

Risk Factors Associated with Oesophageal Malignancy among Ethiopian Patients: A Case Control Study

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Background: *The incidence of Oesophageal cancer is increasing worldwide. Genetics, obesity, smoking, and alcohol consumption are among the known risk factors for this deadly cancer. Although Oesophageal cancer was noted to be common in Arsi and Bale regions of Ethiopia, the risk factors predisposing to this cancer have not yet been identified or reported to the best of our knowledge. The main objective of this study was to identify the risk factors associated with oesophageal cancer among the study population.*

Methods: *A case-control study where volunteer adult patients aged 18 and above with diagnosis of oesophageal cancer (cases) and non-oesophageal cancer patients (controls) were included was conducted in 2015 in Addis Ababa. The patients with dysphagia were referred to Adera Medical and Gastroenterology center from various regions of the country for Endoscopy. Patient data on socio-demographic and socio-economic variables, family history of similar illness and dietary history were collected using a pre specified questionnaire Patients' clinical features, Endoscopic diagnosis and histology reports were retrieved from patients chart. Data were entered and analyzed using SPSS version 20 software. Frequency tables and figures were used to describe cases and controls. Odds ratio and 95% confidence interval were used to establish the strength and the significance of the association between independent and outcome (development of Esophageal Cancer) variables, respectively.*

Results: *A total of 215 patients were diagnosed to have esophageal cancer at the center during April 1,2014 through March 31, 2015. A total of 115 (55%)of cases were females with a mean age of 50 years while 96 (45%) were males with a mean age of 55 years. Most of the patients were Muslim farmers from rural Arsi and Bale regions of the country where consumption of hot wheat porridge is very common as staple diet. Majority had mid esophageal mass lesion followed by distal and proximal lesions, in 45%, 34%, and 21% of the patients, respectively. Most (88%) of the patients had Esophageal squamous cell cancer (SCC) while the rest 12% had adenocarcinoma on histologic diagnosis.*

Conclusion: *Oesophageal cancer was noted to be more common among the farmers from Arsi and Bale regions of the country. Consumption of hot porridge for long time was noted to be significantly associated with having oesophageal cancer among the farmers from the two regions possibly due to the thermal effect, which could lead to dysplasia and later cancer.*

Key words: Oesophageal cancer, Risk factors, Ethiopia

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Introduction:

The global incidence of Oesophageal cancers varies by nearly 16-fold. The highest rates (90% being SCC) are found in Southern and Eastern Africa as well as Eastern Asia along the Oesophageal cancer belt. However, incidence has been noted to be low in Western and Middle Africa and Central America in both males and females^{1,2}. Oesophageal carcinoma is rare in young people but increases in incidence with age, peaking in the 7th and 8th decades of life. Squamous cell carcinoma accounts for about 90% of cases of oesophageal cancer worldwide. Adenocarcinoma is 3-4 times more common in men due to obesity and associated GERD while squamous cell carcinoma is equal in both genders. Oesophageal SCC has been observed to be

declining over the past three decades while adenocarcinoma has been progressively rising mainly due to increasing obesity and associated GERD following life style changes^{3, 4}. The annual risk of adenocarcinoma is estimated to be around 1% in low grade dysplasia Barrett but the risk is up to 5% in high grade dysplasia. Hence endoscopy surveillance is recommended every three years for its early diagnosis and intervention among patients with GERD^{5,6}.

Epidemiological data suggest that aspirin and other NSAIDs, which inhibit cyclooxygenase (COX), might protect against development of oesophageal cancer, particularly in the setting of Barrett's esophagus⁷. Poor nutritional status, low intake of fruits and vegetables, and drinking beverages at high temperatures are thought to be associated risk factors. But in low-risk areas such as the United States and several Western countries, smoking and excessive alcohol consumption has been associated with about 90 percent of the total cases of Oesophageal Squamous Cell Carcinoma^{8,9,10}.

High intake of red meats, fats, and processed foods are also associated with an increased risk of both types of esophageal cancers, whereas high intake of fiber, fresh fruit, and vegetables are associated with a lower risk^{11,12}. Drinking hot tea (≥ 60 degrees C) was also noted to be associated with Oesophageal SCC in a case-control study from northern Iran¹³. Several other dietary factors like zinc, selenium, and folate deficiencies increase the risk of oesophageal cancer. Among infectious risk factors, human papilloma virus (especially serotypes 16 and 18) has been implicated in the pathogenesis of Oesophageal SCC¹³⁻¹⁶.

In Ethiopia, different observational studies have shown oesophageal cancers to be common particularly in Arsi and Bale regions of the country. However, to the best of our knowledge, risk factors that could be associated with it have not yet been identified, which is the purpose of this study.

Patients and Methods

This is a case-control study where volunteer adult patients aged 18 and above with diagnosis of oesophageal cancer were included in the study as cases. These patients were referred to Adera Medical and Gastroenterology center from various regions of the country for Endoscopy when they present with dysphagia. Endoscopies were done by a senior consultant Gastroenterologist at the center using Olympus video Endoscopes under conscious sedation with diazepam and xylocaine oral spray. Endoscopic findings of fungating raised mass lesions were recorded and biopsies were taken from esophageal mass lesions for histologic examination by a senior pathologist. Histological examination used standard procedures. Only those biopsies that were reported as esophageal cancers (irrespective of the types of the cancers and sites of the location of the lesions) were considered as cases. Patients with positive histological findings were interviewed regarding their residence, occupation, family history of similar illness, dietary history, past medical history, and comorbid illnesses.

Clinical features of the cases, Endoscopic diagnosis and histology reports were retrieved from the chart records. Abdominal and chest imaging were also done to stage the tumors and to plan for specific treatment. Patients who underwent Gastroscopy by the same Endoscopist and at the same center but without esophageal cancer (negative histological results) were used as controls. Data collection tools and settings were exactly the same for both cases and controls. The collected data were entered and analyzed using SPSS version 20 software. Frequency tables and figures were used to describe cases and controls. Odds ratio and 95% confidence interval were used to establish the strength and the significance of the association between independent and outcome (development of Esophageal Cancer) variables, respectively.

Results

A total of 215 patients were diagnosed to have oesophageal cancer at Adera Medical center during April 1, 2014 through March 31, 2015. Hundred fifteen (55%) were females with a mean age of 50 years while 96 (45%) were males with a mean age of 55 years. Most of the patients were Muslim farmers from rural Arsi and Bale regions of the country where consumption of hot wheat porridge is very common as a traditional staple diet. Majority had mid Oesophageal mass lesion followed by distal and proximal lesions, in 45%, 34%, and 21% of the patients, respectively. Most (88%) of the patients had Esophageal squamous cell cancer (SCC) while the rest 12% had adenocarcinoma on histologic diagnosis. About 90% of the patients were referred to the center with sever progressive dysphagia and cachexia of more than six months after trying various acid suppressants and/or traditional herbs as they were unaware of the disease and possible risk factors.

Table 1. Distribution of cases and controls by socio-demographic characteristics

	Cases	Controls	Total
Age			
<35 years	9 (10.5)	77 (89.5)	86
35-44 years	39 (48.8)	41 (51.2)	80
45-54 years	70 (63.6)	40 (36.4)	110
55+ years	97 (63.0)	57 (37.0)	154
Mean Age	52.8 (51.1,54.5)	43.2 (41.1, 45.4)	48 (46.6, 49.5)
Sex			
Male	96 (42.5)	130 (57.5)	226
Female	119 (58.3)	85 (41.7)	204
Region			
Addis Ababa	12 (9.9)	109 (90.1)	121
Oromia	122 (72.2)	47(27.8)	169
Amhara	14 (40)	21 (60)	35
SNNP	27 (73)	10 (27)	37
Somali	37 (74)	13 (26)	50
Others	3 (16.7)	15 (83.3)	18
Occupation			
Unemployed	9 (15.5)	49 (84.5)	58
Employed	6 (9.0)	61 (91.0)	67
Farmers	143 (88.8)	18 (11.2)	161
Housewives	43 (54.4)	36 (45.6)	79
Merchants	14 (21.5)	51 (78.5)	65
Dietary History			
Injera	82 (30.6)	186 (69.4)	268
Rice	32 (80.0)	8 (20.0)	40
Porridge	78 (83.9)	15 (16.1)	93
Kocho	23 (79.3)	6 (20.7)	29

Table 2: Logistic Regression Analysis of Association between Oesophageal Cancer and Various Risk Factors

	Cases	Controls	COR, 95%CI	AOR,95%CI
Age				
<35 years	9 (10.5)	77 (89.5)	1.00	1.00
35-44 years	39 (48.8)	41 (51.2)	8.1 (3.6, 18.4)	3.4 (1.2, 9.9)
45-54 years	70 (63.6)	40 (36.4)	14.9 (6.8, 33.1)	7.3 (2.6, 20.7)
55+ years	97 (63.0)	57 (37.0)	14.6 (6.8, 31.3)	6.4 (2.4, 17.3)
Sex				
Male	96 (42.5)	130 (57.5)	1.00	1.00
Female	119 (58.3)	85 (41.7)	1.9 (1.3, 2.8)	2.6 (1.2, 5.5)
Residence/Region				
Addis Ababa	12 (9.9)	109 (90.1)	1.00	1.00
Oromia	122 (72.2)	47(27.8)	23.6 (11.9, 46.7)	4.4 (1.8, 10.9)
Amhara	14 (40)	21 (60)	6.1 (2.5, 14.9)	3.5 (1.2, 10.8)
SNNP	27 (73)	10 (27)	24.5 (9.6, 62.7)	8.1 (2.0, 32.8)
Somali	37 (74)	13 (26)	25.8 (10.8, 61.6)	5.1 (0.85, 30.3)
Others	3 (16.7)	15 (83.3)	1.8 (0.46, 7.2)	0.41 (0.07, 2.4)
Occupation				
Unemployed	9 (15.5)	49 (84.5)	1.00	1.00
Employed	6 (9.0)	61 (91.0)	0.54 (0.18, 1.6)	0.86 (0.24, 3.1)
Farmers	143 (88.8)	18 (11.2)	43.3 (18.2, 102.6)	19.2 (6.4, 57.9)
Housewives	43 (54.4)	36 (45.6)	6.5 (2.8, 15.0)	3.0 (1.00, 8.8)
Merchants	14 (21.5)	51 (78.5)	1.5 (0.59, 3.8)	1.5 (0.5, 4.8)
Dietary History				
Injera	82 (30.6)	186 (69.4)	1.00	1.00
Rice	32 (80.0)	8 (20.0)	9.1 (4.0, 20.5)	6.0 (0.89, 39.4)
Porridge	78 (83.9)	15 (16.1)	11.8 (6.4, 21.7)	2.5 (1.1, 5.9)
Kocho	23 (79.3)	6 (20.7)	8.7 (3.4, 22.2)	1.1, (0.24, 4.8)

Cigarette smoking, chat chewing, and alcohol consumption were reported by 5%, 3%, and 2% the patients with Oesophageal cancer, respectively. None of the patients reported history of similar illness among their family members while vomiting was reported by 55 % of the patients who were wasted due to the malignancy as well as chronic malnutrition due to prolonged dysphagia. Consumption of fruits and vegetables was not common among cases and controls as well. Human papilloma virus could not be tested, as the test was not available in the country.

Discussion

The variable of interest that showed significant association with esophageal cancer development in this study is diet. Accordingly, people whose staple diet is reported to be hot porridge were about three times more likely to develop esophageal cancer than those whose stable diet is injera, [AOR=2.60, 95%CI 1.09, 6.17]. Porridge is consumed regularly in almost all parts of the country but its consumption while it is burningly hot is the tradition in Arsi and Bale where esophageal cancer was observed to be endemic in previous studies¹². Similar case control observation was reported from Iran and Asia among people who drink hot teato be associated with oesophageal SCC¹³.

High temperature beverages and foods may increase the risk of esophageal cancer by causing thermal injury to the oesophageal mucosa^{13,17-19}. In a systematic review of 59 studies, more than 50 percent of the studies found that higher temperatures of fluid intake were associated with a significant increase in the risk of oesophageal cancer^{13,19}. Cigarette smoking, chat chewing, and alcohol consumption were rarely reported by the patients with oesophageal cancer.

Age was one of the important variables that have shown significant association with the esophageal cancer in our study. It was shown that as age increases the chance of developing esophageal cancer also increases. Taking those people who were under the age of 35 years as a reference category, it was depicted that those who are in the age of 35-44 years were more than 3 times more likely to develop Esophageal cancer compared to those who were below the age of 35 years, [AOR=3.47, 95%CI (1.2, 10.2)]. Similarly those who were in the age range of 45 and 54 were about 7 times more likely to develop Esophageal cancer, [AOR=7.3, 95%CI, 2.57, 20.8)] and those who were 55+ years were more than 6 times more likely to develop esophageal cancer compared to those who were below the age of 45 years, [AOR=6.2, 95%CI (2.28, 16.8)]. Increasing age was also noted to be associated with the development of Esophageal cancers in other studies from Asia, USA and Europe. A significant increase in the incidence was observed among persons aged 45 to 65²⁰⁻²².

In this study, Females were noted to be more than twice more likely to develop oesophageal Ca as compared to males, [AOR=2.45, 95%CI, (1.16, 5.17)] unlike male preponderance reports among patients with adenocarcinoma which is associated with obesity and GERD^{20,22}. Globally, the incidence of oesophageal SCC varies considerably among geographic regions. The highest rates are found in Asia (particularly in China and Singapore), Africa, and Iran (the so-called "esophageal cancer belt")²³⁻²⁵.

Similar regional variations were noted in within countries as well. Likewise, in this study, Oromia, Amhara and Southern nations (SNNP) regions of the country showed significant association with esophageal cancer while the remaining regions didn't show significant association. People from Oromia region were more than 8 times more likely to develop Esophageal Ca compared to people from Addis Ababa, [AOR=4.45, 95% CI (1.79, 11.08)]. On the other hand people from Amhara were about 4 times more likely to develop Esophageal Ca compared to those from Addis Ababa, [AOR=3.7, 95%CI (1.21, 11.32)]. Similarly, people from SNNP were about 4 times more likely to develop Esophageal cancer compared to same reference people from Addis Ababa, [AOR=8.03, 95%CI (1.99, 32.3)]. Lower socioeconomic status was associated with oesophageal SCC in a large population-based study²⁶. Occupation was also one of the identified risk factors in this study possibly due to deficiency of vitamins and micronutrients that could be associated with development of Esophageal cancers as reported in other works. Farmers and housewives were most at risk. Farmers were about 19 times more likely to develop Esophageal Ca compared to those unemployed citizens, [AOR=18.85, 95%CI (6.25, 56.9)] while housewives were about 3 times more likely to develop esophageal Ca compared to those unemployed citizens, AOR=3.05, 95%CI, 1.03, 9.05)].

Reflux symptoms were associated with adenocarcinoma of the Oesophagus (odds ratio 7.7) and gastric cardia (odds ratio 2.0) in a large case control study from Sweden²². The risk was greatest among patients with long-standing (>20 years) and severe symptoms (odds ratio 43.5 and 4.4 for esophageal and gastric cardia adenocarcinoma, respectively). Hence, Endoscopic surveillance for oesophageal cancers in people who are at high risk will help for early diagnosis and cure by Endoscopic mucosal resection of the dysplasia or early cancer. However, almost all our patients presented with advanced obstructive Esophageal mass lesions, severe luminal stenosis, and protracted malnutrition due to late presentation and diagnosis. At this advanced stage, palliative care will be the only treatment option available since most are inoperable and resistant to Radio chemotherapy.

Conclusion

Esophageal cancer was noted to be more common among the farmers from Arsi and Bale regions of the country. Consumption of hot porridge for long time was noted to be significantly associated with having Esophageal cancer among the farmers from the two regions possibly due

to the thermal effect, which could in turn lead to dysplasia and cancer. This finding has useful implication for prevention, early diagnosis, and treatment of this dismal cancer.

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