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ORIGINAL ARTICLE

Sepsis mortality and the Human Development Index in Brazilian capitals: 1990-2016

Mortalidade por sepse e Índice de Desenvolvimento Humano nas capitais brasileiras: 1990-2016

Mortalidad por sepsis e Índice de Desarrollo Humano en las capitales brasileñas: 1990-2016

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ABSTRACT

Background and Objectives: the Human Development Index is among the determinants associated with access to health services and sepsis assistance. This study aimed to describe the frequency of mortality from sepsis in Brazilian capitals and verify its correlation with the Human Development Index (HDI), in three-year periods that represented from the early 90's to 2016. **Methods:** a time series ecological epidemiology study, with consultation in secondary database involving Brazilian capital variables, population, deaths from sepsis and HDI. Correlation was assessed with Pearson's/Spearman's correlation coefficient. **Results**: the three highest mean coefficients of mortality from sepsis were observed in Rio Branco (9082.50), Manaus (6367.25) and Macapá (6085.25). A significant correlation was found between the mean mortality rate and the mean HDI in Aracaju (-0,999; p=0.001), Brasília (-0,991; p=0.009), Campo Grande (-0,977; p=0.023), Cuiabá (-0.983; p=0.017), Florianópolis (0.999; p=0.001), Goiânia (-0.997; p=0.003), Maceió (-0.987; p=0.013), Natal (-0.962; p=0.038), Palmas (-0.982; p=0.018) and Vitória (-0.998; p=0.002). **Conclusion:** there is a general correlation between the mean mortality coefficients and HDI. As HDI increases, there is a decrease in mortality from sepsis.

Keywords: *Social Determinants of Health. Mortality. Sepsis.*

ABSTRATO

Justificativa e Objetivos: o Índice de Desenvolvimento Humano está entre os determinantes associados ao acesso aos serviços de saúde e assistência à sepse. Este estudo teve como objetivo descrever a frequência de mortalidade por sepse nas capitais brasileiras e verificar sua correlação com o Índice de Desenvolvimento Humano (IDH), em triênios que representaram do início da década de 90 a 2016. **Métodos:** estudo epidemiológico ecológico de

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série temporal, com consulta em banco de dados secundário envolvendo variáveis da capital brasileira, população, óbitos por sepse e IDH. A correlação foi avaliada com o coeficiente de correlação de Pearson/Spearman. **Resultados:** os três maiores coeficientes médios de mortalidade por sepse foram observados em Rio Branco (9.082,50), Manaus (6.367,25) e Macapá (6.085,25). Foi encontrada correlação significativa entre a taxa média de mortalidade e o IDH médio em Aracaju (-0,999; p=0,001), Brasília (-0,991; p=0,009), Campo Grande (-0,977; p=0,023), Cuiabá (-0,983 ; p=0,017), Florianópolis (0,999; p=0,001), Goiânia (-0,997; p=0,003), Maceió (-0,987; p=0,013), Natal (-0,962; p=0,038), Palmas (-0,982; p=0,018) e Vitória (-0,998; p=0,002). **Conclusão:** existe uma correlação geral entre os coeficientes médios de mortalidade e o IDH. À medida que o IDH aumenta, há uma diminuição na mortalidade por sepse.

Palavras-chave: *Determinantes Sociais da Saúde. Mortalidade. Sepse.*

RESUMEN

Justificación y Objetivos: el Índice de Desarrollo Humano se encuentra entre los determinantes asociados al acceso a los servicios de salud y asistencia a la sepsis. Este estudio tuvo como objetivo describir la frecuencia de mortalidad por sepsis en las capitales brasileñas y verificar su correlación con el Índice de Desarrollo Humano (IDH), en períodos de tres años que representaron desde principios de la década de 1990 hasta 2016. **Métodos:** estudio de epidemiología ecológica de serie temporal, con consulta en base de datos secundaria involucrando variables de la capital brasileña, población, muertes por sepsis e IDH. La correlación se evaluó con el coeficiente de correlación de Pearson/Spearman. **Resultados:** los tres mayores coeficientes medios de mortalidad por sepsis se observaron en Rio Branco (9082,50), Manaus (6367,25) y Macapá (6085,25). Se encontró una correlación significativa entre la tasa de mortalidad media y el IDH medio en Aracaju (-0,999; p=0,001), Brasilia (-0,991; p=0,009), Campo Grande (-0,977; p=0,023), Cuiabá (-0,983 ; p=0,017), Florianópolis (0,999; p=0,001), Goiânia (-0,997; p=0,003), Maceió (-0,987; p=0,013), Natal (-0,962; p=0,038), Palmas (-0,982; p=0,018) y Victoria (-0,998; p=0,002). **Conclusión:** existe una correlación general entre los coeficientes medios de mortalidad y el IDH. A medida que aumenta el IDH, disminuye la mortalidad por sepsis.

Palabras clave: *Determinantes Sociales de la Salud. Mortalidad. Septicemia.*

INTRODUCTION

Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection and is an important global public health concern. Estimates indicate that it is one of the main causes of mortality in the world.[1]

Data from the first study to produce global estimates of sepsis incidence and mortality in 195 countries and territories suggest that in 2017, there were 48.9 million incident cases of sepsis and 11 million deaths, accounting for 19.7% of all worldwide deaths. Middle and low-income countries where 80% of the population live concentrate the highest indicators.[2,3]

In Brazil, considered a middle-income country, a survey using data from the hospital information system of the Unified Health System (*Sistema Único de Saúde*) between 2006 and 2015 revealed an increase in sepsis incidence by 50.5%, and in mortality by 85.0%. Moreover, patients who survive sepsis have physical, psychological and cognitive sequel, with social and health care repercussions.[1,4,5]

Given this reality, sepsis control is a priority of the World Health Organization, with the approval of a resolution recognizing sepsis as a threat to patient safety and global health, encouraging member countries to develop measures aimed at prevention, recognition and treatment. For this to happen, joint efforts by health managers, researchers, health professionals and policymakers are needed.[6]

Furthermore, the scarcity of epidemiological data reduces the success of such actions. Monitoring, knowing and following up on concrete data is important to understand determinants, avoid underreporting of sepsis and would be the effective course for a better strategy to change reality and reduce mortality.[7]

Several areas relate to the impact on sepsis, whether in water supply, sanitary, nutritional conditions, vaccination, awareness of the lay population and health professionals, access to health services and health care associated infections. Among the determinants associated with access to health and care services, we have the Human Development Index (HDI). This describes the relationship between various socioeconomic aspects, and is composed of data on life expectancy at birth, education and gross domestic product per capita. It is known that when the HDI is high, there is an improvement in the supply and access of health care.[8,9,10]

Therefore, this study was developed with the aim of describing the frequency of mortality from sepsis in Brazilian capitals and verifying its correlation with the HDI, in three-year periods, from the early 1990s to 2016.

METHODS

A time series ecological epidemiology study was carried out. Data on deaths and the resident population were obtained, respectively, from the Mortality Information System (SIM - *Sistema de Informação sobre Mortalidade*) and the Brazilian Institute of Geography and Statistics (IBGE - *Instituto Brasileiro de Geografia e Estatística*), both available in the tabulator (TABNET) of the SUS

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Department of Informatics (DATASUS - *Departamento de Informática do SUS*).

Deaths were collected for four three-year periods: 1990-1992, 1999-2001, 2009-2011 and 2014-2016 (the most recent data on deaths in the capitals available at the time of collection). For the calculation of mortality indicators, the population of the middle of the triennium was used. In the years 1990, 1992, 2014, 2015 and 2016, there were no population data available when data collection was performed, so the population was projected for those years. The population projection data not available in the SIM was as follows: 1) the mean of the population growth of the triennium 2009-2011 was calculated, in each capital by the quotient: (population 2010/population 2009)/(population 2011/2010); 2) the mean population growth was multiplied by the population of the previous year with available data (2011), in each capital; 3) the value found in the multiplication of step 2 was considered the population projection of the specific capital. Subsequently, the populations of the following years were projected, based on the projection of the previous year.

The mortality coefficient was compensated for by ill-defined causes to minimize the influence of ill-defined deaths on those from sepsis. Adjustment was performed as follows: mortality from compensated sepsis for ill-defined causes = (mean number of deaths from sepsis in the triennium + mean number of deaths from ill-defined causes in the triennium) x mean number of deaths from sepsis in the triennium/(mean number of deaths from all causes in the triennium – mean number of deaths from ill-defined causes defined in the triennium). The value found for deaths from sepsis compensated for ill-defined causes was divided by the population in the middle of the period and the result was considered the coefficient of deaths from sepsis adjusted for ill-defined causes.

Finally, the coefficient for sepsis adjusted for ill--defined causes was standardized by the Brazilian population, in order to minimize the impact of different population distributions by age group between the capitals, and was calculated as follows: coefficient compensated by ill-defined deaths multiplied by the proportion of the Brazilian population according to each age group used in the research (<1, 1-4, 5-9, 10-14, 15-19, 20-29, 30-39, 40-49, 50-59, 60-69 , 70-79, 80 and older) and multiplied by one hundred thousand.

In statistical analysis, the mean coefficients of mortality from sepsis were described for each three--year period, adjusted and compensated, as well as the capital's HDI in each three-year period. Mortality coefficient means from sepsis were calculated in the four analyzed three-year periods and the mean of the HDI of the period for each capital. Data distribution normality was verified by the Shapiro-Wilk tests. Then, the correlation between mortality coefficients and HDI was assessed with Pearson's or Spearman's correlation coefficient (depending on data compliance with the normal distribution), and the data were arranged in line and dot graphs for better visualization for each capital and region of the country. The temporal trend of the mean mortality rate from sepsis was verified in a simple regression analysis, with Brazilian capitals as dependent variable and the triennium as independent variable. Linear and Poisson regression models were used for symmetrical and non-symmetrical distributions, respectively. All analyzes were performed using SPSS 21.0 (SPSS Inc. Headquarters, Chicago, USA).

This study aimed to describe the mortality profile of sepsis in the country (through secondary data available on the internet) and its relationship with HDI, included in larger research entitled "*Internamentos de recém nascidos atendidos em unidades de terapia intensiva neonatal dos Campos Gerais, Paraná, Brasil*". Despite the data collected involved in the present research being in the public domain and being available on the internet for public consultation, the aforementioned research project was submitted to the Institutional Review Board of the *Universidade Estadual de Ponta Grossa* (COEP/UEPG), being approved under Protocols 2,321,013/2017 (first version of COEP/UEPG opinion) and 3,362,107/2017 (latest version of opinion). The ethical and legal aspects described in Resolution 466/2012 were followed.

RESULTS

Between 1990 and 2016, the three highest mean mortality rates from sepsis were observed in the Rio Branco, Manaus and Macapá capitals. While the smallest were presented in Curitiba, Porto Alegre and São Paulo (Table 1).

In relation to HDI, the highest mean values were present in Florianópolis, Vitória, Porto Alegre, Curitiba, Brasília and São Paulo, ranging from 0.78 to 0.74. However, in 16 Brazilian capitals, the mean HDI for the period studied was less than 0.70 (Table 1).

Temporal trends in mortality from sepsis in Brazilian capitals between 1990 and 2016

In a regression analysis, assessing the mortality rate from sepsis linear trend in Brazilian capitals, there was a growth trend between 1990 and 2016 only for Porto Velho (*p=0.0338*). On the other hand, the trend was downward for Fortaleza, Maceió, Aracaju, Florianópolis, Campo Grande, Cuiabá, Goiânia and Brasília (Table 2).

In the Midwest region, Cuiabá was the capital that had the greatest reduction in deaths from sepsis, from 1,200 deaths/100,000 inhabitants to less than 100 deaths/100,000 inhabitants (Graph 1-A). However, in this region there was a reduction in all capitals, even those that started the study with lower coefficients.

In the Northeast region, João Pessoa, São Luiz do Maranhão and Fortaleza had more pronounced declines in mortality from sepsis between the triennium 1990-1992 and 2014-2016 (Graph 1-B). At the end of the period, despite all capitals having experienced a drop in death rates from sepsis, Fortaleza still remained with a coefficient of 963/100,000 inhabitants, while Teresina ended up with 155/100,000 inhabitants and Salvador again showed growth.

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Table 1. Correlation between the mean mortality rates from sepsis and the Human Development Index in Brazilian capitals. Brazil: 1990-2016.

	Total mean mortality	Mean HDI	Correlation coefficient	p-value
Midwest region				
Brasília	458.50	0.74	-0.991	0.009*
Campo Grande	717.75	0.70	-0.977	0.023*
Cuiabá	5194.25	0.70	-0.983	0.017*
Goiânia	959.25	0.72	-0.997	0.003*
Northeast region				
Aracaju	1997.25	0.68	-0.999	0.001*
Fortaleza	3859.50	0.67	-0.943	0.057
João Pessoa	4015.75	0.68	-0.922	0.078
Maceió	1420.00	0.63	-0.987	0.013*
Natal	1148.25	0.69	-0.962	0.038*
Recife	507.75	0.69	-0.869	0.131
Salvador	1476.25	0.68	-0.618	0.382
São Luís	2489.25	0.68	-0.463	0.537
Teresina	717.25	0.65	-0.873	0.127
North region				
Belém	1872.50	0.67	-0.245	0.755
Boa Vista	1057.25	0.67	0.394	0.606
Macapá	6085.25	0.65	-0.090	0.910
Manaus	6367.25	0.64	-0.852	0.148
Palmas	1002.00	0.66	-0.982	0.018*
Porto Velho	2612.75	0.64	0.830	0.170
Rio Branco	9082.50	0.63	-0.648	0.352
Southeast region				
Belo Horizonte	904.50	0.73	0.377	0.623
Rio de Janeiro	3203.50	0.73	0.518	0.482
São Paulo	251.25	0.74	-0.928	0.072
Vitória	323.25	0.77	-0.998	0.002*
South region				
Curitiba	169.25	0.75	-0.353	0.647
Florianópolis	507.25	0.78	-0.999	0.001*
Porto Alegre	230.50	0.75	-0.919	0.081

**statistically significant correlations*

Table 2. Linear trend analysis of mortality from sepsis in Brazilian capitals. Brazil, 1990-2016.

Capital	Regression coef-ficient*	p**	(95%) CI
Porto Velho	955.1	0.0338	602.05; 1308.08
Rio Branco	-5158	0.3600	-13734.81; 3417.72
Manaus	-2017	0.2524	-4500.74;466.21
Boa Vista	44.58	0.7316	-177.19; 266.35
Belém	-399.8	0.573	-1572.23;772.68
Macapá	-883.8	0.796	-6761.14; 4993.63
Palmas	-1012.0	0.1218	-1775.96; -248.09
São Luís	-1184	0.495	-3988.53; 1619.74
Teresina	-446.4	0.1558	-839.16; -53.55
Fortaleza	-2192.6	0.0460	-3147.84; -1237.31
Natal	-623.6	0.0879	-1012.11;235.02
João Pessoa	-2699.2	0.1054	-4567.65; -830.68
Recife	-292.2	0.1737	-568.29; -16.13
Maceió	-809.4	0.0357	-1117.62; -501.01
Aracaju	-1337.1	0.0443	-1907.98; -766.16
Salvador	-144.7	0.642	-668.15; 378.80
Belo Horizonte	1.65	0.9878	-186.04;189.35
Vitória	-281.57	0.0699	-435.72; -127.42
Rio de Janeiro	534.2	0.411	-480.35; 1548.84
São Paulo	-105.3	0.1310	-188.38; 22.18
Curitiba	-19.82	0.756	-128.88; 89.24
Florianópolis	-422.0	0.058	-630.43; -213.56
Porto Alegre	-180.0	0.236	-390.88; 30.90
Campo Grande	-440.3	0.1216	-772.37; -108.24
Cuiabá	-4260.8	0.0435	-6061.67; -2459.93
Goiânia	-785.7	0.0849	-1265.50; -305.90
Brasília	-338.3	0.0817	-540.46; -136.18

**linear or Poisson regression coefficient depending on distribution; **referring to the model hypothesis test; CI = confidence interval (95%) for the regression coefficient*

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In relation to the North region, the highest mean coefficients were observed in all the 4 three-year periods analyzed, when compared to the other regions of the country (Graph 1-C).

In the Southeast region, the oscillation of deaths from sepsis in Rio de Janeiro calls for attention to historical moments of lower mortality, with alternating high coefficients (Graph 1-D).

The South region (Graph 1-E) was the territory with capitals that showed the lowest mean mortality rates in the 1990s: 1,285, 685 and 178/100,000 inhabitants in Florianópolis, Porto Alegre and Curitiba, respectively. At the end of the analyzed historical periods, these coefficients were 55, 103 and 196/100,000, respectively, for Florianópolis, Porto Alegre and Curitiba. This information points to Brazilian interregional disparities and to a slower reduction in deaths from sepsis in capitals that already had lower indicators at the beginning of the historical series.

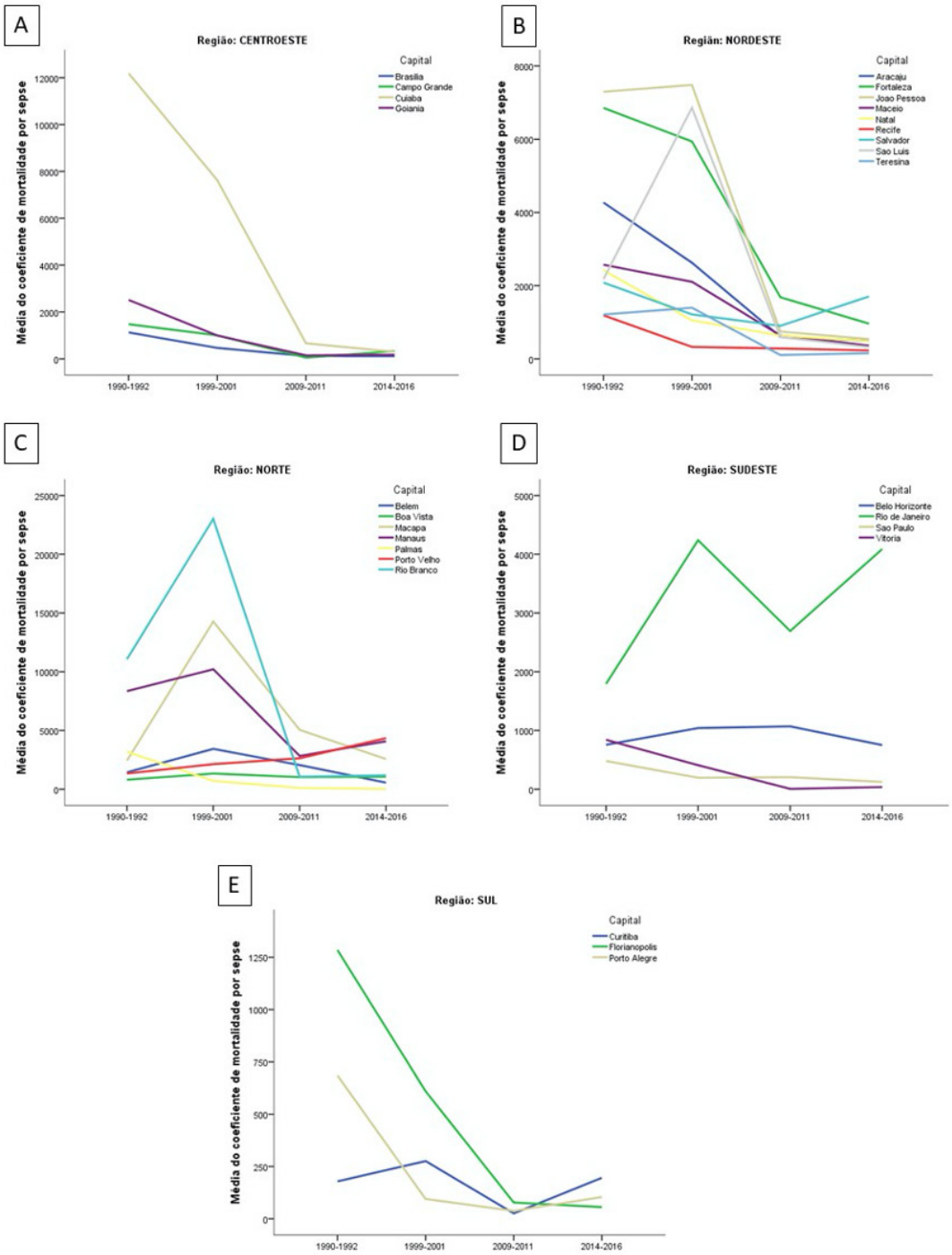

Figure 1. Sepsis mortality coefficient in Brazilian capitals. Brazil: 1990-2016.

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In the supplementary material, temporal trends in mortality from sepsis are presented, according to the age groups of those most susceptible to death from this condition (<1 year and older adults: 60-69 years; 70-79 years; >80 years), with linear regression coefficients and their confidence intervals.

Correlation between mortality from sepsis and the Human Development Index in Brazilian capitals

In general, there is a correlation between the mean mortality coefficients and the HDI. As the HDI increases, the mean mortality rate due to sepsis decreases (Table 1). A statistically significant correlation was found between the mean mortality rate and the mean HDI in Aracaju, Brasília, Campo Grande, Cuiabá, Florianópolis, Goiânia, Maceió, Natal, Palmas and Vitória. In these capitals, there was a strong negative (coefficient above -0.9) and negative correlation, i.e., the higher the mean HDI, the

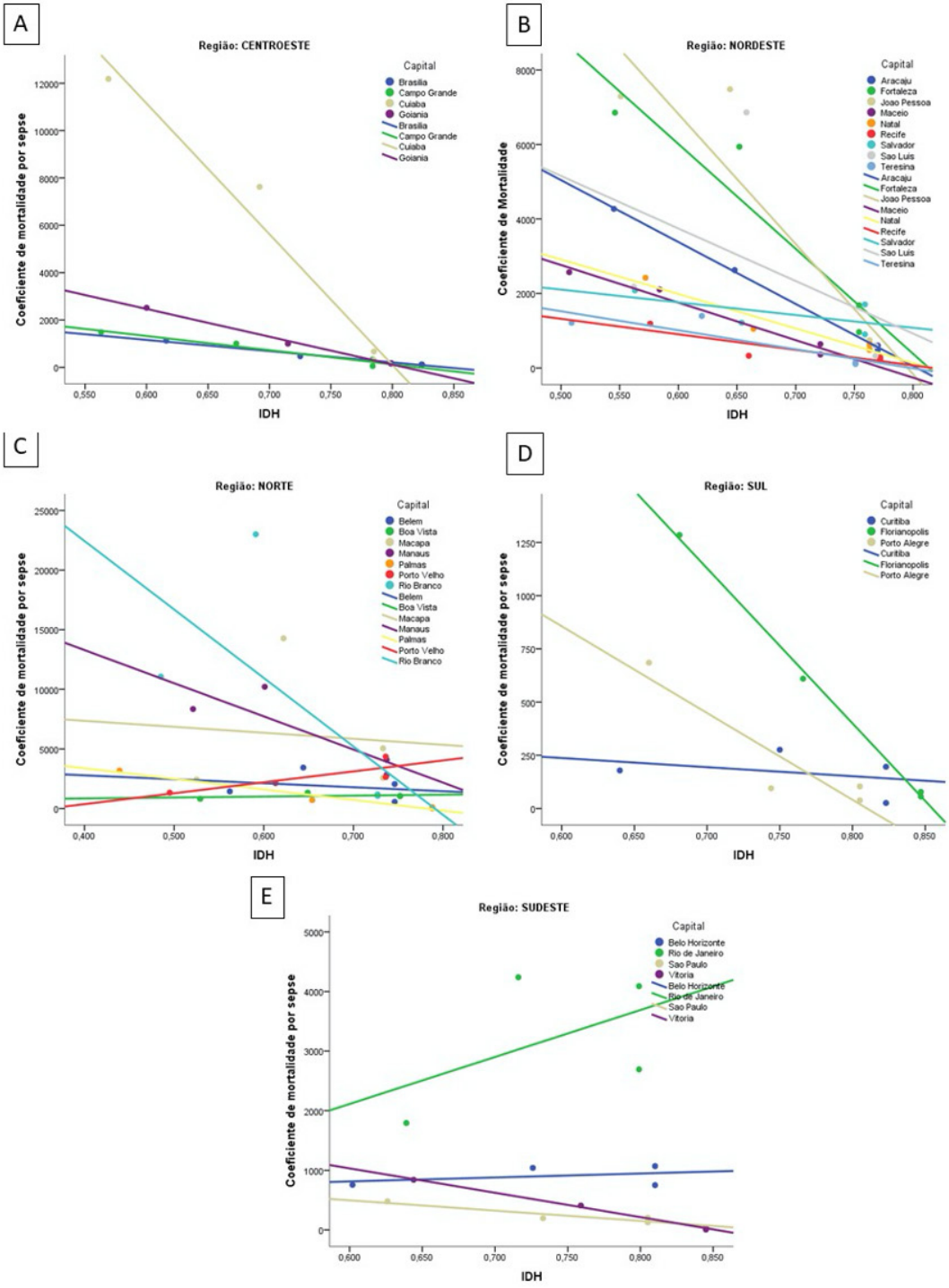

Figure 2. Sepsis mortality coefficient and correlation with the Human Development Index in Brazilian capitals. Brazil: 1990-2016.

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lower the mean mortality, as the capital's HDI increased, its mortality coefficient decreased. The values of the correlation coefficients between the mean HDI and the mortality coefficient, without considering the time, are shown in table 1.

In the Midwest region, Brasília started and ended with the best HDI, 0.62 and 0.82, respectively, correlating with a drop from 1126 deaths/100,000 inhabitants to 115 deaths/100,000 inhabitants. Despite all capitals showing this fact, Cuiabá obtained values with greater difference. In 1990-1992, it had a HDI of 0.57 for 1,200 deaths/100,000 inhabitants, in 2014-2016, the HDI reached 0.79 for less than 100 deaths/100,000 inhabitants (Graph 2-A).

In relation to the Northeast region, Salvador shows a disparity with the other data, despite the HDI 0.76 being maintained from 2009-2011. For 2014-2016, mortality from sepsis increased from 901 deaths/100,000 population to 1,705 deaths/100,000 population (Graph 2-B).

The North region had the lowest HDI and the highest mean coefficients when compared to other regions. Porto Velho presented an inverse correlation with the others, i.e., as the HDI increased, deaths increased. In 1990-1992, the HDI was 0.50, with 1,332 deaths/100,000 inhabitants. In 2014-2016, the HDI reached 0.74, with 4,349 deaths/100,000 inhabitants (Graph 2-C).

This same correlation occurred in the Southeast region with Rio de Janeiro. In 1990-1992, as the HDI was 0.64, with 1,792 deaths/100,000 inhabitants. In the last analyzed period, the HDI reached 0.80, with 4,089 deaths/100,000 inhabitants (Graph 2- E).

In relation to the South region, the capitals present the best results; however, even maintaining their HDIs in recent years, Curitiba and Porto Alegre once again showed growth in mortality rates due to sepsis (Graph 2-D).

DISCUSSION

Among the study limitations, there were no other causes of mortality that could be related to sepsis. Furthermore, different diagnostic criteria between capitals may contribute to discrepancies. As it is an ecological study, the measures calculated in this research have the group as the unit of analysis and do not take into account the sociodemographic characteristics of the cases.

This is the first study encompassing all Brazilian capitals with a twenty-six-year historical series on sepsis incidence and mortality, a portrait of the implementation and evolution of the Unified Health System in Brazil. The findings reinforce the association already reported on social determinants of health, offering relevant and comparative data for the assessment of actions carried out in the period and their impacts, and providing support for further research.[11]

It was shown that the highest mean mortality coefficients from sepsis were in the capitals of the North region, diverging from the epidemiological study, which assessed Brazilian capitals in 2015, in which the Southeast region had the highest mortality rate with 49.51%, but corroborating that the South region has small rates, compared to the others with a rate of 39.2%. This fact may be associated with the isolated assessment of a given year and the factors that influenced it, such as information transmission and care conditions. The North region concentrates the worst rates of use of health services in the country, facing even doctors' low availability, being 7 times less than the capitals of the South.[12,13]

Regarding the HDI, or Brazil, in 2018, reached 0.761, 79th in the ranking of 189 countries. However, when the value of the HDI of Brazil has discounted inequality, it shows a loss of 24.5% in the index; the share of the richest 10% in Brazil concentrates around 42% of the country's total income. Few capitals present their HDI among the ideals, demonstrating this inequality and the reflection of their administrations and local characteristics.[14]

The HDI was a predictor that showed a negative correlation with the mean coefficients of mortality from sepsis in part of Brazilian capitals, as well as other studies reveal its influence on access to health services and mortality rates. The importance of deaths from sepsis in the organization of health systems is demonstrated as well as the evidence of the HDI as a component for their understanding. An international study corroborates this finding and also reveals that the inverse relationship between sepsis and HDI is stronger for mortality than for incidence.[3,15,16]

During the period analyzed in the Midwest region, Cuiabá obtained the greatest reduction in deaths from sepsis, demonstrating a possible improvement in its notifications for basic causes, which requires training of professionals and continuous investigations. The underlying cause of death is related to the triggering of the factors that led to death, being important in the sense of preventing the initiating cause. When sepsis is confirmed as the underlying cause of death, it loses the specificity of diagnosis, causing loss of information about its origin. The underlying causes of death recorded as sepsis are considered not very useful and are classified as garbage codes, which should not be used for coding the underlying cause of death, as they refer to intermediate or final causes and do not support the planning of health actions.[17]

The need for continuous actions to prevent sepsis and its outcomes can be seen when we look at data from the capitals of the Northeast and their oscillations. Salvador, capital of the state of Bahia, even with the HDI evolution and maintenance, showed an increase in deaths again. An ecological study with data on deaths caused by sepsis, recorded between 2010 and 2016 in northeastern Brazil, demonstrates the same as the present study, reinforcing the search for actions for sepsis prevention and treatment.[18]

As for the Northern region with the highest rates of deaths, Porto Velho constructs a reverse path, and the improvement in HDI has led to an increase in deaths from sepsis. A study carried out in 2017, which analyzed the underlying causes after investigation of deaths from sepsis in 60 municipalities, shows that the capital Porto Velho had more than 50% of investigations of deaths reclassified, indicating that the result presented may differ from reality.[17]

The same scenario is observed with Rio de Janeiro, in the Southeast region. Here, possibly, income, goods

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and services are concentrated in the hands of a few people. Inequality affects access, knowledge and the chance of diagnosis and treatment for sepsis or any other diseases. In this context, evidence reveals that the association between health and income is not a direct relationship, better health conditions are in a society with a more balanced income distribution.[19]

Capitals in the Southern region with the best coefficients have a slower reduction in deaths from sepsis. The high life expectancy in these capitals is known, increasing the number of older adults. Population most threatened by sepsis during hospitalization causes death rates to increase.[4]

The sepsis survival campaigns brought many benefits in the acquisition of pathophysiological knowledge, developing more adequate and effective treatments, reflecting in death trend reduction. We can, therefore, conclude that the levels that are still worrying are possibly linked to socioeconomic factors, requiring intervention in social factors with more resolute public policies and a hospital structure that can meet the demand.[20,21]

Sepsis continues to cause many deaths in all Brazilian regions, and measures of constant monitoring and investments in the various sectors of society are important for a reflection on health care. The results reinforce the importance of efforts in the country to regionalize and territorialize health care, in order to be aware of and care for people, close to their daily lives fully and longitudinally. To change the reality of the high incidence and mortality of sepsis in the country, activities are suggested, built in a participatory way and for action planning and prioritization, starting with the dissemination of knowledge of sepsis among society.

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AUTHORS' CONTRIBUTIONS

Letícia Aires do Rosário and **Camila Marinelli Martins** contributed to article planning, conception, design, analysis, review and final approval. **Taís Ivastcheschen** contributed to article design, analysis, writing, review and final approval. **Luciane Patrícia Andreani Cabral, Wesley Sousa Borges and Erildo Vicente Müller** contributed to article planning, conception, design, review and final approval. **Pollyanna Kássia de Oliveira Borges** contributed to article planning, conception, design, analysis, writing, review and final approval.

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