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A spatio-temporal analysis of very low-birth-weight and low-birth-weight prevalence in Brazil from 2010 to 2023

Short title: VLBW and LBW prevalence in Brazil, 2010-2023

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MLZ: Methodology, Visualization, Writing – review & editing. AAMS: Visualization, Writing – review & editing. MAAB: Methodology, Software, Formal analysis, Writing – review & editing.

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A spatio-temporal analysis of very low-birth-weight and low-birth-weight prevalence in Brazil from 2010 to 2023

Abstract

Background: Given the strong link between low-birth-weight (LBW) and neonatal mortality, reducing neonatal mortality to at least 12 per 1,000 live births is one of the Sustainable Development Goals (SDGs) for 2030. **Objective:** The objective of this ecological study is to perform a spatio-temporal analysis of the prevalence of LBW and very low-birth-weight (VLBW) in Brazil between 2010 and 2023. **Methods:** This is an ecological study using data from 510 immediate regions in Brazil obtained from official health information systems. A Bayesian spatio-temporal model using integrated nested Laplace approximations (INLA) was employed, where spatial and temporal effects respectively used a conditional autoregressive dependence structure and a random walk of order two. **Results:** A total of 38,772,489 birth records from 2010 to 2013 were identified, being the average VLBW and LBW rates were estimated at 1.03% and 7.10%, respectively. An increase in the temporal trend of VLBW and LBW relative risks on a national scale was observed in the period, being a more expressive increase starting in 2020. The highest rates were observed in the Brazilian Southeast and South regions, compared to other regions. Regions with a higher number of physicians per inhabitant tend to have a higher number of cases of VLBW per 100 live births. Higher percentages of illiteracy are associated with lower VLBW rates, while higher gross domestic product (GDP) per capita is associated with higher VLBW rates in the immediate regions. **Conclusions:** The prevalence of LBW and VLBW has increased in Brazil and, in line with the LBW paradox, is higher in less vulnerable regions.

Keywords: Very-Low-Birth-Weight Infant; Low-Birth-Weight Infant; Bayes Theorem; Brazil

Análise espaço-temporal da prevalência de recém-nascidos com muito baixo peso e baixo peso ao nascer no Brasil, de 2010 a 2023

Resumo

Justificativa: Dada a forte associação entre baixo peso ao nascer (BPN) e mortalidade neonatal, reduzir a mortalidade neonatal para pelo menos 12 por 1.000 nascidos vivos é um dos Objetivos de Desenvolvimento Sustentável (ODS) para 2030. **Objetivo:** O objetivo deste estudo ecológico é conduzir uma análise espaço-temporal da prevalência de BPN e muito baixo peso ao nascer (MBPN) no Brasil entre 2010 e 2023. **Métodos:** Trata-se de um estudo ecológico que utiliza dados de 510 regiões imediatas do Brasil obtidos de sistemas oficiais de informação em saúde. Foi usado um modelo espaço-temporal bayesiano utilizando o método INLA (*integrated nested Laplace approximations*), em que os efeitos espaciais e temporais seguem, respectivamente, uma estrutura de dependência autorregressiva condicional e um passeio aleatório (*random walk*) de ordem dois. **Resultados:** Um total de 38.772.489 registros de nascimentos de 2010 a 2013 foram identificados, sendo que as taxas médias de MBPN e BPN foram estimadas em 1,03% e 7,10%, respectivamente. Observou-se um aumento na tendência temporal dos riscos relativos de MBPN e BPN em escala nacional no período, sendo um aumento mais expressivo a partir de 2020. As taxas mais elevadas foram observadas nas regiões Sudeste e Sul do Brasil, em comparação com outras regiões. Regiões com maior número de médicos por habitante tendem a apresentar maior número de casos de MBPN por 100 nascidos vivos. Maiores porcentagens de analfabetismo estão associadas a menores taxas de MBPN, enquanto maior produto interno bruto (PIB) per capita está associado a maiores taxas de MBPN nas regiões imediatas. **Conclusões:** A prevalência de BPN e MBPN aumentou no Brasil e, em consonância com o paradoxo do BPN, é maior em regiões menos vulneráveis.

Palavras-chave: Recém-Nascido de muito Baixo Peso; Recém-Nascido de Baixo Peso; Teorema de Bayes; Brasil

Análisis espaciotemporal de la prevalencia del muy bajo peso al nacer y bajo peso al nacer en Brasil entre 2010 y 2023

Resumen

Justificación: Dada la fuerte relación entre el bajo peso al nacer y la mortalidad neonatal, reducir esta última a menos de 12 por cada 1000 nacidos vivos es uno de los Objetivos de Desarrollo Sostenible para 2030. **Objetivo:** El objetivo de este estudio ecológico es analizar la prevalencia del bajo peso al nacer (BPN) y del muy bajo peso al nacer (MBPN) en Brasil entre 2010 y 2023.

Métodos: Se trata de un estudio ecológico que utiliza datos de 510 regiones inmediatas de Brasil obtenidos de los sistemas oficiales de información sanitaria. Se empleó un modelo bayesiano espaciotemporal que utiliza el método INLA (*integrated nested Laplace approximations*), en el que los efectos espaciales y temporales utilizaron, respectivamente, una estructura de dependencia autorregresiva condicional y un paseo aleatorio (*random walk*) de orden dos. **Resultados:** Se identificaron un total de 38.772.489 registros de nacimientos entre 2010 y 2013, y las tasas medias de MBPN y BPN se estimaron en un 1,03 % y un 7,10 %, respectivamente. Se observó un aumento de la tendencia temporal de los riesgos relativos de MBPN y BPN a escala nacional durante el período, siendo este aumento más significativo a partir de 2020. Las tasas más altas se observaron en las regiones sudeste y sur de Brasil en comparación con otras regiones. Las regiones con mayor número de médicos por habitante tienden a presentar un mayor número de casos de MBPN por cada 100 nacidos vivos. Los porcentajes más altos de analfabetismo se asocian con tasas más bajas de MBPN, mientras que un mayor producto interior bruto (PIB) per cápita se asocia con tasas más altas de MBPN en las regiones analizadas. **Conclusiones:** La prevalencia del BPN y el MBPN ha aumentado en Brasil y, en consonancia con la paradoja del BPN, es mayor en las regiones menos vulnerables.

Palabras clave: Recién Nacido de muy Bajo Peso, Recién Nacido de Bajo Peso, Teorema de Bayes, Brasil.

Introduction

Among other adverse birth outcomes, low birth weight (LBW) is defined as a newborn weighing less than 2,500 g irrespective of the gestational age, while very low birth weight (VLBW) is defined as a birth weight of newborn of 1,500 g or less. Both LBW and VLBW infants typically experience a reduced prenatal duration, predisposing them to a range of perinatal and neonatal complications, as well as developmental problems that may impact their overall growth and development during infancy and throughout childhood¹⁻⁴. The duration of gestation and fetal growth are influenced by a variety of factors relating to the infant and the mother, all of which subsequently influence birth weight^{5,6}. These factors include teenage pregnancy, low socioeconomic status, exposure to tobacco, inadequate nutritional intake, low access to health facilities, maternal hypertension, and maternal anemia, among others^{7,8}.

Several ecological studies have suggested that maternal and child factors are interrelated with the surrounding environment and may be important indicators of birth weight⁹⁻¹³. These environmental factors can include maternal exposure to extreme temperatures¹⁴ or to atmospheric fine-particulate matter^{15,16} during pregnancy, or cultural and socioeconomic characteristics of the regions where the individuals, as neighborhood poverty, gross domestic product, percentage of the population with unsatisfied basic needs, and the dimensions of the human development index (HDI)¹⁷⁻¹⁹. Paradoxically, some studies have suggested that LBW is less prevalent in less developed and poorer areas. This phenomenon is described in the literature as “low birth weight paradox”, and has been studied in different countries, as Sweden²⁰, Spain²¹, Colombia¹⁸, and Brazil²²⁻²⁶. Álvarez-Castaño et al.¹⁸ claim that, in Colombia, the paradox may be more accurately by underreporting of birth weight information in poorer municipalities than by an actual socially determined cause. In Brazil, Silva et al.²³ hypothesizes that improved medical interventions for preterm newborns towards the end of pregnancy or errors in determining gestational age may explain low birth weight rates. According to these authors, this is due to the greater availability of technologies that ensure higher live birth rates in more developed municipalities, even among children at high risk of low intrauterine growth caused by pregnancy complications²³.

The objective of this ecological study is to perform a spatio-temporal analysis of the prevalence LBW and VLBW in Brazil between 2010 and 2023, using open-access data from official health information systems aggregated by 510 immediate regions. The World Health Assembly (WHA) set a target to reduce the number of LBW newborns by 30% between 2012 and 2025²⁷. Given the strong link between LBW and neonatal mortality, this target is also considered to be part of the 2030 Sustainable Development Goals (SDGs), which aim to reduce neonatal mortality to at least 12 per 1,000 live births. Therefore, results from ecological studies are important to monitor health indicators associated with birth weight. This allows us to verify pre-established targets and identify regions requiring greater attention.

A variety of applications involving spatio-temporal data can make use of Bayesian models, which are a useful tool for handling very complex models²⁸. One such model is the Bayesian conditional autoregressive (CAR) model, which is commonly used for areal data and includes a term in the mean regression equation to account for spatial random effects. In this article, we employed a Bayesian model with integrated nested Laplace approximations (INLA), where the spatial effects followed an intrinsic CAR dependence structure and the temporal effects were based on a random walk of order two (RW2). This model allows for interaction between space and time, which could explain the differences observed in the time trends of LBW and VLBW in different areas²⁹.

Methods

Setting and study design

We conducted an ecological study based on secondary data of live births at the Brazilian immediate regions level. According to the Brazilian Institute of Geography and Statistics (IBGE), immediate regions comprise several municipalities and represent regional geographic divisions associated with social, political and economic processes observed throughout the country³⁰. First, we conducted an analysis from 2010 to 2023 to describe the spatial and temporal patterns of LBW and very low birth weight VLBW prevalence. Secondly, we examined the association between the number of LBW and VLBW infants per 100 live births in 2022 and some socioeconomic

indicators. This analysis used data from 2022, as this is the most recent year for which IBGE census data is available.

Measurements

The number of LBW and VLBW infants, as well as the number of live births in each Brazilian municipality was obtained from the Brazilian Information System on Live Births (SINASC)³¹ for the period from 2010 to 2023. Twin births were not included.

The number of LBW and VLBW infants per 100 live births in 2022 was hypothesized to be associated with the following indicators:

- The number of physicians per 1,000 inhabitants was used as a proxy variable for the provision of healthcare services in each immediate region. This data was obtained from the National Register of Health Establishments (CNES) of the Department of Informatics of SUS (DATASUS), a national database that collects mandatory information monthly from all health facilities for a wide range of indicators, such as capacity and human resources. Data for December 2022 were considered.
- The percentage of illiterate people aged 15 and over was used as a proxy for educational performance in each region. This information was obtained from the IBGE Automatic Recovery System (SIDRA) for the 2022 Demographic Census.
- The gross domestic product (GDP) per capita was used as a proxy measure for the economic conditions of the immediate regions. The total GDP for each municipality was calculated by multiplying the GDP per capita by the municipality's population. These totals were then aggregated for each immediate region to obtain the overall GDP at immediate regional level. GDP per capita for each region was calculated by dividing the region's total GDP by its population. This information also was obtained from SIDRA, and data for 2021 were considered.

Data at municipality-level were downloaded from the website of the Brazilian Health Informatics Department (DATASUS, <https://datasus.saude.gov.br>) and were then aggregated into immediate

region level. Data from the DATASUS health information system is publicly accessible and anonymized. Thus, obtaining ethical approval for the study was not necessary.

Statistical analysis

The number y_{it} of LBW (or VLBW) individuals in the i -th immediate region and in the year t was modelled as

$$y_{it} \sim \text{Poisson}(\rho_{it}E_{it}),$$

where E_{it} is the number of live births in the immediate region i ($i = 1, \dots, 510$) and in the year t ($t = 1$ for 2010, $t = 2$ for 2011, etc.)³². Our analysis was based on the following model specifications:

$$\eta_{it} = \log \rho_{it} = \alpha + \xi_i + \gamma_t + \phi_t + \delta_{it},$$

where α is the intercept, $\xi_i = \nu_i + v_i$ combines two area specific effects, γ_t is a temporally structured effect modelled dynamically using a random walk of order two (RW2), ϕ_t is specified by means of a Gaussian exchangeable prior, and δ_{it} is the interaction term between space and time, accounting for any residual spatiotemporal variation that was not captured by the spatial or temporal main effects. Note that, in this formulation, $\exp(\alpha)$ represents the average LWB (or VLBW) rate across all 510 immediate regions over the entire period from 2010 to 2013. In addition, the temporal effect $\exp(\gamma_t + \phi_t)$ measures the ratio between the rate in the year t and the average rate over the entire period. In the expression $\xi_i = \nu_i + v_i$, the effect ν_i is a spatially structured residual, modelled using an intrinsic conditional autoregressive (iCAR) structure where weights were assigned to each region according to adjacency, based on a reparametrization of the Besag-York-Mollié specification known as ‘BYM2’^{33,34}, and v_i is a parameter representing an unstructured residual, modelled using an exchangeable normal prior²⁹. The area-specific relative risk or the spatial trend is calculated from the posterior means of the random effects $\exp(\xi_i) = \exp(\nu_i + v_i)$ for the 510 immediate regions. The higher the value of $\exp(\xi_i)$, the higher the risk of LBW in the given region i , over the whole period 2010 to 2023³⁵.

To associate the number of LBW and VLBW infants per 100 live births in 2022 with an independent variable denoted by x_i , the following specification for the Poisson model was used:

$$\eta_i = \log \rho_i = \alpha + \xi_i + \beta x_i,$$

where β is the correspondent regression coefficient. Bayesian 95% credible intervals (95%CI) were obtained from the posterior distribution of β , where 95%CI that does not contain zero suggest evidence of association between the independent variable and the number of LBW (or VLBW) infants (similar to usual $p < 0.05$). Due to the high multicollinearity observed among the independent variables (number of physicians per 1,000 inhabitants, percentage of illiterate people aged 15 and over, and GDP per capita), they were examined through separate models rather than employing multiple linear regression analysis. In these models, all these indicators were transformed into logarithms due to their highly skewed distributions.

The parameters of all the models were estimated using the INLA method³⁶. Other nested models with simpler formulations were also fitted to the same set of data, and the deviance information criterion (DIC) was used to compare between them. The model with the lowest DIC value was considered the better model.

All analyses were performed using R software version 4.4.1. The 'sp', 'spdep', 'sf' and 'mapview' packages were used to handle the spatial data and generate maps based on the shapefile for the immediate regions available on the IBGE website. The 'INLA' package was used to implement Bayesian estimation³⁷.

Results

A total of 38,772,489 birth records from 2010 to 2013 were identified. Based on the fit of the Bayesian models, the average VLBW rate across all 510 immediate regions over the entire period from 2010 to 2013 was estimated at 1.034%, while the average LBW rate was estimated at 7.096%.

Figure 1 shows the yearly increase in the risk of VLBW (Panel (a)) and LBW (Panel (c)) in relation to the mean of the period 2010 to 2023, and the maps of the spatial pattern of VLBW (Panel (b)) and LBW (Panel (d)) risks, obtained from the Bayesian model. Panels (a) and (c) of Figure 1 show an increase in the temporal trend of VLBW and LBW relative risks on a national scale between 2010 and 2023. Panel (c) highlights a more expressive increase starting in 2020. The VLBW rate increased from 1.10% to 1.28% between 2010 and 2023. The LBW rate increased from 7.38% to 8.21% over the same period.

Maps representing the spatial patterns of VLBW and LBW risks over the study period are presented in panels (b) and (d) of Figure 1. These maps indicate higher risks in the Brazilian Southeast and South regions compared to the North, Northeast and Central-West regions.

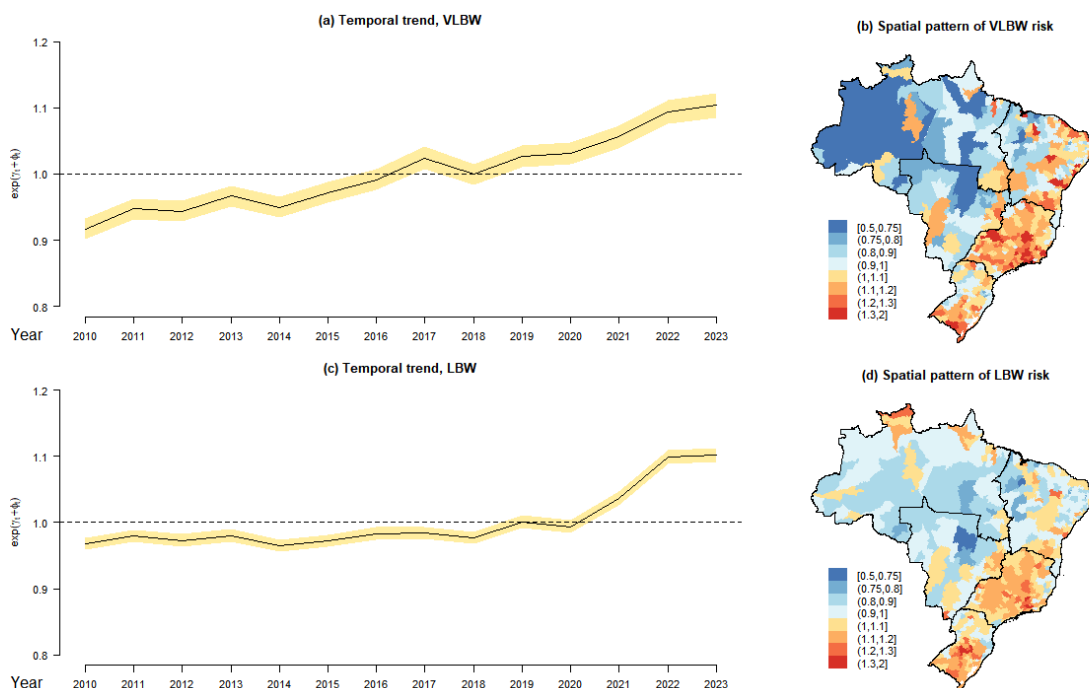


Figure 1. Spatial and temporal effects estimated by the Bayesian model. (a) Common temporal trend of VLBW relative risks on a national scale given by $\exp(\gamma_t + \phi_t)$. The yellow region is a 95% credible interval. (b) Map of the spatial pattern of VLBW risk given by $\exp(\xi_i) = \exp(v_i + v_i)$. (c) Common temporal trend of LBW relative risks on a national scale. (d) Map of the spatial pattern of LBW risk. The maps highlight the five major regions of Brazil (North, Northeast, Central-West, Southeast, and South).

Figures 2 and 3 show the maps of the smoothed Bayesian estimates for the number of cases of VLBW and LBW per 100 live births, respectively, in each immediate region between 2010 and 2023, stratified by octiles categories. These maps newly evidence that regions Southeast and South have the highest rates of VLBW and LBW.

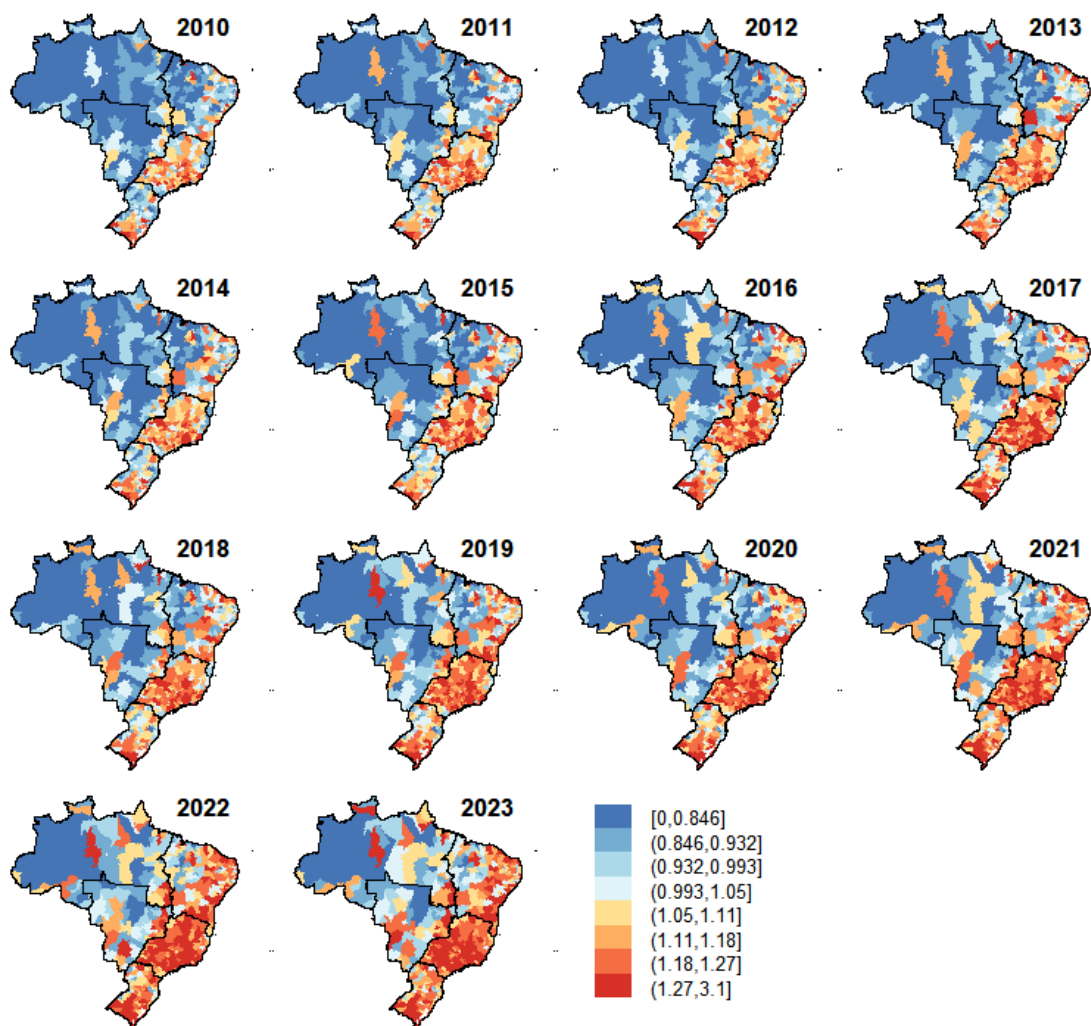


Figure 2. Cases of VLBW per 100 live births between 2010 and 2023, estimated by the Bayesian spatio-temporal INLA model and stratified by octiles categories.

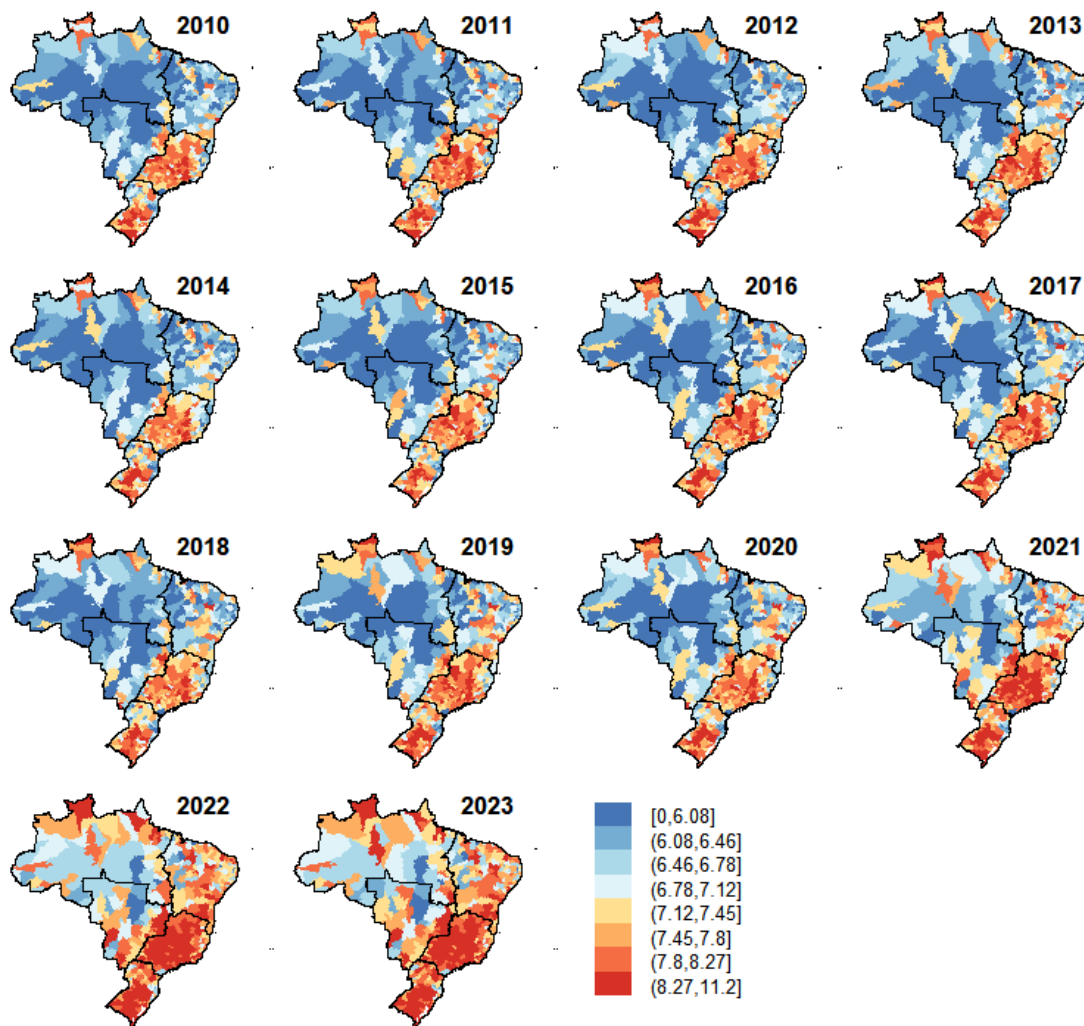


Figure 3. Cases of LBW per 100 live births between 2010 and 2023, estimated by the Bayesian spatio-temporal INLA model and stratified by octiles categories.

The graphs in Figure 4 show the relationship between the number of physicians per 1,000 inhabitants, percentage of illiterate people aged 15 and over, GDP per capita, and the number of cases of VLBL and LBW per 100 live births in 2022. In Panel (a), the β regression coefficient is estimated at 0.149 (95%CI: 0.113, 0.185), indicating that regions with a higher number of physicians per inhabitant tend to have a higher number of cases of VLBW per 100 live births. In Panels (b) and (c) the β regression coefficients are given by -0.203 (95% CI: -0.255, -0.151) and 0.09 (95%CI: 0.043, 0.138) for the effects of the percentage of illiterate people aged 15 and over and GDP per capita respectively. These coefficients also suggest significant effects of these variables on VLBL rates. Higher percentages of illiteracy are associated with lower VLBW rates,

while higher GDP per capita is associated with higher VLBW rates in the immediate regions. In Panel (d), the β regression coefficients is 0.06 (95%CI: 0.039, 0.081), also indicating a positive effect of the number of physicians per inhabitant on the LBW rates. Panel (e) shows that higher percentages of illiteracy are associated with lower LBW rates ($\beta = -0.069$, 95%CI: -0.100, -0.038). Finally, the graph in Panel (e) shows no evidence of an association between GDP per capita and the LBW rates ($\beta = 0.016$, 95% CI: -0.009, 0.042; the interval includes the value zero).

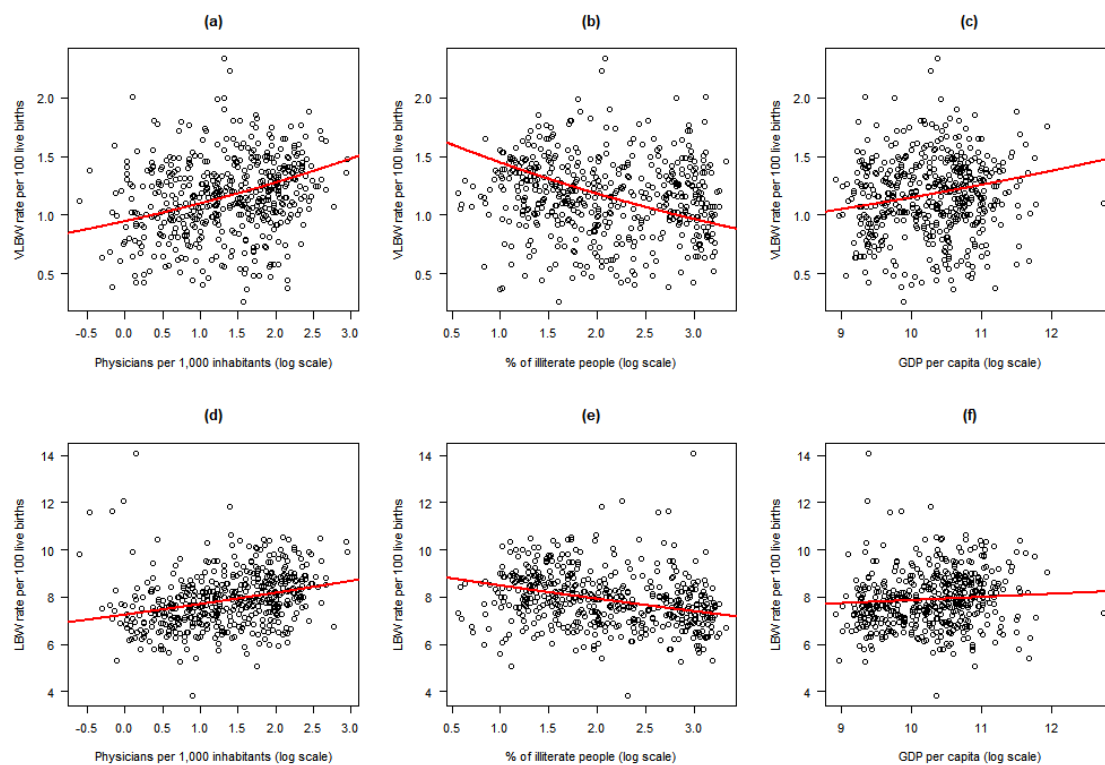


Figure 4. Relation between the number of physicians per 1,000 inhabitants, percentage of illiterate people aged 15 and over, and GDP per capita (log scale) with the number of cases of VLBL and LBW per 100 live births in 2022.

Discussion

Identifying spatial patterns of LBW and VLBW and its determinants is important for understanding the epidemiology of this public health challenge, while the temporal patterns are essential for surveillance practices. The present study highlights two main findings in this regard.

Firstly, the results reaffirm the low-birth-weight paradox by showing that regions subject to greater social vulnerability have lower rates of LBW and VLBW. Secondly, Brazil will find it difficult to comply with the Sustainable Development Goals (SDG) target of reducing neonatal mortality to at least 12 per 1,000 live births by 2030, given the observed increase in the prevalence of LWB and VLWB.

Our findings indicate that 7.38% of Brazilian newborns were born with LBW in 2010, increasing to 8.21% in 2023. This last prevalence rate is comparable to that observed in Latin America and the Caribbean in 2015 (8.7%), but much lower than that observed in Southern Asia (26.4%)³⁸. As examples of studies conducted in other countries, the prevalence of LBW in infants was found to be 10.4% in Malaysia³⁹, 15.3% in Nepal⁴⁰, 14.3% in Bangladesh⁴¹, and 39.1% in Taiz City, Yemen⁴². Additionally, a secondary data analysis⁴³ based on Demographic and Health Surveys (DHS) showed that the prevalence of LWB in 35 sub-Saharan African countries varied from 6.3% in Guinea to 16.21% in Ethiopia, yielding an overall prevalence of 9.47%. While the frequency of LBW in Brazil in 2023 appears to be modest when compared to other nations, it is greater than in North America (7.9%), Europe (6.5%), and Australia and New Zealand (6.4%)³⁸. This is concerning because the well-known health effects extend beyond infant death to include long-term morbidities and unfavorable outcomes such as obesity, diabetes, elevated leptin levels, and cognitive impairments^{44,45}. Our results also show that, between 2010 and 2023, the VLBW prevalence in Brazil rose from 1.10% to 1.28%. VLBW is associated with an increased risk of physical, cognitive and developmental challenges during childhood which may persist into adolescence and adulthood^{46,47}, as well as a higher mortality rate than LBW⁴⁸.

Our findings suggest that LBW and VLBW are more prevalent in Brazil's South and Southeast areas, which are noted for their higher economic and social development. A Bayesian regression model with spatial components showed that the VLBW prevalence in 2022 is positively associated with the number of physicians per 1,000 inhabitants and GDP per capita and inversely related to the percentage of illiterate people aged 15 and over. The LBW prevalence was positively associated with the number of physicians per inhabitant and inversely related to

illiteracy rates. This confirms the low-birth-weight paradox, which states that LBW and VLBW rates are lower in more vulnerable regions. In addition to the increasing availability of technology that ensures higher birth rates in more developed regions, as indicated by Silva et al.²³, we can hypothesize some other factors that could be investigated in future research. In Brazil, regions with lower Human Development Index values have a higher proportion of live births to adolescent mothers⁴⁹, although these rates are declining⁵⁰. However, a U-shaped link between maternal age and LBW is possible. Delayed childbearing may be more common in more developed locations and be associated with LBW, although this relationship is controversial in the literature^{51,52}. The Brazilian National Abortion Survey, carried on in 2021, showed that higher rates of abortion were detected among women residing in poorer regions⁵³. The higher frequency of pregnancy interruptions in more vulnerable regions, which could be related to low birth weight, could also be related to the paradox.

Disparities in access to fetal monitoring technologies, such as adequate ultrasound, and health infrastructure in less developed regions increase the likelihood of at-risk fetal pregnancies resulting in stillbirth, given the lack of resources for intervention and rescue. In more developed regions, however, the widespread availability of advanced perinatal technologies and a network of Neonatal Intensive Care Units enables the early identification and intervention of a significantly larger number of vulnerable neonates. While this capacity reduces stillbirth rates, it paradoxically contributes to an increase in the proportion of live births with low birth weight and/or prematurity, as these neonates, who would previously have been stillborn, are now rescued and classified as LBW newborns. In conclusion, the low-birth-weight paradox can be a complex phenomenon, with many related factors.

The increased prevalence of LWB and VLWB throughout the period from 2010 to 2023 could be a consequence of improvements in the technologies available in public health services, as part of the low-birth-weight paradox. While the potential improvement in resource availability for the population is seen as a positive development, the increase in the number of LBW children indicates the need for adjustments to health services to ensure they are prepared to care for these

infants. Additionally, considering that LWB and VLWB are important determinants of morbidity and mortality, particularly during the neonatal period, strategies aimed at reducing preventable infant deaths must prioritize the prevention of prematurity by ensuring adequate prenatal care for women⁵⁴.

The fundamental limitation of this study is its ecological design, which prevents the extrapolation of regional-level relationships discovered to the individual level (known as ecological fallacy). Additionally, data obtained from the national information systems may be subjected to underreporting⁵⁵. For convenience, we used the number of physicians per 1,000 inhabitants, the percentage of illiterate people aged 15 and over, and GDP per capita as proxy variables for the provision of healthcare services, educational performance, and the economic conditions of each region, respectively. However, we cannot guarantee that these variables are the most valid representation of these indicators. Despite these limitations, this study provides important information on the prevalence of LWB and VLWB throughout the period from 2010 to 2023, as well as their geographical distribution.

Conclusion

Applying a Bayesian spatio-temporal model revealed an increase in the prevalence of LBW and VLBW newborns in Brazil between 2010 and 2023, particularly in the most developed regions. This finding is consistent with the low-birth-weight paradox, whereby greater resources are associated with higher rates of LBW and VLBW. This paradox can be explained by the ability to 'rescue' vulnerable pregnancies, transforming potential stillbirths into LBW newborns. While a decrease in stillbirths has been observed, adjustments to health services for high-risk neonates are required to contribute to target 3.2 of the Sustainable Development Goals for 2030, which aims to end preventable newborn deaths.

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