

Gastric Cancer Mortality in Ceará in Brazil's Northeastern, 2000-2022: Spatio-Temporal Study

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Mortalidade por Câncer Gástrico no Ceará, Nordeste do Brasil, 2000-2022: Estudo Espaço-Temporal

Mortalidad por Cáncer Gástrico en Ceará, Nordeste del Brasil, 2000-2022: Estudio Espacio-Temporal

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ABSTRACT

Introduction: In recent decades, the prevalence of gastric cancer (GC) has increased in Brazil's Northeastern, especially in the state of Ceará. **Objective:** To analyze temporal trends and spatial patterns of GC mortality over a 23-year period in Ceará. **Method:** All registered death certificates (DC) (GC registered as any cause of death) from 2000 to 2022 were included. Temporal trends were assessed by joinpoint regression models, while spatial patterns were assessed by spatial autocorrelation, using the local Moran index based on Local Indicators of Spatial Association (LISA). **Results:** GC was detected in 16,670 DCs (1.5% of all deaths). Age- and sex-adjusted mortality was 8.44/100,000 population. The highest mortality rates were found in the southern parts of the state and around a northern major urban center. Analysis over time showed a rising trend (Average Annual Percent Change: AAPC 1.2; 95%CI 0.6;2.1), especially in males (AAPC 1.6; 95%CI 1.1;2.1), individuals <45 years (AAPC 2.1;3.7), residents of the central region (AAPC 3.2, 95%CI 1.8;5.1) and high deprivation index municipalities (AAPC 2.6, 95%CI 1.3;5.0). Spatial-temporal clusters of high risk for GC-related mortality from 2000 to 2017 were identified, with no statistical significance in the period 2018-2022: clusters were identified in the south until 2011 and in the northwest from 2006 to 2017. **Conclusion:** GC mortality has increased in Ceará during the study period. High risk areas for GC mortality were identified, enabling focused integrated actions to strengthen prevention, diagnosis, surveillance and control networks.

Key words: Stomach Neoplasms/epidemiology; Demography/trends; Spatial Analysis; Epidemiology/trends; Mortality/trends.

RESUMO

Introdução: Nas últimas décadas, a prevalência de câncer gástrico (CG) tem aumentado no Nordeste do Brasil, especialmente no Estado do Ceará. **Objetivo:** Analisar tendências temporais e padrões espaciais da mortalidade por câncer gástrico, durante um período de 23 anos no Ceará. **Método:** Foram incluídas declarações de óbito (DO) registradas (CG registrado como qualquer causa de morte) de 2000-2022. Tendências temporais foram avaliadas por modelos de regressão *joinpoint*. Padrões espaciais foram avaliados por autocorrelação espacial, usando índice de Moran local com base nos Indicadores Locais de Associação Espacial (LISA). **Resultados:** O CG foi detectado em 16.670 DO (1,5% de todas as mortes). A mortalidade ajustada por idade e sexo foi de 8,44/100 mil habitantes. Taxas de mortalidade altas foram encontradas no Sul do Estado e em torno de um grande centro urbano no Norte. A análise ao longo do tempo mostrou uma tendência de aumento (Variação Percentual Anual Média [VPAM] 1,2; IC95% 0,6;2,1), em homens (VPAM 1,6; IC95% 1,1;2,1), pessoas com menos de 45 anos (VPAM 2,1;3,7), residentes da região central (VPAM 3,2, IC95% 1,8;5,1) e municípios com alto índice de privação (VPAM 2,6, IC95% 1,3;5,0). Foram identificados *clusters* espaço-temporais de alto risco para mortalidade relacionada ao CG de 2000-2017, sem significância estatística no período 2018-2022: os *clusters* foram identificados no Sul até 2011 e Noroeste de 2006-2017. **Conclusão:** A mortalidade por CG aumentou no Estado do Ceará no período do estudo. Foram identificadas áreas de alto risco para mortalidade por CG, possibilitando ações integradas focadas para fortalecer redes de prevenção, diagnóstico, vigilância e controle.

Palavras-chave: Neoplasias Gástricas/epidemiologia; Demografia/tendências; Análise Espacial; Epidemiologia/tendências; Mortalidade/tendências.

RESUMEN

Introducción: En últimas décadas, la prevalencia del cáncer gástrico (CG) ha aumentado en nordeste de Brasil, especialmente en el Estado de Ceará. **Objetivo:** Analizar tendencias temporales y patrones espaciales de mortalidad por cáncer gástrico durante un período de 23 años en Ceará. **Método:** Se incluyeron certificados de defunción (CD) registrados (CG registrado como cualquier causa de muerte) entre 2000-2022. Tendencias temporales se evaluaron mediante modelos de regresión *joinpoint*. Patrones espaciales se evaluaron mediante autocorrelación espacial, utilizando el índice de Moran local basado en los Indicadores Locales de Asociación Espacial (LISA). **Resultados:** Se detectó CG en 16 670 CD (1,5% de todas las muertes). La mortalidad ajustada por edad y sexo fue de 8,44/100 000 habitantes. Se observaron tasas de mortalidad elevadas en el sur del Estado y alrededor de un gran centro urbano en el norte. El análisis a lo largo del tiempo mostró una tendencia ascendente (Variación Porcentual Anual Media [VAPM] 1,2; IC95% 0,6;2,1), en hombres (VAPM 1,6; IC95% 1,1;2,1), personas menores de 45 años (VAPM 2,1;3,7), residentes de la región central (VAPM 3,2; IC95% 1,8;5,1) y municipios con un alto índice de privación (VAPM 2,6; IC95% 1,3;5,0). Se identificaron *clusters* espacio-temporales de alto riesgo de mortalidad relacionadas con el CG entre 2000 y 2017, sin significación estadística en el período 2018-2022: los *clusters* se identificaron en el sur hasta 2011 y en el noroeste entre 2006-2017. **Conclusión:** La mortalidad por CG aumentó en el Estado de Ceará durante el período de estudio. Se identificaron áreas de alto riesgo de mortalidad por CG, que permitió acciones integradas focalizadas para fortalecer redes de prevención, diagnóstico, vigilancia y control.

Palabras clave: Neoplasias Gástricas/epidemiología; Demografía/tendencias; Análisis Espacial; Epidemiología/tendencias; Mortalidad/tendencias.

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INTRODUCTION

As the fifth most common malignant neoplasm and the fourth leading cause of death worldwide, gastric cancer (GC) represents a significant public health challenge. In 2022, GC was responsible for almost one million new cases and an estimated 659,853 deaths¹. If current GC rates persist, 1.8 million cases and 1.3 million deaths will occur in 2040. These figures are 66% and 71% higher than those estimated in 2020².

The number of GC cases and mortality rates has been declining worldwide since the mid-20th century, particularly in North America, Northern Europe, Australia, Japan, and Korea¹. It is noteworthy that the decline in GC is primarily due to distal disease, the most common subtype (accounting for approximately 82% of all GC cases worldwide), which is also known as “non-cardia” GC and is associated with *Helicobacter pylori* infection³. The incidence of proximal GC, or “cardia cancer,” has been increasing and is thought to be linked to the rise in gastro-esophageal reflux disease (GERD) and obesity².

The global decline in GC incidence and mortality is associated with improvements in socioeconomic development, a reduction in the prevalence of *H. pylori* infection (the most significant risk factor for distal GC), a decrease in smoking and high salt intake, and the availability of refrigeration and better sanitation¹. In addition, population screening for early detection of GC and population-level eradication of *H. pylori* in high-risk regions have contributed to this decline^{4,5}.

Conversely, the high incidence and increased mortality of distal GC are still observed, particularly in the most underserved regions with low Human Development Index (HDI)².

In Brazil, GC is the fourth and sixth most common internal malignant neoplasm in men and women, respectively⁶. Over the last two decades, there has been a significant decrease in the incidence of GC in developed regions, while there has been an increase in less developed areas – North and Northeast – which have the worst health indicators in the country⁷⁻⁹. Exposure to risk factors in addition to different cultures and habits also contribute to these inequalities⁹.

In the Northeast region, GC has the second highest incidence (10.70/100,000 men and 4.96/100,000 women)⁸. The state of Ceará has the highest incidence and mortality rates of GC, one of the most common internal malignancies in men in the state, along with lung, and prostate cancer⁶. Nevertheless, the number of local studies addressing the epidemiology of GC is limited¹⁰.

The study of the dynamics as well as the mapping of the geographical patterns of GC mortality in Ceará can

help to plan, evaluate and implement public policies to control GC. This study aims to analyze the spatial patterns and temporal trends of GC mortality in the state of Ceará, Brazil, from 2000 to 2022.

METHOD

This is a statewide population-based ecological study based on spatial and temporal analysis of GC mortality. Official secondary data from the Ministry of Health National Mortality System (SIM), based on death certificates (DCs), were used. The units of analysis were the 184 municipalities of Ceará.

Ceará is located in Brazil's Northeast region. It has a tropical climate, a population of 9.2 million inhabitants in 2024 and a population density of 59.07 inhabitants per square kilometer. The state is divided into 184 municipalities, and is operationally organized into 22 health micro-regions and 5 health macro-regions (Figure 1¹¹).

SIM data for the period 2000-2022 were obtained from the databases of the Computer Department of the Brazilian National Health System (DATASUS) of the Ministry of Health (MoH)¹².

All GC-related death records as the underlying or associated causes were selected using the International Statistical Classification of Diseases and Related Health Problems in its tenth revision (ICD-10). The following ICD-10 codes were included: C16-malignant neoplasm of stomach, C16.0-malignant neoplasm of cardia, C16.1-malignant neoplasm of fundus of stomach, C16.2-malignant neoplasm of body of stomach, C16.3-malignant neoplasm of pyloric antrum, C16.4-malignant neoplasm of pylorus, C16.5-malignant neoplasm of small curvature of stomach, unspecified, C16.6 - malignant neoplasm of large curvature of stomach, unspecified, C16.8 - malignant neoplasm of stomach with invasive lesion, and C16.9 - malignant neoplasm of stomach, unspecified¹³.

The population data were obtained from the “*Instituto Brasileiro de Geografia e Estatística* (IBGE)” through DATASUS¹⁴. It was based on the Brazilian 2000, 2010 and 2022 censuses, as well as municipal population estimates through intercensal projections (2001-2009; 2011-2021). This dataset included demographic information as age and sex¹⁴.

A total of 23 SIM files were downloaded for Ceará. The files were available in .dbc format and were subsequently merged into a single database using TabWin 4.15¹⁵ software, which was also saved in “.dbc” format for recognition by statistical analysis programs. The database was managed, and statistical analyses were performed using Stata¹⁶ software version 11.2.

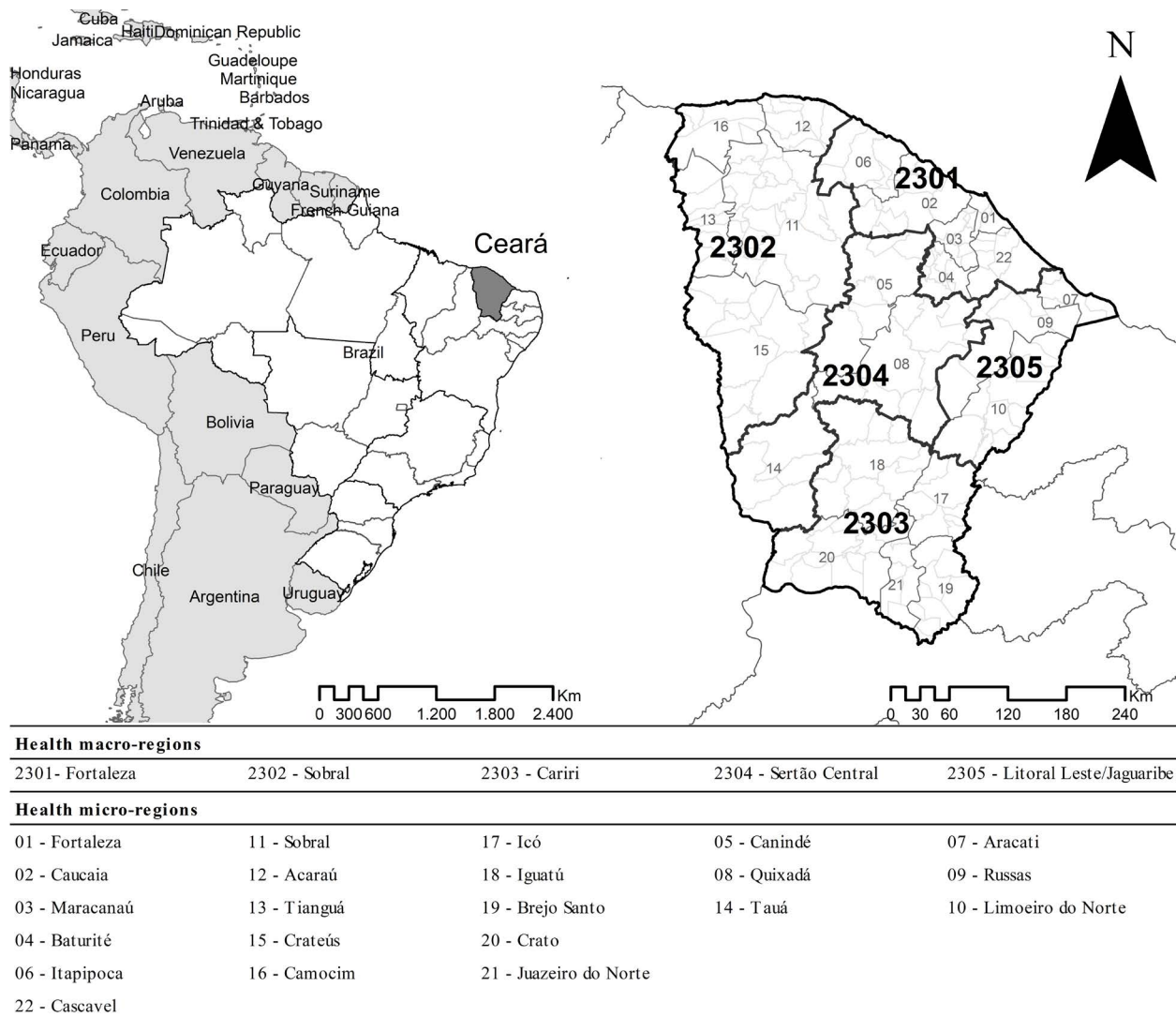


Figure 1. Study area: Ceará state in Brazil's Northeastern, health macro-regions and health micro-regions

Source: IBGE¹¹.

The relative frequencies of sociodemographic variables in relation to specific GC mortality were calculated, including the following sociodemographic variables: sex (male and female), age groups (group 1: <15, 15-29, 30-39, 40-49, 50-59, 60-69, ≥70 and group 2: <45, ≥45 years), ethnicity (Caucasian, Afro-Brazilian, Asian, Pardo-Brazilians, Indigenous), health macro-region (Litoral, Leste/Jaguaribe, Sertão Central, Cariri, Sobral, Fortaleza), residence in the capital, (yes, no), and municipality size (small size I, ≤20,000 inhabitants; small size II, 20.001;50,000 inhabitants; medium size, 50.001;100,000 inhabitants; large size: >100,001 inhabitants).

The Brazilian Deprivation Index (IBP) is a tool designed to measure social inequalities in the country, at the level of census sectors in small areas and is suitable to be used in municipalities. This index is based on three variables extracted from the 2010 IBGE Census¹⁷: (1) the percentage of

households with per capita income of less than or equal to half minimum wage; (2) the percentage of illiterate individuals aged 7 and over; and (3) the mean percentage of individuals with inadequate access to sanitation, water, garbage collection and no toilet/shower, combined in a single measure¹⁸.

Crude and age- and sex-adjusted GC mortality rates were calculated, based on the mean number of deaths during the period, with 2010 as the population reference period per 100,000 inhabitants.

Age- and sex-adjusted rates per 100,000 inhabitants were calculated over time for the health macro-regions. The data on the respective rates in the time series were presented in graphical form. The relative risks (RR) and corresponding 95% confidence intervals (CI) were calculated. Pearson's chi-squared test (χ^2) was used to identify the significance of differences related to the socio-demographic variables included in the study.

To assess the trend of the socio-demographic indicators over time, the Poisson regression analysis with joinpoints was applied, which determines statistical significance, using the Monte Carlo permutation method, recognizing the line of best fit at each follow-up. The analyses produced two results: annual percent change (APC) and average annual percent change (AAPC), with the respective 95%CI. The APC/AAPC results can be interpreted as an increase (positive results) or a decrease (negative results), both with statistical significance, or as no trend (no statistical significance)¹⁹. Joinpoint²⁰ Regression® software version 5.0.0 was used for these analyses.

To analyze the municipal spatial patterns of GC mortality, age- and sex-adjusted mortality rates were calculated per 100,000 inhabitants for the period 2000-2022, using the direct method and the age structure of the 2010 Brazilian census.

To determine the presence of spatial autocorrelation, the local Moran index was calculated, which is based on the Local Indicators of Spatial Association (LISA), recognizing specific areas. The results indicate the presence of significant clustering among municipalities with similar values²¹. The spatial analysis was carried out using ArcGIS²² software version 9.3 (Environmental Systems Research Institute, Redlands, CA, USA) to calculate autocorrelation indicators and create thematic maps.

The Jenks natural breaks method (per 100,000 inhabitants) was used to determine the class breaks of the age- and sex-adjusted mortality rate indicators. The spatial unit of analysis was the municipality of residence (n=184), excluding DCs with unknown municipalities and/or invalid coding.

The Ethics Review Board of “Universidade Federal do Ceará” (Fortaleza, Brazil) approved the study in 2015, report number 1,320,661, (CAAE submission for ethical review 50537415.3.0000.5054) for the analysis of GC mortality data from 2000 to 2022 in compliance with Directive 510²³ dated April 7, 2016 of the National Health Council (CNS).

RESULTS

A total of 16,670 deaths by GC were recorded between 2000 and 2022, accounting for 1.5% of the state's 1,133,334 deaths. GC was the underlying cause in 15,722 (94.3%) deaths. The mean adjusted mortality rate was 8.44/100,000 inhabitants (95%CI 8.31;8.57) (Table 1). Mortality rate was higher among males (n=10,612; 63.7%, adjusted mean rate 11.04/100,000 inhabitants, 95%CI 10.83;11.25), and in individuals aged 45 years and older (n=15,428; 92.5%, adjusted mean rate 5.75/100,000 inhabitants, 95%CI 5.53;5.97).

A higher proportion of GC deaths was observed among individuals living in rural cities (n=12,073,

72.4%, adjusted mean rate of 8.32/100,000 inhabitants, 95%CI 8.17;8.47), in municipalities with very high IBP (n=10,056, 60.3%, mean adjusted rate of 8.29/100,000 inhabitants, 95%CI 8.12;8.45), in the macro-region Fortaleza (n=7,820, 46.9%, mean adjusted rate of 8.46/100,000 inhabitants, 95%CI 8.27;8.64), and large cities (>100,000 inhabitants) (n=7,084, 42.5%, mean adjusted rate of 8.78/100,000 inhabitants, 95%CI 8.57;8.98) (Table 1).

There was a higher risk of death by GC among men, compared to women (RR: 1.84, 95%CI 1.58;2.14, $p < 0.0001$), those aged 45 years or older compared (RR: 38.49, 95%CI 29.17;50.78, $p < 0.0001$) to 45 years or less, those aged 70 or over compared to those aged 40-49 (RR: 14.51, 95%CI 10.97;19.19, $p < 0.0001$), and those living in the macro-region Cariri compared to Fortaleza (RR: 1.26, 95%CI 1.03;1.54, $p = 0.0220$) (Table 1).

The temporal evaluation identified up to three (3) breakpoints (joinpoints) in the temporal trends of the sociodemographic indicators. The overall time trend showed an increase (AAPC 1.2, 95%CI 0.6;2.1), which was more pronounced in males (AAPC 1.6, 95%CI 1.1;2.1), age <45 years (AAPC 2.1, 95%CI 0.8;3.7), and Pardo-Brazilians (AAPC 3.7, 95%CI 2.9;4.9). The increases were more significant among residents of the macro-region Sertão Central (AAPC 3.2, 95%CI 1.8;5.1), in municipalities with higher IBP (AAPC 2.6, 95%CI 1.3;5.0), in medium-sized cities (AAPC 1.9, 95%CI 1.2;2.6), and in rural municipalities (AAPC 1.3, 95%CI 0.8;1.9) (Table 2).

The geographical distribution of GC mortality rates adjusted for age and sex showed heterogeneity, with rising rates during the study period. High-risk areas (mortality rates $\geq 8.45/100,000$ inhabitants) were significantly more common in the southern and western regions of the state, as well as in municipalities close to the capital (Figure 2).

The LISA method identified municipalities with elevated mortality rates located near other municipalities with similarly elevated mortality rates in the period (Moran's $I=0.142638$, $z\text{-score}=3.983685$, $p = 0.000068$), with statistical significance. Spatial autocorrelation using the local Moran's index identified municipalities with a spatial correlation in the west, at the border with the state of Piauí, and in municipalities close to the capital (Figure 3).

DISCUSSION

This is the first study to examine the spatial patterns and temporal trends of GC mortality over a 23-year period in 184 municipalities in Ceará. During the study period, the age- and sex-adjusted GC mortality rates demonstrated an upward trend across the entire state as well as in all health macro-regions, even in the context of

Table 1. Number and percentage, crude rate, and adjusted rate (per 100,000 inhabitants), and relative risk of gastric cancer mortality by sociodemographic variables. State of Ceará, Brazil's Northeast, 2000-2022

Indicator/Variables	Deaths			RR (95%CI)	p
	Deaths %	Crude mortality rate	Adjusted mortality rate (95%CI)		
Total	16.670 (100.0)	8.41	8.44 (8.31;8.57)	-	-
Sex					
Female	0.58 (36.3)	5.96	5.97 (5.82;6.12)	Ref	
Male	10,612 (63.7)	10.97	11.04 (10.83;11.25)	1.84 (1.58;2.14)	<0.0001
Age group 1 (years)*					
<15	6 (0.0)	0.01	0.01 (0.00;0.02)	0.00 (0.00;0.06)	0.0001
15-29	144 (0.9)	0.26	0.26 (0.22;0.31)	0.04 (0.02;0.10)	<0.0001
30-39	573 (3.4)	1.99	1.94 (1.79;2.10)	0.36 (0.23;0.58)	<0.0001
40-49	1.307 (7.8)	5.49	5.62 (5.31;5.92)	Ref	
50-59	2.518 (15.1)	15.72	14.74 (14.17;15.32)	2.84 (2.06;3.91)	<0.0001
60-69	3.975 (23.8)	36.05	34.96 (33.87;36.05)	6.55 (4.85;8.83)	<0.0001
≥70	8.142 (48.8)	80.02	79.68 (77.95;81.41)	14.51 (10.97;19.19)	<0.0001
Age group 2 (years)*					
< 45	1.237 (7.4)	0.83	0.53 (0.49;0.57)	Ref	
≥ 45	15.428 (92.5)	31.88	25.75 (25.35;26.15)	38.49 (29.17;50.78)	<0.0001
Ethnicity*					
Caucasian	4.456 (26.7)	7.24	-	Ref	
Afro-Brazilian	664 (4.0)	7.49	-	1.04 (0.70;1.53)	0.8514
Asian-descendant	76 (0.5)	3.18	-	0.40 (0.13;1.25)	0.1135
Pardo-Brazilians	10.288 (61.7)	8.49	-	1.17 (0.99;1.38)	0.0681
Indigenous	28 (0.2)	6.09	-	0.69 (0.10;4.92)	0.7111
Macro health region*					
Litoral Leste/Jaguaripe	1.129 (6.8)	9.31	8.40 (7.91;8.89)	1.22 (0.90;1.64)	0.1997
Sertão Central	1.434 (8.6)	9.99	8.63 (8.18;9.09)	1.30 (0.99;1.70)	0.0573
Cariri	3.184 (19.1)	9.65	8.70 (8.40;9.00)	1.26 (1.03;1.54)	0.022
Sobral	3.098 (18.6)	8.50	8.15 (7.86;8.44)	1.11 (0.91;1.36)	0.285
Fortaleza	7.820 (46.9)	7.64	8.46 (8.27;8.64)	Ref	
Resident in the capital					
No	12.073 (72.4)	8.59	8.32 (8.17;8.47)	1.08 (0.92;1.27)	0.3686
Yes	4.592 (27.5)	7.96	8.88 (8.62;9.14)	Ref	
IBP*					
Very low	-	-	-	-	-
Low	-	-	-	-	-
Medium	4.592 (27.5)	7.98	8.88 (8.62;9.14)	0.89 (0.76;1.06)	0.1875
High	2.017 (12.1)	7.09	8.58 (8.20;8.96)	0.80 (0.63;1.00)	0.0499
Very high	10.056 (60.3)	8.95	8.29 (8.12;8.45)	Ref	
Size of municipality*					
Small Size I	2.387 (14.3)	9.52	8.30 (7.96;8.63)	Ref	
Small Size II	4.006 (24)	9.19	8.34 (8.08;8.60)	0.96 (0.75;1.23)	0.7561
Medium Size	3.188 (19.1)	8.21	8.14 (7.86;8.42)	0.86 (0.67;1.11)	0.2549
Large Size	7.084 (42.5)	7.80	8.78 (8.57;8.98)	0.82 (0.65;1.02)	0.0745

Captions: Significantly different ($p < 0.05$); 95% CI: 95% confidence intervals; RR: Relative risk; IBP: Brazilian Deprivation Index; Ref: Reference; -: Not calculated; N: Number; %: percent. * Data not available in all cases.



Table 2. Joinpoint regression analysis by sociodemographic variables of GC mortality, Ceará State, Brazil, 2000-2022

Indicator/Variables	Trends		Entire period
	Period	APC (95%CI)	AAPC (95%CI)
Total	2000-2018	2.0* (1.6;5.6)	1.2* (0.6;2.1)
	2018-2022	-2.2 (-10.0;1.3)	
Sex			
Female	2000-2015	2.7* (1.8;8.1)	1.3* (0.4;2.5)
	2015-2022	-1.5 (-8.9;1.0)	
Male	2000-2022	1.6* (1.1;2.1)	1.6* (1.1;2.1)
Age group 1 (years)			
<15	2000-2022	-1.6 (-5.2;1.6)	-1.6 (-5.2;1.6)
15-29	2000-2022	1.0 (-1.7;3.9)	1.0 (-1.7;3.9)
30-39	2000-2022	0.4 (-1.2;2.3)	0.4 (-1.2;2.3)
40-49	2000-2022	-0.6 (-1.5;0.2)	-0.6 (-1.5;0.2)
50-59	2000-2022	-0.8 (-2.0;0.5)	-0.8 (-2.0;0.5)
60-69	2000-2018	-0.1 (-0.8;3.0)	
	2018-2022	-6.9* (-17.7;-1.4)	-1.4* (-2.2;-0.3)
≥70	2000-2006	3.6* (0.2;20.7)	
	2006-2022	-0.8 (-6.0;0.0)	0.4 (-0.7;1.7)
Age group 2 (years)			
<45	2000-2022	2.1* (0.8;3.7)	2.1* (0.8;3.7)
≥45	2000-2022	-0.5 (-1.0;0.0)	-0.5 (-1.0;0.0)
Ethnicity			
Caucasian	2000-2007	3.8* (1.3;15.0)	
	2007-2022	-0.2 (-3.3;0.6)	1.1* (0.2;2.0)
Afro-Brazilian	2007-2022	-0.2 (-3.3;0.6)	-2.2* (-4.3;-0.1)
Asian-descendant	2000-2022	-21.4* (-24.3;-18.4)	-21.4* (-24.3;-18.4)
Pardo-Brazilians	2000-2007	10.7* (5.2;21.1)	
	2007-2018	2.2* (1.0;14.9)	3.7* (2.9;4.9)
	2018-2022	-3.9 (-12.1;0.7)	
Indigenous	2000-2022	-4.1* (-7.1;-0.8)	-4.1* (-7.1;-0.8)
Health Macro-region			
Litoral Leste/Jaguaribe	2000-2022	0.8 (-0.3;2.0)	0.8 (-0.3;2.0)
Sertão Central	2000-2008	8.3* (4.1;28.8)	
	2008-2022	0.4 (-3.1;1.9)	3.2* (1.8;5.1)
Cariri	2000-2019	1.8* (0.9;8.6)	
	2019-2022	-6.0 (-16.3;1.3)	0.7 (-0.2;2.0)
Sobral	2000-2022	1.6* (0.5;2.8)	1.6* (0.5;2.8)
Fortaleza	2000-2022	1.6* (1.2;2.1)	1.6* (1.2;2.1)
Living in the capital			
No	2000-2018	2.4* (1.9;3.3)	
	2018-2022	-3.3 (-10.2;0.4)	1.3* (0.8;1.9)
Yes	2000-2022	0.9* (0.4;1.6)	0.9* (0.4;1.6)
IBP^a			
Very low	-	-	-
Low	-	-	-
Medium	2000-2022	0.9* (0.4;1.5)	0.9* (0.4;1.5)
High	2000-2018	4.0* (2.8;18.0)	
	2018-2022	-3.8 (-17.3;3.2)	2.6* (1.3;5.0)
Very high	2000-2018	2.1* (1.7;3.1)	
	2018-2022	-3.1 (-9.8;0.4)	1.2* (0.6;1.7)
Size of municipality			
Small Size I	2000-2022	1.6* (1.0;2.2)	1.6* (1.0;2.2)
Small Size II	2000-2008	4.7* (2.0;19.1)	
	2008-2022	0.2 (-5.0;1.3)	1.8* (0.7;3.2)
Medium Size	2000-2016	3.2* (2.5;4.6)	
	2016-2022	-1.6 (-6.6;0.9)	1.9* (1.2;2.6)
Large Size	2000-2022	1.4* (0.8;2.0)	1.4* (0.8;2.0)

Captions: *Significantly different from 0 ($p < 0.05$); 95% CI: 95% confidence intervals; APC: annual percent change; AAPC: average annual percent change; IBP: Brazilian Deprivation Index.

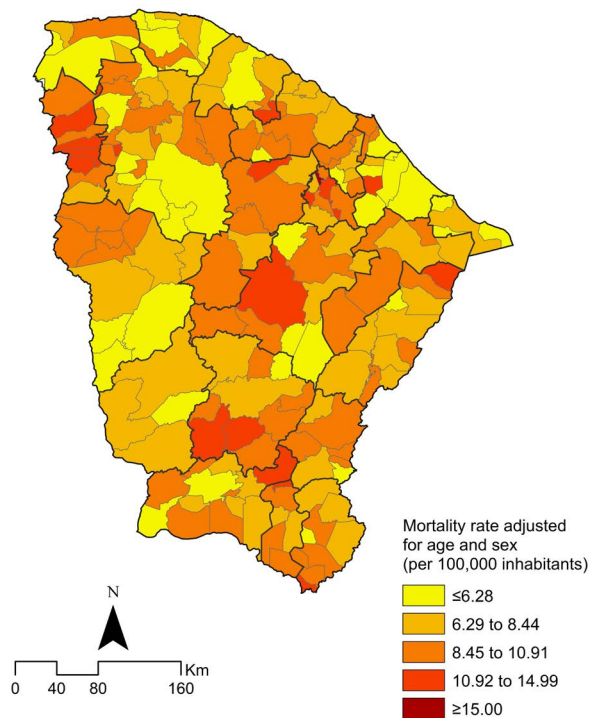


Figure 2. Distribution of age and sex-adjusted GC mortality rates (per 100,000 inhabitants), by municipality of residence in Ceará State, Brazil, 2000-2022

Source: The authors, based on SIM¹⁴ and IBGE¹⁷.

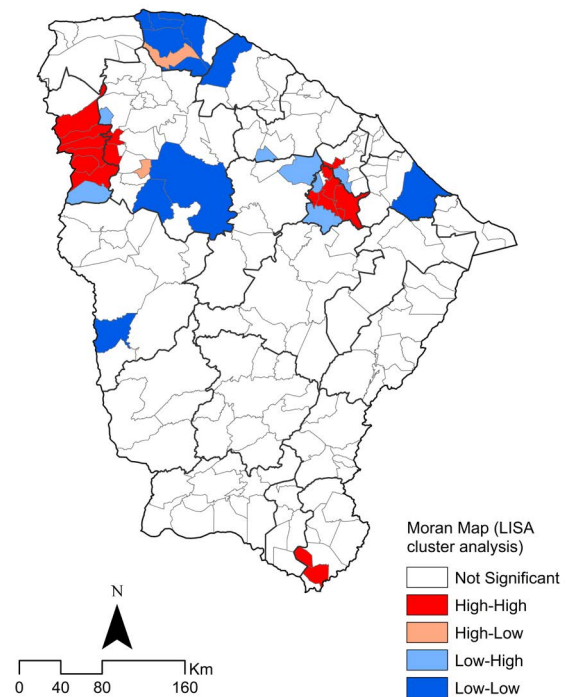


Figure 3. Spatial and spatiotemporal LISA cluster analysis (Moran map) of GC mortality rates (per 100,000 inhabitants) by municipality of residence in Ceará State, Brazil, 2000-2022

Source: The authors, based on SIM¹⁴ and IBGE¹⁷.

the COVID-19 pandemic after 2020. Previous national studies evaluating GC mortality from 2000 to 2019 had already indicated that mortality rates in the state exhibited a rising rate that had not been consolidated. Operational issues related to access to timely diagnosis and appropriate treatment within SUS care network remain critical for improving GC detection^{24,25}.

Higher GC mortality rates among individuals residing in large cities (>100,000 inhabitants) were observed, as well as in municipalities characterized by greater social vulnerability, lower educational attainment, and higher levels of poverty, as indicated by a high IBP index. Ceará is one of the northeastern states with the highest concentration of individuals without access to sanitation in 2022.

Social vulnerability is a recognized factor contributing to increased GC incidence and mortality worldwide¹ and in Brazil²⁶. The primary risk factor for distal GC, *Helicobacter pylori* infection, is associated with low economic development, poor sanitation, and limited educational attainment in most countries^{1,3}. Previous studies conducted in the municipality of Fortaleza have demonstrated that the overall prevalence of *H. pylori* infection is high²⁷, as is the prevalence of the more virulent *CagA* and *VacA* strains, which are significantly associated with GC²⁸. Further research should be conducted to assess the prevalence of *H. pylori* infection throughout

Ceará over recent decades. Indeed, controlling *H. pylori* infection could have a substantial impact on reducing both GC incidence and mortality²⁹.

Furthermore, the limited availability and accessibility of health care resources for the early detection and treatment of GC as endoscopy, as well as the lack of GC screening guidelines for high-risk individuals within the Brazilian health care system may contribute to the higher GC mortality rates observed. This issue is particularly evident in disadvantaged areas as Ceará⁸. Population-based screening using upper gastrointestinal endoscopy has been shown to reduce GC mortality significantly in high-risk East Asian countries, including Japan and Korea⁵. The criteria for GC screening are determined by population risk, regional incidence, and individual risk factors. Accordingly, population-based screening is recommended in high-risk countries³⁰.

A high-risk country is defined as one where the age-standardized incidence rate of GC is 10–12 cases or greater per 100,000 individuals per year, which usually mirrors the GC mortality rate. Additional criteria include a high prevalence of *Helicobacter pylori* infection, which is a well-established risk factor, along with the presence of other contributing factors. In regions with low incidence, population-wide screening is generally not cost-effective. Instead, screening efforts focus on individuals at increased

risk, identified by factors as age, ethnicity, first degree history of GC, hereditary syndromes, premalignant gastric lesions, and *Helicobacter pylori* infection status³⁰.

Another potential factor contributing to the observed increase in GC rates in Ceará is changes of dietary habits, including greater access to processed foods, high salt intake, and low intake of fresh vegetables and fruits³¹. Smoking is considered an important risk factor for GC³², although it has decreased in Brazil in recent decades, including the Northeast region³³.

An increased risk of GC has been reported for some professional groups as agricultural workers, fishermen, and environmental exposures to coal, asbestos dust, organic solvents, pesticides and herbicides, nitrogen oxides, N-nitroso compounds, and ionizing radiation³⁴. In Brazil, epidemiological studies suggest that agricultural workers have higher mortality rates by esophageal and stomach cancers than non-agricultural workers and that these disparities may be increasing³⁵. As agribusiness has expanded in several regions of Brazil including Ceará³⁶, it will be important to assess potential occupational exposures among agricultural workers in future studies.

Overall GC mortality and time-trend mortality rates were higher in males than in females. These findings are consistent with the literature^{1,26,36}. One explanation is the higher incidence of GC in men, twice than in women¹. In addition, men are more exposed to risk factors as tobacco, and alcohol use, and there are also biological differences as sex hormones and metabolic system³⁷.

Most studies have shown that GC mortality increases significantly with age^{1,26,36,37}. Similarly, in the present study, a higher percentage of GC was observed in the group aged 70 years or older. A temporal rising mortality trend was observed in men aged 45 years or younger, which is termed early-onset gastric cancer (EOGC)³⁸. This finding has been reported in other Brazilian studies^{39,40}, as well as in low-incidence countries as USA and United Kingdom⁴¹. The overall mortality rate of EOGC was 7.6%, similarly to previous studies performed in Fortaleza, Ceará³⁹, and lower than in São Paulo (9%)⁴⁰. The rates of EOGC vary between 2.7% and 15%, depending on the population studied⁴¹. The increase in EOGC is worrisome because several years of life are lost due to cancer-related disability or death⁴¹.

Increased GC mortality rates have been observed in Pardo-Brazilians (individuals with different ethnic ancestries). Similar results have been found in studies evaluating GC over time in Brazil^{36,42}. There are few studies evaluating the association between racial inequality and GC in Brazilian public health system, however, the available data on GC disparities suggest that Black and Brown/Pardo populations face longer diagnostic delays,

reduced access to specialized care, and worst prognoses⁴⁰. Tackling this requires public health interventions and improved access to prevention and treatment in historically underserved populations.

However, no higher GC rates or temporal rising trend were found in indigenous populations. In contrast, increasing mortality among indigenous was observed in Siberians, the Mapuche in South America, the Inuit in the Arctic areas of Greenland, Canada and Alaska, the Māori in New Zealand⁴³ and Amerindians in Brazil³⁵. Furthermore, in Taiwan, New Zealand, United States, American Indians/Alaska Natives have been found to have a rising GC incidence and higher mortality rate compared to their non-Indigenous counterparts⁴⁴.

The significant GC mortality in Ceará does not show a homogeneous distribution pattern among municipalities. High mortality rates ($\geq 12.16/100,000$ inhabitants) were more significant in the south of the state, in the macro-region of Cariri, and in the north, near the city of Sobral. From this perspective, in the period 2000-2017, municipalities with high mortality rates were identified, surrounded by other municipalities with similarly high mortality rates, with no statistical significance in the period 2018-2022. In addition, municipalities with a spatial correlation were identified in the south of the state until 2011, in the northwest from 2006-2017, and in municipalities near the capital since 2012. These areas share not only a process of historical organization of their space based on social and economic dimensions, but also the structuring of local health systems⁴⁵.

Differences in the quality of mortality surveillance among municipalities in Ceará may have affected the results, especially in less developed municipalities, which is one of the study limitations. Additionally, the lack of information on the topographic subsite of GC does not allow the classification of GC as proximal (cardia) or distal (non-cardia).

Despite these limitations, one of the strengths of the study was the use of a nationwide database, and multiple causes of death, which included all death certificates referencing GC in any field. This approach is more accurate than the underlying causes of death.

CONCLUSION

In summary, GC mortality has shown a rising pattern for the state over the 23-year period analyzed. Relevant high-risk areas with a higher concentration of GC mortality were identified for future integrated actions to strengthen care, surveillance, and control networks.

GC represents a public health problem in the state, especially in younger than 45 years of age. The

results reinforce the need for prevention strategies to be implemented to reduce future deaths for this population, as well as in high mortality areas.

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Lucia Libanez Bessa Campelo Braga, Helio De Almeida Nobre Junior, Anderson Fuentes Ferreira, and Alberto Novaes Ramos Jr. contributed to the study design, data analysis and interpretation, writing, and critical review of the intellectual content. Ana Suzete Lopes, Jorg Heukelbach, Edson Luiz de Oliveira, Vitor de Sousa Tomé, Daniele Calheiros Campelo Maia, and Taynara Lais Silva collaborated to the data analysis and interpretation, writing, and critical review of the intellectual content. All the authors approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

DATA AVAILABILITY STATEMENT

The dataset generated and reviewed during the study are available at the repository of DATASUS <https://datasus.saude.gov.br/transferecia-de-arquivos/> and <ftp://ftp.datasus.gov.br/dissemin/publicos/SIM/CID10/DORES/>

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