Epidemiology Of Hospitalizations For Malignant Pancreatic Neoplasm In Brazil

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ABSTRACT

Introduction: Pancreatic cancer is one of the most lethal tumors because it develops in a silent manner, without specific signs, so that when it is diagnosed, many patients are already in advanced stages. Pancreatic ductal adenocarcinoma is the most common primary malignant neoplasm and the most aggressive type of the disease. This exocrine tumor corresponds to 90% of the diagnosed cases and affects mostly the head of the organ. Its risk factors are smoking, obesity and diabetes. Objective: To determine the epidemiology of hospitalizations for malignant neoplasm of the pancreas in Brazil from 2015 to 2021. Methodology: This is an epidemiological, quantitative, and retrospective study, with data collection in DATASUS, by consulting the SUS Hospital Admissions System (SIH/SUS) http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sih/cnv/nrmg.def of the Brazilian Ministry of Health. The numbers of hospitalizations, age group, gender, regimen, character of care, and deaths were analyzed. Results: We identified 80,960 hospitalizations for malignant neoplasm of the pancreas during the years 2015 to 2021. According to the age range, 24.42% of cases are between 50-59 years and 32.14% between 60-69 years. Furthermore, according to the hospitalizations by gender, there was a slight predominance of males with 50.38%. The mortality rate in Brazil was 23.97. As for the type of care, most of the cases were urgent (71.4%), private (5.47%), and the average total length of stay was 7.3 days. Conclusion: We conclude that pancreatic neoplasms are more prevalent among men, with an increasing incidence after 50 years of age. Therefore, avoiding risk factors can help prevent the disease, and early diagnosis is still a difficulty in the medical environment.

Keywords: Epidemiology, Pancreatic cancer, Hospitalizations.

1 INTRODUCTION

Cancer is one of the leading causes of death and a major barrier to increased life expectancy in every country in the world. According to estimates by the World Health Organization (WHO) in 2019, cancer is the first or second leading cause of death before the age of 70 in 112 out of 183 countries. In 2020, there was an estimate of 19.3 million new cancer cases and 10 million deaths worldwide. For pancreatic neoplasm, there were 495,773 new cases and 466,003 deaths.(SUNG *et al.,* 2021)

The highest age-standardized incidence is seen in Europe and North America, and the lowest in Africa and South Central Asia (MCGUIGAN *et al.,* 2018). According to *Cancer Research UK*, pancreatic cancer is the tenth most common cancer in the UK and has increased its incidence by approximately 10% in the last ten years. It is predicted that pancreatic neoplasm will soon overtake breast cancer as the third

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leading cause of cancer death in the European Union. In the United States, it is projected to become the second leading cause of death in the next twenty to thirty years.(MIZRAHI *et al.,* 2020)

According to the National Cancer Institute (INCA) (2022), Brazil is expected to register 704,000 new cases of cancer in each year of the triennium 2023-2025, among them, 10,980 new cases of pancreatic cancer, which represents a little more than 1% of all cancers diagnosed, and accounts for 5% of all deaths from the disease.

Most pancreatic cancers are characterized as ductal adenocarcinoma (about 90%) and therefore represent the malignancy of the exocrine pancreas, while a minority represent neuroendocrine tumors. Most ductal adenocarcinomas arise from precursor lesions, named pancreatic intraepithelial neoplasms, which progress through a gradual process in which they acquire genetic alterations and thereby culminate in the development of ductal adenocarcinoma. The molecular progression from grade 1 and 2 intraepithelial neoplasms to ductal adenocarcinoma are characterized, in about 90%, by point mutations in the KRAS oncogene (MIZRAHI *et al.,* 2020).

Approximately 60 to 70 percent of exocrine pancreatic cancers are located in the head of the organ, while 20 to 25 percent are in the body or tail, and the remainder involve the entire pancreas. When compared to tumors located in the body or tail of the gland, tumors in the head of the pancreas most often present with jaundice, steatorrhea, and weight loss (MIZRAHI *et al.,* 2020).

Modifiable risk factors associated with the development of pancreatic cancer include type 2 diabetes, tobacco use, diet with high intake of saturated fat and/or meat, particularly smoked or processed meats, and alcohol.(MIZRAHI *et al.,* 2020) The estimated fraction of the population in which tobacco is attributed as a cause of death from pancreatic cancer is 11 to 32 percent. In several cohort and case-control studies, the relative risk of developing pancreatic cancer among smokers was at least 1.5, and it is estimated that quitting smoking could eliminate approximately 25 percent of pancreatic cancer deaths in the United States. On obesity and physical inactivity, studies show that a BMI of at least 30 kg/m^2 was associated with a significantly increased risk of pancreatic cancer compared with a BMI of less than 23 kg/m^2 , and that overweight and obese individuals develop pancreatic cancer at a younger age than normal-weight patients, and that they also have lower rates and shorter survival duration when pancreatic cancer is diagnosed.(CASTILLO; JIMENES, 2022).

There are also hereditary risk factors, where approximately 5 to 10 percent of individuals with pancreatic cancer have a family history of the disease. Peutz-Jeghers syndrome, which results from a mutation in the tumor suppressor gene STK11 (also known as LKB1), results in a 35 percent increased risk of developing pancreatic cancer. Similarly, hereditary breast and ovarian cancer syndrome, most commonly attributed to mutations in the BRCA1 or BRCA2 genes; germline mutations in CDKN2A (familial atypical multiple melanoma); and mutations in genes important for DNA damage response (e.g., ATM) and DNA repair (e.g., LKB1).: ATM) and DNA repair (MLH1, MSH2, MSH6 as seen in Lynch syndrome, PALB2) are also associated with the risk of developing pancreatic malignancy (MIZRAHI *et al,* 2020).

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Chronic pancreatitis is a well-known risk factor for the development of pancreatic cancer, with a 40% lifetime risk of this type of cancer in patients with hereditary pancreatitis syndromes associated with mutations in SPINK1 and PRSS1.(MIZRAHI et al., 2020)

In 2010, the International Consortium for Pancreatic Screening (CAPS) was formed to help organize guidelines for pancreatic cancer screening, and included several experts from different countries. In 2011, the group agreed that screening was not recommended for the general population because the incidence risk was low (1.3% lifetime risk), but on the other hand, it was recommended for individuals considered to be at high risk (lifetime risk >5%), with family history being the main determinant. Consensus was not reached for the age to start screening or discontinue surveillance. It was agreed that initial screening should include endoscopic ultrasound and/or magnetic resonance imaging/magnetic resonance cholangiopancreatography (CANTO, *et al.,* 2013). In 2018, CAPS reconvened, and they decided not to change the surveillance goals (identify high-grade dysplastic precursor lesions and T1N0M0 pancreatic cancer), but agreed that for those with familial risk, surveillance should not begin until age 50 or 10 years of the youngest relative with pancreatic cancer, but were split on whether to begin at age 50 or 55. (GOGGINS, *et al.,* 2020). However, it is worth noting that screening is not recommended by INCA.

Surgical resection is the only potentially curative treatment. But unfortunately, because of late presentation of signs and symptoms, only 15 to 20 percent of patients are candidates for pancreatectomy (CASTILLO, 2022). The disease often causes few or no symptoms before progressing to advanced stages. And usually, those who do develop symptoms have nonspecific complaints - epigastric or back pain, nausea, bloating, abdominal fullness, or change in stool consistency - symptoms often attributed to alternative, benign causes, which can delay diagnosis (MIZRAHI *et al.,* 2020).

Thus, the 5-year survival rate is only 5% (INCA, 2022). This value varies according to the stages of the disease, and in localized disease (restricted to the pancreas) is 37%, in regional disease (involvement of lymph nodes and nearby structures) is 12%, and distant disease (involvement of areas far from the pancreas) is 3% (AMERICAN CANCER SOCIETY, 2020).

Therefore, the present study aims to determine the epidemiology of hospitalizations for malignant pancreatic neoplasms in Brazil.

2 METHODOLOGY

This is a retrospective, descriptive, quantitative, documentary-based study with comparative-statistical procedure. Its research universe was the database of the SINASC/TABNET system developed by DATASUS, regarding the epidemiology of pancreatic cancer occurring in Brazil, in the period from January 2015 to December 2021. The data were obtained from TABNET, an application developed by DATASUS, thus making available the information from the databases of the Unified Health System at the electronic address (http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sih/cnv/nrmg.def).

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Data collection occurred in January 2023 using the SINASC program (TABNET). The tabulation of the records found for the research included studied variables, which were: sociodemographic (age range and sex) and clinical (number of pancreatic malignancies per year and region; character of care; mortality rate; as well as the costs of hospitalizations and deaths).

A descriptive analysis of the variables was performed, with frequency, percentage, and average number of cases recorded. *Microsoft Office Excel® software was* used for data management and analysis.

Considering that the research was based on data made available electronically by the Ministry of Health, which are in the public domain, and due to the fact that there is confidentiality about the identification information inherent to the human beings involved, this study does not require the review and approval of the Research Ethics Committee.

3 RESULTS

In the period from January 2015 to December 2021, a total of 80,960 hospitalizations for malignant neoplasm of the pancreas were recorded in Brazil. The number ranged from 8,819 to 14,865, with an average of 11,566 cases. It is observed that each year there was an increase in the amount of hospitalizations when comparing with the previous year, with a greater increase in the year 2019 (13.76%).**(Figure 1).**

Figure 1: Number of hospitalizations for malignant neoplasm of pancreas in Brazil, 2015 to 2021.
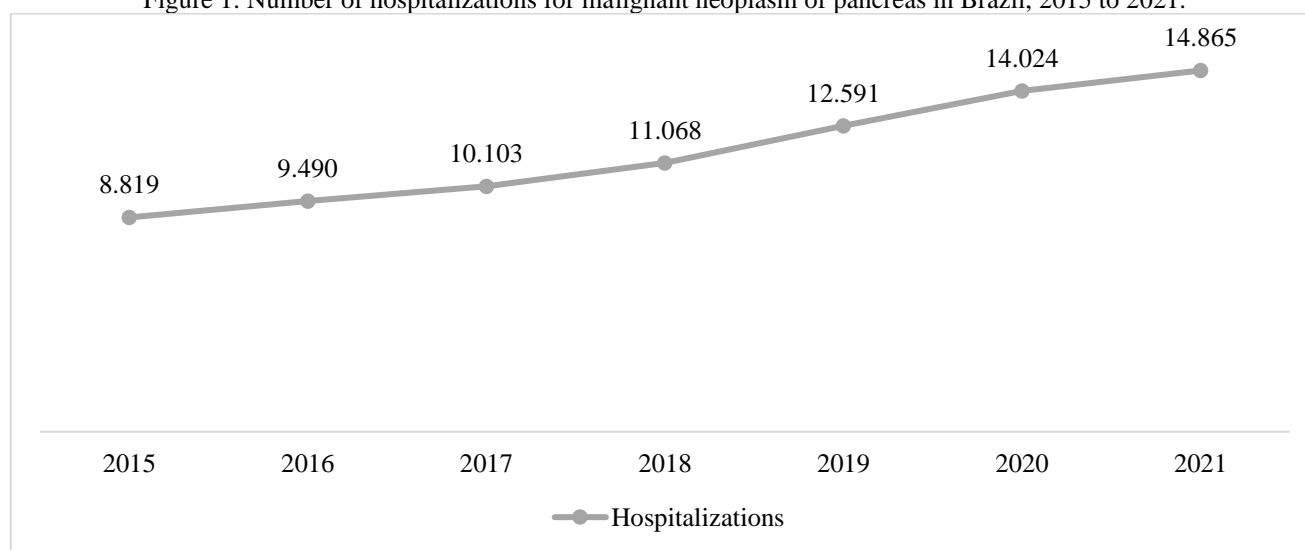
Source: Ministry of Health - SUS Hospital Information System (SIH/SUS).

In reference to the distribution of hospitalizations for pancreatic cancer according to the regions of the country, there was a greater number of notifications in the Southeast (n. 39,217/48.4%) and South (n. 20,939/25.9%) regions. The mortality rate in Brazil was 23.97, being higher in the North (28.31) and Southeast (24.63) regions **(Figure 2).**

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Figure 2: Number of hospitalizations and mortality rate for malignant neoplasm of pancreas in Brazil, 2015 to 2021.
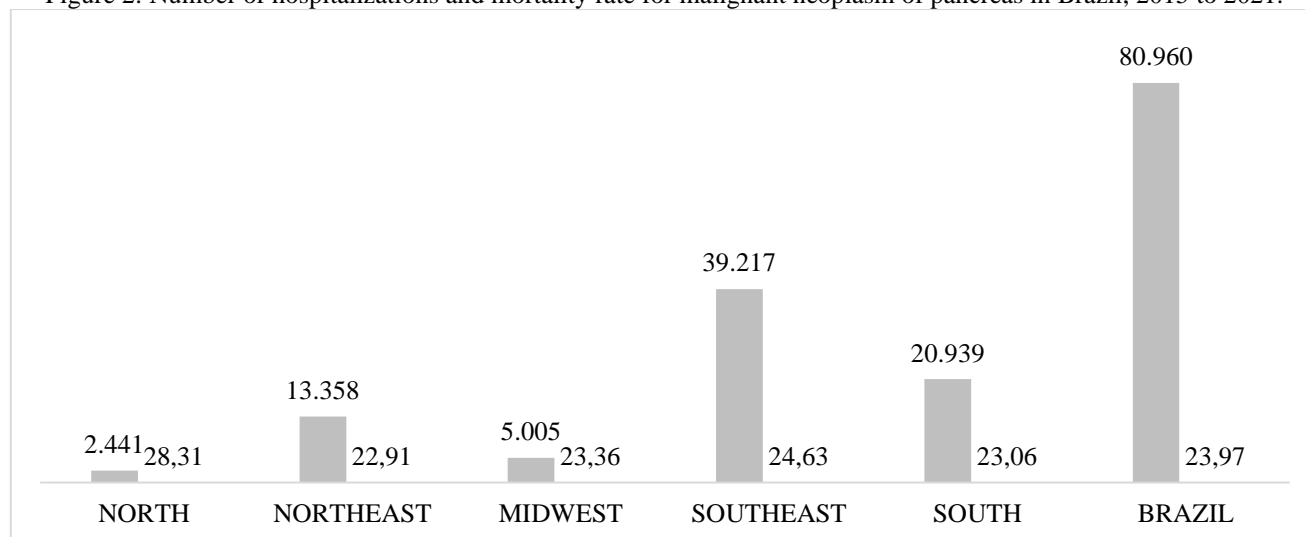
Source: Ministry of Health - SUS Hospital Information System (SIH/SUS).

Regarding the sociodemographic and clinical data of patients, there is a predominance of hospitalizations for pancreatic cancer in the age groups 50 to 59 years (n. 19,775/ 24.42%) and 60 to 69 years (n. 26,024/ 32.14%). There was no significant difference between genders (0.76% more for males). As for the type of care, most of the cases were urgent (n. 57,803/ 71.4%), in the private system (n. 4,430/ 5.47%) and the average total stay was 7.3 days, being higher in the public system with 10.6 days versus 7 days in the private system. Moreover, in the period analyzed there were 19,408 deaths.

As for the expenses related to pancreatic cancer, the total amount was 164,602,374.88 reais, of which 5.87% went to private institutions, 3.48 to public ones, and 90.65% were ignored **(Table 1).**

Variables	Total Hospitalizations	% Hospitalizations
Total	80.960	**100**
Age Group		
Less than 10 years old	136	**0,17**
10 to 14 years old	159	**0,20**
15 to 19 years old	239	**0,30**
20 to 29 years old	847	**1,05**
30 to 39 years old	2.495	**3,08**
40 to 49 years old	7.908	**9,77**
50 to 59 years old	19.775	**24,42**
60 to 69 years old	26.024	**32,14**
70 to 79 years old	17.153	**21,19**
80 years and older	6.224	**7,69**
Sex		
Male	40.788	**50,38**
Female	40.172	**49,62**
Regime		
Public	2.915	**3,6**
Private	4.430	**5,47**
Ignored	73.615	**90,92**
Character		
Elective	26.157	**28,6**
Urgency	57.803	**71,4**
Deaths		
Deaths	19.408	**100**
Average Stay		

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Public	10,6	
Private	7,0	
Ignored	7,2	
Total	7,3	
Total Value		
Public	5.731.522,58	**3,48**
Private	9.661.811,87	**5,87**
Ignored	149.209.040,43	**90,65**
Total	164.602.374,88	**100**

4 DISCUSSION

A significant and gradual increase in the number of hospitalizations for pancreatic cancer is observed during the period analyzed in Brazil. When comparing the years 2015 to 2021, an increase of 68.5% in the number of hospitalizations is evident.

Analyzing the distribution of hospitalizations for pancreatic neoplasms according to the regions of Brazil, there is a higher number of notifications in the Southeast (48.4%) and South (25.9%), this is due to the fact that the highest incidences are found in more developed countries and regions, which can be attributed to lifestyle (MCGUIGAN *et al.,* 2018). The mortality rate was high in Brazil (23.97), in the period analyzed, being higher in the North (28.31) and Southeast (24.63) regions, a fact that may be related to the fact that the North region has less development and difficulty in access to health services and the Southeast region for having the highest numbers of cases.

According to INCA (2022), the estimated number of new cases of pancreatic cancer is 10,980, of which 5,290 in men (48.18%) and 5,690 in women (51.82%). Although pancreatic cancer is not among the leading cancers in incidence, it ranks seventh in mortality in men and fifth in women, according to INCA (2020), with an estimated 11,893 deaths, 5,552 in men and 6,011 in women.

Pancreatic cancer is one of the tumors that causes most mortality. In this sense, the American Cancer Society estimates that in 2023, about 64,050 people will be diagnosed with pancreatic cancer, 33,130 men (51.7%) and 30,920 women (48.3%), with approximately 50,550 deaths, which represents 3% of all cancers in the United States and about 7% of all cancer deaths.(AMERICAN CANCER SOCIETY, 2019). The results presented in this study showed a similar relationship to Brazil between the years 2015 to 2021, with regard to gender, with the prevalence in males being 50.38% and 49.62% in females.

Pancreatic cancer is typically a disease of old age. It is extremely rare for patients to be diagnosed before the age of 30, and 90% of newly diagnosed patients are over the age of 55, with most in their seventh and eighth decade of life.(MCGUIGAN *et al.,* 2018). The data of the present study corroborates with those existing in the literature, given that, 85.44% of hospitalization cases occurred after the age of 50 years, suggesting that aging is a non-modifiable risk factor for the pathology.

The results revealed a significant number of emergency admissions (71.4%), in the private sector (5.47%) (of which 90.92% were ignored), with a mean length of stay of 10.6 days in the public sector and 7 days in the private sector.

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As for the expenses related to hospitalizations, the total value was 164,602,374.88 reais, of which 5.87% went to private institutions, and 90.65% were ignored.

A study that evaluated the epidemiology of pancreatic cancer in southern Brazil from 2010 to 2016 showed that the state of Rio Grande Sul had the highest number of cases among the states of the southern region, just as Porto Alegre was the southern capital that had the highest incidence of pancreatic cancer, followed by Curitiba and then Florianópolis. One of the hypotheses pointed out for the difference in incidence between the states is the amount of smokers in each one of them, since smoking is responsible for about 30% of the cases of the disease. Thus, Rio Grande do Sul is the state with the highest number of daily smokers in the population, 18.4%, followed by Paraná with 15.8% and Santa Catarina in seventh, with 15.1% (KUAIVA; CHIELLE, 2018).

Patients with a familial risk of pancreatic ductal adenocarcinoma are a potential target for screening. However, there is no consensus on the optimal age, the time interval at which screening should be performed, or the best imaging technique. Further retrospective and prospective studies that follow these patients with familial pancreatic cancer over time will help gain a better understanding of the course of this disease and allow for the introduction of effective methods of screening and treatment.(MCGUIGAN *et al.,* 2018).

Some limitations should be considered when evaluating the results of this study. The SIH-SUS data depict only publicly funded hospitalizations for malignant pancreatic neoplasia, it does not depict the totality of cases that occur in the entire population with pancreatic neoplasia.

Although there are limitations, the SIH/SUS database should be used in epidemiological studies because it represents the universe of publicly funded hospital admissions in Brazil and, when analyzed together with results from other sources, can subsidize the setting of policy plans and the allocation of public resources in a community (VERAS; MATHIAS, 2014).

5 CONCLUSION

The results of this study show an increase in the number of hospitalizations for malignant pancreatic neoplasms in Brazil in recent years. The highest number occurs in the Southeast and South regions, and they have high mortality rates. There was no significant difference between genders, and the age group with more hospitalizations was 60 to 69 years. The financial expenses, for the most part, were ignored, as well as the care regimen.

Thus, it is concluded that pancreatic cancer remains a devastating malignancy with limited effective treatment options. Improved patient outcomes will depend on multidisciplinary advances in imaging, surgical techniques, radiation, and therapies. And avoiding risk factors can help prevent the disease, and early diagnosis is still a difficulty in the medical setting.

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