Disparities on Pancreatic Cancer Mortality Trends and Human Development Index (HDI) in Brazil

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Abstract

Pancreatic cancer mortality is greatest in countries with a high and very high Human Development Index (HDI). The aim was to evaluate the pancreatic cancer mortality rates and trends related to HDI in Brazil by state. An ecological study was conducted on pancreatic cancer mortality in Brazilian states between 1979 and 2019. Age-standardized mortality rates (ASMR) and Annual Average Percent Change (AAPC) were calculated. Pearson's correlation test was applied to compare rates over the 3 decades from 1986-2015 to verify correlation between change in HDI from 1991 to 2010. A total of 209,425 deaths from pancreatic cancer were reported in Brazil from 1979 to 2019. In men, ASMRs ranged from 2.9/100,000 in 1979 to 6.1/100,000 in 2019, with AAPC of 1.5% per year, and in women, ASMR ranged from 2.1/100,000 in 1979 to 4.7/100,000 in 2019, with AAPC of 1.9% per year. Mortality rates and trends increase with higher % of HDI improvement with a correlation between ASMRs and HDI above $r>0.80$. The mortality trends in pancreatic cancer were uneven increase in Brazil, there was an upward trend in mortality in both genders, but higher among women. Pancreatic cancer mortality trends were higher in those states where there was greatest increase in HDI, regions as North and Northeast. However, mortality rates remain higher in South, Southeast and Central-West of Brazil.

Introduction

Pancreatic cancer is one of the most lethal malignant neoplasms worldwide, ranking 11th in number of cases and 7th in cancer-related deaths¹⁻³. An estimated 466,000 deaths were recorded in 2020 (1-2), with half (55.8%) from developed countries⁴. Projections from 2018 to 2040 regarding trends estimate a 79.9% (345,181) increase in deaths, been +114.8% in Africa, +101.0% in Latin America and the Caribbean while lower increment in rates were predicted for Europe (+31.6%)⁵. It has been anticipated this malignancy will surpass breast cancer as the third-cause of death by 2025 in 28 European countries⁶.

In Brazil, the highest mortality rates for pancreatic cancer were observed in the South and Southeast areas from 1980 to 1995⁷. There were 112,533 deaths, among men ranging from 4.2/100,000 in 2000 to 5.1/100,000 in 2014⁸. The prognosis of adenocarcinoma remains unclear, with no overall survival (OS) improvement in Brazil⁹.

Due to lethality the mortality incidence ratio is close to 98%, and more common among males, increases with age after 55^{3,10}. Differences in mortality of pancreatic cancer can be attributed to risk factors such as lifestyle (smoking, alcohol consumption, physical inactivity, obesity), diabetes, inherited genetic disorders and environmental exposures^{3,10-16}. Regarding morphological classification It can be classified in two groups: pancreatic adenocarcinoma, (85%) it involves exocrine glands having poor prognosis, with average 5-year survival of 9%; neuroendocrine tumor, accounts less than 5% and occurs in the endocrine glands with better survival³.

Some studies have described a correlation between high mortality rates of pancreatic cancer with high and very high HDI areas^{10-11, 17}, whereas lowest rates were found in low and medium HDI areas¹⁸. Mortality trends of pancreatic cancer in the Southeast Brazil showed a decline among women, having an inverse correlation with cancer mortality and HDI¹⁹.

However, there are few studies investigating trends in pancreatic cancer mortality in Brazil and HDI. This study aims to correlate pancreatic cancer mortality rates and trends and Human Development Index (HDI) in Brazil.

Methods

An ecological study of pancreatic cancer mortality was conducted in Brazil from 1979 to 2019 by state. Mortality data was taken from Mortality Information System publicly available in the website at the Ministry of Health²⁰ it includes deaths due to pancreatic cancers (ICD-9 code 157 for 1979-1995; ICD-10 code C25 for 1996-2019)²¹. Population data was obtained from Institute of Geography and Statistics²² while Human development index (HDI) was taken from the United Nations Development Program (UNDP)²³. HDI differences from 1991 to 2010 was calculated as percentage.

Age-standardized mortality rates were calculated by gender, and world standard population of Segi modified by Doll (1966). Mortality rate was smoothed using a 3-year average for 1979-2019 and calculated for three decades (1986-1995, 1996-2005 and 2006-2015). Age-specific mortality rates were calculated for the 5 geographical regions (North, Northeast, Central-west, Southeast and South) and Brazil.

The Annual Average Percent Change (AAPC) was estimated for mortality rates, except in females from Acre (North) and Tocantins (North), for which data collection started from 1989 onwards; it was calculated a linear regression model using the Joinpoint Regression software, version 4.9.0.0²⁴.

Two analyses were performed to evaluate pancreatic cancer mortality correlation: (1) correlation between the age-standardized pancreatic cancer mortality rates and HDI, in 3 periods for 10 years around the HDI. Being rates of period 1986-1995 for HDI 1991, 1996-2005 for HDI 2000 and 2006-2015 for HDI 2010 considering that the higher the correlation is, the higher the increase is; (2) percentage of difference in HDI from 1991 to 2010 versus AAPC.

Pearson's correlation test was applied using STATA version 15 (College Station, Texas, USA, 2017), with p-value <0.05 considered significant. A Brazilian map by state and regions was produced with mortality rates and HDI expressed in terciles by periods and plotted on Tabwin software. All the procedures were performed in accordance with the relevant guidelines and regulations.

Results

In Brazil about 209,425 deaths of pancreatic cancer were reported comprising 106,825 in men and 102,600 in women from 1979 to 2019 (Supplementary Table 1). Pancreatic cancer age-standardized mortality rates in men ranged from 2.9/100,000 in 1979 to 6.1/100,000 in 2019, with a 1.5% increase per year

(95% CI 1.3;1.6), while in women ranged from 2.1/100,000 in 1979 to 4.7/100,000 in 2019, with a 1.9% increase per year (95% CI 1.7;2.0) (Table 1, Supplementary Table 1). The highest mortality rates were in the South, Southeast and Central-West regions for both genders in 2006-2015 (Table 1, Figure 1).

Table 1
Age-Standardized Mortality Rates (ASMR) for pancreatic cancer and Average Annual Percentage Change (AAPC) among Brazil.

States	Male					Female									
	HDI			Percentage difference (HDI) 1991 to 2010	ASMR per 100,000 inhabitants					AAPC (95% CI) 1979-2019	ASMR per 100,000 inhabitants				
	1991	2000	2010		1986-1995	1996-2005	2006-2015	1979	2019		1986-1995	1996-2005	2006-2015	1979	2019
Brazil	0.493	0.612	0.727	47%	3.4	3.7	4.3	2.9	6.1	1.5 (1.3;1.6)	2.5	2.9	3.4	2.1	4.7
North															
Acre (AC)	0.402	0.517	0.663	65%	1.8	0.9	2.9	1.2	4.5	2.4 (0.7;4.1)	1.0	2.0	1.5	-	3.7
Amazonas (AM)	0.430	0.515	0.674	57%	1.5	2.4	3.3	1.1	4.7	4.4 (4.0;4.7)	1.3	1.5	3.0	0.6	3.3
Pará (PA)	0.413	0.518	0.646	56%	1.6	1.5	2.0	1.0	2.9	1.3 (0.8;1.9)	1.5	1.2	1.7	0.8	3.2
Rondônia (RO)	0.407	0.537	0.690	70%	1.8	2.6	2.9	3.0	5.6	3.9 (2.7;5.1)	1.9	2.2	2.4	0.1	6.1
Roraima (RR)	0.459	0.598	0.707	54%	1.8	3.5	2.9	0.1	7.4	5.4 (2.8;8.0)	1.8	1.3	3.9	0.1	3.8
Tocantins (TO)	0.369	0.525	0.699	89%	0.7	1.5	3.0	-	4.2	*	0.6	1.6	2.5	-	3.4
Northeast															
Alagoas (AL)	0.370	0.471	0.631	71%	1.0	1.2	2.5	1.1	2.8	3.4 (2.8;4.1)	0.9	1.2	1.8	0.5	3.5
Amapá (AP)	0.472	0.577	0.708	50%	3.2	3.2	2.6	2.2	2.4	0.4 (-0.6;1.4)	3.3	1.4	2.4	3.4	1.9
Bahia (BA)	0.386	0.512	0.660	71%	1.5	1.6	2.7	1.3	4.6	2.7 (2.2;3.2)	1.1	1.4	2.2	0.7	3.4
Ceara (CE)	0.405	0.541	0.682	68%	1.0	2.0	3.0	1.1	4.6	4.4 (3.9;4.9)	0.8	1.5	2.6	0.6	3.4
Maranhão (MA)	0.357	0.476	0.639	79%	0.6	0.9	1.9	0.4	2.4	5.3 (4.4;6.1)	0.5	0.7	1.8	0.1	2.3
Paraíba (PB)	0.382	0.506	0.658	72%	1.3	1.2	3.0	0.5	4.2	3.6 (2.7;4.5)	0.7	1.0	2.2	0.4	3.2
Pernambuco (PE)	0.440	0.544	0.673	53%	1.9	2.5	3.4	1.7	5.1	2.6 (2.2;2.9)	1.6	2.3	3.0	1.0	3.6
Piauí (PI)	0.362	0.484	0.646	78%	0.8	1.4	2.4	0.1	3.1	5.9 (5.2;6.5)	0.6	1.2	2.0	0.2	3.5
Rio Grande do Norte (RN)	0.428	0.552	0.684	60%	2.0	1.9	3.3			3.3 (2.7;3.9)	1.6	1.6	2.6		
Sergipe (SE)	0.408	0.518	0.665	63%	0.9	1.6	2.6	1.0	5.1	4.8 (3.7;5.9)	1.3	1.8	2.6	0.9	3.7
Central-West															
Distrito Federal (DF)	0.616	0.725	0.824	34%	6.0	5.5	5.1	4.1	9.1	0.3 (-0.1;0.7)	4.3	4.5	4.3	4.6	5.5
Goiás (GO)	0.487	0.615	0.735	51%	2.4	2.9	3.9	1.3	5.7	2.4 (2.1;2.8)	1.8	2.6	2.8	2.0	4.3
Mato Grosso (MT)	0.449	0.601	0.725	61%	1.8	3.1	3.5	0.8	4.8	4.1 (3.6;4.6)	1.5	2.2	2.8	0.1	4.0
Mato Grosso do Sul (MS)	0.488	0.613	0.729	49%	3.5	3.7	4.7	3.4	5.9	1.6 (1.2;1.9)	2.2	2.9	3.4	2.4	4.5

* Acre (North) had insufficient data for females, while Tocantins (North) lacked data for both genders.

Human Development Index (HDI). Confidence Interval (CI). AAPC in bold = p<0.05

					Male					Female						
Southeast																
Espírito Santo (ES)	0.505	0.640	0.740	47%	3.0	3.3	4.3	2.9	6.4	1.8 (1.4;2.3)	2.3	2.5	3.2	2.1	4.7	
Minas Gerais (MG)	0.478	0.624	0.731	53%	3.0	3.2	3.6	2.6	5.0	1.4 (1.2;1.7)	2.1	2.5	2.9	1.9	4.1	
Rio de Janeiro (RJ)	0.573	0.664	0.761	33%	4.4	4.4	4.7	4.8	6.7	0.5 (0.3;0.7)	3.3	3.3	3.7	2.8	4.7	
São Paulo (SP)	0.578	0.702	0.783	35%	3.3	4.1	5.4	2.4	7.7	2.5 (2.4;2.7)	3.4	4.0	4.1	3.3	5.7	
South																
Paraná (PR)	0.507	0.650	0.749	48%	4.5	5.0	5.7	3.6	7.9	1.2 (1.0;1.4)	3.2	3.7	4.3	2.5	5.6	
Rio Grande do Sul (RS)	0.542	0.664	0.746	38%	6.7	6.3	7.0	6.0	9.0	0.7 (0.5;0.9)	4.5	4.8	5.3	3.5	7.2	
Santa Catarina (SC)	0.543	0.674	0.774	43%	4.6	5.2	5.6	2.9	8.1	1.5 (1.2;1.7)	2.8	3.8	4.3	2.0	6.1	
* Acre (North) had insufficient data for females, while Tocantins (North) lacked data for both genders.																
Human Development Index (HDI). Confidence Interval (CI). AAPC in bold = p<0.05																

Age-specific mortality rates were highest in the 65-69 age group with the lowest rates observed in the North and Northeast, while the highest were observed in the South (Figure 2).

There was an increase in pancreatic cancer mortality trends (AAPC) in all states, with highest trends in North (Roraima, 5.4%) and Northeast (Piauí, 5.9%). The HDI from 1991 to 2010 increased unequally in Brazil, ranged from 54–89% in North, 50–79% in Northeast, while Southeast region varied from 33–53% and South 38–48% (Table 1).

A positive correlation ($r>0.80$) was observed between mortality rates and HDI over three decades in which the highest rates were observed the regions with the highest HDIs (Figure 3, Table 1).

Correlation was found between AAPC for pancreatic cancer mortality with percent increase in HDI from 1991 to 2010. In states with highest HDI, greater mortality trends were present ($r = 0.75$ men; $r=0.78$ women). The greatest increase in HDI was observed in Maranhão state (Northeast region) 79% associated with a 5.3% (95%CI 4.4;6.1) increase in mortality, and in Piauí state (Northeast region) AAPC of 78% with a 5.9% (95%CI 5.2;6.5) increase in mortality (Figure 4, Table 1).

Discussion

In Brazil pancreatic cancer mortality trends were higher in North and Northeast regions with greatest increase in HDI. There was a tendency toward increase in mortality in both genders, but higher among women.

The pancreatic cancer mortality rates observed in the period were similar to those seen in countries with very high HDI, as in Australia and China¹. South, Southeast and Central-West regions of Brazil, mortality rates were comparable to developed countries as New Zealand, United Kingdom and Iceland. Mortality rates in the North and Northeast were similar to El Salvador and Indonesia². There was a trend of increasing mortality among men, in Russia, Spain and Germany, but there was a decreasing trend among women^{10–11}, in contrast with present study found increased mortality among women in Brazil.

The North and Northeast showed the highest mortality trends for pancreatic cancer, which may be related to the improvement in the quality of notification of deaths¹⁹, in addition to the increase in the HDI. There are disparities among the diagnosis and treatment access for cancer in Brazil, South, Southeast and Central-West regions having higher HDIs and greater provision of healthcare facilities, compared to the North and Northeast²⁵.

The pancreatic cancer mortality increase it may be associated with urbanization and socioeconomic development as a result of lifestyle changes. Pancreatic cancer is an aggressive malignant neoplasm, and is also related to increased longevity, in some regions of the world it is predicted to become the second leading cause of death from cancer. Some studies have proposed to avoid modifiable risk factors including smoking, diabetes and obesity, as a strategy as consequence reduce mortality, due to lethality the mortality incidence ratio is close to 98%^{1,3,10–11,26}.

In Brazil, the smoking prevalence has been declined from 35% in 1990 to 11.3% in 2017²⁷. However, the consumption of alcoholic beverage has increased from 15.6% (2006) to 18.8% (2019) in men and 7.7–13.3% among women, in the Central-West, Southeast and South regions²⁸. The overweight prevalence increased from 43.2% in 2006 to 51.0% in 2012, with annual increase of 1.37% for both genders (1.62% for women), in the North, Northeast and Midwest regions the largest increment was observed. Obesity increased from 11.6–17.4% in all regions with highest increase among women from 11.8–18.2% (AAPC 1.04%)²⁹. The diabetes prevalence reduced 30% for men and 26% for women from 1990 to 2017³⁰. This rising pancreatic cancer mortality trend of may be

associated with an unknown risk factor, since there are differences in prevalence of risk factors between Brazilian regions^{28–32}, this could be the reason in disparities of the mortality rates.

South, Southeast and Central-West regions, had the highest HDI (0.724 to 0.825), also the highest mortality rates for pancreatic cancer (3.6 to 7.0). However, the North and Northeast had the greatest increases in HDI (50–89%) and in mortality trends in both genders. These results are in agreement with studies that found a positive correlation with higher pancreatic cancer mortality for both genders, in countries with very high HDI^{1,11,18}.

This study has limitations proper of ecological studies due to the impossibility of inferring causality at the individual level. Another limitation is the lack of information on histological type in mortality database precluding stratification in histological types. However, this study allows populational inferences regarding pancreatic cancer mortality in Brazil, and to analyses regional differences due to improvement of HDI over the period³³.

The mortality trends in pancreatic cancer were uneven increase in Brazil, there was an upward trend in mortality in both genders, but higher among women. Pancreatic cancer mortality trends were higher in those states where there was greatest increase in HDI, regions as North and Northeast. However, mortality rates remain higher in South, Southeast and Central-West of Brazil. For malignant neoplasms, such as pancreatic cancer, whose early diagnosis and treatment are still limited, prevention of associated risk factors remains the best strategy to reduce incidence and mortality.

Declarations

Author contributions

D.R.M.S.: conceptualization, data curation, formal analysis, writing—original draft, and writing—review and editing. M.M.O.: formal analysis, writing—review and editing. G.A.F.: conceptualization, writing—review and editing. M.P.C.: conceptualization, supervision, and writing—review and editing.

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Figures

Figure 1

Age-standardized mortality rates per 100,000 inhabitants for pancreatic cancer over three decades (1986-1995, 1996-2005, 2006-2015) by gender and tercile for Brazil.

Figure 2

Age-standardized specific mortality rates for pancreatic cancer by age group, gender in Brazil over three decades.

Figure 3

Correlation between average age-standardized mortality rates over three decades and Human Development Index (HDI, 1991, 2000 and 2010) based on gender, in Brazil. *p-value < 0.05.

Figure 4

Pancreatic cancer mortality correlation between average annual percentage change (AAPC) for and percentage increase of HDI in Brazil. *p-value < 0.05

Supplementary Files

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- [SupplementaryTable1.docx](#)