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Original Article

Spatio-temporal analysis of congenital syphilis in Rio Grande do Norte, Brazil, from 2008 to 2022

Análise espaço-temporal da sífilis congênita no Rio Grande do Norte, Brasil, de 2008 a 2022
Análisis espacio-temporal de la sífilis congénita en Rio Grande do Norte, Brasil, de 2008 a 2022

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ABSTRACT

Background and Objectives: Rio Grande do Norte state is experiencing an epidemic of congenital syphilis cases, with an average incidence above the national rate. In this context, this study aims to identify the Health Regions of Rio Grande do Norte most affected by congenital syphilis through spatial analysis and, from there, define the temporal trend of infection in these areas. **Methods:** This is an ecological study using secondary data, using spatial analysis techniques, and temporal trends of congenital syphilis in Rio Grande do Norte from 2008 to 2022. **Results:** The incidence of congenital syphilis in 2022 reached 525 new cases in the state, approximately 100 fewer cases compared to 2021. Of these, the 7th health region had a substantially higher average than the other regions. The 3rd health region has the highest average number of congenital syphilis cases per 1,000 live births in the territory, with 25.51 cases. Regarding the temporal trend, the most significant increase is expected in the 8th, 3rd, and 7th health regions, respectively.

Conclusion: A greater incidence of congenital syphilis exposure was found in the 1st, 3rd, 7th, and 8th health regions. Given the data studied, an increase in these health regions is expected, which may result in service overload. Therefore, appropriate management of infected pregnant women should be reinforced in Primary Care, as well as investment in prevention and health education actions.

Keywords: Nursing. Congenital Syphilis. Vertical Transmission of Infectious Diseases. Spatial Analysis. Time Series Studies.

RESUMO

Justificativa e Objetivos: O Rio Grande do Norte vive uma epidemia de casos de sífilis congênita, com incidência média acima da taxa brasileira. Nesse contexto, o estudo tem como objetivo identificar quais as Regiões de Saúde do Rio Grande do Norte mais acometidas pela Sífilis Congênita por meio de análise espacial e, a partir disso, definir a tendência temporal da infecção nessas áreas. **Métodos:** Trata-se de um estudo ecológico, com uso de dados secundários, com técnicas de análise espacial e tendência temporal da sífilis congênita no Rio Grande do Norte no período entre 2008 e 2022. **Resultados:** A incidência da sífilis congênita no ano de 2022 atingiu 525 novos casos no estado, cerca de 100 casos a menos quando comparado ao ano de 2021. Desses, a 7ª região de saúde obteve uma média substancialmente maior que a das outras regiões. A 3ª região de saúde possui a maior média de sífilis congênita por 1000 nascidos vivos do território, com 25,51 casos. No que se refere a tendência temporal, o aumento mais expressivo é esperado na 8ª, 3ª e 7ª regiões de saúde, respectivamente. **Conclusão:** Constatou-se um maior acometimento pela exposição à sífilis congênita nas 1ª, 3ª, 7ª e 8ª regiões de saúde. Diante dos dados estudados, espera-se um aumento nas regiões de saúde que podem resultar em uma sobrecarga no serviço. Dessa maneira, o manejo adequado das gestantes infectadas deve ser reforçado na Atenção Básica, assim como o investimento em ações de prevenção e educação em saúde.

Descriptores: Enfermagem. Sífilis Congênita. Transmisión Vertical de Enfermedades Infecciosas. Análisis Espacial. Estudios de Series Temporales.

RESUMEN

Justificación y Objetivos: Rio Grande do Norte atraviesa una epidemia de sífilis congénita, con una incidencia media superior a la tasa nacional. En este contexto, el objetivo del estudio fue identificar cuáles Regiones de Salud de Rio Grande do Norte han sido más afectadas por Sífilis Congénita a través del análisis espacial y, con base en esto, definir la tendencia temporal de la infección en esas áreas. **Métodos:** Se realizó un estudio ecológico con uso datos secundarios, empleando técnicas de análisis espacial y análisis de tendencia temporal de la sífilis congénita en Rio Grande do Norte desde 2008 hasta 2022. **Resultados:** En 2022 la sífilis congénita registró 525 nuevos casos en el estado, aproximadamente 100 casos menos en comparación con 2021. De estos, la 7ª región de salud tuvo un promedio sustancialmente mayor que las otras regiones. La 3ª Región de Salud mostró la mayor media de sífilis congénita por 1,000 nacidos vivos, con 25,51 casos. En cuanto a la tendencia temporal, se espera que el aumento más significativo ocurra en las 8ª, 3ª y 7ª regiones de salud, respectivamente. **Conclusión:** Se constató un mayor impacto de la sífilis congénita en las 1ª, 3ª, 7ª y 8ª regiones de salud. Dada la información estudiada, se anticipa un aumento en estas regiones de salud, lo que podría resultar en sobrecarga de los servicios. Por lo tanto, se refuerza la necesidad de un manejo adecuado de las gestantes infectadas en la Atención Primaria, así como invertir en acciones de prevención y educación en salud.

Palabras Clave: Enfermería. Sífilis Congénita. Transmisión Vertical de Enfermedades Infecciosas. Análisis Espacial. Estudios de Series Temporales.

INTRODUCTION

Syphilis Syphilis is a systemic infection caused by *Treponema pallidum* (*T. pallidum*), transmitted primarily through vertical and sexual routes.¹ The ease of transmission and the complications associated with its chronic progression pose a persistent public health challenge, as a high incidence of the infection is still observed in the Brazilian population despite the availability of preventive measures.² Diagnosis during pregnancy increases the risk of spontaneous abortion, prematurity, congenital malformations, and neonatal death.¹

Congenital syphilis (CS) results from vertical or transplacental transmission of *T. pallidum* from an infected pregnant woman who has not received adequate treatment to the fetus. Among the possible outcomes of CS, it is estimated that at least 11% of pregnancies result in term stillbirths, while approximately 20% of exposed newborns present signs suggestive of infection.¹

The elimination of vertical transmission of syphilis is a global priority defined by the World Health Organization (WHO) and the Pan American Health Organization (PAHO). However, the increasing number of cases remains constant and highly challenging.³ In 2016, the WHO reported that CS surpassed half a million notifications worldwide, resulting in 200,000 deaths, including stillbirths and neonatal deaths.⁴

In Brazil, syphilis is a notifiable disease under the Information System for Notifiable Diseases (SINAN), as established by Ordinance No. 542 of December 22, 1986, which mandated the reporting of CS in the country, and is currently regulated by Ordinance No. 264 of February 17, 2020.⁵ Despite the reduction in birth rates, vertical transmission of CS remains high.⁶

According to the Epidemiological Bulletin published by the Ministry of Health (MS) in October 2023, 26,468 CS cases and 200 related deaths were recorded in 2022, representing a 16% increase compared with 2019. Of this total, 27.6% of diagnoses occurred in the Northeast, the second most affected region after the Southeast. In the state of Rio Grande do Norte (RN), the CS detection rate in the capital, Natal, exceeds the national average, approaching 50 cases per 1,000 live births.⁷

Given the current syphilis epidemic in Brazil, particularly in RN, it is necessary to identify the areas most affected by the infection and to understand its future incidence trends in order to support public health policies for prevention and control. Furthermore, spatial analysis is an efficient and relevant method for epidemiological surveillance, as it enables the development of targeted strategies for the most vulnerable territories.

Accordingly, the objective of this study is to identify the Health Regions of Rio Grande do Norte most

affected by congenital syphilis through spatial analysis and, subsequently, to examine the temporal trends of infection in these areas.

METHODS

Study design

This is an ecological study based on secondary data, employing spatial analysis and temporal trend techniques to evaluate outcomes related to congenital syphilis (CS) in Rio Grande do Norte (RN) between 2008 and 2022. During this period, 70,213 births of children diagnosed with CS were reported in the state. According to the most recent census conducted by the Brazilian Institute of Geography and Statistics (IBGE) in 2022, the population of RN was estimated at 3,302,729 inhabitants.⁸

The territorial division of the state follows the Master Regionalization Plan (PDR/RN), which aims to expand access to referral and high-complexity health services within regional boundaries. RN is composed of 167 municipalities, organized into two health macro-regions and eight Health Regions (HR). Macro-region I, headquartered in the capital city, includes the 1st, 3rd, 4th, 5th, and 7th HRs, while Macro-region II comprises the 2nd, 6th, and 8th HRs.

In October 2023, the reported cases were obtained from the Information System for Notifiable Diseases (SINAN), through the Department of Informatics of the Unified Health System (DATASUS). SINAN is continuously updated by states and municipalities with information on conditions listed as nationally notifiable diseases, allowing for ongoing monitoring of the epidemiological situation in the country.

Study variables

The dependent variables were: absolute number of live births, absolute number of CS cases by place of residence, and average incidence rate of the disease from 2008 to 2022. The independent variables were Health Region and year of diagnosis.

Data analysis

Data were organized and tabulated in Microsoft Excel spreadsheets. For spatial analysis, a thematic map of CS incidence by Health Region in RN was developed. Crude rates and smoothed rates using simple moving averages were calculated with the open-source software TerraView 4.2.2, considering 1,000 live births as the constant. Purely spatial analysis was performed using SaTScan 9.6, and all maps were generated with QGIS 2.4.17.

Trend analysis of detection rates was performed using a Poisson regression model with the Joinpoint Regression Program, version 4.7.0.0, applying the following parameters: no geographical overlap of

clusters, maximum cluster size of 50% of the exposed population, circular clusters, and 999 replications.⁹ Joinpoint is widely used in trend analyses due to its accessible interface, free availability, and methodological robustness, although it has limitations, such as only accepting aggregated data with a normal distribution.

Ethical considerations

As this study was based on secondary data publicly available from DATASUS, it complied with the principles of Resolution No. 466/2012. Therefore,

approval by the Research Ethics Committee of the Federal University of Rio Grande do Norte (CEP/UFRN) was waived.¹⁰

RESULTS

In 2008, the total number of live births in Rio Grande do Norte was 50,246 children. Since then, the state has shown a decreasing trend in four of the eight RS, with 40,542 births recorded in 2022 (Figure 1).

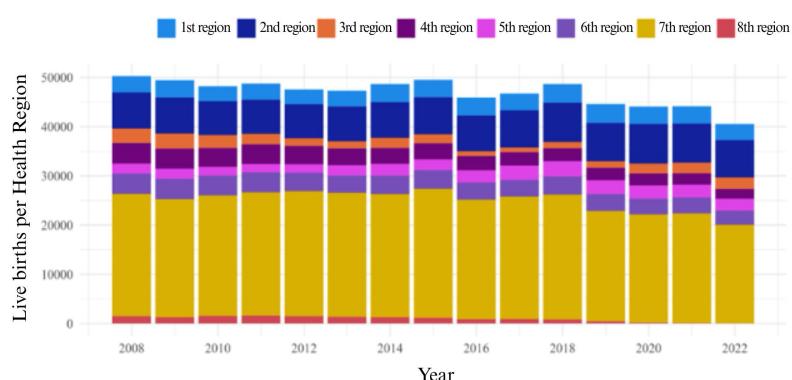


Figure 1. Live births per Health Region in Rio Grande do Norte, from 2008 to 2022. Rio Grande do Norte, 2023.

Despite the observed decline, the 7th Health Region (HR) maintained the highest absolute number of live births. Conversely, the 4th HR experienced a substantial decrease, with an approximate 50% reduction over the period, corresponding to 2,147 fewer births.

Regarding the incidence of congenital syphilis (CS) across the health regions, the 7th HR exhibited the highest rates, with a consistent upward trend throughout the years analyzed. Similar patterns were identified in the 1st, 2nd, 4th, and 8th HRs, which also demonstrated a gradual increase in reported cases. In contrast, the 3rd HR showed a decline in incidence during the last three years evaluated (2020–2022), while the 5th HR presented a significant reduction following a peak in 2020 (Figure 2).

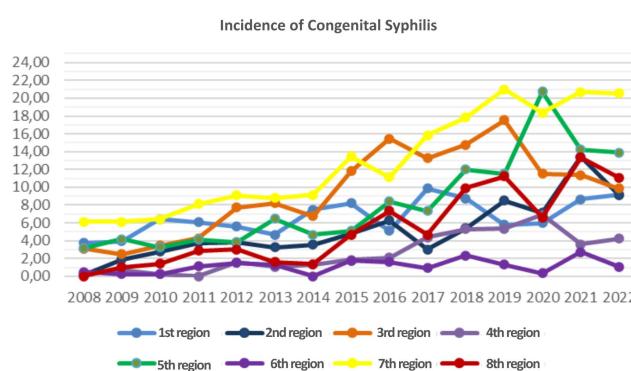


Figure 2. Incidence of Congenital Syphilis Cases in Newborns per 1,000 Live Births, 2008 to 2022. Rio Grande do Norte, 2023.

In 2022, a total of 525 new cases of CS were reported in the state, approximately 100 fewer than in 2021 (Figure 3). Of this total, the 3rd Health Region (HR) accounted for 322 cases, exhibiting a markedly higher average rate than the other regions, at 25.51 cases per 1,000 live births. The lowest average rates were observed in the 6th, 4th, and 2nd HRs, with 1.04, 2.15, and 3.46 cases per 1,000 live births, respectively.

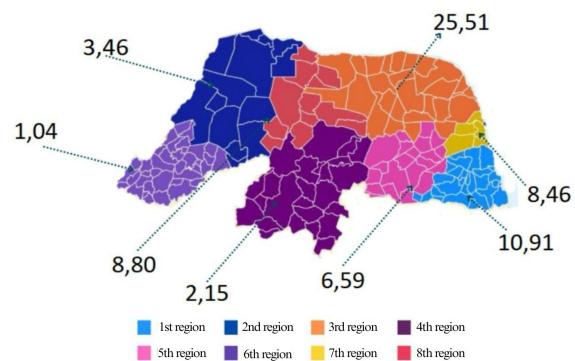


Figure 3. Average incidence of congenital syphilis cases per 1,000 live births in Rio Grande do Norte, from 2008 to 2022. Rio Grande do Norte, 2023.

Although the 3rd HR accounts for the fourth largest share of the population in Rio Grande do Norte, it maintained the highest average number of CS cases during the study period, followed by the 1st HR, with 10.91 cases per 1,000 live births. In 2016, the 3rd HR reached an alarming average of 67.91 cases per 1,000 live births, followed by a gradual decline in subsequent

years and a sharp decrease during the Covid-19 pandemic.

Forecasts suggest that, starting in 2024, the 8th HR will surpass the 3rd HR, reaching the highest projected

average of CS cases, estimated at 175.58 per 1,000 live births. By 2026, this figure is expected to rise to 245.19 cases per 1,000 live births, with a downward trend anticipated from 2027 onward (Figure 4h).

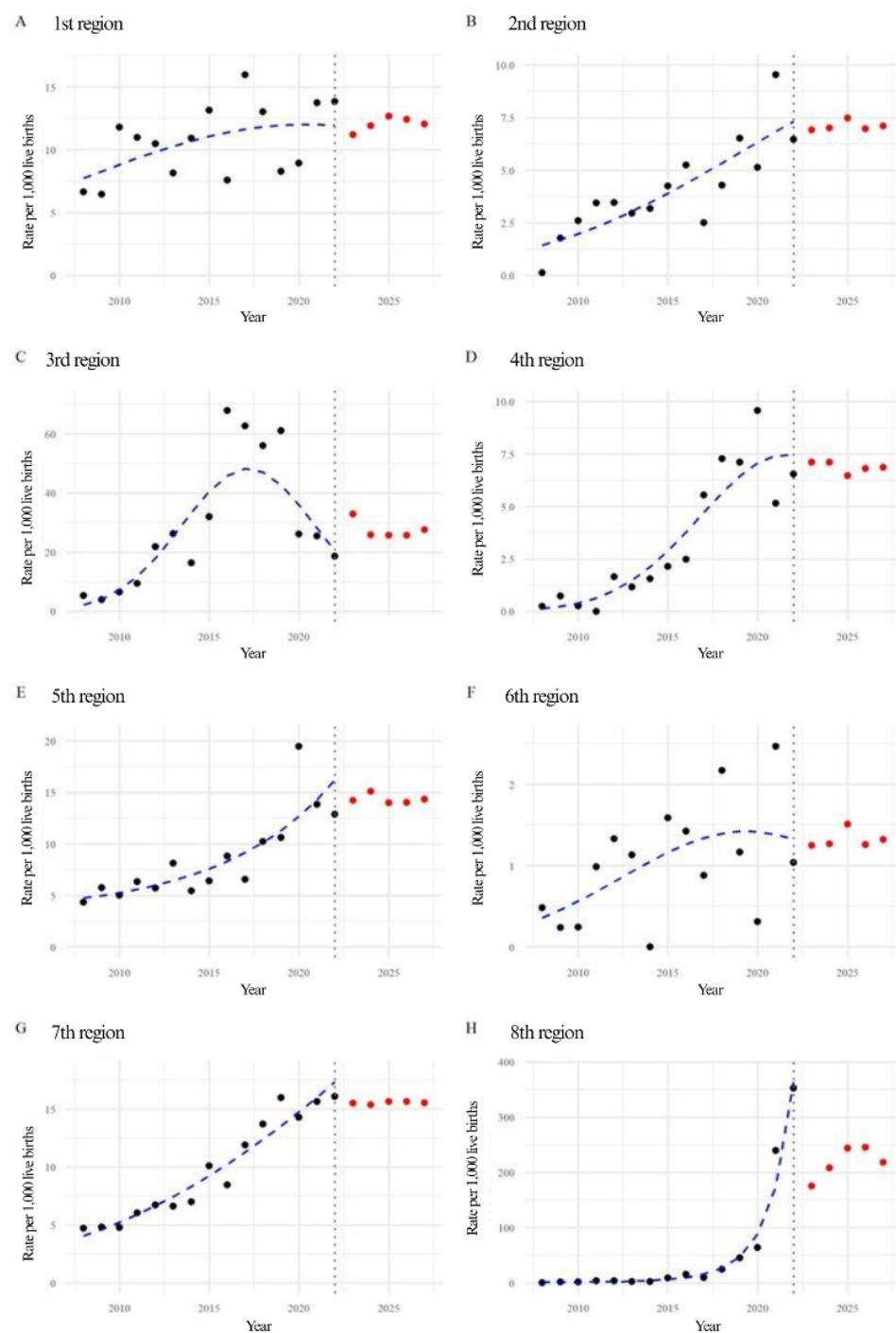


Figure 4. Forecast of the number of cases per 1,000 live births of congenital syphilis in the Health Regions of RN, from 2024 to 2027. Rio Grande do Norte, 2023.

DISCUSSION

The analysis of CS in Rio Grande do Norte revealed a high incidence of cases across the HR, with an upward trend over the study period, increasing from 168 cases in 2008 to 525 in 2022. According to the 2023 epidemiological bulletin, the state ranked fourth in the

Northeast in absolute number of cases, with 527 notifications, and fifth in Brazil in incidence rate (13.2/1,000 live births).⁷

The Pan American Health Organization (PAHO) recommends that CS be reduced to ≤ 0.5 cases per 1,000 live births, a parameter considered indicative of low incidence.³ In the absence of official thresholds,

previous studies have proposed the following classifications: intermediate incidence (0.4–4.0), high (4.01–8.0), and very high (>8.0/1,000 live births).¹¹ Within this framework, none of the HRs in the state met the PAHO goal: the 2nd, 4th, and 6th HRs fell into the intermediate category; the 5th HR into the high category; and the 1st, 3rd, 7th, and 8th HRs into the very high category, as demonstrated in the results (Figure 4).

The HRs with very high incidence, except for the 8th, are part of Macroregion I, which concentrates the largest supply of maternal and child health services and technologies.¹¹ Of note is the 7th HR, corresponding to the metropolitan area, which, despite being the smallest in number of municipalities, has the largest population and recorded the highest incidence rates during the study period. This region includes the state capital, Natal, which in 2022 reported the third highest incidence rate among Brazilian capitals (27.0/1,000 live births).⁷

An ecological study conducted in the Northeast in 2022, using SINAN and SINASC data, found an association between higher CS incidence and geographic location, particularly in metropolitan and coastal municipalities. Another finding was the elevated risk of vertical transmission in Natal. This high detection rate may reflect both increased availability of health services and testing, as well as more structured notification systems.¹²

With regard to diagnosis, treponemal rapid tests, available in Primary Health Care, enable early identification and are incorporated into routine prenatal care in all three trimesters of pregnancy, as well as at hospital admission for delivery.¹³ Nevertheless, the 3rd HR showed the highest incidence in the state (25.51/1,000 live births), despite having 98.72% coverage of the Family Health Strategy (FHS).¹⁴ This finding suggests shortcomings in clinical management of pregnant women, corroborating studies that report increasing CS rates in the Northeast regardless of prenatal care uptake.¹² Another aggravating factor is the recurrent global shortage of benzathine penicillin.¹

In 2021, the Brazilian Ministry of Health updated its technical manual for syphilis diagnosis, recommending the use of treponemal tests combined with clinical evaluation at the start of investigation due to their high sensitivity. However, because they induce a serological scar, treponemal tests should not be used to monitor therapeutic response; non-treponemal tests such as VDRL, RPR, and TRUST are required for follow-up.¹³

Despite the wide availability of diagnostic tests, a national study (2014) showed that fewer than 50% of municipalities in the Northeast and Southeast provided benzathine penicillin in more than half of their Primary Care teams.² Where the drug was available, vertical transmission was reduced. Administration requires

physician support and availability of adrenaline to manage possible anaphylactic reactions, which may discourage municipalities from providing treatment, compounded by shortages of trained professionals.¹⁵

Conversely, the 2nd, 4th, and 6th HRs had the lowest CS incidence, reaching zero cases in the 4th HR in 2011. This reduction may be linked to improvements in maternal and child health care, particularly following the implementation of the Rede Cegonha program, care territorialization, and expansion of the FHS.¹¹ However, underreporting remains a challenge, especially in municipalities with limited technological capacity for data recording.² A previous study documented substantial underreporting of adverse outcomes such as fetal and infant deaths, even in areas with structured surveillance systems.¹⁶

Follow-up of exposed infants is the responsibility of Primary Care, which should refer them when necessary.¹⁴ The protocol includes serial testing (at 1, 3, 6, 12, and 18 months) to avoid unnecessary invasive procedures.¹ Persistence or increased titers requires further investigation, including lumbar puncture.

Despite advances, a study conducted in Natal (2011–2015) revealed late diagnosis among pregnant women, often in the third trimester or only at delivery. Partner treatment was documented in just 10.9% of cases, favoring reinfection.^{14,17} The epidemiological profile of pregnant women with syphilis has been linked to greater social vulnerability, low educational attainment, and brown skin color.^{18–19}

Vertical transmission occurred in approximately 45% of pregnant women in the state in 2022.⁷ It is estimated that 60% of children with CS develop neurosyphilis, particularly those symptomatic at birth.¹⁴ However, a local study identified flaws in neonatal follow-up: 73.5% had no record of lumbar puncture and 47% did not undergo long-bone radiography, despite receiving treatment.¹⁷

Projections for 2024–2027 indicate an increase in cases, particularly in the 8th, 3rd, and 7th HRs. Spatial analysis, therefore, proves to be a crucial tool to guide regionally tailored interventions.²⁰

Given these findings, it is clear that early diagnosis, timely treatment of pregnant women and their partners, assurance of essential supplies, and capacity building of FHS teams must be strengthened. Shortages of professionals and resources in Primary Care undermine the effectiveness of health care and hinder progress toward established goals.

Study limitations include the use of secondary data, subject to incomplete reporting and underreporting. Furthermore, the ecological design did not allow for identification of individual-level characteristics associated with case occurrence.

Finally, the expected rise in CS cases suggests a potential future burden on specialized health services.

Investment in educational interventions, strengthening of Primary Care, and training of health professionals, especially nurses, must be prioritized to prevent new cases and reduce vertical transmission.

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AUTHORS' CONTRIBUTIONS

Dhyanine Morais de Lima Raimundo contributed to project administration, literature review, methodology, discussion, interpretation and presentation of results, conclusions, revision, and statistical analysis. **Richardson Augusto Rosendo da Silva** contributed to project administration, literature review, methodology, discussion, interpretation and presentation of results, conclusions, revision, and statistical analysis. **Rita de Cássia Azevedo Constantino** contributed to the literature review, abstract writing, introduction, methodology, discussion, interpretation and presentation of results, table development, conclusions, revision, and statistical analysis. **Angelo Maximo Soares de Araujo Filho** contributed to methodology, interpretation of results, conclusions, revision, and statistical analysis. **Ketyllem Tayanne da Silva Costa** contributed to abstract writing, introduction, methodology, discussion, interpretation and presentation of results, conclusions, revision, and statistical analysis. **Harlon França de Menezes** contributed to project administration, literature review, methodology, discussion, interpretation and presentation of results, conclusions, revision, and statistical analysis. **Ana Elza Oliveira de Mendonça** contributed to methodology, interpretation of results, conclusions, revision, and statistical analysis.

All authors approved the final version for publication and are collectively responsible for all aspects of the work, including ensuring its accuracy and integrity.

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