Socio-demographic risk factors of esophageal carcinoma: A case control study in a tertiary care hospital, Kabul Afghanistan

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Abstract

Introduction

Esophageal cancer (EC) is 7th most common cancer in world in term of incidence and 6th common cancer in term of mortality. In Afghanistan, EC is the most common cancer in males. The socio-demographic status has been known as associated factor for EC. We carried out this study to determine the associated risk factors with EC in a tertiary hospital in Kabul, Afghanistan.

Methodology

Unmatched case control study of socio-demographic risk factors and EC was conducted at French Medical Institute for Mother and Children (FMIC). We enrolled and analyzed 132 EC cases and 132 normal controls to find out the associated risk factors for EC

Result

In current study Esophageal Squamous Cell Carcinoma (ESCC) was the predominant EC type (75.8%). The mean age of the case group is 59.48 ± 9.9 years and in control group is 48.05 ± 11.02, (OR: 1.070, 95% CI, p-value <0.001). Majority of the cases group are male (69.6%) (OR: 3.538, 95% CI, p-value 0.022). Participants living in rural areas have the 25-times higher risk of EC than living in urban regions. Un-educated and lower education are highly associated with the risk of EC (OR: 11.21, 95% CI, p-value: <0.001) as well as, having low Socioeconomic status was also highly associated with the increased risk of EC (OR: 14.08, 95% CI, p-value: <0.001). Having family history in first degree family highly associated with the risk of EC (OR: 4.581, 95% CI, p-value <0.001). Although, the majority of the EC patients were unemployed (93.3%) of which 75% were farmer comparing to control which comprises 55.3% of unemployed statistically in multivariate analysis it showed no significant association with EC. In addition, living area according country zones and provinces, weight and height and ethnicity showed no significant association with EC.

Conclusion

The study concluded that EC is common cancer in older age groups and, predominance in males. In addition, living in rural areas, being un-educated or having lower education, belonging to low socioeconomic status, and having positive family history in first degree relatives are associated with high risk of EC in our study.

Introduction

Non-communicable diseases are expanding all around quickly, and are now responsible for the majority of global deaths. The vast majority of non-communicable diseases belong to cancer (1). Esophageal cancer (EC) is the 7th most common cancer in term of incidence and 6th common cancer in term of cancer death worldwide. In 2018 worldwide, 572,000 new cases were diagnosed and as overall 509,000

deaths were estimated in 2018 (2). In Afghanistan, no nationwide cancer study has been published to see the incidence and mortality rate of EC, only a single health center study estimated that EC is the first common cancer in male and second common cancer in female (3). EC arises from surface lining cells of the esophageal mucosa. There are two main histologic patterns of EC: Esophageal Squamous Cell Carcinoma (ESCC) and Esophageal Adenocarcinoma (EAC) (4). International Agency for Research on Cancer (IARC) estimated that ESCC comprises 88% of all EC and the remaining 12% are EAC (5). Esophageal cancer is more prevalent in developing and underdeveloped countries (6).

Many risk factors are studied to be possibly related with the risk of EC including gender, race, obesity, smoking, alcohol consumption, hot tea, nutritional deficit, genetic susceptibility and gastroesophageal reflux disease (7). Low socioeconomic status (SES) which has been indicated by income, education, occupation and other variables are suggested to increase the risk of both types of EC (8). SES has been known as associated risk factors for EC in developing countries which has compressed social status. Interestingly, in developed countries in studies with wide range of educational histories and income range, SES is still associated with the risk of EC (8). As the cancer higher incidence belt is from northern Africa, to middle east and central Asia including Afghanistan to parts of China (9). Afghanistan which is a limited resources country, still no study has been published to evaluate the associated risk factors with EC. Current study is the first study conducted to see the associated risk factors with EC.

Methodology:

Design

This was unmatched case control study design to explore the sociodemographic risk factors association with EC.

Study population and setting

The data was collected from EC patients and control groups during time period of January 2019 up to January 2020. A total of 264 (132 cases and 132 controls) participants were included in the study. All EC cases were diagnosed and confirmed by histopathologic examination at the department of Pathology and Clinical Laboratory at French Medical Institute for Mother and Children (FMIC). The control groups were selected from adult participants who were visiting the hospital for routine health check-up with no cancer, cancer history and signs of cancer. All the questions were asked by direct interview from participants in local languages (Pashto & Farsi) following informed consent and using a structured questionnaire.

Risk factors

Variable included; Age by year, gender is selected as an independent/exposure variable both male and female are included in this case-control study, provinces (country zone) of living. The living situation is

also classified as rural and urban area. The urban living defined as living in the capital or center cities of the provinces while living in the districts and villages of the country defined as rural area.

Weight and height counted by Kg and cm, respectively. Ethnicity is classified according to available ethnicity groups in the country. The common ethnicity group in Afghanistan are Pashtun, Tajik, Hazara, Turk (Uzbek and Turkmen) and the remaining population which make less percentage are labeled as other ethnicity group.

Education level was categorized as illiterate/primary school (who never gone school or completed only elementary school), Secondary/high school or higher (beyond secondary school, graduated from high school or more).

The SES was categorized as low-income, middle/high-income as follows; Participants who don't have own house, permanent job, and other property are known as low-income, while participants who have own house, car, and other property are known as middle/high-income.

Family history of the cancer for each participant was asked about the history of cancer in first degree family as yes or no. The cancer history was classified for site of the cancer history as esophageal and non-esophageal and also relation of study participant with family member who had cancer.

Histopathology

The tissue biopsies were submitted in formalin. Grossly, all the tissues were small gray-white endoscopic biopsied specimens. Microscopic slides of the tissue block were made and stained with hematoxylin and Eosin (H&E) stain. The stained slides were seen under microscope for diagnosis and histologic subtype of the tumor.

Statistical analysis

Statistical Package for the Social Sciences (SPSS, version 25) was used for analyzing the data. Mean and standard deviation were calculated for continuous variables (age, weight and height of the participants), frequency and proportion were calculated for categorical variables. Binary logistic regression test of univariate analysis was used to estimate the risk of hypothesized risk factors for their unadjusted associations with EC. Significant variables (p-value < 0.05) in univariate logistic regression were further analyzed in multivariant logistic regression model to see independent associations with EC.

Results

Among total number of 132 EC cases, ESCC was the predominant type (74%) and 26% were EAC cases. Majority of our study population was male (54.5%). Table 1 shows the detail descriptive information of risk factors.

Table 1
Descriptive data of case and controls

Variables	Controls (n = 132)	Cases (n = 132)
	Number (%)	Number (%)
Age group (year)		
25–34	10 (7.6%)	0 (0%)
35–44	43 (33%)	9 (6.8%)
45–54	45 (34%)	27 (20.5%)
55–64	20 (15%)	52 (40.2%)
>=65	14 (11%)	44 (33.3%)
Mean age (SD)	48.05 ± 11.02 Y	59.48 ± 9.9 Y
Gender		
Male	52 (39.4%)	92 (69.7%)
Female	80 (60.6%)	40 (30.3%)
Ethnicity Group		
Pashtun	37 (28%)	42 (31.8%)
Tajik	58 (43.9%)	41 (28.1%)
Hazara	28 (21.2%)	25 (18.9%)
Turk (Uzbek-Turkmen)	7 (5.3%)	21 (15.9%)
Others	2 (1.5%)	3 (2.3%)
Residency		
Rural	56 (42.4%)	122 (92.4%)
Urban	76 (57.6%)	10 (7.6%)
Country zone		
Center	64 (48.5%)	49 (37.4%)
North-East	15 (11.4%)	28 (21.2%)
North	12 (9.8%)	20 (15.2%)
West	13 (9.1%)	8 (6.1%)
South	5 (3.8%)	4 (3.1%)
South-East	15 (11.4%)	18 (13.7%)

Variables	Controls (n = 132)	Cases (n = 132)
East	8 (6.1%)	5 (3.8%)
Occupation		
Non-employee	73 (55.3%)	124 (93.9%)
Employee	59 (44.7%)	8 (6.1%)
Socio-economy status		
Low	18 (13.6%)	110 (83.3%)
Middle	114 (86.4%)	22 (16.7%)
Education		
Uneducated/primary school	43 (32.6%)	126 (95.5%)
Secondary/High school or more	89 (67.4%)	6 (4.5%)
Family history		
No	113 (85.6%)	74 (56.5%)
Yes	19 (14.4%)	57 (43.5%)
Family history cancer site		
Esophageal cancer	1 (5.6%)	12 (38.7%)
Non-esophageal cancer	15 (83%)	11 (35.5%)
Unknown site	2 (11%)	8 (25.8%)

Age group of EC cases ranged from 30–85 years. 55–64 year was the common age group for cases with mean age of 59.48 ± 9.9 years compared to control group mostly in the age group of 45–54 years with mean age of 48.05 ± 11.02 years. Statistically it showed the risk of the getting EC is higher in older age group (OR: 1.070, 95% CI, *p*-value < 0.001). In Tables 2 and 3 the detail information of univariate and multivariate analysis for cases and controls are described, respectively.

Table 2
Univariate analysis

Characteristics	OR	95% CI		*p*-Value
Age				
	1.103	1.073	1.134	< 0.001
Gender				
Male	3.538	2.126	5.89	< 0.001
Female	1			
Residency				
Central zone	1			0.196
North-East zone	1.225	0.377	3.977	
North zone	2.88	0.798	10.393	
West zone	2.462	0.659	9.192	
South Zone	1.067	0.255	4.463	
South-East zone	1.28	0.228	7.187	
East zone	1.92	0.518	7.121	
Living area				
Rural	16.557	7.969	34.402	< 0.001
Urban	1			
Weight	0.986	0.963	1.009	0.24
Height	1.027	0.997	1.058	0.08
Ethnicity				
Pashtun	1			0.021
Tajik	0.386	0.148	1.007	
Hazara	0.237	0.092	0.609	
Turk (Uzbek-Turkmen)	0.298	0.108	0.818	
Education level				
Illiterate/ Primary school	43.465	17.738	106.505	< 0.001
High school or more	1			
Socio-economy status				

Characteristics	OR	95% CI		*p*-Value
Low SES	31.667	16.111	62.241	< 0.001
Middle and high SES	1			
Occupations				
Unemployed	12.527	5.668	27.687	< 0.001
Employed	1			
Family history				
No history	1			
Yes	4.581	2.524	8.316	< 0.001
Cancer site				
Esophagus	10.737	1.26	91.473	0.03
Non-esophagus	1			
Relation				
Parents	0.361	0.103	1.257	0.109
Sister & brothers	1			

Table 3
Multivariate analysis

Characteristics	OR	95% CI		*p*-Value
Age	1.114	1.06	1.172	< 0.001
Gender				
Male	3.394	1.182	9.745	0.023
Female	1			
Education level				
Illiterate/primary school	11.21	2.565	48.991	0.001
High school/Higher	1			
Living area				
Rural	25.161	6.855	92.356	< 0.001
Urban	1			
Socioeconomic status				
Low	14.08	4.602	43.075	< 0.001
Middle or High	1			
Family history				
No history	1			
Yes	4.715	1.407	15.795	< 0.001

A larger proportion of EC cases (69.4%) than control (39.4%) were male, showing that being male as risk factor for EC (OR: 1.070, 95% CI, *p*-value < 0.001).

Majority of the cases and control group participants were living in central zone of the country 48.5% and 37.4%, respectively. This is following by North-East and North zone of the country. No statistically significant association was identified between residency zones and risk of EC in our study. However, 92.4% of the EC patients were residing in rural areas of the country comparing to control group (42.4%) (OR: 25.16, 95% CI, *p*-value: <0.001).

According to ethnicity the control subjects are 43.95% were Tajik, 28% were Pashtun, 21.2% were Hazara, 5.3% were Turk (Uzbek-Turkmen) and 1.5% were other ethnicity groups. In cases subjects the Pashtuns made 31.8%, Tajiks 28.1%, Hazaras 18.9%, Turk (Uzbek-Turkmen) 15.9% and other ethnicity groups (Sadat and Arabs) made 2.3%. We found no significant relation of any ethnicity group with risk of EC in our study.

Among the EC cases majority (95.4%) are uneducated or only having primary education and 4.5% have completed the secondary school or high school comparing to control group 32.6% are uneducated or having primary education. Statistical analysis showed significant association of uneducated and lower education with risk of EC (OR: 11.21, 95% CI, *p*-value: <0.001). In addition, vast majority of the EC cases are belonging to low SES (83.3%) while in control group 13.6% are belong to low SES (OR: 14.080, 95% CI, *p*-value: <0.001). Approximately, 43.5% of the EC patients had the history of cancer in first degree family members whereas in control group 14.4% had positive family history of the EC suggesting that positive family history was significantly associated with developing risk of EC (OR: 4.715, 95% CI, *p*-value: <0.001). The family history of cancer according to the cancer site, 38.7% were EC, 35.5% were non-EC and in 25.8% the patient couldn't remember the exact site. However, site of cancer in family history and relation to the patient was not statistically significant.

According to occupation the majority are EC patients unemployed (93.9%) out of this 75% were farmer. Statistically it showed no significant association with EC in our study.

Discussion

The great majority of the EC cases are ESCC and EAC which are making 95% of all EC cases. Among these two most common types ESCC is more prevalent in under-developed countries and EAC is prevalent in developed countries (10, 11). However, the ESCC remains the most common histologic subtype of EC worldwide (12). Since the esophagus is lined by squamous epithelium, it could be a reason ESCC is more predominant. Moreover, other risk factors are also having important role. In our study the predominant subtype was ESCC (68%).

EC occurs mostly in older age groups. The risk rises with age, with an average age of 67 years at diagnosis (13). In our study the mean age of case groups was 59.4 years old compared to mean age of control (48 years). Study in India (14),Tanzania (15) and China (16) reported the majority of EC cases occurred in age group of > 60 years, > 65 years, and 60–69 years, respectively. Although EC occurs in the older age groups the lowest age for EC in the present study is 30 years. Study in more endemic area for EC, such as China, Japan and Iran also reported that EC starting from 30 years old age onward (17). The likely reason why EC occurs in older age maybe due to increase in the exposure to environmental risk factors and certain specific genes that are more likely to be altered and mutated by increasing age.

The EC most commonly affect males than female population. The incidence of EAC is 6–10 times higher in male than female and the incidence of ESCC is 2–3 times higher (18). In our study most of the EC cases were in males and showed 3.3-time associated risk of EC in male groups. Similar distribution were reported by study was conducted in Tanzania (15), an ecological study, which conducted based on GLOBOCAN project of World Health Organization (WHO) for Asian counters estimated that 70.33% incidence of EC cases in male and 29.87% in female (19). In addition, American Society of Cancer (20) and cancer research from United Kingdom (UK) countries reported the higher incidence of EC in male over female (21). Equally or higher distribution of EC among females is a rare epidemiologic feature of EC

which is reported in Linxian, China. This may show a single, very powerful risk factor shared by both genders (22). By the reviewing of literatures, it was not clear why the EC cases occur more in male than female, but probably due to the exposure to different environmental factors. As, the EC most common in farmers and workers in agricultures as men commonly do these works in rural areas. Others risk factors such as smoking, alcohol consumption and snuff dipping are also common among males.

The current study showed belonging to low SES comparing to middle/high SES, has the higher associated risk with EC (OR = 14.08). In addition, according to the education level, participants who were illiterate/having primary school education comparing to those who studied up to high school or more are at higher risk of EC (OR = 11.21). Many studies and different countries reported low SES and low education are related to the increase incidence of EC. Study was obtained in India indicated that 30.91% of EC patients were illiterates, 73.91% patients belonged to lower SES (23). Case control studies are conducted in Chinese and Iranian population sample revealed strong association between low SES and an increased risk of EC (24, 25). Low SES and increases the risk of EC incidences, are also reported in developed countries than might be expected. A case-control analysis in the United States by Gammon et al. estimated that the risk of EC among those with low income and low education was higher (26). The correlation of low SES and EC was documented by a case control study in Sweden, the unqualified employees were at 3.7 times the risk of AC and 2.1 times the risk of ESCC (27). Low education has also had negative impact on the prognosis and survival rate of the EC. In this regard a cohort study in Sweden reveals clear association between lower education and increased mortality after esophagectomy of EC patients (28).

Very large number of the EC patients in current study were living in rural areas (92.4%) and suggest an increased associated risk of EC among people living in rural areas (OR = 25.16). This findings are in line with study has been conducted in Turkey and reported the association of EC and rural population ($p < 0.001$) (29) and study in India also showed high prevalence of EC in rural areas (30).

Despite, the occupation did not show significant association with risk of EC in multivariate model in our study, but the majority of the EC patients were unemployed (93.9%). Of these unemployed EC patients 75% were farmer and all female EC patients were housewives. Studies in Brazil and Iran reported the that EC was more prevalent in farmers in high prevalent areas (25, 31). The work environment in agriculture is complex, with many potential hazardous exposures, such as pesticides, herbicides, fertilizers, dusts, zoonotic microbes, and sunlight (32). The reason why it is not significant in our study, will be belongs to small sample size and this need larger and wide study on this class population.

Weight and height did not show statistically significance association with EC in our study. A meta-analysis study showed high risk of obesity with EAC but inverse association to ESCC (33). Another study in Netherland also showed significant association between obesity and overweight with EC (34). No significance of EC and body mass index (BMI) in our study is because all cancer patients had the weight loss during the time of the diagnosis of the cancer.

In addition to environmental risk factors, hereditary susceptibility in esophageal carcinogenesis is another noticeable risk factor. Meanwhile, the co-occurrence of EC in family members is not always related to hereditary susceptibility but it also be consider as environmental factors (35). A study by Chen et al (36), reported that EC patients with positive family history increased 2-fold risk of developing of EC, while for whose both parents had history of cancer, 8-fold risk had been observed. Another study in high endemic area of the Iran showed more than 2-times risk for people who had positive first-degree family history of the cancer (37).

In the present study, the same association between family history of cancer in first degree family and EC was identified (OR = 4.71). The specific genetic expression related to EC in Afghanistan, however, have not been researched yet, which is important in prevention and treatment of EC. However, a multi-center case-control study in USA revealed no statistically significant risk of positive family history with EC (38). The inconsistency in the result from different articles might be due to different genetic susceptibility and different type environmental risk factors exposures.

To the best of our knowledge, this is the first study in Afghanistan in case control design which estimate the associated risk factors with EC. The study has been conducted in one of the main pathology centers of the country which receive biopsy samples from all around the country.

The limitations of this study includes small sample size due to the limited number of oncology center in the country. Secondly due to a smaller number of the EC cases in particular EAC cases, we were not able to run statistical analyses for both subtypes of EC separately. Thirdly, the risk factors are not studied in details because this is the first research assessing the risk factors in Afghanistan.

Conclusion

There is a growing occurrence of EC in Afghanistan, but very limited data are available. Our study concluded that EC is common cancer in older ages groups (> 65y) and in male over female. Our study also provided the evidence that living in rural areas, being un-educated or having lower education, belonging to low SES, and having family history in first degree relatives may contribute to the etiology of EC. These positive associations can help to suggest EC preventive measures and screening programs in early detection of EC in people who affected by above positive risk factors.

Abbreviations

EC: Esophageal carcinoma, ESCC: Squamous cell carcinoma, EAC: Esophageal adenocarcinoma, FMIC: French Medical Institute for Mothers and Children, SPSS: Statistical package for the Social Sciences, SES: Socioeconomic Status, IARC: International Agency for Research on Cancer, UK: United Kingdom

Declarations

Ethics Approval: The research project was approved by Ethical Review Committee of the FMIC (37-FMIC-ER-18).

Consent for publication: Prior to participation, each participant was autonomous to accept or reject to be part of this research and the detailed information about the study was provided to each participant as well. Informed consent form developed in local languages and translated to English was obtained from each participant.

Availability of data and materials: All data generated or analyzed during this study are included in this published article. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests

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Authors' contributions: The hypotheses were made by RS. RS collected the data. The data analyzed by RS, NA and TA. RS wrote the manuscript and reviewed the literatures. NA, TA, JAG and RS were the major contributors for critically revising the manuscript for important intellectual content. JAG has given expert opinion and final approval of the version to be published. All authors read and approved the final manuscript.

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