Trends of oesophageal carcinoma and increasing number of young patients with oesophageal carcinoma in Southern Punjab, Pakistan

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ABSTRACT
Background: Oesophageal cancer (OC) is a cancer that develops in the gastrointestinal tract and is caused by a variety of circumstances. It has quite an uneven geographic distribution with male predominance and squamous cell carcinoma being most frequent type of oesophageal carcinoma in developing countries. As Pakistan lacks any proper cancer registry this study was needed to have an idea of the OC statistics in South Punjab region. Objective was to determine the prevalence of OC in the general population and in young people of South Punjab, Pakistan
Methods: Retrospective cross-sectional study. Two hundred and twenty-three patients who presented to Multitest lab from 2014 to 2018 were included in the study.
Results: The 186 patients were positive for OC. Sixty patients were below 40 years of age. Male to female ratio was 1.24:1. Most frequent symptom was dysphagia and squamous cell carcinoma was histological subtype.
Conclusions: In our study based on South Punjab region, oesophageal carcinoma has become a common condition and is more prevalent in males. It commonly involves upper oesophagus and squamous cell carcinoma is the most frequent type. It can also be concluded that it is in increasing in young population of South Punjab.

Keyword: Oesophageal carcinoma, Young patients, Cancer in South Punjab

INTRODUCTION
Oesophageal cancer (OC) is a highly malignant and aggressive tumour commonly effecting the elderly which is complicated by late diagnosis, low cure rate that is less than 10%.¹ It has high metastasis rate with almost 50% cases having metastasis at the time of diagnosis. According to World statistics, it is the eighth most common cancer and the sixth most common cause of cancer related. Its frequency and prevalence experience global variability, most frequent in Africa, Afghanistan, Iran and China whereas in western countries its incidence is low.²⁷ In USA data obtained from National Centre for health statistics estimated that 16,980 new OC cases would be diagnosed in 2015 and in this year publication the estimation has reached to 18,440 new cases.⁸⁹

Median age of presentation of oesophageal malignancy is 55 years. It is more frequent in males with male to female ratio 1.2:1. Most frequent area of oesophagus involved is upper part followed by middle part and lower part.²¹⁰

A number of risk factors are involved as a causative factor in OC. Tobacco smoking is a strongly associated risk factor and one study has shown that more than 78% patients have history of tobacco use. Tobacco smoking increases the risk of squamous cell carcinoma around-10 folds and adenocarcinoma two folds. Other risk factors implicated are alcohol abuse, helicobacter pylori infection and dietary habits. Family history and genetics are also involved and confer poor prognosis. Genetic changes involved include over expression of oncopGenes and suppression of tumour suppressor genes. Some of these
genes are cyclin-D, Rb, P53 etc. Pakistan has poor socioeconomic status, use of naswar specially in Pukhtoons of Baluchistan that has attributed towards high rates of squamous cell oesophageal carcinoma in this population setting.\textsuperscript{2,7,11,12}

In Pakistan OC is very common in some areas and experience regional variability. It is more common in Northwest frontier province (NWFP). Though we do not have cancer registry in Pakistan, studies conducted in Karachi and Lahore have shown that OC is the sixth most common malignancy in Pakistan. It is on number fifth among most invasive malignancy in a study conducted in Shaukat Khanum memorial hospital and research centre (SKMH and RC) in Lahore.\textsuperscript{2,3,6,13-15}

It is a rare malignancy in young people and also has different histological type as compared to older people. Young patients mostly suffer from oesophageal adenocarcinoma whereas majority of older patients are diagnosed with squamous cell carcinoma. OC usually presents late in young patients and have a bad prognosis. Despite giving young patients adjuvant therapy there is no significant difference observed in the outcomes between them and older patients.\textsuperscript{7,16-19} Due to the lack of a similar study in this area, this study was done to determine the frequency of OC in Southern Punjab and its prevalence among young people. We also wanted to know male to female ratio in population and to confirm whether it follows ratios described in literature or not.

**METHODS**

It was a retrospective cross-sectional descriptive study conducted at Multitest laboratory and research centre in southern Punjab. Cases were selected by reviewing the medical record of seven years from January 2014 to December 2020. Record of all the patients whose oesophageal biopsy was done and sent to the Multitest laboratory for histopathological examination and diagnosis, were evaluated and included in study. Patients of both gender and all ages were included in the study.

The tumour was classified according to the international classification of disease for oncology with revision, clinical modification ICD-9-CM. As it was a laboratory-based study so stage of the disease was not included nor author collected data for it.

During this period a total of 223 patient’s oesophageal biopsies were submitted for diagnosis and evaluation. Data regarding gender, age, presenting complaints, type of the oesophageal malignancy and location of the tumour was collected by reviewing the record. Data regarding risk factor could not be collected due to retrospective nature of study.

Data was collected, entered and analysed by using SPSS 20. Frequencies and percentages were calculated by using descriptive statistics. \( P<0.05 \) was considered significant. Study was approved by institutional ethical committee.

**RESULTS**

A number of 223 oesophageal biopsies were examined during seven years starting from January 2014 till December 2020. Oesophageal carcinoma was found in 186 biopsies. Male to female ratio was 1.24:1 (Figure 1).

**Figure 1: Gender distribution of study population.**

Of the total 186 OC diagnosed cases 126 (67.7\%) were above 40 years of age as shown in Figure 2.

**Figure 2: Frequency of cases among age groups.**

In 84 out of 186 (45.1\%) cases, the tumour was located in upper third of the oesophagus. Rest of the locations and their percentages are depicted in the Figure 3.

**Figure 3: Location of the oesophageal involvement by tumour.**
Most common tumour was found to be squamous cell carcinoma followed by adenocarcinoma (Table 1).

Table 1: Types of oesophageal carcinoma.

| Type of OC               | No. of cases | Percentage (%) |
|-------------------------|--------------|----------------|
| Squamous cell carcinoma | 159          | 85.4           |
| Adenocarcinoma          | 15           | 8.06           |
| Adenosquamous carcinoma | 03           | 1.61           |
| Undifferentiated        | 04           | 2.15           |
| Intraepithelial carcinoma| 02           | 1.07           |
| Leiomysarcoma            | 01           | 0.53           |
| Signet ring cell carcinoma | 01         | 0.53           |
| Spindle cell carcinoma  | 01           | 0.53           |

Dysphagia was the commonest presenting complaint as expected, its number and percentages with other symptoms are shown in the Table 2.

Table 2: Presenting complaint of the patients.

| Presenting complaint | No. of cases | Percentage (%) |
|----------------------|--------------|----------------|
| Dysphagia            | 170          | 91             |
| Pain chest and throat| 06           | 3.22           |
| Dry cough            | 01           | 0.53           |
| No history           | 09           | 4.83           |

One thing which was observed in our study was that most of the cases lack proper history, which is very important and helpful for the histopathologist to proceed in the case. Other thing which was alarming, was high number of young patients. It was considered to be the malignancy of the old age but 60 out of 186 (32.25%) diagnosed cases in our study were below 40 years of age. Not only that the number of young patients suffering from OC has increased with the passage of time as shown in Figure 4.

Figure 4: Increasing number of young patients with time.

DISCUSSION

OC observes geographic variability in incidence and prevalence with huge burden in south East Asia. United States and the western countries are considered low risk areas but despite that it was estimated that 15,070 people died from OC in 2012 in US which increased to 15590 deaths in 2015 and further increasing to16,170 deaths in 2020. Cancer belt is described in the literature, which encompass Iran to Turkmenistan, North Afghanistan, Uzbekistan, Kazakhstan, Northern China and Mongolia. Specificity of this belt region is that, it has very high disease burden and is almost in the state of an epidemic. The risk factors and the reasons for increased incidences in this belt have not been identified yet. Some areas of Pakistan have also high disease burden especially areas bordering Afghanistan. Studies conducted in Pakistan have shown that OC is prevalent in NWFP and Punjab. This may be due to factors like eating habits, use of tobacco products, smoking, alcohol intake, chewing pan, hot beverages, GERD and many more. These risk factors are described in the literature.

The most frequent type of oesophageal malignancy in our study was squamous cell carcinoma followed by adenocarcinoma. Our findings are in conformity with studies conducted previously. The most frequent type of carcinoma oesophagus in developing countries is squamous cell and in developed countries it is adenocarcinoma. These may be due to change in lifestyle, eating and drinking habits. As Pakistan comes under developing countries, so we also have same findings as other developing countries.

OC is more frequent in the males with male to female ratio of 1.2:1 as described in various studies. The value varies in developing and developed countries. Hafeez et al has reported male to female ratio of 1.3:1. Our study has also shown that males suffer from OC more as compared to females and ratio found in our study was 1.24:1. The most frequent presenting complaint in oesophageal carcinoma is dysphagia or inability to eat. Same finding was observed in this study where 91% patients complained of dysphagia.

One of the important observations in our study was high number of young people though OC is considered to be the malignancy of old age. In low endemic areas like U.S., Zeng et al has reported that 8.37% diagnosed EC cases were below 40. On the other hand, in high endemic areas like Kenya 38% cases were below 40. In our study population 32.25% cases were below the age of 40 years. Dawsey et al also reported that in Kenya from 1989 to 1998 11% of EC were under 40 years old which increased to 38% during 1999 to 2007. Our study has also showed that the numbers of young patients with EC are increasing with the passage of time. This is an alarming finding, though it may be biased because it’s a single centre study and is a private institution. But this finding, is in need of further exploration as oesophageal carcinoma has a poor
prognosis and usually presents late with most of the patients having metastasis at the time of diagnosis. So, if it is rising in the young people in this area, factors responsible for this need to be addressed. Malignancy at a young age means that it will affect many people related to him, so family member will have psychological effects. Previous studies conducted have shown that oesophageal carcinoma in young is of adenocarcinoma, advanced at time of diagnosis, has lower oesophageal involvement, male predominance, need more aggressive treatment as compared to older population. To confirm this finding population-based studies should be conducted.  

The oesophageal carcinoma mostly affects the upper third of the oesophagus. Studies conducted locally and internationally confirm this finding. In this study it was the same finding.

In our study we did not include risk factors. Another limitation of our study was that it was based in a private institution where only referred cases came so its finding cannot be generalized. More population-based studies are needed to evaluate risk factors and prevalence and incidence of the disease in population. This is important as we lack local statistics of cancer, by doing so recommendation can be made to modify risk factors in an attempt to lower the incidence of the disease.

CONCLUSION

The findings in this study reflect the almost endemic state of EC in South Punjab. The study demonstrated that EC is more common in males and mostly involve upper oesophagus with squamous cell carcinoma being the most frequent type. It can also be concluded that its incidence is increasing in young population which needs to be addressed.

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