

DEMOGRAPHIC VARIANCE OF PRIMARY ESOPHAGEAL CANCER, BASED ON LOCATION AND HISTOPATHOLOGY IN PUNJAB-PAKISTAN

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ABSTRACT

Objective: To determine the demographic variance in location and histopathological findings of esophageal carcinoma in Punjab-Pakistan.

Study Design: Observational cross sectional study.

Place and Duration of Study: This study was conducted in Multicentre Tertiary Care Hospitals of Combined Military Hospital/Pak Emirates Military Hospital/Army Medical College Rawalpindi, Combined Military Hospital Kharian and Combined Military Hospital Multan from 2010 to 2017.

Methodology: Patients with dysphagia and histopathology proven malignancy were included in this study. All patients had undergone flexible upper gastrointestinal endoscopy. Patients with lesions other than carcinoma, causing dysphagia and those with inconclusive histopathology were excluded from our study. The morphological site of the carcinoma were divided into upper, middle, lower and at gastro-esophageal junction. Histopathologically proven carcinoma of esophagus was reviewed for subtype of grading differentiation. Statistical analysis was done using IBM version SPSS 22.

Results: Out of 150 patients, 85 (57%) were males and 65 (43%) were females. Their age ranged between 30 to 85 ± 12.33. Among one hundred and fifty patients 107 (71.33%) had Squamous Cell Carcinoma, 42 (28%), Adenocarcinoma and metastasis in two cases. Frequency of distribution of esophageal carcinoma in North, East and South Districts of Punjab was 73%, 18% and 9% respectively. Esophageal Carcinoma in upper, middle, lower and Gastroesophageal junction was 22.5%, 35%, 15% and 27.5% respectively. Frequency of well differentiated SCC was 46 (30.6%) and well differentiated AC 31 (20.7%) respectively.

Conclusion: SCC with male preponderance is more common in North of Punjab. Lower 1/3rd and GE junction esophageal tumor are the commonest sites in all North, East and South Punjab. Histopathological differentiation revealed Well Differentiated SCC along with significant rise in Adenocarcinomas compared to previous national studies.

Keywords: Adenocarcinoma, Dysphagia, Esophageal Malignancy, Squamous cell carcinoma.

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INTRODUCTION

Esophageal is a stern malignancy in terms of aggressive nature and mortal outcome. Its 8th most common cancer and 6th leading cause of death world over with rapidly increasing incidence¹. There are two main hispathological types of esophageal carcinoma squamous cell and adenocarcinoma². Geographically histopathological types vary country to country. Couple of decades before SCC was the most common esophageal

malignancy in the USA, now there is steady rise in AC³. Esophageal cancer is 20 to 30 times higher in China than in USA. A cancer belt predominantly SCC extends from northeast China to Middle East⁴. Smoking, alcohol, red meat consumption, caustic injury, history of head and neck malignancy and radiotherapy are associated with SCC. Barret's Esophagus and obesity are related with AC⁵. Previously the studies carried out in Pakistan SCC was more common esophageal malignancy in northern area^{6,7} in current scenario adenocarcinoma was more prevalent in western population as compared Asians where SCC still dominates^{8,9}. In our observation, AC was being

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reported more. As survival depicts histology type and site of the esophageal malignancy¹⁰, this study was carried out to find out any change in the previous trend of esophageal malignancy. Our objective was to determine the variance in the site and histopathology of esophageal carcinoma demography in the province of Punjab (Pakistan).

METHODOLOGY

Study was conducted at Gastroendoscopy and Histopathological Departments of three main centres; AM College, CMH Kharian and CMH Multan. AM College receives histopathology samples from Pak Emirates Military Hospital (PEMH) and CMH Rawalpindi. PEMH and CMH Rawalpindi represent the North zone of the Punjab. CMH Kharian represents East of Punjab and CMH Multan is in South-Punjab. The study was conducted from Jan 2010 to Dec 2017, duly approved by the Ethical Committee of the Hospitals. Informed verbal consents were taken from all the patients. All patients presenting with dysphagia underwent upper GI Endoscopy in GI Department and Histopathological evaluation in Pathology Department of the respective Hospitals. Patients with lesions other than carcinoma causing dysphagia and those with inconclusive histopathology were excluded. Esophageal lesion locations were divided into four zones. Upper esophageal lesion was from lower end of cricoid cartilage i.e., 16 cm to 24 cm (point of tracheal bifurcation), mid esophagus lesions was from 25 cm to 32 cm (approximate at the level of inferior pulmonary vein), lower esophagus was from 32 to 40 cm. The entrance of esophagus into stomach was junctional zone lesion. This was a pilot study but the sample size was 150 based on the referral of patients for endoscopy with sample calculator, it gives 95% confidence interval. The demographic features i.e, sex, age, site of esophageal carcinoma and histopathological pattern were collected. Descriptive analysis of data, mean /standard deviation, mode, frequencies were analysed by the IBM SPSS version 22.

RESULTS

Out of 150 patients 85 (57%) were males and 65 (43%) were females. Their minimum age was

Table-I: Age wise distribution of esophageal carcinoma with their percentage.

Age of patients in years	No of patients with Percentage n(%)
30-50	34 (23)
51-60	68 (45)
61-70	30 (20)
71-85	18 (12)
Total	150 (100)

Table-II: Demography of esophageal carcinoma.

Gender and site of esophageal involvement	Squamous Cell CA n(%)	Adeno CA n(%)	Others
Female n=65	40 (62)	23 (35)	
Upper	20 (50)	-	2 (3%)
Middle	8 (20)	-	(Mets)
Lower	12 (30)	8 (34)	1%
GE Junction	-	15 (65)	
Male n=85	52 (61)	33 (39)	
Upper	15 (29)	-	Mets
Middle	30 (57.6)	9 (27)	-
Lower	7 (13.4)	4 (12)	
GE Junction	-	20 (60)	

Table-III: Histopathological type and grade of esophageal carcinoma.

Type	n=150
Well differentiated Adenocarcinoma (AC)	31 (20.7%)
Moderately differentiated AC	10 (6.7%)
Poorly differentiated AC	8 (5.3%)
Poorly differentiated signet ring cell AC	7 (4.7%)
Well differentiated Squamous Cell CA(SCC)	46 (30.6%)
Moderately differentiated SCC	31 (20.6%)
Poorly differentiated SCC	15 (10%)
Mets and other malignancies	2 (1.4%)

30 and maximum was 85 years with mean SD 59 ± 12.33 . Age distribution of the carcinoma is shown in table-I. Sixty eight (45%) patients were in range 51-60 years. AC was more common in men as shown in table-II. Distribution of SCC, AC and other malignancy infiltrating the esophagus leading to dysphagia is highlighted in fig-1. It is evident by the results that SCC is more common in North Punjab. There is minimal difference

between the two malignancies in East and South Punjab. Out of all these patients, 107 (71.33%) had squamous Cell Carcinoma (SCC), 42 (28%) had Adenocarcinoma (AC) and one case showed Metastasis. Demography of esophageal carcinoma according to gender and site of involvement is shown in table-II. SSC was present in 60% of cases among both males and females. In females, it was more common in upper one third of esophagus i.e. 50% while in males, it presented more in mid esophagus i.e., 57.6%. Adenocarcinoma was common in lower esophagus and at GE junction. It was representing 35% of esophageal carcinoma in both males and females' groups. Frequency of GE tumour was statistically equal in both genders. As mentioned in (table-III), when esophageal tumours graded histopathologically, it was found that most common tumours were Well differentiated SCC 46 (30.6%) followed by Moderately differentiated SCC 31 (20.6%) and well differentiated AC was 31 (20.7%) at GE junction.

DISCUSSION

Mathieu *et al* observed gender disparity in adenocarcinoma, being more in males, as females has partial protection due to oestrogen exposure during fertility period¹¹. Esophageal adenocarcinoma was more common in males in our study. In the same study maximum numbers of patients were between 50-54 years of age, so is the case in our study, with 45% from 50-60 years of age. SCC was more common in males compares with findings explained by Wheeler *et al*¹². Male to female ratio of 1.3: 1 is also comparable in both studies. SCC frequency in North, East and South Punjab was 82, 18 and 10% respectively. Increased frequency of SCC in North as compared to South Punjab may be due to its demographic location in close to Asian Esophageal Cancer belt secondary to genetic and ethnic factors^{4,13,14}. Frequency of AC in North, East and South Punjab was 28, 15, and 8% respectively. If we compare with a similar study that was done in 2005 by Badar *et al*¹⁵. There was no change in the prevalence of SCC in North Punjab but there is significant reduction of carcinoma in East/South Punjab. On the other hand in our study there

were more cases of AC in North Punjab as compared to East/South Punjab as shown in (fig-2) indicating rising trend of AC in North Punjab. Although SCC is still a common esophageal

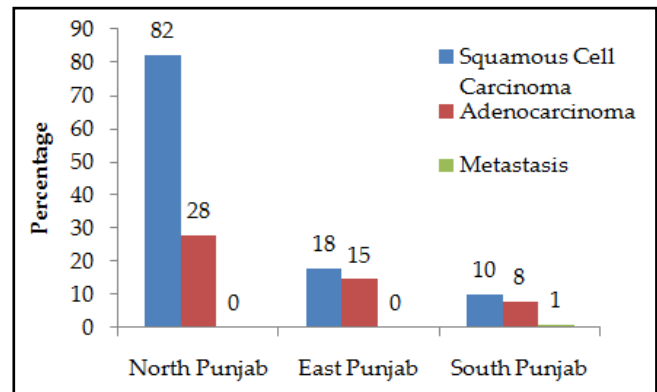


Figure-1: Types of carcinomas in different parts of Punjab.

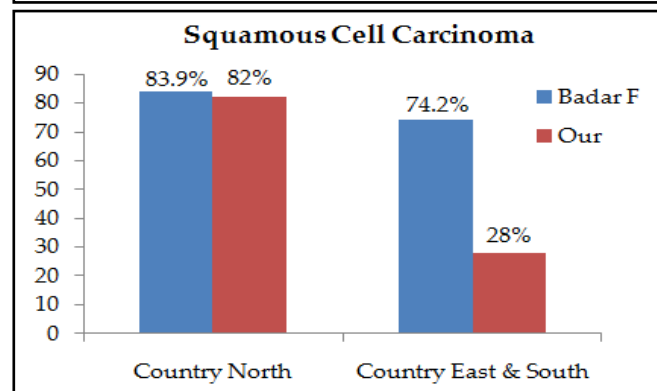
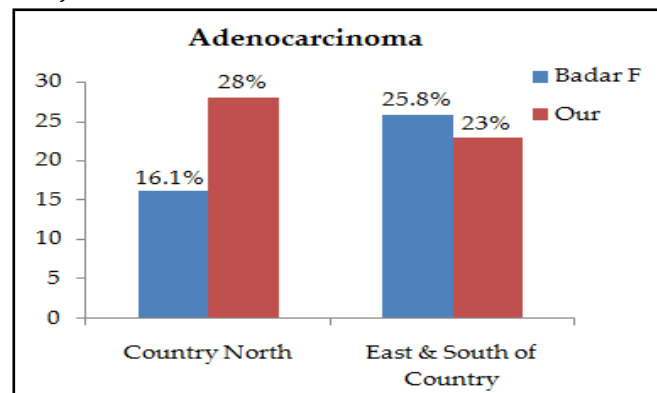


Figure-2: Histopathological trends of Esophageal Carcinoma.

malignancy but a number of studies show rising trend of AC in developed countries like USA, UK and Denmark^{16,17}. A few studies reported from China also showed rising incidence of AC¹⁸. In order to determine similar changing trends of AC

especially in North Punjab, further studies are required as previous studies showed raised prevalence of SCC. Esophageal carcinoma was found to be more common in lower 3rd of esophagus including GE junction followed by mid and upper 3rd of esophagus as compared to study done by Alema *et al*, where the frequency of incidence was midesophagus followed by lower and upper esophagus¹⁹. Well differentiated SCC followed by Moderately differentiated SCC was the sequence in our study as compared to that of Ali *et al* where moderately differentiated SCC was more common than well differentiated SCC⁶.

Well differentiated AC was common in our study in contrary to moderately differentiated adenocarcinoma reported by Hassan *et al*²⁰. Studies show that esophageal carcinoma which are well differentiated has good prognosis²¹⁻²². Most of the esophageal cancers in our study were well differentiated, which implies that early diagnosis and a good monitoring system for high risk individuals may have better outcome.

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CONCLUSION

SCC with male preponderance is more common in North Punjab. Lower 1/3rd and GE junction are the commonest sites in all North, East and South Punjab. Histopathological evaluation revealed Well Differentiated SCC/AC to be the most common type of esophageal cancers. However our study has limitation because of less number of patients. Moreover it could be a biased representation as it was depended upon the referral patients from other hospitals. A larger study from other centres should be conducted to get the meta-analysis of distribution of pattern of esophageal carcinoma in Pakistan.

CONFLICT OF INTEREST

There is no conflict of interest to be declared by any author.

REFERENCES

- Pennathur A, Gibson MK, Jobe BA, Luketich JD. Oesophageal carcinoma. *Lancet* 2013; 381(9864): 400-12.
- Cambell F, Bogomoletz WV, Williams GT. Tumours of esophagus/stomach. In: D Christopher, Fletcher M, eds. *Diagnostic Histopathology of Tumours* 2nd ed. Philadelphia: Churchill Livingstone; 2003. p.313-683.
- Thrift AP. The epidemic of esophageal carcinoma: Where are we now? *Cancer Epidemiol* 2016; 41(1): 88-95.
- Rahmani H, Sarabi Asiabar A, Niakan S, Hashemi SY, Faramarzi A, Manuchehri S, et al. Burden of esophageal cancer in Iran during 1995-2015: Review of findings from the Global Burden of Disease studies. *Med J Islam Repub Iran* 2018; 32(1): 55-60.
- Ward MH, Cross AJ, Abnet CC, Sinha R, Markin RS, Weisenburger DD. Heme iron from meat and risk of adenocarcinoma of the esophagus and stomach. *Eur J Cancer Prev* 2012; 21(2): 134-38.
- Ali A, Naseem M, Khan TM. Oesophageal Cancer In Northern Areas Of Pakistan. *J Ayub Med Coll Abbottabad* 2009; 21(2): 148-50.
- Roohullah, Khursheed MA, Shah MA, Khan Z, Haider SW, Burdy GM, et al. An alarming occurrence of Esophageal cancer in Balochistan. *Pak J Med Res* 2005; 44(2): 101-04.
- Zhang HZ, Jin GF, Shen HB. Epidemiological differences in esophageal cancer between asian and western populations. *Chin J Cancer* 2012; 31(6): 281-86.
- Domper Arnal MJ, Ferrández Arenas Á, Lanás Arbeloa Á. Esophageal cancer: Risk factors, screening and endoscopic treatment in Western and Eastern countries. *World J Gastroenterol* 2015; 21(26): 7933-43.
- Faivre J, Trama A, De Angelis R, Elferink M, Siesling S, Audisio R, et al. Incidence, prevalence and survival of patients with rare epithelial digestive cancers diagnosed in Europe in 1995-2002. *Eur J Cancer* 2012; 48: 1417-24.
- Mathieu LN, Norma F, Kanarek, Tsai HL, Charles M, Rudin, et al. Age and Sex Differences in the Incidence of Esophageal Adenocarcinoma: Results from the Surveillance, Epidemiology and End Results (SEER) Registry. *Dis Esophagus* 2014; 27(8): 757-63.
- Wheeler JB, Reed CE. Epidemiology of esophageal cancer. *Surg Clin North Am* 2012; 92(5): 1077-87.
- Arnold M, Soerjomataram I, Ferlay J, Forman D. Global incidence of oesophageal cancer by histological subtype in 2012. *Gut* 2015; 64(3): 381-87.
- Idrees R, Fatima S, Raheem JAA, AhmadZ. Cancer prevalence in Pakistan: meta-analysis of various published studies to determine variation in cancer figures resulting from marked population heterogeneity in different parts of the country. *World J Surg Oncol* 2018; 16(1): 129-39.
- Badar F, Anwar N, Mahmood S. Geographical Variation in the Epidemiology of Esophageal. Cancer in Pakistan. *APJ Cancer Prev* 2005; 6(2): 139-42.
- Pohl H, Welch HG. The role of overdiagnosis and reclassification in the marked increase of esophageal adenocarcinoma incidence. *Natl Cancer Inst* 2005; 97(2): 142-46.
- Abbas G, Krasna M. Overview of esophageal cancer. *Ann Cardiothorac Surg* 2017; 6(2): 131-136.
- Fan YJ, Song X, Li JL, Li XM, Liu B, Wang R, et al. Esophageal and gastric cardiacancers on 4238 Chinese patients residing in municipal and rural regions: a histopathological comparison during 24 year period. *World J Surg* 2008; 32(1): 1980-88.
- Alema ON, Iva B. Cancer of the esophagus: histopathological sub-types in northern Uganda. *Afr Health Sci* 2014; 14(1): 17-21.

20. Hassan A, Majeed Y, Bashir H, Nawaz MK. Correlation between standardized uptake value and histopathology of oesophageal carcinoma: a single center analysis. *J Cancer Allied Spec* 2015; 1(1): 1-3.
 21. Francisco T, Cintia M, Sakurai K, Flavio Roberto T, Rodrigo Hideki U, Aissaret RA, et al. Prognostic factors and survival analysis in esophageal carcinoma. *Arq Bras Cir Dig.* 2016 29(3): 138-141
 22. Griffiths EA, Pritchard SA, Mapstone NP, Welch IM. Emerging aspects of esophageal and gastro-oesophageal junction cancer: histopathology-updates for the surgical oncologist. *World J Surg Oncol* 2006; 4(1): 82-96.
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