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EPIDEMIOLOGICAL FEATURES OF ESOPHAGEAL CARCINOMA IN PAKISTAN

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Abstract

Background: *Esophageal cancer is often fatal disease with one of the most common type of cancers worldwide, having two main histopathological variants, esophageal squamous cell carcinoma and esophageal adenocarcinoma. The main risk factors for cancer of esophagus include smoking, poor diet, hot beverages, obesity, gastroesophageal reflux disease (GERD) and Barret's esophagus. The prognosis of this tumor also varies across the region and populations. One of the most common symptoms include dysphagia, vomiting and weight loss. Diagnostic procedures for esophageal cancer include endoscopy, endoscopic ultrasound, computed tomography (CT scan).*

Objective*: The main objective of this study was to compile the different research outputs to emphasize the recent epidemiological aspects of both histo-pathological subtypes of esophageal cancer and to highlight the distinct characteristics of esophageal carcinoma occurring in Pakistan.*

Design of the study*: This study is designed to cover the trends of occurrence for esophageal cancer using past data available.*

Conclusion: *In Pakistan the research on Health-care department is an ignored discipline. Particularly, data regarding the epidemiological studies of esophageal cancer in Pakistan is in scanty. Therefore, data-based studies are needed to measure the exact burden of esophageal cancer in Pakistan. This study will help to implement surveillance programs and to aware our nation towards the incidence, risk factors related to life style for causing cancer of esophagus in Pakistan.*

Keywords: *Computed tomography (CT scan), Esophageal cancer (ESC), Esophageal adenocarcinoma (EAC), Esophageal squamous cell carcinoma (ESCC), Gastroesophageal reflux disease (GERD), Magnetic resonance imaging (MRI)*

INTRODUCTION

Esophageal carcinoma (ESC) is a serious lethal death threat these days. It stands at eight most common found cancers globally and sixth most prevalent death causing tumor. Esophageal cancer mostly occurs in un-industrialized nations, showing the highest frequency in Africa and Asia (1, 2). Cancer of esophagus is associated with a poor prognosis and in spite of advancement in diagnosis and treatment, the inclusive survival rate of five years for esophageal cancer suffering patients is 15-20% in the US and worldwide (3). Primarily ESC consists of two main two histopathological variants referred to as esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC). Approximately 95% malignant cancers of esophagus constitute of the subtypes, which are not deliberated here, including melanomas, lymphomas, sarcomas and carcinoid tumors (4, 5). The esophageal cancer incidence varies in populations and across the regions. In 2018, about 570,000 individuals were estimated to have been detected with esophageal carcinoma, which aggregated 3.2% of the total diagnosed tumor (6). Another retrospective study was conducted in the northern area of Pakistan in 2009 to assess the gender and age frequency for esophageal cancer. Majority of the patients were diagnosed with esophageal squamous cell carcinoma (ESCC), while mean age of the patients was 53 years in women (W) and 42 years in men (M) giving 3:1 ratio for both genders. Approximately all patients showed clinical symptoms of dysphagia in the advanced stage of disease in this study (7).

The main focus of the present study was to compile the different research outputs of esophageal cancer to develop data from Pakistan and to investigate the research publications categories of esophageal

cancer published from Pakistan. This study will provide significant information of this prevalent cancer in Pakistan which can facilitate the method for designing epidemiological, screening, diagnostic, prognostic and therapeutic strategies for suffering patients from this cancer.

HISTOPATHOLOGICAL VARIENTS OF ESC

ESOPHAGEAL SQUAMOUS CELL CARCINOMA (ESCC)

Esophageal squamous cell cancer accounts for 90% of cases globally and is the most prevalent variant of esophageal carcinoma (ESC) outside of the US (8). Majority of the cases occur in Central Asia, China, South and East Africa (9). The incidence of ESCC is almost 3/100,000 per person every year in the US (10). The prevalence peaks in age from 60-70 years and shows consistency among gender i.e., higher in black males (11). Some common risk factors for ESCC include alcohol, smoking and achalasia (12, 13).

ESOPHAGEAL ADENOCARCINOMA (EAC)

In Europe and North America EAC is the major type of esophageal carcinoma (8). A study conducted in 2013 from the NCI (National Cancer Institute), reported most incidence of cases occurs in people more than the age of 50 years while the prevalence among 65 years and/or older is 16.3 per 100,000 per person every year. This study also reported high risk in male as compared to females and white as more prone to EAC than blacks (14). The most frequent etiological factors for EAC include obesity, gastroesophageal reflux disease (GERD) and smoking (15-17). According to another study a much known precursor for EAC is Barrett esophagus with a low rate of alteration (7, 18).

EPIDEMIOLOGICAL FEATURE OF ESC

Globally total tumor burden of esophageal cancer comprises 90% of esophageal squamous cell carcinoma (19). According to research almost 80% of the cases arise from the evolving countries (20). Some countries of Asia and Africa are identified as high-risk areas (referred to as “Asian belt” and “African belt”). The maximum incidence of esophageal carcinoma has been reported in north-eastern Iran, China, South Africa and Southeast of the USA (21). According to the recent United States distribution of esophageal carcinoma, two histological variants esophageal adenocarcinoma (EAC) accounts 31% and esophageal squamous cell carcinoma (ESCC) includes 64% of total tumor burden of esophagus, whereas 5% are transitional, basal, and other unspecified cancers (22). Esophageal cancer has a high mortality rate because it is not often diagnosed before it has progressed or metastasized to other regions of the body. In the 2020 yearly report of the US reported that only 18% of esophageal carcinomas were found confined to the prime site at the time of diagnosis (22). Whereas, 40% of cases were demonstrated as metastasized to distant organs which indicates even worse prognosis of esophageal cancer (22). Globally adenocarcinoma is predominant in highly developed regions including Europe and North America. Both ESCC and EAC have different geographical trends, patterns, etiologies and risk factors but the incidence of ESCC is higher to some extent in elderly women (19). Balochistan, the province of Pakistan also reported the highest figure of cases of esophageal cancer (7, 23). Previous research data from the Cancer Registry of Karachi also showed cancer of esophagus as one of the most prevalent cancers in Karachi (24, 25). A recent study conducted in 2021 in Pakistan reported a majority of the patients suffering from ESCC while the rest were diagnosed with EAC (26). Similarly, in some other regions of Pakistan, the frequency of esophageal cancer is even higher, including the district of Balochistan ‘Quetta’ reported high prevalence of esophageal cancer in both male and females (27,28). Another report in Balochistan from a cancer center reported cancer of esophagus as the third most frequently diagnosed tumor (29, 30).

RISK FACTORS OR CAUSES OF ESC

Cancer of esophagus shows strong relevance in use of tobacco likewise a study conducted, reported 78% of tobacco users among all cases. Betel nut and naswar usage is also considered as a risk factor. A common fact about smoking is that it raises the risk of developing EAC by 2-folds and ESCC by 5-10 folds. Majority of the risk factors for cancer of esophagus includes obesity, cigarette smoking, Barrett's esophagus and chronic gastroesophageal reflux disease (GERD) (31-33).

Some etiological factors including GERD, Barrett's esophagus and obesity are might be attributed due to rise in incidence of adenocarcinoma of esophagus in West populations (United States, United Kingdom, France and Australia). A study reported around 1-3% of patients will develop EAC which are already suffering with Barrett's Esophagus and 3% will develop dysplasia of high grade, and 15% will develop low grade dysplasia (34, 35). In contrast consumption of alcohol, smoking, hot beverages usage, an excessive salty diet and/or diet lacking salt, betel nut chewing, low socioeconomic lifestyles, a chronic cancer history of family and viral agents (e.g., human papillomavirus) are common etiological factors for ESCC in the 'Asian cancer belt' (31, 36). Usage of impure water and low socioeconomic lifestyle are noticeable risk factors in some regions (Saudi Arabia and China). Whereas, low socioeconomic status and lifestyle is reported as a predominant factor for causing esophageal cancer in Iran (37, 38).

In Pakistan registration on national scale for cancer does not exist (39), however Cancer Registry of Punjab published some reports indicating cancer of esophagus as the fourth most prevalent cancer in adults in 2013 (40) and risk factors affecting populations of Bangladesh, India, Afghanistan and Pakistan are, excessive consumption of alcohol, hot beverages, smoking, lack of nutrition from vegetables and fruits, betel nut chewing and vitamins that are fat soluble, are also one of the prominent factors (Saudi Arabia) (41, 42).

AGE

Primarily cancer of esophagus evolves in the mid-high aged people ranging from 40 to 60 years (43). In Asia the mean age of patients diagnosed with esophageal cancer is in the range of 51 to 60 years (44, 45). Globally the ASR (age standardized range) for patients from Asia suffering with esophageal cancer is 7.7/100000 cases with the maximum 12.5 to 12.7/100000 ASR reports in Bangladesh and China. Whereas, the ASR is reported as 4.1/100000 cases in Pakistan (21, 46). A study reported a standard age of patients suffering with ESC in females were 53.3-54.3 years while males were 53.3-55.8 years in Karachi (25).

GENDER

A gender affinity is seen more towards male than female worldwide in contrast to other malignancies, showing 3-fold higher risk for men. Moreover, a report from Globocan 2012 reported esophageal cancer in Pakistan as the ninth most prevalent cancer in men and fifth most frequent cancer in women (47). Furthermore, cancer registry based on pathology (the Dow University of Health Sciences, Karachi) also analyzed registering of patients during the year of 2010-2014 indicating esophageal cancer as the third most prevalent cancer in females while fifth most frequent in male. Though national level registration of a cancer incidence is absent in Pakistan on account of which a very large frequency of esophageal cancer is still not reported and given data advocate a high burden in country with the cancer of esophagus. Another study conducted in 2010 in Karachi reported a 60% of esophageal cancer incidence in males (48). In contrast a study conducted in Pakistan reported a female ratio higher than male mainly diagnosed with ESCC (26).

ETHNICITY

Ethnicity is one of the factors that can indicate origin of disease and especially genetic and environmental factors can easily be known by this. Numerous tumors have been simplified by racial variances and several studies constructed on major differences in frequency rates, features of disease on patient's survival through ethnicity. The capital of Balochistan as well as the largest city (Quetta) consists of several ethnicities including Pathan (Pashtun), Punjabi, Hazara, Baloch and other ethnic groups. In Balochistan only one care center is present that treats cancer modalities named as CENAR (Centre for Nuclear Medicine and Radiotherapy) (30). The data from Quetta based on cancer genetics, racial differences and environmental, varies from Northwest province (27).

CLINICAL PRESENTATION OR SYMPTOMS FOR ECS

Usually, the ESC in early stages is often asymptomatic. Though patients suffering with advanced stage of ESC complains about progressive dysphagia (difficulty with swallowing solids first than followed by liquids as the disease progresses), odynophagia (painful swallowing, often noticed initially with dry

foods), accidental weight loss (10% or more in the preceding 3-6 months), chest pain, vomiting, heartburn or indications of blood less. The most common clinical symptoms are dysphagia alone or with sudden weight loss and vomiting in patients suffering from esophageal cancer found in Pakistan, Bangladesh, Afghanistan, Iran, India and China, while Saudi Arabia reported weight loss as the second most prevalent manifestation. According to other reports some further uncommon signs present only in 10% of patients at the time of analysis include hematemesis, cervical adenopathy, hoarseness along with dysphagia is most prevalently reported (in India, Iran, Afghanistan, China, Pakistan and Bangladesh) followed by weight loss frequently reported in Saudi Arabia. Whereas, other symptoms are retrosternal burning pain, odynophagia, hoarseness, anemia, blood in the vomit (23, 49, 50). Patients suffering from ESC mainly reported dysphagia for solid while in advanced stages of disease; dysphagia is reported for both solid and liquid.

DIAGNOSTIC MEASURES AND TREATMENT FOR ESC

For the initial diagnostic estimation, the patients are prescribed to undergo upper endoscopy (51, 52). Other signs warranting endoscopy include consistent upper abdominal indications in patients >45 years and medical therapy (53). For further evaluation of esophageal cancer following modalities are used magnetic resonance imaging (MRI), computed tomography (CT scan), chromoendoscopy, fiberoptic endoscopy, endoscopic ultrasound, endoscopy with Iodine, positron emission tomography, narrow-band imaging, high-resolution magnification endoscopy (42, 49, 50). Afterwards, when diagnosis is confirmed with endoscopic biopsies, some additional laboratory tests are performed which may be helpful in estimating the stage of cancer. The complete blood count (CBC) reports are required to detect the anemia which will influence the treatment that patient requires chemotherapy (52).

The treatment of esophageal cancer for both adenocarcinoma and squamous cell carcinoma depends mainly on the stage of tumor at the time of diagnosis. All the processes including chemotherapy, chemoradiotherapy and curative surgical therapy have shown to raise survival rate and progress the quality of life related to health of patients (54, 55).

CONCLUSION

Nevertheless, the scientific data to define the status of esophageal cancer is not present in Pakistan. Research related to health-care is a neglected discipline in Pakistan and cancer of esophagus ranking high among other cancers in both male and female of Pakistan is no exception. Hence it is extremely necessary to prioritize the research on esophageal cancer in Pakistani health care program. Specifically, there is not any availability of data regarding the overall incidence and risk factors affecting patients of esophageal cancer possessing different age, gender, geographic region, dietary habits, smoking, ethnicity, types and stages in Balochistan.

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