ORIGINAL RESEARCH ARTICLE

Investigating Influence of Multiple Risk Factors on Survival Likelihood in Esophageal Cancer Patients: Evidence from Assam, North-East India

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ABSTRACT

Background: To comprehend the complex interplay of multiple risk factors impacting survival at a localized level is imperative. This study aimed to explore survival patterns and identify the underlying causal factors linked to mortality risk in the region.

Methodology: Data from 200 patients with esophageal cancer treated at three prominent hospitals over the course of one year is collected for the study purpose. The Kaplan–Meier curve and Cox proportional hazard regression model were employed.

Results: This study identified smokeless tobacco consumption habits showing a 6-fold elevated mortality risk (HR 6.22, p<0.001). Subsequently, cultivator (HR 4.85, p=0.001) and male gender (HR 4.24, p=0.001) showed higher mortality risk. Additionally, a significantly higher prevalence of death among smokers with comorbidity (66.0%) is found compared to smokers without comorbidity (44.1%), p=0.043. The survival probability shows a declining trend, i.e. 84.50% in the first year to 13% in the 6th year. With an 82% change, this variation was greatest between the 3rd and 4th years.

Conclusions: To better understand mortality risk, certain risk factors, such as salted fish, fertilizer and pesticide exposure, and length of marriage, need to be thoroughly investigated in future studies due to limited knowledge about this exposure at a localized level.

Keywords: Oesophagus, Smoking, Traditional alcoholic drinks, Risk factors, Tobacco, Survival

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INTRODUCTION

Esophageal cancer poses a significant global health concern in terms of both its incidence and mortality rates. In addition, its incidence is highly varied, with sharply demarcated geographic areas exhibiting high rates of incidence.[1] Generally, countries with higher human development indices tend to have lower incidence rates of the disease. Specifically, Asian and African countries are more vulnerable to esophageal cancer than developed regions such as Europe and America.[2] According to the report of Global Cancer Observatory (GLOBOCON) 2022, the mortality rate (13.4%) due to esophageal cancer is the 7th highest, with an estimated 445391 (4.57%) cases globally. The report's findings put India in 5th position in terms of mortality out of all cancers explored, with an estimated mortality of 66410 (7.2%) and a cumulative risk of 0.55. The same report mentioned that the Age-standardized rate (ASR) for mortality based on the world population among Indians is 4.7, which also ranks esophageal cancer in terms of ASR at the 5th position among the 15 most common cancers explored.[3] Despite advancements in treatment techniques, there has been limited progress in improving the prognosis and survival rates of patients with this disease. This raises questions about the implementation and effectiveness of public health measures such as screening facilities, early diagnosis, and treatment in enhancing survivability outcomes.[4-6] The prognosis for esophageal cancer patients is also generally poor due to late-onset symptoms and delayed diagnosis, hindering definitive surgical intervention.[7] The chances of survival are significantly greater when the disease is detected at an early stage and remains localized to its original site at the time of diagnosis. As the cancer spreads to distant organs, the likelihood of survival decreases.[8-9] Reports indicate that 5-year survival rates for esophageal cancer worldwide range from 4% to 30%.[10]

The prediction of survival and its association is a difficult task for this type of cancer because at the time this cancer is detected, it spreads to distant locations, and response bias may hinder understanding.[11] Additionally, there are no specific studies at the local level aimed at understanding the risk of multiple exposures and survivability, and studies performed within the country have shown mixed results. As an early strategy for prevention, a strong understanding of the possible causative factors for the disease, along with proper predictability, may increase the likelihood of the disease and possibly increase patient survival.[12]

This study aimed to assess the survival pattern of esophageal cancer patients in Assam, India, and to estimate the effects of different exposures on survival. We also aimed to evaluate the association between comorbidities and the risk of death. This is an attempt to understand the cause of a significant proportion of mortality in the region.

METHODOLOGY

Study setting and time of study; Esophageal cancer patients were identified from three prominent tertiary care hospitals in Assam. These hospitals are located in the Dibrugarh and Guwahati districts of Assam. Each hospital has a dedicated cancer unit for patient registration and initial reporting of diseases. Patients are diagnosed at these facilities using endoscopic screening for the esophagus, CT scans, MRI scans, biopsy sampling, and by assessing esophageal cancer-related symptoms such as dysphagia chronic cough, hoarseness, and weight loss. Additionally, many referral patients visit these hospitals for definitive treatment options, including chemotherapy, radiotherapy, and surgery. The hospitals also have the capacity to admit cancer patients for treatment.

The investigation is carried out between the 1st of February 2022 and the 31st of January 2023, spanning a period of one year. The study subjects are followed over a period of one year, i.e., from the day of investigation until the end of the survey period, to observe the event of interest, death. The study participants whose follow-up information was lost at the end of the study period are censored. A total of 87 deaths is observed at the end of the study period.

Sample size: A total of 200 patients were included in the present study based on a case-control study design studied earlier, (the sample size was calculated based on the review of literature, aiming at an odds ratio of 2.0 with a 20% exposure level in the community, the power of the study was set to 80%, and at a 5% level of significance, by using a standard formula for case-control study design), a total sample size of 180 was obtained. An additional 20 samples were added to account for nonresponse or to cover any missing observations, resulting in a total of 200 case subjects), all of whom were confirmed through histopathological testing.

Inclusion and exclusion criteria; Patients eligible for the study were confirmed by histopathology testing. In contrast, patients with recurrent cancer were excluded from the study.

Study tool: The data were recorded using a self-administered questionnaire. If the patient could not speak, a reliable family member approached for information.

Statistical analysis; Descriptive statistical analysis was used to present the categorical measurement in frequency and percentage. The effect of exposure on cancer mortality is analyzed using a Cox proportional hazard regression model. The variables found to be significant at 25% and certain additional variables that have clinical significance for disease outcome according to the log-rank test were taken into account before being fit into the multivariable Cox model. The Kaplan–Meier method was used to observe the survival probability over time. The hazard ratio (HR) and 95% confidence interval (CI) were es-

timated using the Cox model. A P value less than 0.05 between two groups is considered to indicate statistical significance. Missing information is taken care of by exclusion from analysis. Categorical variables are presented in frequency tables, forest plots, and bar graphs. We used SPSS v25 (IBM, Armonk, New York, USA), STATA v17, and Anaconda v3.7 for the processing and description of the data.

Ethical statement: The study is presented before the research committee of Manipur University, Manipur, and approved under order no. MU/3-3/2019/PhD (MPS)/424 dated 23rd December 2021. The study did not involve any clinical parameters, animals, or invasive procedures before the commencement of the survey clearance from respective institutions is also sought and obtained for data collection viz. Aditya diagnostics and hospitals, Sanjivani diagnostics and hospitals, and health city hospitals. Informed consent was also obtained from the participants before the data were collected; the privacy and confidentiality of the participants were maintained.

RESULTS

Socio-demographic and Socio-economic characteristics of the patients: This study investigated the sociodemographic characteristics of 200 esophageal cancer patients, representing 34.50% of the female population and 64.50% of the male population. In Table 1, descriptive statistics explored the median age of the studied population was 57 years, with an interquartile range of 52-62 years. Among the studied population, 60% are from rural areas, and the majority belong to the Hindu community. In addition, 92% of them were non-scheduled tribes, while the rest were from the scheduled tribe population. In terms of education, 14% of the population is illiterate, and only 10% have a college degree or above. The majority of the participants were married (97.50%), and those with a length of marriage < 26 years had the highest percentage of patients with the disease (45.40%). Two children per household constituted the majority of these families, while 7.90% of the married population did not have any children. In terms of income, a significant portion belonged to the higher income category based on the percentile distribution, i.e., above 31000 rupees per month constituted 35%.

Risk of mortality associated with various exposure in the participants and their median survival time: Table 2 shows the results of the multivariate Cox proportional hazard model, which was used to evaluate the impact of multiple exposures on mortality risk. In addition, the median times of survivability concerning these exposures are also discussed. The exposures significantly associated with mortality risk in the model were family income <20000, smokeless tobacco, salting fish, alcohol consumption, smoking, primary to middle, fertilizer use, pesticide use, gum disease, betel nut, sex, age, tooth loss >4, length of marriage >38 years, first child age <22 years, cultivating/agricultural worker, and only 2 children.

Based on the findings model revealed that smokeless tobacco consumption (HR-6.226; 95% CI 1.030-2.864, p-value 0.038) was associated with a greater risk of death than other factors. However, having two children (HR 0.437) is found to be associated with an increased likelihood of survival from the disease.

Table 1: Sociodemographic characteristics of the studied population

Sociodemographic characteristics	Participants (%)
Age (median) IQR(Q3-Q1)	57 (52-62)
Gender	
Male	131 (64.5)
Female	69 (34.5)
Residence	
Urban	65 (32.5)
Semiurban	15 (7.5)
Rural	120 (60)
Religion	
Hindu	164 (82)
Muslim	33 (16.5)
Christian	3 (1.5)
Ethnicity	
Non-schedule tribe	185 (92.5)
Schedule tribe	15 (7.5)
Education	
Illiterate	28 (14)
Primary school	23 (11.5)
Middle school	47 (23.5)
High school	59 (29.5)
Secondary school	20 (10.5)
College	15 (7.5)
Other	3 (1.5)
PG	5 (2.5)
Occupation	
Unemployed	8 (4)
Cultivator	66 (33)
Business	9 (4.5)
Service	50 (25)
Housewife	66 (33)
Other	1 (0.5)
Marital status	
Married	195 (97.5)
Unmarried	5 (2.5)
Age at marriage	
<=26 years	104 (52)
27-30 years	44 (22)
>=31 years	34 (17)
Length of marriage	
<26 years	88 (45.4)
26-38 years	47 (24.2)
>38 years	59 (30.4)
Income category	
<12000 INR/<143 USD	17 (8.5)
12000-20000 INR/ 143-240 USD	47 (23.5)
20001-31000 INR/ >240-370USD	66 (33)
>31000 INR/ >370 USD	70 (35)
Number of children	
No children	27 (14.3)
Only one child	58 (30.37)
Two children	74 (38.74)
Three children	27 (14.14)
Four children	5 (2.61)

Table 2: Median survival, log-rank test, and estimated hazard ratio of the significant variables of the multivariable Cox proportional hazard regression model

Category	Subjects	Median time of survivability (95% CI)	Log-rank test (p-value)	Partial Likelihood	HR (95%CI)	p-value
Family income <20000						
No	134	38(30-64)	0.006	0.004	1.898(1.047-3.439)	0.035
Yes	66	20(14-31)				
Tobacco						
No	136	38(31-68)	0.0001	0.0002	6.226(2.671-14.51)	<0.001
Yes	64	20(14-26)				
Salted fish						
No	139	37(25-58)	0.2057	<0.001	3.595(1.687-7.66)	0.001
Yes	61	30(18-38)				
Alcohol consumption						
No	129	41(31-60)	0.2057	0.008	2.622(1.285-5.35)	0.008
Yes	71	24(18-30)				
Smoking						
No	131	51(37-73)	<0.001	<0.001	2.145(1.11-4.145)	0.023
Yes	69	22(16-26)				
Primary to middle education						
No	130	41(33-71)	0.2928	0.242	3.937(1.751-8.854)	0.001
Yes	70	24(14-26)				
Fertilizer use						
No	127	58(32-73)	<0.001	<0.001	3.77(1.826-7.786)	<0.001
Yes	73	22(14-26)				
Pesticide use						
No	135	37(30-64)	0.0003	0.0004	2.062(1.123-3.788)	0.020
Yes	65	21(13-35)				
Gum disease						
No	120	60(37-68)	<0.001	<0.001	3.103(1.501-6.416)	0.002
Yes	80	20(15-28)				
Betel nut consumption						
No	98	39(32-41)	<0.001	<0.001	2.876(1.254-6.595)	0.013
Yes	101	24(16-31)				
Gender						
Male	131	30(24-37)	0.1359	0.129	4.249(1.861-9.702)	0.001
Female	69	38(21-69)				
Age	-	-	0.0179	0.036	1.053(1.007-1.245)	<0.001
Tooth lose						
<4	110	37(16-63)	0.3327	0.136	2.333(1.201-4.532)	0.012
>=4 number	87	31(20-41)				
Cultivator						
No	134	49(34-64)	0.2868	0.289	4.854(1.93-12.207)	0.001
Yes	66	38(23-69)				
Length of Marriage						
<=25 years	90	37(26-61)	0.2578	0.32	4.069(1.63-10.159)	0.003
26-38 years	42	33(18-60)				
>38 years	62	25(14-35)				
First child age<22 years						
No	122	43(11-52	0.2789	0.154	2.85(1.19-6.824)	0.019
Yes	55	41(23-51)				
Two children in the family						
No	111	30(14-63)	0.2458	0.234	0.437(0.214-0.895)	0.024
Yes	70	26(19-51)				

Kaplan-Meier survivability curve for the patients and identified mortality risk factors:

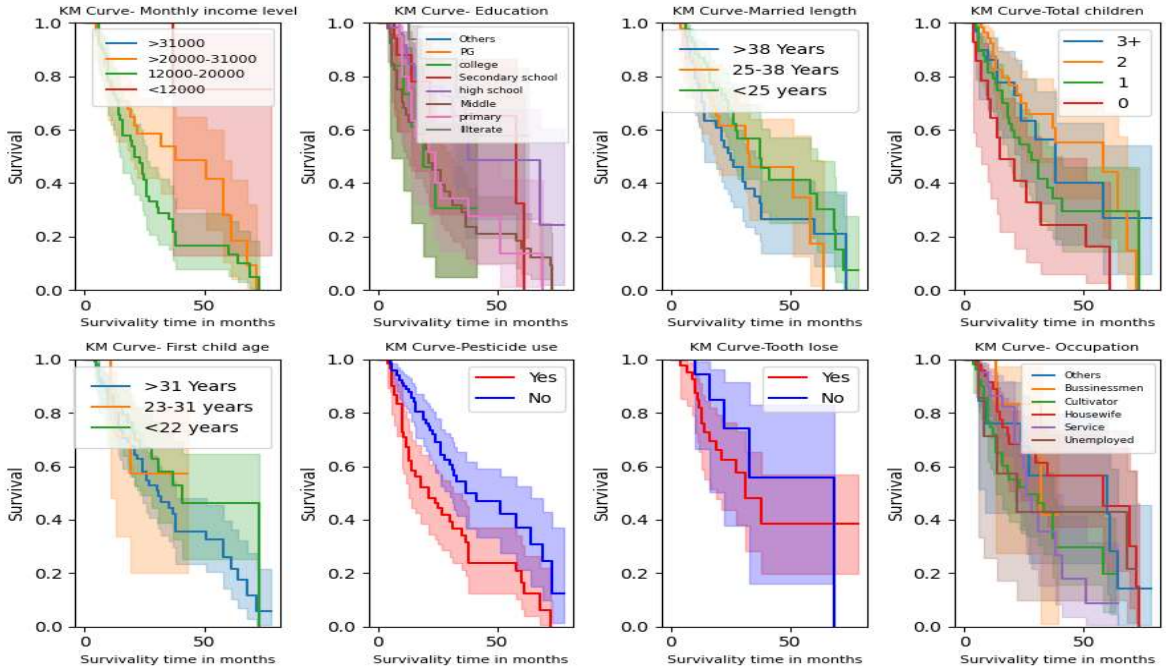
Figure 1(a) is a representation of Kaplan–Meier curves based on sociodemographic characteristics, while Figure 1(b) represents survivability based on lifestyle-related exposures. These figures illustrate a comparison of survival rates among the significant variables observed in the multivariable Cox analysis. The exposures (red line) that were significantly associated with the disease showed lower survival rates than those without exposure.

Figure 2 illustrates survival over time based on the Kaplan–Meier curve and reveals that the first mortality occurred at the end of the 4th month. During this period, the survivability was 99.5%. By the end of the 1st year, the survivability further decreased to 81.4%. Over the consecutive years, the rate further declined to 60.7% in the second year, 42.9% in the 3rd year, 35.5% in the 4th year, and 28.5% in the 5th year, and at the end of the sixth year, survival reached only 13.1%.

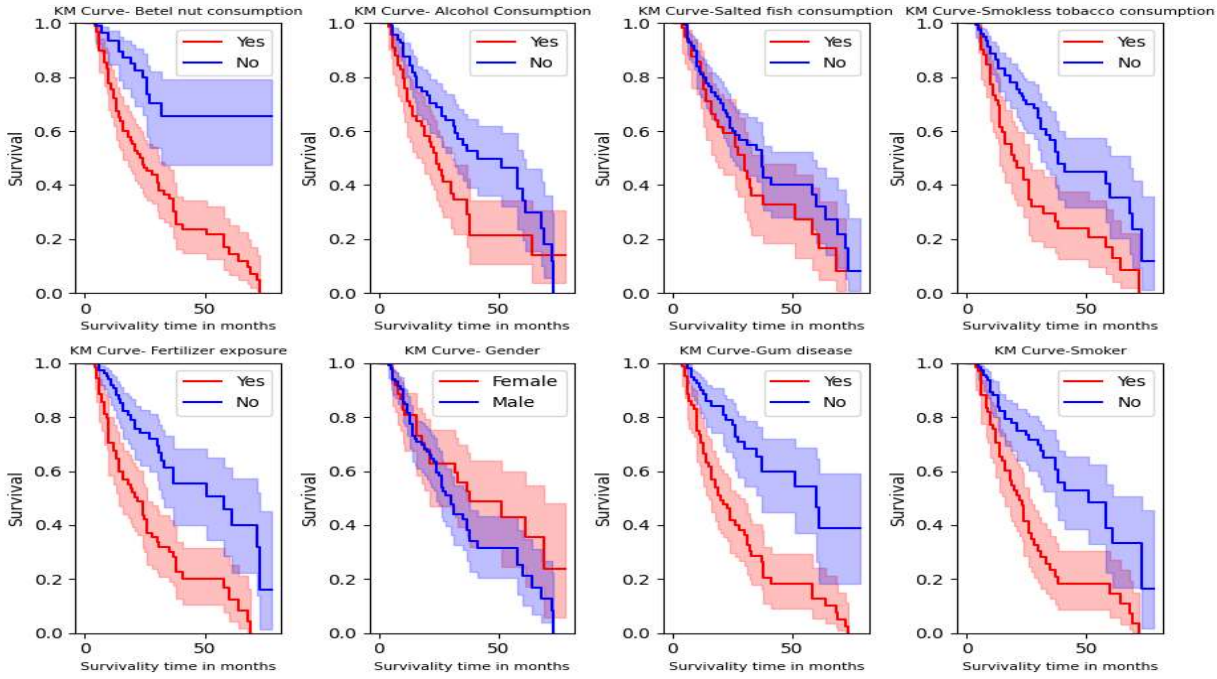
Association of comorbidity and mortality due to the exposures:

Table 3 presents the relationship between comorbidity status and mortality proportion among the investigated esophageal cancer patients. The mortality

proportion was highest among the participants who consumed betel nut, for both with (79%) and without (87.9%) comorbidities. Among those with comorbidities, fertilizer exposure, and periodontal/gum disease, both together showed the second highest proportion of mortality (76.3%). Conversely, participants who had only two children in their families had the lowest proportion of mortality with comorbidities (15.6%). The group who had "First child aged less than 22 years" showed the lowest proportion of mortality in the group without comorbidities (17.9%). The study found smoking habits (p-value 0.043) and exposure to fertilizer (p-value 0.012) independently associated with comorbidities-related death among esophageal cancer patients.



(a)



(b)

Figure 1 (a, b): Kaplan–Meier survival curve based on the significant covariates in the hazard regression model

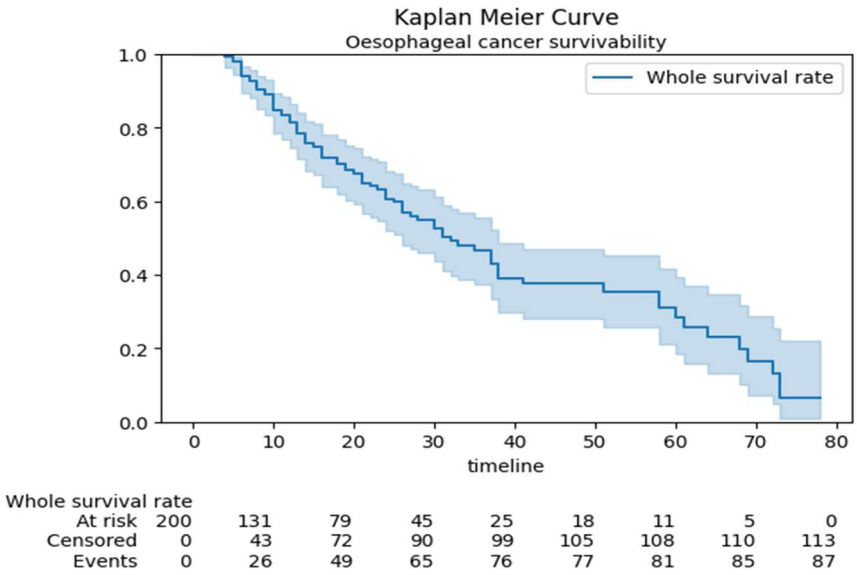


Figure 2: Kaplan–Meier curve for survival probability over time

DISCUSSION

At the time of this study, research has been scarce at the local level aimed at understanding the effect of multiple exposures on mortality risk. Most studies have focused primarily on the risk factors associated with the incidence of cancer. These past studies lacked a comprehensive approach to studying the effect of multiple exposures on mortality risk across different dimensions of life. To address this gap in previous studies, the present study investigated the effect of multiple exposures in a more comprehensive manner tailored toward understanding at the local level.

Overall, the study concluded that 34.5% of the mortality risk from the disease can be prevented in females if the findings showing evidence of their association with the disease are accounted for, while in males, the rate is 64.5%. By investigating the effect of multiple exposures on mortality risk, the current study identified several exposures that directly influence mortality risk. For instance, the findings of income and its association with mortality align with past studies, which show that socioeconomic disparities, encompassing low income, play a substantial role in cancer disparity. Typically, low socioeconomic status may be associated with lower utilization of screening facilities and advanced stages of the disease[13]; consequently, access to advanced treatments is compromised, impacting patient survival[14]. Limited availability of healthcare facilities in rural settings and low levels of health literacy among the lower socioeconomic group, coupled with lower awareness about the symptoms of the disease and lifestyle choices among different groups of the population, make the situation even worse for the low-income population.[15-19] The risk of incidence of betel nut, a lifestyle choice among the indigenous population, has been previously investigated, but as a risk factor for mortality, this topic has yet to be properly explored. The present study provides evidence of their association. The carcinogenic potential of betel nuts was explored in one study conducted in Taiwan. Based on saliva samples from betel nut consumers, traces of potent carcinogens, such as 3-methyl nitrosamine propionitrile, and other compounds, such as safrole-type DNA adducts, were found in the samples.[20-21] Furthermore, the presence of the mutagenic and genotoxic alkaloid arecoline in betel nut also poses a contributing risk factor for this disease.[22-28] The effect of aging was also explored in the present study, and a positive association was observed. Zarean et al. (2018) explored gender as a risk factor for mortality among the Iranian population and noted a greater mortality risk among males than females. The consumption behaviour of women, which was less correlated with lifestyle factors such as smoking, tobacco use, and alcohol consumption, could account for the lower mortality risk observed among females.[29] Tooth loss is a risk factor for mortality, and many previous studies have linked this risk. Poor oral hygiene, poor dentition, lack of access to dental services, etc., are certain contributors to tooth loss.[30-33] The mechanism of poor oral hygiene may be the accumulation of bacteria and overgrowth of microorganisms in the affected parts and their surroundings, which convert nitrates into nitrites and then to amines, ultimately forming carcinogenic nitrosamines.[34-36]

Smokeless tobacco consumption as a hazard risk has been investigated; this habit is more common among the population of India[37] than the use of snuff, and the same is observed in the state of Assam. Smokeless tobacco (ST) use can lead to addiction and various health issues, such as oral leukoplakia, gingival recession, and damage to the oral mucosa, potentially resulting in inflammation and lesions in the esophagus, leading to significant morbidity and mortality.[38]

Table 3: Proportion of death due to the presence of comorbidities

Variables	No comorbidities* Death (%)	Comorbidities* Death (%)	Total death (%)	P value
Family income 10000-20000				
No	27 (79.4)	44 (83.1)	71 (81.6)	0.671
Yes	7 (20.6)	9 (16.9)	16 (18.4)	
Smokeless tobacco consumer				
No	16 (47.1)	29 (54.7)	45 (51.7)	0.485
Yes	18 (52.9)	24 (45.3)	42 (48.3)	
Salted fish consumer				
No	21 (61.8)	33 (62.3)	54 (62.1)	0.962
Yes	13 (38.2)	20 (37.7)	33 (37.9)	
Alcohol Consumption				
No	21 (61.8)	24 (45.3)	45 (51.7)	0.522
Yes	13 (38.2)	29 (54.7)	42 (48.3)	
Smoker				
No	19 (55.9)	18 (34)	37 (42.5)	0.043
Yes	15 (44.1)	35 (66)	50 (57.5)	
Education				
Illiterate	2 (5.9)	2 (3.8)	4 (4.6)	
Primary School	6 (17.6)	9 (17)	15 (17.2)	
Middle School	15 (44.1)	22 (41.5)	37 (42.5)	
High school	5 (14.7)	11 (20.8)	16 (18.4)	0.979*
Secondary School	3 (8.8)	3 (5.7)	6 (6.9)	
College	2 (5.9)	4 (7.5)	6 (6.9)	
Other	1 (2.9)	2 (3.8)	3 (3.4)	
Fertilizer use				
No	18 (52.9)	14 (26.4)	32 (36.8)	0.012
Yes	16 (47.1)	39 (73.6)	55 (63.2)	
Pesticide use				
No	17 (50)	26 (49.1)	43 (49.4)	0.931
Yes	17 (50)	27 (50.9)	44 (50.6)	
Gum/periodontal disease				
No	13 (38.2)	14 (26.4)	27 (31)	0.245
Yes	21 (61.8)	39 (73.6)	60 (69)	
Betel nut consumer				
Non-Chewer	4 (12.1)	11 (20.4)	15 (17.4)	0.323
Chewer	29 (87.9)	43 (79.6)	72 (82.6)	
Gender				
Male	22 (64.7)	40 (75.5)	62 (71.3)	
Female	12 (35.3)	13 (24.5)	25 (28.7)	0.278
Tooth lose >4				
No	19 (59.4)	22 (40)	41 (47.2)	
Yes	13 (40.6)	33 (60)	46 (52.8)	0.08
Occupation cultivator				
No	23 (67.6)	35 (66)	58 (66.7)	0.876
Yes	11 (32.4)	18 (34)	29 (33.3)	
Married length>38 years				
No	27 (79.4)	35 (66)	62 (71.3)	0.178
Yes	7 (20.6)	18 (34)	25 (28.7)	
FCA less than 22 years				
No	23 (82.1)	32 (63.3)	55 (71.4)	0.115
Yes	5 (17.9)	17 (34.7)	22 (28.6)	
Number of children only two				
No	30 (71.4)	38 (84.4)	68 (74)	0.142
Yes	12 (29.6)	7 (15.6)	19 (26)	

*Fisher exact test

Smoking as a mortality risk was explored by Menon et al. (2014). This study examined the roles of current smokers, ex-smokers, and never-smokers in esophageal cancer, noting a decreasing hazard risk from current smokers to ex-smokers and then to never-smokers. The hazard risk for current smokers was 1.41 (95% CI: 0.63–3.16), and for ex-smokers, it decreased to 0.69 (95% CI: 0.32–1.45). The use of periodontal disease as a risk factor for disease has been investigated, and periodontal disease is linked to disease mortality.[39] In the United Kingdom, Michaud et al. (2008) reported a hazard risk of death of 1.44 with a 95% CI in the range between 0.98 and 2.11, suggesting an increased risk of mortality due to periodontal/gum disease, without reaching statistical significance.[40] However, the findings of the present study demonstrated a significant association between periodontal disease and mortality (HR 2.34,

95% CI 1.009-9.008), corroborating the results of Nwizu et al. (2017).[31]

A statistically significant correlation between pesticide exposure and the risk of mortality was observed in this study. The mechanism likely involves DNA and chromosomal damage caused by pesticide ingestion, leading to genotoxic effects and potential carcinogenesis. Animal studies also suggest that oxidative stress due to pesticide consumption is a contributing factor. Severe esophageal injury from pesticide ingestion can result in lumen stricture or decreased esophageal motility, causing esophageal stasis and chronic inflammation, which can lead to carcinogenesis.[41] Knekt et al. (1999) reported that the consumption of salted fish increased the risk of mortality by 2.58 times.[42] Similarly, the present study revealed a significantly greater risk of mortality among esophageal cancer patients who consumed salted fish, indicating that salted fish pose a serious health risk in the context of this study. Choi et al. (2017) conducted a cohort study among the South Korean population and observed that consumption of mild to moderate alcohol the risk increases the mortality risk by 1.52 times, while heavy drinkers are associated with a hazard of 3.13 times greater risk of death from esophageal cancer when compared to the non-drinkers.[43]

Thrift et al. (2012) compared drinkers with lifelong non-drinkers of alcohol and reported that those who consumed 7 to 20 drinks per week and more than ≥21 drinks per week had hazard risks of 2.21 (95% CI in the range of 1.27 to 3.84) and 2.08 (95% CI in the range of 1.18 to 3.69), respectively.[44] The study also revealed that traditional alcoholic drinks as a risk of esophageal cancer incidence, and Menya et al. (2019) reported this association in Kenya. However, their association needs to be further investigated.[45]

In terms of survival, the first mortality event occurred within 4 months, resulting in a survival rate of 99.95%. Subsequently, the survival rate showed a declining trend over time, reaching 84.50% at the end of the first year after diagnosis, 60.2% at the end of the second year, 42.9% at the end of the third year, 35.5% at the end of the fourth year, 28.50% at the end of the fifth year, and 13% at the end of the sixth year. Chen et al. (2017) reported a decrease in the survival rate from 52% to 22% from the first to third years. Their study on survivability based on several categories of treatment strategies revealed that the median survival time was 2.46 years (95% CI: 1.98–2.96 years) for patients who opted for surgery as a treatment procedure, 0.85 years (95% CI: 0.82–0.95 years) for those who received definitive chemotherapy, and 0.61 years (95% CI: 0.54–0.76 years) for those who received supportive and palliative treatment.[46] Similarly, Mahbobe et al. (1973) reported a median survival rate of 9 months, with first-year, third-year, and fifth-year survivability rates of 23%, 15%, and 13%, respectively.[47] Another study by Saddoughi et al. (2019) investigated the survival rate of patients aged <=45 years relative to those aged >=45 years and reported rates of 89.9%, 53.7%, and 44.5% for the first year, third year, and fifth year, respectively, in the <=45 years group. However, for the >=45 years age group, the percentages were 79.2%, 50.2%, and 39.1%, respectively.[48]

The findings of these studies suggest that there is a decline in survivability over time. In these studies, the survivability was found to be as high as 89% (Saddoughi et al., 2019)[48] for the first year and as low as 23% (Mahbobe et al., 1973).[47] The higher survival rate noted by Saddoughi et al. (2019) is attributed to the better response of the younger population to therapy compared to that of the older population, who face additional health challenges over time. Furthermore, the older group was less likely to pursue treatment, as recommended by radiologists and oncologists.[46]

Limitations

In the present study, a lack of understanding about the duration of certain lifestyle habit choices may weaken the association of evidence. In addition, the information obtained was based on self-administered questionnaires, and there may be response bias. This limitation needs to be accounted for in future studies.

Conclusion

In conclusion, this investigation identified several risk factors that independently and in combination significantly decrease the likelihood of survival, and these risk factors need to be further investigated. These factors are strongly linked to mortality risk among the investigated population, and they have been unaccounted for in past studies at the local level. Therefore, to strengthen the findings of this study, future research must focus on understanding these risk factors more thoroughly by incorporating them and delving more into the specific region under investigation. In addition, the decrease in the survival rate observed over time underscores the poor quality of life among patients. To comprehend this finding, efforts must be made to provide screening facilities through health checkups at regular intervals and to increase awareness of these risk factors. An increase in quality of life also needs to be considered. Emphasis should be placed on educating people and discouraging the availability of harmful products. These steps are crucial for limiting disease incidence and mortality and improving health outcomes.

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REFERENCES

1. Sobti RC, Thakur M, Kaur T. Cancer: Epidemiology, Racial, and Geographical Disparities. InMolecular Biomarkers for Cancer Diagnosis and Therapy. Springer Nature Singapore. 2024 Jun 30:31-52.
2. Teng Y, Xia C, Cao M, Yang F, Yan X, He S, Cao M, Zhang S, Li Q, Tan N, Wang J, Chen W. Esophageal cancer global burden profiles, trends, and contributors. Cancer Biol Med. 2024 Jul 26;21(8):656–66.
3. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012: Globocan 2012. Int J Cancer. 2015;136(5):E359-86.
4. American Cancer Society. Cancer facts and statistics. https://cancerstatisticscenter.cancer.org/#!/ cancer-site/Esophagus. Accessed December 11, 2023.
5. Stabellini N, Chandar AK, Chak A, et al. Sex differences in esophageal cancer overall and by histological subtype. Sci Rep. 2022;12(1):5248.
6. Tella SH, Mara K, Chakrabarti S, Jin Z, Mahipal A. A glimpse into the future of esophageal carcinoma in the United States: predicting the future incidence until 2040 based on the current epidemiological data. J Gastrointest Oncol. 2023 Feb 28;14(1):1-10. doi: 10.21037/jgo-22-729.
7. Lu SW, Niu KY, Pai CP, Lin SH, Chen CB, Lo YT, Lee YC, Seak CJ, Yen CC. Novel Prediction Score for Arterial-Esophageal Fistula in Patients with Esophageal Cancer Bleeding: A Multicenter Study. Cancers (Basel). 2024 Feb 16;16(4):804.
8. Qu HT, Li Q, Hao L, Ni YJ, Luan WY, Yang Z, Chen XD, Zhang TT, Miao YD, Zhang F. Esophageal cancer screening, early detection and treatment: Current insights and future directions. World J Gastrointest Oncol. 2024 Apr 15;16(4):1180-1191
9. Zhu J, Xu B, Li Y, Pang X, Ji S, Lian J, Lu H. Epidemiology, prognostic factors, and survival analysis in small cell esophageal carcinoma: A population-based study with external validation. Biomol Biomed. 2024 Sep 3. doi: 10.17305/bb.2024.11090
10. Ashok, A., Jiwnani, S., Karimundackal, G., Pramesh, C.S. (2024). Esophageal Cancer. In: Badwe, R.A., Gupta, S., Shrikhande, S.V., Laskar, S. (eds) Tata Memorial Centre Textbook of Oncology. Springer, Singapore. Doi: 10.1007/978-981-99-3378-5_36
11. Park K, Ali A, Kim D, An Y, Kim M, Shin H. Robust predictive model for evaluating breast cancer survivability. Eng Appl Artif Intell. 2013;26(9):2194–205. Available from: http://dx.doi.org/10.1016/j.engappai.2013.06.013
12. Marabotto E, Pellegatta G, Sheijani AD, Ziola S, Zentilin P, De Marzo MG, et al.Prevention strategies for esophageal cancer-an expert review. Cancers (Basel). 2021;13(9):2183. Doi: 10.3390/cancers13092183
13. Warren Andersen S, Blot WJ, Lipworth L, Steinwandel M, Murff HJ, Zheng W.Association of race and socioeconomic status with colorectal cancer screening, colorectal cancer risk, and mortality in southern US adults. JAMA Netw Open. 2019; 2(12): e191 7995. Doi: 10.1001/jamanetworkopen.2019.179 95
14. Tasnim, Sadia & Sudarshan, Monisha. (2024). Identifying and improving disparities in esophageal cancer care: a narrative review. 10.21037/ccts-23-24.
15. Kim S, Kwon S, Subramanian SV. The impact of socioeconomic status on survival after cancer in the United States: findings from the National Program of Cancer Registries Patterns of Care Study 12. 2015;26:1617–25.
16. Tewari M. Cancer Care in India. Indian J EndocSurg Res 2022; 17(1):1–3.
17. Dessalegn B, Getachew S, Yirgu R, Enqueselassie F, Assefa M, Addissie A. Time intervals from first symptom recognition to pathological diagnosis among patients with oesophageal cancer in Ethiopia: a cross-sectional study. BMJ Open. 2022 Aug 4;12(8):e060812. doi: 10.1136/bmjopen-2022-060812.
18. Sandström N, Johansson M, Jekunen A, Andersén H. Socioeconomic status and lifestyle patterns in the most common cancer types-community-based research. BMC Public Health. 2023;23(1):1722. Doi.org/10.1186/s12889-023-16677-6
19. Housten AJ, Gunn CM, Paasche-Orlow MK, Basen-Engquist KM. Health literacy interventions in cancer: A systematic review. J Cancer Educ. 2021;36(2):240–52. Doi: 10.1007/s13187-020-01915-x
20. Chen PH, Mahmood Q, Mariottini GL, Chiang TA, Lee KW. Adverse Health Effects of Betel Quid and the Risk of Oral and Pharyngeal Cancers. Biomed Res Int. 2017;2017:3904098. doi: 10.1155/2017/3904098.
21. Chen CL, Chi CW, Chang KW. Safrolelike DNA adducts in oral tissue from oral cancer patients with a betel quid chewing history. Carcinogenesis. 1999;20:2331–4.
22. IARC Monographs Vol 128 group. Carcinogenicity of acrolein, crotonaldehyde, and arecoline. Lancet Oncol. 2021 Jan;22(1):19-20. doi: 10.1016/S1470-2045(20)30727-0.
23. Ashek Elahi Noor, Boyapati Ramanarayana, Relationship of smokeless tobacco uses in the perspective of oral cancer: A global burden, Oral Oncology Reports, Volume 10, 2024, 100516, ISSN 2772-9060 Doi: 10.1016/j.oor.2024.100516.
24. Zisis Kozlakidis, Io Hong Cheong, Hui Wang; Betel Nut and Arecoline: Past, Present, and Future Trends. Innovations in Digital Health, Diagnostics, and Biomarkers 1 January 2022; 2 (2022): 64–72
25. Xie, H., Jing, R., Liao, X. et al. Arecoline promotes proliferation and migration of human HepG2 cells through activation of the PI3K/AKT/mTOR pathway. Hereditas 159, 29 (2022).
26. Sun H, Yu W, Li H, Hu X, Wang X. Bioactive Components of Areca Nut: An Overview of Their Positive Impacts Targeting Different Organs. Nutrients. 2024; 16(5):695
27. Muthukumaran, R. B., Bhattacharjee, P., Bhowmick, P., Zote, L., Malsawmtluangi, Kumar, N. S., Jahau, L., Cooke, M. S., Hu, C. W., & Chao, M. R. (2023). Genetic and epigenetic instability induced by betel quid associated chemicals. Toxicology reports, 10, 223–234.
28. Saikia JR, Schneeweiss FH, Sharan RN. Arecoline-induced changes of poly-ADP-ribosylation of cellular proteins and its influence on chromatin organization Cancer-Lett. Cancer-Lett. 1999;139:59–65.
29. Zarean E, Azizmohammad Looha M, Amini P, Mahmoudi M, Azimi T. Factors affecting long-survival of patients with esophageal cancer using non-mixture cure fraction model. Asian Pac J Cancer Prev. 2018;19(6):1677–83. Doi: 10.22034/APJCP.2018.19.6.1677
30. Meyer MS, Joshipura K, Giovannucci E, Michaud DS. A review of the relationship between tooth loss, periodontal disease, and cancer. Cancer Causes Control. 2008;19(9):895–907. Doi: 10.1007/s10552-008-9163-4
31. Nwizu N, Wactawski-Wende J, Genco RJ. Periodontal disease and cancer: Epidemiologic studies and possible mechanisms. Periodontol 2000. 2020; 83(1): 213–33. Doi: 10.1111/prd.12329
32. Ji Zhang, Rino Bellocco, Gunilla Sandborgh-Englund, Jingru Yu, Margaret Sällberg Chen, Weimin Ye; Poor Oral Health and Esophageal Cancer Risk: A Nationwide Cohort Study. Cancer Epidemiol Biomarkers Prev 1 July 2022; 31 (7): 1418–1425. Doi:10.1158/1055-9965.EPI-22-015121.1
33. Zhang S, Yu P, Wang J-B, Fan J-H, Qiao Y-L, Taylor PR. Association between tooth loss and upper gastrointestinal cancer: A 30-year follow-up of the Linxian Dysplasia Nutrition Intervention Trial Cohort. Thorac Cancer. 2019;10(4):966–74. Doi: 10.1111/1759-7714.13037

34. Peterson LA. Formation, repair, and genotoxic properties of bulky DNA adducts formed from tobacco-specific nitrosamines. J Nucleic Acids. 2010 Sep 5;2010:284935. doi: 10.4061/2010/284935.

35. Bernard R, Fazili I, Rajagopala SV, Das SR, Hiremath G. Association between Oral microbiome and esophageal diseases: a state-of-the-art review. Dig Dis. 2022; 40: 345–354

36. Chiang HC, Hughes M, Chang WL. The role of microbiota in esophageal squamous cell carcinoma: A review of the literature. Thorac Cancer. 2023 Oct; 14(28): 2821-2829. doi: 10.1111/1759-7714.15096.

37. The health consequences of using smokeless tobacco: Report of the Advisory Committee to the Surgeon General. NIH Publication No. 86-2874. Bethesda, MD: US Department of Health and Human Services. Public Health Service. 1986;

38. Gupta, J., Gupta, K. K., Samadi, F. M., & Kabiraj, A. (2012). Smokeless tobacco and oral cancer: A review. *Indian J Oral Sci*, *3*(2), 74-78.

39. Menon S, Nightingale P, Trudgill N. Is hormone replacement therapy in post-menopausal women associated with a reduced risk of oesophageal cancer? United European Gastroenterol J. 2014;2(5):374–82. Doi: 10.1177/ 2050640614543736

40. Michaud DS, Fu Z, Shi J, Chung M. Periodontal disease, tooth loss, and cancer risk. Epidemiol Rev. 2017;39(1):49–58. Doi: 10.1093/epirev/mxx006

41. Mu H-W, Chen C-H, Yang K-W, Pan C-S, Lin C-L, Hung D-Z. The prevalence of esophageal cancer after caustic and pesticide ingestion: A nationwide cohort study. PLoS One. 2020; 15(12): e0243922. Doi: 10.1371/journal.pone.0243922

42. Knekt, P., Järvinen, R., Dich, J., & Hakulinen, T. (1999). Risk of colorectal and other gastro-intestinal cancers after exposure to nitrate, nitrite and N-nitroso compounds: a follow-up study. *International journal of cancer*, *80*(6), 852–856. Doi: 10.1002/(sici)1097-0215(19990315)80:6<852::aid-ijc9>3.0.co;2-s

43. Choi YJ, Lee DH, Han KD, Kim HS, Yoon H, Shin CM, Park YS, Kim N. The relationship between drinking alcohol and esophageal, gastric or colorectal cancer: A nationwide population-based cohort study of South Korea. PLoS One. 2017 Oct 3;12(10):e0185778. doi: 10.1371/journal.pone.0185778.

44. Thrift AP, Nagle CM, Fahey PP, Russell A, Smithers BM, Watson DI, et al. The influence of prediagnostic demographic and lifestyle factors on esophageal squamous cell carcinoma survival. Int J Cancer. 2012;131(5). Doi: 10.1002/ijc.27420

45. Menya D, Kigen N, Oduor M, Maina SK, Some F, Chumba D, et al. Traditional and commercial alcohols and esophageal cancer risk in Kenya. Int J Cancer. 2019;144(3):459–69. Doi: 10.1002/ijc.31804

46. Chen M-F, Chen P-T, Lu M-S, Lee C-P, Chen W-C. Survival benefit of surgery to patients with esophageal squamous cell carcinoma. Sci Rep. 2017;7(1). Doi: 10.1038/srep46139

47. Mahboubi E, Kmet J, Cook PJ, Day NE, Ghadirian P, Salmasizadeh S. Oesophageal cancer studies in the Caspian littoral of Iran: The Caspian cancer registry. Br J Cancer. 1973;28(3):197–214. Doi: 10.1038/bjc.1973.138

48. Saddoughi SA, Taswell J, Spears GM, Harmsen WS, Allen MS, Blackmon SH, et al. Patients younger than 45 years of age have superior 5-year survival in advanced esophageal cancer. Shanghai Chest. 2019;3:42–42. Doi: 10.21037/shc.2019.07.01