OR=3.7, $p<0.05$), betel quid with tobacco (adjusted OR=12.8, $p<0.05$), snuff dipping (adjusted OR=4.3, $p<0.05$) and smoking (adjusted OR=2.9, $p<0.05$).²⁵ In the present majority of the patients with ESCC subtype had moderately differentiated tumor ($n=93$), lower site ($n=78$) and stage 2 of cancer ($n=51$). The relationship was found statistically significant between type of EC and tumor site, grade and stage ($p<0.05$). Zeybek and coauthors in their study found that 57% of the patients had moderately differentiated tumor grade, 60.3% had lower site & 31% had stage IIIB of tumor.³⁰ In another study Yendamuri and friends found majority of the EC had EA subtype (60.6%) whereas 38.5% had ESCC subtype, among patients with EA most of them had grade III & IV (45%), stage IIb-IVa (35%) and lower site (80%) and the relationship was statistically significant.³¹ Ahmad and coauthors reported 65% of the patients had lower third location of tumor followed by middle third (13.5%) and upper third (4.1%).¹⁰

CONCLUSION

The burden of esophageal squamous cell carcinoma is dramatically increasing in Pakistani population and squamous cell carcinoma was the most common histopathological types.

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