

TEMPORAL ANALYSIS OF ESOPHAGEAL CANCER MORTALITY IN THE BRAZILIAN STATE OF THE AMAZON REGION; AMAPÁ (2012- 2021)

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Abstract: Goal: This study aims to analyze the temporal trend of mortality from esophageal cancer between 2012 and 2021 in a state in the Amazon region of Brazil: the state of Amapá. **Methods:** This time series included the mortality rate from esophageal cancer, by year, according to location, by federative unit, reported in the Online Atlas of Mortality of the National Cancer Institute (INCA), from 2012 to 2021. The search followed the underlying cause coded in the ICD-10 Category in C15 (malignant neoplasm of the esophagus). The data extracted from the information system were for the variables: year of occurrence (2012-2021), sex (male and female) and age group (30-39; 40-49; 50-59; 60-69; equal to or greater than 80). **Results:** the study in the State of Amapá between 2012 and 2021 recorded 103 deaths from esophageal cancer, predominantly among men (90.3%) and in the age group of 60-69 years (33.01%). The average mortality rate was alarming, reaching 3,116 per 100,000 inhabitants, with significant variation over time. Men had an average mortality rate 5.63 higher than that of women (0.601). **Conclusion:** Temporal analyses revealed an increase in the mortality rate from esophageal cancer in Amapá, while in Brazil there was an opposite trend, indicating advances in preventive measures and treatments at the national level. The association between alcoholism and esophageal cancer highlights the need for public policies and effective interventions to reduce these risks, indicating the importance of continuous epidemiological surveillance and the implementation of preventive strategies to control cases of esophageal cancer in the population. Evidence of the need for targeted interventions in relation to esophageal cancer is a premise for the formulation of public health policies adapted to the specific characteristics of each region.

Keywords: esophageal cancer; mortality; risk

factors; epidemiology; temporal trend.

INTRODUCTION

Millions of people are diagnosed with cancer every year. Data from the 2020 Global Cancer Observatory (apud MORGAN, E. et.al, 2020) linked to the World Health Organization (WHO) estimate that by 2040, 30.2 million new cases of the disease may arise. Among the various types of cancer, malignant neoplasia of the esophagus has a high incidence and constitutes an important cause of morbidity and mortality in the world population. In 2020, there were 604,100 cases of esophageal cancer recorded, with 544,076 deaths attributed to the disease (GLOBOCAN, 2020 apud MORGAN, E. et.al, 2020). In Brazil, the National Cancer Institute (INCA) points to esophageal cancer as the 5th cancer with the highest mortality rate in men, accounting for 5.5% of all cancer deaths in this population. For the North region of the country, esophageal cancer was described with an incidence rate of 2.28/1,000 inhabitants for 2023, considered the lowest value among the five national regions (INCA, 2023).

Clinically, esophageal cancer is classified into squamous cell carcinoma, the most common, and adenocarcinoma (SUZUKI et al., 2023). Its risk factors include socioeconomic and behavioral aspects, such as smoking, alcoholism, obesity, consumption of hot beverages, micronutrient deficiencies, increased consumption of red meat and processed foods (UHLENHOPP et al., 2020; ZHAO; LIM, 2020).

In addition, there are also some uncommon dietary risk factors, such as the intake of salty foods and beverages, non-piped drinking water, and foods with a high glycemic index (GHOSH; JONES, 2022). Associations with other clinical conditions are also evidenced, such as Barrett's esophagus pathology, gastroesophageal reflux disease and viral and

bacterial infections, such as HPV, Epstein-Barr, polyoma and *Helicobacter pylori* (EL-ZIMAITY et al., 2018; UHLENHOPP et al., 2020).

Recent epidemiological analyses of cancer indicate that economic and social factors in low- and middle-income countries are determining factors in increasing exposure to risk factors that predispose to cancer. Therefore, understanding the dynamics of cancer incidence and mortality in populations is an essential strategy for directing health actions and evaluating the efficiency of current interventions (BRAY et al., 2012; SILVA et al., 2020). For this reason, considering the magnitude of the disease in Brazil and worldwide and its different dynamics over time, this study aimed to analyze the trend in mortality from esophageal cancer in the state of Amapá, from 2012 to 2021.

A risk factor indirectly indicates the chance of contracting a disease, and different types of diseases present different risk factors (AMERICAN CANCER SOCIETY, 2020). Some, such as smoking, can be controlled; others, such as age and family history, cannot. Although risk factors can influence the development of cancer, most do not directly cause the disease. (AMERICAN CANCER SOCIETY, 2020)

To have one or even several risk factors does not imply the objective consolidation of the disease, since many people who contract the disease may not be subject to any known risk factors. If a person with esophageal cancer has a risk factor, it is often very difficult to know how much this factor may have contributed to the development of the disease. (AMERICAN CANCER SOCIETY, 2020).

The chance of contracting esophageal cancer increases with age, with less than 15% of cases being diagnosed in people under the age of 55. In addition, men are more likely to develop this disease compared to women.

Another important factor is the consumption of tobacco products, such as cigarettes, cigars, pipes and chewing tobacco, which doubles the risk of esophageal adenocarcinoma compared to non-smokers. Alcohol consumption also increases the risk, especially of squamous cell cancer. In addition, people with gastroesophageal reflux or Barrett's esophagus have a higher risk of developing adenocarcinoma. In this case, the presence of dysplasia in the glandular cells can develop into cancer. Finally, obesity is a risk factor, as it is associated with increased gastroesophageal reflux (AMERICAN CANCER SOCIETY, 2020).

Other risk factors include diet, physical activity and certain specific medical conditions. For example, a diet rich in fruits and vegetables can reduce the risk of esophageal cancer, while a diet rich in processed meat and frequent consumption of very hot liquids can increase it (AMERICAN CANCER SOCIETY, 2020). Regular physical activity, in turn, can reduce the likelihood of adenocarcinoma. Regarding medical conditions, people with achalasia have a slightly higher risk, usually diagnosed 15 to 20 years after the diagnosis of achalasia. In addition, tylosis, a rare hereditary disease, increases the risk of squamous cell carcinoma and requires medical monitoring. Esophageal webs associated with Plummer-Vinson syndrome also increase the risk. Injuries to the esophagus caused by corrosive agents such as caustic soda can lead to cancer decades after the injury. In addition, a history of other cancers, such as lung, mouth and throat, and HPV infection in certain regions of the world, are factors that increase the risk of esophageal cancer.

With special regard to alcoholism, a case-control study conducted by Jozala (1983) in order to understand the relationship between alcoholism, smoking and esophageal cancer concluded that the relative risk of developing

esophageal carcinoma in relation to alcoholism was 26.7 (statistically significant), reinforcing the idea of an association between alcoholism and esophageal cancer. Menezes (2007) points out that if there were a total elimination of smoking, it would lead to the prevention of 54% of esophageal cancer.

Another study conducted by Gimeno (1995), pointing out the results of the multivariate analysis, suggests that alcohol and smoking are independent risk factors for the disease. Suggesting that there is an evident dose-response relationship for the different levels of exposure to smoking and drinking strengthens the hypothesis that these factors play an important role in the etiology of this disease.

METHODS

This is a time series study dedicated to analyzing the trend in mortality from malignant esophageal neoplasm in the State of Amapá, drawing comparisons with the national scope. Amapá, located in the Amazon region, in the north of Brazil, has an estimated population of 877,613 people and a Human Development Index (HDI) of 0.740, according to data from 2021 (*Companhia de Desenvolvimento dos Vales do São Francisco e do Parnaíba* - CODEVASF, 2021). It borders the state of Pará to the south, with its several islands with riverside communities and indigenous Amazonian peoples. To the north, east and west, it has international borders with French Guiana and Suriname. These geographic borders give Amapá not only a strategic position, with a rich cultural and natural diversity, but also a reference position in health services, concentrated mainly in the city of Macapá, the state capital. The mortality rate from esophageal cancer, by year, according to location, by federative unit, reported in the INCA Online Mortality Atlas, from 2012 to 2021, were included. The search

followed the underlying cause coded in the ICD-10 Category in C15 (malignant neoplasm of the esophagus). The data extracted from the information system were for the variables: year of occurrence (2012-2021), sex (male and female) and age group (30-39; 40-49; 50-59; 60-69; equal to or greater than 80). The data obtained were organized and analyzed using the Python 3.10.12 language, using the library: Pandas 2.0.3. Matplotlib 3.7.3 and Sklearn 1.2.2

For the trend analyses of this time series, the simple linear equation model was used with the variables 'mortality rate from esophageal cancer' (dependent variable) and 'years evaluated' (independent variable). Furthermore, for comparative purposes, it was decided to analyze the rates of the dependent variable at the local and national levels (State of Amapá and Brazil), in the same time interval.

The analyses were also tested in polynomial, quadratic, cubic and exponential models. After that, given the consistency of the results, the simple linear method was adopted. The equation adopted in the general polynomial model of the time series was: $Y^{\wedge} = \beta_1 X + \beta_0$; where Y^{\wedge} represented the mortality rate from esophageal cancer for each year (2012-2021) determined in X, β_1 represents the angular coefficient of the model, that is, the slope of the line. The significance level adopted in the F test of analysis of variance was $p \leq 0.05$ and all rates were expressed per unit of 100,000 inhabitants.

RESULTS AND DISCUSSION

Between 2012 and 2021, 103 deaths (n=100%) from esophageal cancer were recorded in the State of Amapá. Of these, 93 were male, representing 90.3% of the total number of cases; only 9.7% (n=10) of deaths were female.

The predominant age group among deaths

from esophageal cancer in the State of Amapá (2012-2021) was among individuals aged 60-69 years (33.01%, n=34). For those aged 30-39, there was only one death in the period (0.97%), for those aged 40-49, 12 deaths (11.65%), for those aged 50-59, 17 were recorded (16.50%), for those aged 70-79, 29 (28.15%), and, finally, for those aged over 80, this was the case for 9.71% (n=10) of the total.

During the period studied, the average general mortality rate was 3,116 per 100,000 inhabitants, with a standard deviation of $\pm 2,831$, indicating a considerable variation in mortality rates over time.

When comparing the mortality averages between men and women, a significant difference was observed. Men had an average mortality rate of 5.63, with a standard deviation of ± 1.615 , while for women, the average rate was 0.601, with a standard deviation of ± 0.514 .

Statistical analysis using Student's t-test demonstrated a p-value of 2.356, indicating statistically significant differences between the groups of men and women.

Figure 1 shows the dynamics of mortality rates during the study period, and it is possible to distinguish the increasing trend of the general mortality rate for men and the stationary rate in the female population.

In contrast to Amapá, when observing the data for Brazil (2012-2021), the analysis of the data, in general, it is possible to see that mortality rates decreased throughout the period studied, both for men and women (Figure 1), indicating possible advances in preventive measures or treatments, although, similar to Amapá, it reveals significant patterns of mortality and disparities between men and women.

The results also indicated that in Brazil the predominant age group among deaths in Brazil was 60 to 69 years old, representing 30.33% of the total deaths recorded. 30 to 39 being 886 (1.1%), 40 to 49 being 6,674 (8%),

50 to 59 20,809 (25.1%), 60 to 69 being 25,146 (30.33%), 70 to 79 being 18,206 (21.9%), 80 or over 11,268 (13.6%). The distribution of deaths by age group revealed an increasing trend with advancing age, following a pattern similar to that of Amapá (Figure 2).

The average overall mortality rate in Brazil observed was 7,364, with a standard deviation of 4,542, indicating significant variability in the data. When disaggregating by gender, a striking disparity is observed: while the average mortality rate for men reaches 11,757, with a standard deviation of 0.78, for women, this value is considerably lower, with an average of 2,972 and a standard deviation of 0.255.

The difference between the means is statistically significant, as indicated by the p-value of the Student's t-test, which was found to be 9.517, suggesting a strong association between gender and the mortality rate from esophageal cancer. These results highlight the importance of differentiated prevention and treatment strategies, adapted to the specific characteristics of each population group, aiming to reduce the impact of this public health condition.

The data also indicate that it is possible to demonstrate that men tend to have higher mortality rates in all age groups, with more pronounced differences in the older age groups. This suggests the need for more effective preventive measures, especially among older men, who appear to be more vulnerable to esophageal cancer.

These results highlight the importance of differentiated prevention and treatment strategies, adapted to the specific characteristics of each population group, aiming to reduce the impact of this public health condition. The data also indicate that it is possible to demonstrate that men tend to have higher mortality rates in all age groups, with more pronounced differences in the

Esophageal cancer mortality rate, comparison between Amapá and Brazil (2012-2021)

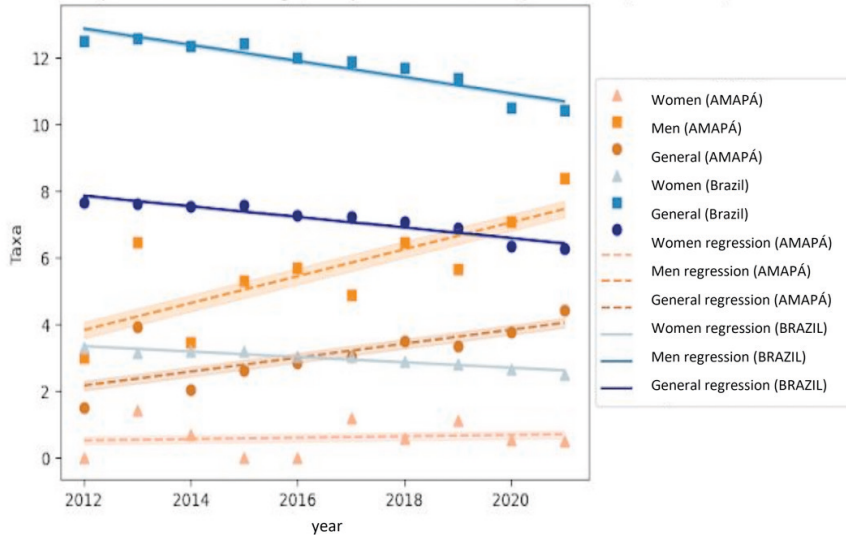


Figure 1: Esophageal cancer mortality rate in Amapá and Brazil by gender (2012-2021)
Source: the authors, 2023.

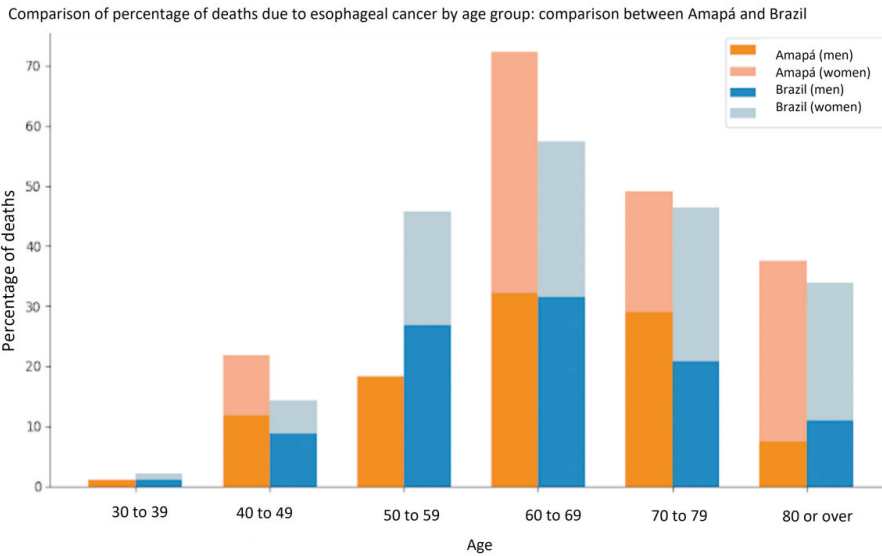


Figure 2: Percentage distribution of esophageal cancer mortality by age group: Comparison between Brazil and Amapá (2012-2021)
Source: the authors, 2023.

Age	Men (Amapá)	Women (Amapá)	Men (Brazil)	Women (Brazil)
30 to 39	1.08	0	1.09	0.98
40 to 49	11.83	10	8.73	5.63
50 to 59	18.28	0	26.81	18.97
60 to 69	32.26	40	31.53	25.96
70 to 79	29.03	20	20.91	25.57
80 or over	7.53	30	10.93	22.89

Table 1: Percentage distribution by age group and sex, comparison between Brazil and Amapá
Source: the authors, 2023.

older age groups. This suggests the need for more effective preventive measures, especially among older men, who appear to be more vulnerable to esophageal cancer.

When we compare Brazil and Amapá more objectively, in relation to the age range of deaths, although there are similarities in the predominant age range (60-69 years) between the two scenarios, Amapá presents a more uniform distribution across age ranges, with a relatively lower proportion of cases in older age groups compared to Brazil. This may indicate differences in the age structure of the population and in exposure to specific risk factors in each region.

When comparing the percentages of deaths from esophageal cancer among men and women in the state of Amapá relative to Brazil (Table 1), we can observe distinct patterns in different age groups. Notably, men in Amapá have a higher mortality rate in almost all age groups compared to men in Brazil. For example, in the age group of 50 to 59 years, the mortality rate among men in Amapá is significantly higher (18.28%) than in Brazil (26.81%), suggesting a possible disparity in risk factors or in the effectiveness of preventive measures. Furthermore, women in Amapá, although they have a lower mortality rate than men, still face challenges related to older age groups, with these rates being higher for women in Amapá when compared to other regions of Brazil. Although they have a lower mortality rate than men, they still face challenges, especially in older age groups, where mortality rates are higher compared to women in other regions of Brazil.

When examining the data by age group, it is evident that gender disparities in esophageal cancer mortality persist in both contexts, both in Amapá and in Brazil as a whole (Table 1). However, it is important to note that the differences in mortality rates between the two settings vary across different age groups. For

example, while women in Amapá face higher mortality rates than women in Brazil in the age group 80 years and older, this trend is not observed across all age groups.

This analysis highlights the need for targeted prevention and intervention strategies, tailored to the specific characteristics of each region and demographic group, aiming to reduce the impact of esophageal cancer and improve population health outcomes.

CONCLUSIONS

Data analysis reveals a comprehensive picture of esophageal cancer mortality, highlighting distinct patterns between men and women, as well as between different age groups. In the state of Amapá, between 2012 and 2021, an average overall mortality rate of 7,364 per 100,000 inhabitants was observed, with significant variability in rates over time. The disparity between genders is notable, with men presenting an average mortality rate of 11,757 per 100,000 inhabitants, in contrast to the average of 2,972 per 100,000 inhabitants for women. This difference is statistically significant, indicating a strong association between gender and the esophageal cancer mortality rate.

Furthermore, the analysis of the distribution by age group reveals that the 60-69 age group is the most affected, accounting for 33.01% of registered deaths. In comparison, younger age groups have relatively lower proportions of cases. However, it is important to note that, although the overall mortality trend is increasing, especially among men, the mortality rate in the period studied decreased in Brazil as a whole, indicating advances in preventive measures or treatments. The comparison between Brazil and Amapá reveals differences in the distribution of deaths by age group, suggesting variations in the age structure of the population and in the exposure to specific risk factors in each region.

These results point to the need for differentiated prevention and treatment strategies, considering the gender disparities in mortality from esophageal cancer, but paying special attention to groups of greater vulnerability, such as older men. Understanding these mortality patterns is crucial to inform targeted and effective public health policies, aiming to reduce the impact of esophageal cancer and improve health outcomes for the population.

The figures observed in the gender variable show that there is a significant difference in mortality rates between men and women, both in Amapá and in Brazil. This suggests the need for differentiated prevention and treatment strategies for each gender group.

Regarding the analyses of temporal trends, they show that, while mortality rates from esophageal cancer in Brazil decreased over the period studied, this trend was not observed

in Amapá. This highlights the importance of investigating the reasons behind these differences and implementing measures to reverse this trend in the state.

The results highlight the importance of preventing esophageal cancer, especially through controlling risk factors such as smoking, alcohol consumption, obesity and diet. Early identification of conditions such as Barrett's esophagus is also essential to reduce the risk of developing esophageal cancer. Finally, this work highlights the importance of continued research on the epidemiology of esophageal cancer, including analyses of temporal trends and regional comparisons, in order to improve the implementation of screening programs, public education on risk factors and equitable access to health services, in addition to being a fundamental part of organizing the health care network in the spheres of complexity in this studied region.

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