

Dietary Risk Factors for Oesophageal Cancer: A Case Control Study from Assam, India

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ABSTRACT

Introduction: World Health Organization (GLOBOCON 2018) stated Oesophageal cancer ranks 6th among most cancers in India with an incidence 5.04%. As per Population Based Cancer Registry (PBCR) India, Cancer of the Oesophagus is the leading site in the registries in states of Assam, Meghalaya, Mizoram and Nagaland. In Assam, there are various tribes with diverse cultural and dietary practices where food habit and cooking practice are different and unique. Keeping all these views, the present study was undertaken to find out various dietary risk factors with risk of developing Oesophageal cancer in Assam, India. **Materials & Methods:** A Hospital based case control study was conducted from an apex institution of Assam, Gauhati Medical College and Hospital (GMCH) and State Cancer Institute, a branch of GMCH from August 2020 to July 2021. Considering 80% power, 5% alpha error and odds ratio to be 2.6 a total sample size of 144 was calculated. Among cases and control ratio is taken to be 1:1. After matching age and sex, data collected from both cases and controls by face-to-face interview method. Collected data compiled, analyzed in MS excel and results were tabulated. **Results:** Majority of cases and controls were aged ≥ 50 years. Statistically significant association was seen between infrequent intake of green leafy vegetables, higher frequency of intake of fermented, preserved food with Kala Khar and risk of developing Oesophageal cancer. **Conclusion:** A holistic approach with the aim of prevention of dietary risk factors is crucial in reducing higher incidence of Oesophageal cancer.

KEY WORDS: Oesophageal cancer, Kala Khar, Green leafy vegetables.

Introduction

Oesophageal cancer is one of the common malignant tumor of the Gastrointestinal (GI) tract. As per the World Health Organisation GLOBOCON 2018, Oesophageal cancer ranks 7th among the most common cancers (3.2%) in the world with 5,72,000 new cases and mortality ranks 6th (5.3%), with 5,09,000 deaths. It is 6th most common cancer in India with an incidence 5.04%.^[1] As per Population Based Cancer

Registry (PBCR) India, Cancer of the Oesophagus is the leading site in the registries in the states of Assam, Meghalaya, Mizoram and Nagaland.^[2] This North-East region of India came under “Oesophageal Cancer belt” which extends from Northeast China to the Middle East. Here, reported cancer incidences 150-200 cases per lakh population in comparison to national data (80-110 cases per lakh population).^[3] As per three population-based cancer registries in Assam, Kamrup urban district shows an increased trend of Oesophageal cancer from year 2003 to 2016. Amongst male, it increased from 22.4 to 32.6 per 100000 population during this period. Whereas, Dibrugarh district show a decline in crude rate from 13.1 to 11.8 per 1,00,000 population. However, among males’ highest proportion (15.7%) of Oesophageal cancer seen In Dibrugarh district, followed by Kamrup urban (14.3%).^[4]

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There is huge diversity in terms of socio-demographic, religious and cultural factors in North-East region including Assam. In Assam, there are various tribes with diverse cultural and dietary practices where food habit and cooking practice are different and unique. Studies have shown some locally prepared specific food items eg. Kala Khar are probable risk factors for this cancer.^[5] Kala Khar is a highly alkaline substance made from charred false stem, skin of a particular variety of banana, used in Assam as herbal remedy and food additives.^[5] The type of food, preserving practices and cooking habits prevalent in the community will surely help to detect the unidentified risk factors and will definitely help in changing community behaviour through instituting primary and primordial prevention. This will also bring some policy changes in instituting preventive measures. Keeping all these views, the present study was undertaken to find out various dietary risk factors with risk of developing Oesophageal cancer in Assam.

Materials & Methods

A Hospital based, case control study was conducted from one of the apex institutions of Assam, Gauhati Medical college and Hospital and State Cancer Institute, a branch of Gauhati Medical College for cancer speciality. Histologically diagnosed Oesophageal cancer patients from August 2020 to July 2021, aged 40-80 years attended the State cancer institute OPD were enrolled as cases and age, sex matched controls were taken from Gastroenterology (GI) and General Medicine department of Gauhati Medical College and Hospital. Inclusion criteria for cases were histologically diagnosed cancer patients preceding 6 months from the study period, while control were patients attending GI and General Medicine Dept suffering from different diseases other than cancer, who underwent diagnostic endoscopic procedure, found negative results for any Oesophageal diseases. In view of multiple risk factors being studied, considering 80% power in a two-sided test with 5% alpha error and assuming the associated odd ratios to be 2.6^[6], a total sample size was calculated to be 144, taking case control ratio 1:1. During the study period 387 Oesophageal cancer patients were registered in Hospital based cancer registry, out of which 124 were newly diagnosed. Exclusion criteria for this case control study were those, who had exposure history of smoking, alcohol or history of consumption of any form of tobacco with betel products, critically ill patients unable to respond, patients unable to give clear past medical history of

any Oesophageal diseases, already diagnosed with other cancer, having family history of cancer etc. After applying exclusion criteria 72 cases taken for the study.

Smokers here defined as adults smoked more than 100 cigarettes in lifetime either continue smoke every day or occasionally, alcoholic as who drinks more than 12 drinks in lifetime and betel product along with tobacco users as those taking these more than 10 times in lifetime.

Variables of the study were various dietary habits like habit of taking green vegetables and their frequency, habit of taking preserved, fermented, smoked food with Kala Khar, habit of eating meat with frequency and use of various beverages etc. Regrading characteristics of the beverages, very hot taken as consumed immediately or within 5 minutes, hot beverages within 5-10 minutes and mild beverages more than 10 minutes after being served.

The cancer hospital outdoor was visited daily in all working days and patient were interviewed till desired sample size met. After taking informed consent from the patients, all the information were filled up in a predesigned, pretested interview schedule. Interview was conducted maintaining the privacy and confidentiality of the patients. Data was collected, compiled and analyzed in MS excel and Instat graph pad. For data analysis, Chi square test was done, Odds Ratio was calculated, and multiple logistic regression was done. p value less than 0.05 was taken as statistically significant. The reference category was selected as the no exposure or low exposure group. Permission from the instructional ethics committee Gauhati Medical College and Hospital (IEC No.MC/190/2007/Pt-II/Mar-2020/75 on Date: 4/6/2020) was obtained as per institutional norms.

Results

On analyzing basic characteristics for both cases and controls, males accounts for 73.6% in both. The average age of the cases and controls were 60.9 ± 13.1 and 61.2 ± 12.8 years respectively. Majority (72.3%) of both cases and controls were aged ≥ 50 years. While studying the relationship between socio-economic characteristics and occurrence of Oesophageal cancer, no statistically significant association was seen religion with development of Oesophageal cancer with odds 1.1 (95% CI, 0.6-2.2). Similarly, no statistically significant association was

Table 1: Relationship among cases and controls for various dietary habits and patterns

Dietary factors	Cases (N=72)	Control (N=72)	Total (N=144)	p value	OR (95% CI)
Habit of eating Green leafy vegetables					
Yes	29(40.3)	46(63.9)	75(52.0)	0.007	0.3 (0.2-0.7)
No	43(59.7)	26(36.1)	69(48.0)		
Frequency of eating Green leafy vegetables (per week)					
≤ once/week	20(68.9)	18(39.1)	38(50.6)	0.022	3.4 (1.2-9.2)
> once/week	09(31.1)	28(60.9)	37(49.4)		
Habit of eating preserved/fermented/smoked foods and Kala Khar					
Yes	23(31.9)	19(26.4)	42(29.2)	0.582	1.3 (0.6-2.6)
No	49(68.1)	53(73.6)	102(70.8)		
Frequency of eating preserved/fermented/smoked foods and Kala Khar					
≤ 1/month	05(6.9)	09(12.5)	14(9.7)	-	1 (reference)
1-3/month	06(8.3)	07(9.7)	13(9.0)	0.898	0.9 (0.2-2.9)
>3 /month	12(16.7)	03(4.1)	15(10.4)	0.046	4.3 (1.1-16.2)
Frequency of eating meat					
Yes	49(68.0)	51(70.8)	100(69.4)	0.856	0.8 (0.4-1.7)
No	23(32.0)	21(29.2)	44(30.6)		
Characteristics of drinking beverages (Thermal temperature)					
Mild	14(19.4)	32(44.4)	46(31.9)	-	1 (reference)
Hot	42(58.3)	31(43.1)	73(50.7)	0.007	3.1 (1.4-6.7)
Very hot	16(22.3)	9(12.5)	25(17.4)	0.013	4.1 (1.4-11.3)

seen between castes and occurrence of Oesophageal cancer. However, odds of developing Oesophageal cancer was found to be 6.3 (95% CI, 1.3-29.6) among those having previous history of suffering from any oesophageal abnormalities and it was found to be statistically significant with risk of developing Oesophageal cancer. Regarding family history of cancer, no statistically significant association was seen having family history of cancer with risk of developing Oesophageal cancer. Table 1 showing a statistically significant association between less and infrequent intake of green leafy vegetables with risk of developing Oesophageal cancer. Similarly, no statistically significant association was seen between habit of taking preserved, fermented, smoked food and Kala Khar with increased risk of Oesophageal cancer. However, the odds (4.3, 95% CI 1.1-16.2), of developing Oesophageal cancer were found to be high among cases who had habit of taking fermented, preserved and smoked food along with Kala Khar more than 3 times per month and it was found to be statistically significant. On analysing habit of eating meat with risk of developing Oesophageal cancer, no statistically significant association was found in Table 1. Similarly, no statistically significant association was seen between increased in frequency

of eating meat with risk of developing Oesophageal cancer. While analysing characteristics of drinking beverages, the odds of developing Oesophageal cancer was found to be 1.9 (95% CI, 1.0-3.8) for those, who had habit of drinking tea compared to coffee and odds of 1.9 (95% CI, 1.0-3.8) for those who had frequency of intake of beverages more than 5 times per day, which were not found to be statistically significant. However, a statistically significant association was found between drinking very hot beverages and risk of developing Oesophageal cancer with odds 4.1 (95% CI 1.4-11.3). After doing the logistic regression in Table 2, taking Oesophageal cancer as the dependent variable we found out that previous history of having any Oesophageal diseases, frequency of Preserved/Fermented/Smoked/Kala Khar intake, temperature at intake of beverages showed positive association. However, no positive association was seen between less and infrequent intake of green leafy vegetables and risk of developing Oesophageal cancer.

Discussion

Oesophageal cancer is an upper digestive tract cancer, prevalent in developing and developed countries with male to female ratio globally 2.7:1 and in India

Table 2: Logistic regression model for risk factors among cases and controls

Risk factors	B	Std. Error	Wald	df	Sig.	Exp(B)	95% Confidence Interval for Exp (B)
Intercept	-1.701	.961	3.133	1	.077		
H/O any Oesophageal abnormality	-3.405	.591	33.222	1	<0.0001	1.9	1.01-4.2
Green leafy vegetables intake	.316	.492	.413	1	.521	1.372	0.52-3.6
Frequency of Green leafy vegetables	0.908	0.685	1.756	1	0.185	2.478	0.64-9.4
Frequency of Pre-served/Fermented/Smoked food/ Kala Khar	2.772	1.040	7.107	1	.008	15.994	2.08-122.7
Initial temperature of beverages	1.497	.546	7.511	1	.006	4.468	1.53-13.0

3:1 respectively.^[7,8] The higher male proportion in present study was in conformity with various studies across the globe.^[9,10] A population based case control study by Cronin-Fenton and co-workers had stated protective role of female hormones and breast feeding for decreased risk of Oesophageal cancer.^[9,10] However, in the present study the predominance of male could be due to exposure to different addictive substances like tobacco. A study by Nanda Kumar and co-workers stated that nearly 49.3% males compared to 22.8% females had exposure to tobacco in North East region of India.^[11] In our study higher prevalence of Oesophageal was cancer amongst ≥ 50 years with mean age group of 60.9 years (57.8-63.9), which was at conformity with observations by SEER programme of NIH.^[12] As per SEER programme of NIH, median age group of an Oesophageal cancer diagnosis is 66 years, which supports our study findings about elderly population. This may necessitate the development of simple screening facilities at primary level during this age of 60.9 years for early identification and confirmation as well as intervention.

Statistically insignificant association was seen when comparing religion among cases and control for Oesophageal cancer that could be explained on biological plausibility ground. However, there may be other factors like cultural and behavioural which can be further studied by including quantitative study design. Similarly, non-significant association was between ethnicity and Oesophageal cancer, could be due to study settings, as it is a single centered hospital-based study. Among various tribes resides in North-East India fermented food, smoking,

home made locally available liquor are considered as normal food habit practices, which are known as risk factors for Oesophageal cancer. Non-significant association between ethnicity and development of Oesophageal cancer could be due to exchange of cultural practices between tribal and nontribal population.

Significant relationship between Oesophageal abnormality and Oesophageal cancer has got a biologically plausible explanation, however less prevalence of Oesophageal abnormalities was found in this study compared to other studies.^[13,14] A study by Kim JH and co-workers stated that prevalence Barrett's Oesophagus 1.6% among general population which increased to 10% among Oesophageal cancer patients, supporting our study findings.^[15] In the present study, history of Oesophageal abnormalities was based on previous medical reports which was limitation of the study. This requires further studies for development of screening tools for early identification of Oesophageal diseases at every level. Unlike Oesophageal abnormalities, no statistically significant association was seen between having history of cancer in the family with risk of developing Oesophageal cancer in this study. Healthy diet and lifestyle play a crucial role for prevention of Oesophageal cancer and helps in inducing or modifying carcinogenic process for development of cancer.^[6] In this study, odds of developing Oesophageal cancer was found to be statistically significant with less and infrequent use of Green leafy vegetables (GLV) in diet. Protective role of Green leafy vegetables in present study was in conformity with studies done by Engel L S et al.^[16] and Li W Q

et al.^[17] These findings would help for further in depth research in future and will help in strategic implementation in relation to consumption of green leafy vegetables as primary preventive measures for development of cancer. This finding can be utilized in formulation of IEC for promoting health, dietary practices including use of GLV.

No statistically significant association was seen between preserved, smoked, fermented foods and Kala Khar intake with risk of developing Oesophageal cancer. However, odds (4.3,95% CI, 1.1-16.2) of developing Oesophageal cancer was found to be statistically significant amongst people who had history of eating preserved, smoked, fermented foods and Kala Khar in their regular meal more than 3 times in a month. This finding of the study is in conformity with a case control study done in Assam by P K Phukan and co-workers.^[5] Kala Khar being charred product and high alkalinity may have a biological plausible relation with risk of developing Oesophageal cancer. Further, in depth and qualitative research work needed in future for better evaluation of this association. No statistically significant association was found between intake of meat, increased in frequency of intake with risk of developing Oesophageal cancer. In contrast to present findings, a systematic review and meta-analysis by Choi Y and co-workers stated odds (1.44,95%CI, 1.16-1.80) of developing Oesophageal cancer is high with high consumption of red meat.^[18] The insignificant association in present study could be due to inability to precisely estimate the amount and frequency of consumed meat because of the study design.

On analysing characteristics of beverages with risk of developing Oesophageal cancer no statistically significant association was seen in between. Findings in the present study was in conformity with a study done by Islami F and co-workers stating no statistically significant association between types of beverages, frequency of drinks and risk of developing Oesophageal cancer. However, study by Islami F and co-workers estimated a significant association between characteristics of beverages based on temperature (mild, hot, very hot) with risk of developing Oesophageal cancer.^[19,20] In present study, odds of developing Oesophageal cancer was found to be high with increased in initial temperature of intake of beverages, which was in conformity with the study by Islami F and co-workers.^[19,20] A biological plausibility is seen as high temperature damages oral and oesophageal mucosa that may

lead to development of Oesophageal cancer. On doing multiple logistic regression (MLR) analysis, trend for h/o any Oesophageal abnormality, increased in frequency for intake of preserved, fermented smoked food with Kala Khar, higher temperature of drinking beverages were found to be statistically significant. On the other hand, regular intake and increased frequency of GLV were not found to be protective against occurrence Oesophageal cancer in MLR analysis.

Conclusion

Oesophageal cancer is a disease related unhealthy food practices. In our study, higher intake of green leafy vegetables was found to be protective against development of cancer, showing that further interventions were required for promotion of these kinds of healthy practices at individual as well as community level. While eating fermented, preserved food and drinking hot beverages were found to be more threat in the causation of cancer, these could be intervened through effective behaviour change communication. A holistic approach with the aim of prevention of risk factors as well as early identification of undiagnosed disease is crucial.

Limitations of the study

One of the important limitations of the study is Recall bias specially in terms of duration of intake of food items, that happens because of study setting. Moreover, Covid pandemic situation attributed to a small sample size for this study that leads to another limitation.

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