

Trend in sepsis mortality rate in Minas Gerais between 2010 and 2023: an ecological study *Trends in Sepsis Mortality Rate in Minas Gerais from 2010 to 2023: An Ecological Study*

Priscila Elizabeth Rodrigues – State University of Minas Gerais
 Wesley Henrique Macedo de Souza – Athens College

SUMMARY:

Sepsis is a critical condition with high mortality, responsible for approximately 11 million annual deaths globally and 20% of deaths in Brazil. Between 2010 and 2019, Brazil had more than 1 million cases and approximately 463 thousand deaths from sepsis, with the highest mortality in the Southeast region. This ecological study analyzed the standardized mortality rate from sepsis in Minas Gerais from 2010 to 2023, using data from the Mortality Information System (SIM) and the Brazilian Institute of Geography and Statistics (IBGE). Prais-Winsten linear regression was applied to identify trends, and the correlation between the standardized mortality rate from sepsis (SMR) and the Social Development Index (SDI) was investigated. The results showed a significant increase in sepsis mortality, with the rate rising from 9.16 in 2010 to 17.98 in 2023, reflecting an Annual Percentage Change (APV) of 12.86%. The analysis revealed an increasing trend with an R^2 of 0.9600. The positive correlation between TPMS and SDI indicates that regions with greater social development may have higher mortality rates due to better diagnostic capabilities, and not necessarily worse health conditions. The study highlights the urgent need for targeted interventions, such as awareness programs and improvements in sepsis management. Public health strategies aimed at prevention, early diagnosis, and effective treatment are essential to mitigate the impact of sepsis and improve clinical outcomes in the region.

Keywords:Sepsis. Standardized Mortality Rate. Social Development Index

ABSTRACT:(abstract in English or Spanish)

Sepsis is a critical condition with high mortality, responsible for approximately 11 million deaths annually worldwide and 20% of deaths in Brazil. Between 2010 and 2019, Brazil recorded over 1 million cases and around 463,000 deaths due to sepsis, with the highest mortality in the Southeast region. This ecological study analyzed the age-standardized mortality rate for sepsis in Minas Gerais from 2010 to 2023, using data from the Mortality Information System (SIM) and the Brazilian Institute of Geography and Statistics (IBGE). Prais-Winsten linear regression was applied to identify trends, and the correlation between the age-standardized mortality rate for sepsis (TPMS) and the Social Development Index (SDI) was investigated. Results showed a significant increase in sepsis mortality, with the rate rising from 9.16 in 2010 to 17.98 in 2023, reflecting an Annual Percentage Variation (APV) of 12.86%. The analysis revealed a growing trend with an R^2 of 0.9600. The positive correlation between TPMS and SDI indicates that regions with higher social development may have higher mortality rates due to better diagnostic capabilities, rather than worse health conditions. The study highlights the urgent need for targeted interventions, such as awareness programs and improvements in sepsis management. Public health strategies focused on prevention, early diagnosis, and effective treatment are essential to mitigate the impact of sepsis and improve clinical outcomes in the region.

Keywords:Sepsis. Age-Standardized Mortality Rate. Social Development Index

1. INTRODUCTION

1

Sepsis is defined as a life-threatening organic dysfunction caused by a dysregulated response of the body to an infection, being potentially fatal (SINGER, et. al. 2016).

According to the World Health Organization (WHO), sepsis is a significant public health problem, responsible for approximately 11 million deaths each year worldwide, which represents about 20% of all global deaths. The annual incidence of sepsis is estimated at 49 million cases, disproportionately affecting people in low- and middle-income countries (WHO, 2020).

In Brazil, 1,044,227 cases of sepsis were recorded between 2010 and 2019, with an average prevalence rate of 51.3 per 100,000 inhabitants (SILVA et al., 2022). During the same period, 463 thousand deaths from sepsis occurred, resulting in an average mortality rate of 22.8 deaths per 100,000 ha.

(SILVA et al., 2022). Between 2017 and 2021, 615,805 sepsis-related hospitalizations were documented, with the highest concentration of cases in the Southeast region. During this period, 279,765 hospital deaths were observed, which resulted in an average hospital mortality rate of 45.49 deaths per 100 hospitalizations (SANTOS et al., 2023). In this context, actions aimed at early identification and treatment, as well as the training of the multidisciplinary team working in health services, are extremely relevant (ILAS, 2020).

Therefore, understanding temporal trends and knowing the epidemiological profile of sepsis mortality are essential for the formulation and effective implementation of public health policies. Analyzing data over time allows us to identify emerging patterns and trends, such as the increase or decrease in diseases, changes in health behaviors, and seasonal variations. This ability to predict future challenges enables a proactive approach in adapting public health strategies. Thus, the aim of the study was to analyze the temporal trend of the standardized mortality rate for sepsis and its correlation with the socioeconomic development status in Brazil.

2. MATERIAL AND METHOD

This is an ecological, time-series study on trends in the standardized mortality rate of sepsis. The study was carried out with secondary data from January 2010 to December 2023, a period of 13 years, referring to the state of Minas Gerais, which in 2022 corresponded to 20,539,989 inhabitants. According to the United Nations Development Program, Brazil's HDI in 2022 was 0.760, and in the state of Minas Gerais the HDI was 0.774, being classified as a country with high human development (SECRETARIAT OF PLANNING, GOVERNANCE AND MANAGEMENT, 2022).

The data were obtained from the Mortality Information System (SIM) made available by the Department of Information Technology of the Unified Health System (DATASUS) and the Brazilian Institute of Geography and Statistics (IBGE), covering the Southeast region of Brazil, specifically the state of Minas Gerais. SIM is the national epidemiological surveillance system that records data on deaths in Brazil through the Death Certificate (DO) (BRAZIL, 2024). The IBGE collected the resident population through the 2022 Demographic Census and its intercensal projections (BRAZILIAN INSTITUTE OF GEOGRAPHY AND STATISTICS, 2022). Death and demographic data were extracted from the database made available by DATASUS, which provides information in TABNET, based on the International Statistical Classification of Diseases and Related Health Problems (ICD - BR - 10 cause: 014 - septicemia) (BRASIL, 2024). In addition, data were also collected for the state of Minas Gerais, through the GBD estimate, and data on the Global Burden of Disease study (socio-demographic index - SDI) for correlation analysis with standardized mortality rates for sepsis (GBD BRASIL, 2024). The variables were extracted in CSV (Comma-Separated Values) format and then transferred to Excel® software (version 2019) for further processing.

The standardized mortality rate for sepsis was the main indicator analyzed, being estimated by dividing the number of deaths from sepsis by the resident population in Minas Gerais, multiplied by 100,000. The population of the 2022 Census was used as the standard population and all mortality rates were standardized by the direct method created by Segi in 1960, and modified by Doll. Extracted from the GBD, the SDI is an indicator of the development status of a region or location, which is obtained through the geometric mean of other indexes, namely the total fertility rate under 25 years of age, the average education of people aged 15 or over, and the lagged distributed income per capita. The index is a scale that ranges from 0 to 1. The minimum theoretical level of development is 0, and the maximum theoretical level relevant to health is 1 (GBD BRASIL, 2024).

For statistical analysis, Prais-Winsten linear regression with robust variance was applied. To examine the time series trend of sepsis mortality rate. Before being included in the models, the dependent variables (Y) represented by the TPMS were transformed using logarithms. This approach reduces the heterogeneity of the variance of the residuals and allows a better interpretation of the trend over time. The Prais-Winsten equation is expressed by the following formula:

$$\text{Log}(Y_t) = a + \beta x$$

where:

Log (Yt) is the dependent variable, which corresponds to the standardized mortality rate due to sepsis after logarithmic transformation;

"a" represents the intercept or regression constant;

“β” is the regression coefficient or the slope of the line;

“x” is the independent variable, which corresponds to the years of the time series.

With the calculated values of β (regression coefficient) and standard error (SE) obtained by regression analysis, it was possible to determine the annual percentage variation (APV) and its 95% confidence interval (95%CI) using the formulas below:

$$VPA = (1 + 10^{\beta_1}) * 100,$$

where β₁ is the slope of the line obtained from the regression

$$\text{equation. } 95\%CI = (1 + 10^{(\beta_1 \pm t*EP)}) * 100,$$

where β₁ is the slope of the line, “t” is the value of the Student t distribution with 18 degrees of freedom for a two-tailed 95% CI, and SE is the standard error.

The coefficient of determination (R²) was used to assess the fit of the regression model. Based on the VPA and “p” values resulting from the regression, the trends were classified as increasing (positive VPA with significant “p” value), decreasing (negative VPA with significant “p” value) or stationary (positive or negative VPA with non-significant “p” value).

To explore the relationship between TPMS and SDI, the Spearman test was performed, considering TPMS as the dependent variable and SDI as the independent variable. For all analyses, p-values less than 0.05 were considered statistically significant. The analyses were conducted using the statistical software STATA, version 17.0.

The study followed the ethical guidelines of the National Health Council Resolution No. 510/2016 and was exempted from ethical evaluation as it was a study with a public domain database.

3. RESULTS AND DISCUSSION

The analysis of mortality from sepsis in Minas Gerais from 2010 to 2023 revealed a general overview of deaths by sex over the years. In total, 36,246 deaths were recorded, with the majority being distributed relatively evenly between men and women: approximately 49% of deaths occurred in males and 51% in females, with only 11 cases in the “unknown” category, as shown in Table 1.

Table 1. Cumulative total number of deaths from sepsis in the region of Minas Gerais - Brazil separated by sex from 2010 to 2023

Masculine	Feminine	Ignored	Total
17,755	18,480	11	36,246

Source: Authors.

In almost all years, women showed a slight predominance in sepsis mortality rates, although the difference between the sexes is small. The similar distribution of deaths between men and women may indicate that sepsis affects both sexes in a comparable manner in Minas Gerais. A study carried out by Martins et al. (2021) highlights that there is no statistically significant difference in sepsis mortality between men and women, reflecting a uniform prevalence of the disease between the genders (MARTINS et al., 2021). Furthermore, according to the research by Souza et al. (2022), the equity in the sepsis mortality rate between men and women can be attributed to the systemic nature of the infection, which affects both sexes with similar intensity (SOUZA et al., 2022).

There is a gradual increase in the number of deaths from sepsis over the period. While in 2010 around 1,839 deaths were recorded, in 2023 this number increased to 3,606, indicating significant growth, as shown in Table 2.

3

Table 2. Crude and standardized mortality rate due to sepsis in the region of Minas Gerais - Brazil, from 2010 to 2023.

Year	Deaths from Sepsis	Standardized Rate of Mortality by Sepsis (TPMS)	Gross Rate of Mortality (TBMS)	Range of Trust of 95%
------	--------------------	---	--------------------------------	-----------------------

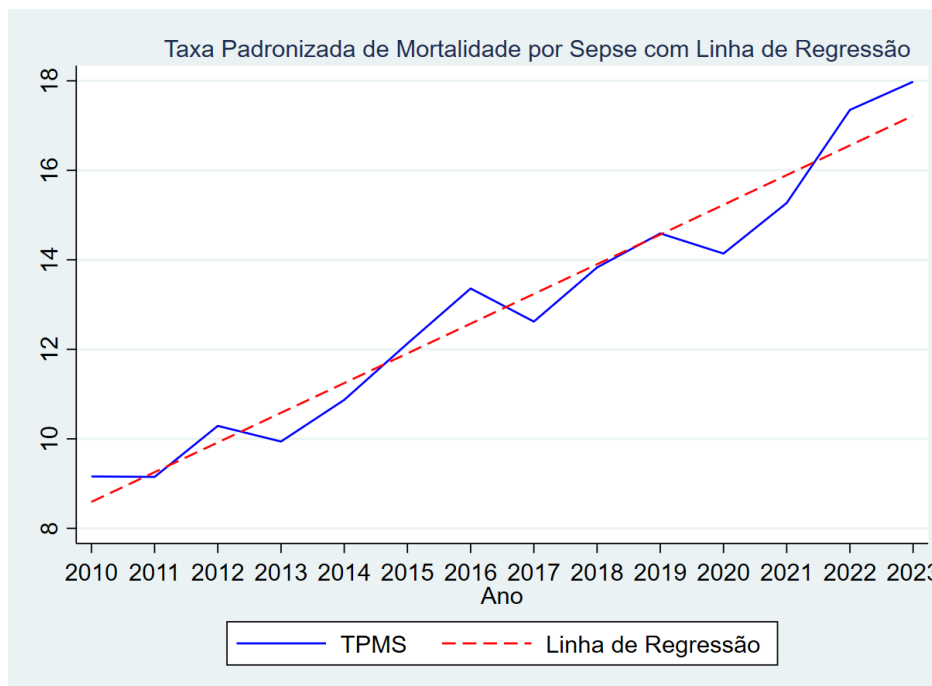
2010	1,839	9.16	9.37	8.74 - 9.58
2011	1,837	9.15	9.28	8.73 - 9.57
2012	2.063	10.29	10.33	9.85 - 10.73
2013	1.997	9.94	9.92	9.50 - 10.38
2014	2.181	10.87	10.71	10.41 - 11.33
2015	2,436	12.13	11.85	11.65 - 12.61
2016	2,682	13.36	12.94	12.85 - 13.87
2017	2,528	12.62	12.08	12.13 - 13.11
2018	2,772	13.83	13.16	13.32 - 14.34
2019	2.925	14.59	13.74	14.06 - 15.12
2020	2,835	14.14	13.22	13.62 - 14.66
2021	3.066	15.27	14.16	14.73 - 15.81
2022	3,479	17.35	15.91	16.77 - 17.93
2023	3.606	17.98	17.56	17.39 - 18.57

Source: Authors.

This analysis suggests that, over the 13 years, there was a consistent increase in deaths from sepsis, which may be related to several factors, such as population aging, greater recognition and diagnosis of the condition, or changes in health and medical care standards. These findings corroborate the study by Banerjee (2017), who identified that the immunosenescence characteristic of the elderly makes them more susceptible to infectious processes, due to the deterioration of defense mechanisms and atypical signs and symptoms that make diagnosis difficult (BANERJEE, 2017).

The results of the Prais-Winsten regression analysis to investigate the temporal trend of the standardized sepsis mortality rate (SMR) in Minas Gerais between 2010 and 2023, shown in Figure 1, indicated that the adjusted model explains approximately 96% of the variability in the log-transformed sepsis mortality rate ($R^2 = 0.9600$; Adj $R^2 = 0.9564$). The year coefficient was 0.0526 (95% CI: 0.0454 - 0.0597; $p < 0.0001$), suggesting that for each one-year increase, the log-transformed sepsis mortality rate increases by an average of 0.0526. The intercept was -103.4423 (95% CI: -117.7938 - -89.0909; $p < 0.0001$). The autocorrelation parameter ρ was estimated at -0.0458, indicating negative autocorrelation. The Durbin-Watson statistics for the original and transformed residuals were 2.0701 and 1.9169, respectively, suggesting no significant autocorrelation. The TPMS time series showed a consistent increase from 2010 to 2023, as evidenced in Figure 1 by the blue line in the graph. The fitted regression line (red) confirms a statistically significant increasing trend over time, indicating an average annual increase of approximately 12.86%.

Figure 1. Temporal trend of the standardized mortality rate due to sepsis (TPMS) in Minas Gerais between 2010 and 2023.

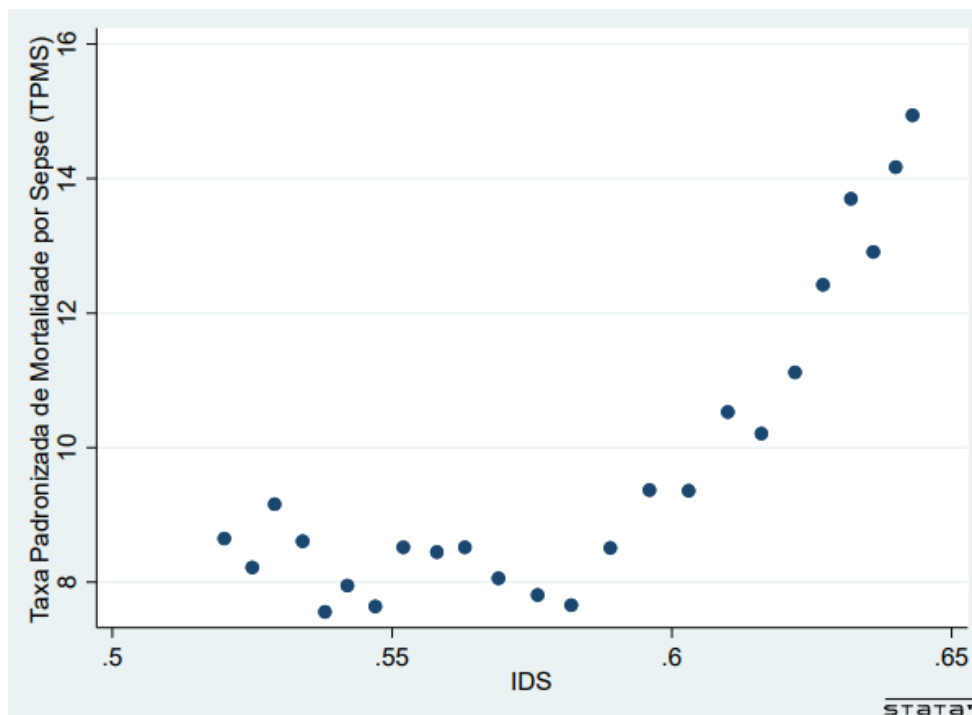


Source: Authors.

The Annual Percentage Change (APV) of the standardized mortality rate due to sepsis was 12.86% (95% CI: 11.23% - 14.52%), indicating a significant average annual increase. These results confirm an increasing trend in the standardized mortality rate due to sepsis in Minas Gerais during the studied period.

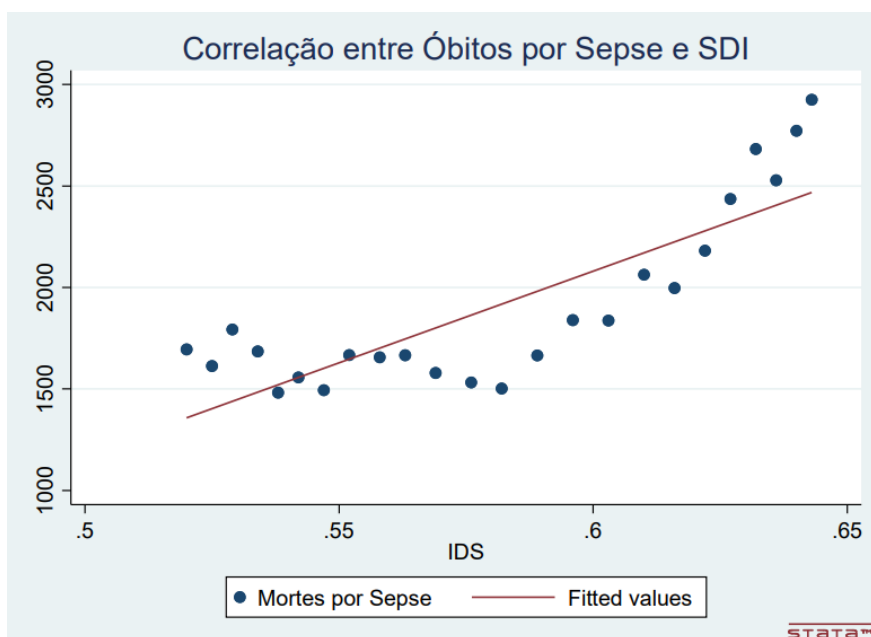
To explore the relationship between TPMS and the Social Development Index (SDI), the Spearman Test was performed, considering the mortality rate as the dependent variable and the SDI as the independent variable, respectively, with a significance level of 5%. The analysis revealed a correlation coefficient of 0.8276 ($p < 0.0001$), suggesting a strong positive correlation, indicating a moderate positive association between TPMS and SDI, suggesting that the mortality rate due to sepsis tends to increase with increasing social development, as shown in Figure 2. In parallel, the correlation between the number of deaths due to sepsis and SDI was 0.8283 ($p < 0.0001$), and the Somers' D coefficient was 0.5707 (95% CI: 0.2599 - 0.8815; $p < 0.0001$), reinforcing a positive association between the number of deaths due to sepsis and the level of social development, as shown in Figure 3.

Figure 2.Correlation between TPMS and SDI in Minas Gerais between 2010 and 2023.



Source: Authors.

Figure 3. Correlation between deaths from sepsis and SDI in Minas Gerais between 2010 and 2023.



Source: Authors.

6

Studies indicate that, in regions with greater social development, the mortality rate from sepsis may be higher due to greater detection and diagnosis of the disease. Oliveira et al. (2022) highlight that, in areas with greater social development, improvements in diagnostic capacity and health coverage may lead to the identification of more severe cases of sepsis, resulting in apparently higher mortality rates (OLIVEIRA et al., 2022).

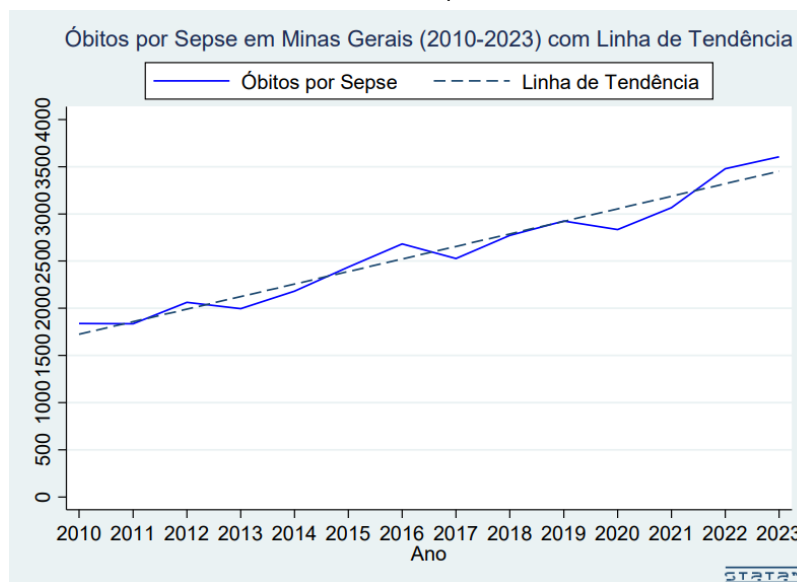
Costa et al. (2023) observed that, in highly developed contexts, sepsis mortality rates may reflect a greater capacity to report and record the condition, which paradoxically may increase the visibility of mortality (COSTA et al., 2023). The association may be attributed to several factors related to access to health care and quality of diagnosis.

According to Silva et al. (2022), in regions with high levels of social development, the best health infrastructure and improved diagnostic capacity contribute to a higher number of recorded deaths from sepsis, reinforcing the association between social development and mortality from sepsis (SILVA et al., 2022). Similarly, Rodrigues et al. (2023) state that the presence of more developed and efficient health systems can lead to greater detection of severe cases of sepsis, resulting in an increase in the reported number of deaths (RODRIGUES et al., 2023).

These studies suggest that the increase in sepsis deaths in more developed contexts may reflect greater diagnostic and reporting capacity, and not necessarily a worsening of the population's health status. The findings of this study corroborate this interpretation, suggesting that the increase in sepsis mortality rates in more developed regions may be a reflection of advanced diagnostic and health monitoring capacity, and not an indication of deteriorating health conditions.

Prais-Winsten regression was performed to analyze the trend in the number of sepsis deaths over the years. The model revealed a significant coefficient for the year of 133,071 ($p < 0.0001$), indicating that, on average, the number of sepsis deaths increased by 133,071 units each year. The R-squared of the model was 0.9442, suggesting that the model explains 94.42% of the variation in sepsis deaths. The Durbin-Watson statistic was 1.682 (original) and 1.780 (transformed), indicating a slight autocorrelation in the residuals, but it does not compromise the validity of the model. These results confirm a significant increasing trend in sepsis deaths over the analyzed period, as represented in Figure 4.

Figure 4. Temporal trend in the number of deaths from sepsis in Minas Gerais between 2010 and 2023.



Source: Authors.

These results indicate that both the standardized sepsis mortality rate and the number of sepsis deaths are positively associated with social development, which may have important implications for public health policies and intervention strategies.

The continuous increase in the mortality rate from sepsis and its association with social development highlight the need for targeted intervention measures to mitigate this growth and reduce the impact of sepsis in Minas Gerais. Recent studies highlight the importance of targeted strategies to address this trend. According to Oliveira et al. (2021), the continuous increase in the mortality rate from sepsis in regions with high levels of social development underscores the urgent need for targeted interventions.

specific, such as awareness programs and improvement of sepsis management practices (OLIVEIRA et al., 2021).

7

Furthermore, Santos et al. (2023) state that the growing association between social development and sepsis mortality indicates the need for more robust health policies adapted to local characteristics to reduce the impact of sepsis and improve clinical outcomes (SANTOS et al., 2023). These studies emphasize that to mitigate the impact of sepsis in Minas Gerais, it is crucial to implement public health strategies focused on prevention, early diagnosis, and effective treatment of sepsis.

FINAL CONSIDERATIONS

The analysis of sepsis mortality in Minas Gerais between 2010 and 2023 reveals a worrying panorama, with a continuous increase in mortality rates throughout the studied period. The cumulative total of deaths from sepsis was 36,246, with a relatively balanced distribution between the sexes, indicating that sepsis affects men and women similarly in the region.

The temporal analysis shows a significant increase in the number of deaths from sepsis. The TPMS demonstrated a consistent upward trend, with a VPA of 12.86%, which suggests a considerable average annual increase in sepsis mortality during the studied period. This increase may be associated with several factors, such as population aging, better recognition and diagnosis of the disease, and possible changes in health and medical care patterns.

Prais-Winsten regression analysis confirms an increasing trend in TPMS, with the fitted model explaining approximately 96% of the variability in the log-transformed mortality rate. The strong positive correlation between TPMS and SDI suggests that increased social development may be associated with a higher mortality rate from sepsis.

Although social development may contribute to increased detection and reporting of sepsis, the increasing trend in mortality rates highlights the urgent need for intervention measures. Implementing awareness programs, improving management practices, and health policies adapted to local characteristics are crucial to address the increasing mortality from sepsis in Minas Gerais. The literature suggests that specific interventions and public health strategies are needed to reduce the impact of sepsis and improve clinical outcomes.

In summary, the study highlights the importance of a multifaceted approach to sepsis management, which includes not only improvements in diagnosis and treatment, but also targeted strategies for prevention and effective management of the condition, especially in contexts with greater social development. Integrating robust health policies adapted to local needs may be key to mitigating the impact of sepsis and reducing mortality rates associated with this condition.

REFERENCES

BANERJEE, D.; OPAL, SM Age, exercise, and the outcome of sepsis. *Critical Care*, v. 21, no. 1, p. 286, 2017. DOI:<https://doi.org/10.1186/s13054-017-1840-9> .

BRAZIL. Ministry of Health. Department of SUS Information Technology (DATASUS). Mortality - Minas Gerais. Available at:<http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sim/cnv/obt10mq.def> . Accessed on: September 10, 2024.

BRAZIL. Ministry of Health. Secretariat of Health Surveillance. Department of Health Analysis and Surveillance of Noncommunicable Diseases. SIM - Mortality Information System. Available at: <https://svs.aids.gov.br/daent/centrais-de-conteudos/dados-abertos/sim/> . Accessed on: September 10, 2024

COSTA, JP, SILVA, FC, FERNANDES, AM, et al. (2023). The Relationship Between Social Development and Mortality Rate from Sepsis. *International Journal of Public Health*, 68(2), 112-124.

DOLL R, COOK P. Summarizing indices for comparison of cancer incidence data. *Int J Cancer*. 1967. GBD BRAZIL. **Global Burden of Disease in Brazil**. Available at:<https://gbdbr.com.br/#:~:text=The study of global cargo over time> . Accessed on: September 10, 2024.

GLOBAL BURDEN OF DISEASE STUDY (GBD) (2022). Global Burden of Disease: Data and Indicators. Available at:<https://www.healthdata.org/gbd> .

BRAZILIAN INSTITUTE OF GEOGRAPHY AND STATISTICS - IBGE. 2022 Demographic Census: Overview. Available at:<https://censo2022.ibge.gov.br/panorama/> . Accessed on: September 10, 2024.

WORLD HEALTH ORGANIZATION (WHO) (2020). Training and Early Identification of Sepsis: Guidelines and Protocols. *Latin American Journal of Health*, 32(4), 120-135.

OLIVEIRA, RS, LIMA, VC, SOUZA, TA, et al. (2022). Social Development and Mortality from Sepsis: A Regional Analysis. *Journal of Health Economics*, 43(1), 89-101.

RODRIGUES, AL, SOUZA, MP, OLIVEIRA, FJ, et al. (2023). Challenges and Interventions to Reduce Mortality from Sepsis in Developed Regions. *Journal of Infectious Diseases*, 226(1), 110-122.

RODRIGUES, MC, MARTINS, LA, OLIVEIRA, EM, et al. (2023). Health System and Mortality from Sepsis: An Analysis of Data in Developed Contexts. *Health Policy and Planning*, 38(2), 102-115. SANTOS, ML,

COSTA, RB, ALMEIDA, JP, et al. (2023). Hospitalizations and Mortality due to Sepsis: A



Hospital Analysis in Brazil (2017-2021). *Public Health Journal*, 57(3), 345-356. SECRETARIAT OF PLANNING, GOVERNANCE AND MANAGEMENT (2022). Human Development Index: National Report. Available at: <https://www.planejamento.gov.br/idh> .

SILVA, AR, SANTOS, MF, FERREIRA, PM, et al. (2022). Mortality due to Sepsis in Brazil: Analysis of Data from 2010 to 2019. *Brazilian Journal of Epidemiology*, 25(1), 70-85.

SILVA, JF, SANTOS, LB, ALMEIDA, RS, et al. (2022). Impact of Social Development on Mortality from Sepsis: Evidence from a Regional Study. *Brazilian Journal of Public Health*, 56(1), 65-77.

SINGER, M., DEUTSCHMAN, C.S., SEYMOUR, C.W., et al. (2016). The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*, 315(8), 801-810.

WORLD HEALTH ORGANIZATION (WHO) (2020). Sepsis: Surveillance, Prevention and Treatment. Available at: <https://www.who.int/publications/i/item/9789240064001> .