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Temporal trend, spatial distribution, and factors associated with detection and mortality from viral hepatitis B and C in Brazil (2010–2019)

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ABSTRACT

Introduction: The elimination of viral hepatitis is one of the goals of the 2030 agenda, particularly because they pose significant public health challenges. **Objective:** To analyze the temporal trend, spatial distribution, and factors associated with the detection and mortality of viral hepatitis B and C in Brazil from 2010 to 2019. **Methods:** Ecological study on Brazilian regions and Federative Units. Annual detection and mortality coefficients were calculated. Trend analysis was performed using polynomial regression models. Thematic maps were constructed to illustrate spatial distribution. And the Spearman correlation coefficient was employed to assess the association with seven socioeconomic indicators. **Results:** Brazil exhibited a decreasing trend in hepatitis detection and mortality. The South and North regions had the highest rates of hepatitis B, with a decreasing and stable trend, respectively. The South and Southeast regions had the highest rates of hepatitis C, both showing a decreasing trend. Hepatitis B detection was more prevalent in Acre and Rondônia, while hepatitis C detection was higher in Rio Grande do Sul and Acre. There was an increase in the detection of infections and a decline in mortality from hepatitis C in Pará and Acre. Hepatitis detection was inversely related to the illiteracy rate and directly related to the human development index, life expectancy, and per capita income. **Conclusion:** Regional and state disparities in the behavior of viral hepatitis B and C in Brazil were evident, with areas (states) of higher development indexes exhibiting higher detection rates of the infections.

Keywords: hepatitis B; hepatitis C; diagnosis; mortality; ecological studies.

INTRODUCTION

The World Health Organization (WHO) has included the elimination of viral hepatitis as one of its goals in the sustainable development agenda for 2030[1]. Globally, viral hepatitis caused over 1.34 million deaths in 2015, with 66% attributed to hepatitis B virus (HBV) and 30% to hepatitis C virus (HCV)[2]—primarily due to cirrhosis and hepatocellular carcinoma[3]. Notably, in 2019, approximately 58 million people were living with HCV and 296 million with HBV worldwide[4].

In Brazil, between 1999 and 2019, there were over 670,000 reported cases of viral hepatitis, with a higher occurrence of cases caused by HCV (37.6%) and HBV (36.8%)[5]. To address these diseases at the national level, the Ministry of Health has committed to expanding diagnosis and treatment within the Brazilian Unified Health System (SUS), aligning with international efforts to eliminate these infections as public health concerns by the end of this decade[5].

Key actions targeted at early diagnosis, vaccination, rapid testing, and antiviral therapy are indispensable measures for controlling hepatitis B and C[4,5]. Globally, adopting these strategies, important milestones were achieved for the reduction of morbidity and mortality from these diseases, with emphasis on vaccination strategies against hepatitis B and the cure of hepatitis C cases, through active search, treatment, and attachment to care[6].

WHO advocates, as one of its strategies for the elimination of viral hepatitis, the qualification and the use of health information to understand epidemiological scenarios, aiming at the logistical direction of responses and interventions[1]. From this perspective, we consider time series analyses as relevant statistical method to evaluate temporal trends of health data at regular intervals, allowing the visualization of their probable behavior in the future[7].

Nevertheless, it is crucial to acknowledge the possible influence of the geopolitical and spatial contexts on the occurrence of hepatitis B and C[8], considering that social, economic and programmatic factors—among which we can mention the low education level, the high prevalence of HBV or HCV, the higher population density, and the lower gross domestic product (GDP) *per capita*—have already been evidenced as important predictors for the high occurrence of these aggravations[9-13].

In this sense, it is pertinent to develop time series and geospatial studies for the description of temporal trends and for the prediction of disease behaviors, as well as for the identification of priority territories and factors associated with their occurrence. Therefore, this study aimed to analyze the temporal trend, spatial distribution, and factors associated with the detection and mortality of viral hepatitis B and C in Brazil from 2010 to 2019.

METHODS

This is a temporal and spatial ecological study, whose analytical units were the Federative Units (FUs) and the Brazilian regions. Brazil, located in South America, has more than 213 million inhabitants, a territorial extension of 8,510,417,771 square kilometers, and a *per capita* GDP of 35,935.74 BRL. The country consists of 5,570 municipalities, distributed in 26 states and the Federal District, which, in turn, are organized in regions: North, Northeast, Midwest, South and Southeast[14].

We conducted an investigation covering the records about cases and deaths from hepatitis B and C in the country, publicly available in national systems. The data came from the Information System of Notifiable Diseases (SINAN) and the Brazilian Institute of Geography and Statistics (IBGE), via the Department of Informatics of the Unified Health System (DATASUS); the Panel of Indicators of Viral Hepatitis (PIVH), from the Ministry of Health; and the Atlas of Human Development of Brazil (AHD).

The period from 2010 to 2019 was considered given the availability of data on mortality until this year. In addition, we decided to work with the pre-pandemic years due to the burden of care and surveillance, preceded by the reorganization of actions and health services to cope with coronavirus disease 2019 (COVID-19). Thus, the detection data of 2020 were disregarded for the possibility of masking the epidemiological scenario, since there may have been under diagnosis and/or underreporting[15,16].

The data collection took place in the first half of September 2022 through the elaboration of an instrument in a Microsoft Excel® 2016 spreadsheet to assist in tabulating the data. Contingency tables were created with the variables of interest of SINAN and PIVH, considering the guidelines of the Ministry of Health[8]: confirmed cases (by laboratory or clinical-epidemiological criteria) or deaths (as a basic cause), year of diagnosis or death and place of notification (Brazil, FUs and regions).

From AHD, the following development indicators of the Brazilian FUs were extracted from the National Household Sample Survey (PNAD) and administrative records of DATASUS, 2017: (i) Human Development Index (HDI); (ii) illiteracy rate among people aged 18 years or more; (iii) Gini index; (iv) infant mortality rate; (v) life expectancy at birth; (vi) *per capita* income; and (vii) percentage of hospitalizations for primary care sensitive conditions (PCSC).

The detection and mortality coefficients were calculated year by year for each analytical unit. To this end, the formula recommended by the Ministry of Health was used, namely: the numerator consisted of the number of confirmed cases or number of deaths due to HBV and HCV, according to the year of diagnosis or death and place of notification; the denominator referred to the population for the respective year, residing in the same place; and the multiplication factor was 100,000 inhabitants (inhab.)[8].

In the calculations of the coefficients, the denominator referred to the IBGE census for the year 2010 and, for the intercensitarian years, to the study of population estimates of the Ministry of Health. With the annual coefficients, the arithmetic mean (ratio of the sum of the coefficients by the total of observations) was calculated for the FUs. We used polynomial regression models for trend analyses, which consisted of the use of a polynomial function to explain the behavior of a time series[17].

The coefficients were considered as the dependent variable (y) and the years of the series as the independent variable (x). To avoid autocorrelation between polynomials, the year variable was transformed into the year-centered variable (year minus the midpoint of the series). In addition, given random variations, the detection and mortality coefficients were smoothed by a three-point moving average (arithmetic mean of the previous year, the same year and the following year)[17].

Scatter diagrams were constructed to check which function best fit the data. First-order models ($y=\beta0\pm\beta1x$) and, when necessary, second-order ($y=\beta0\pm\beta1x\pm\beta2x^2$) and third-order models ($y=\beta0\pm\beta1x\pm\beta2x^2\pm\beta3x^3$) were tested, where $\beta0$ represented the average coefficient (intercept), and $\beta1$, $\beta2$, and $\beta3$ configured the regression coefficients (evolution), determining the annual variation/acceleration and, based on the sign, the increasing (+) or decreasing (–) trend[17].

The choice of the best polynomial model considered the significance by the *F* test (observing, individually, the *t* test for each regression coefficient), the highest coefficient of determination (r^2) (close to 1.00), and the analysis of residuals (true homoscedasticity assumption), verifying them in scatter plots. When the criteria were contemplated/similar for more than one model, the one with the simplest polynomial order was chosen[17].

Maps were constructed for the spatial distribution of the coefficients and the trend for the FUs. The distribution of the coefficients was given by the natural breaks[18] on a scale of blue tones, defining light and dark colors to the minimum and maximum coefficients, respectively. The trend was presented in: light blue, if decreasing; white, if stationary; and dark blue, if increasing. The figures were constructed, from the shape file obtained in IBGE, by QGIS® software, version 2.36.

Finally, the Spearman correlation coefficient (ρ) was used to verify the relationship of development indicators with mean detection and mortality coefficients, since they did not adhere to the normal distribution. The ρ may represent an inverse (–) or direct (+) correlation, classified as weak (±0.31 to ±0.50), moderate (±0.51 to ±0.70), or strong (±0.71 to ±1.00)[19]. The analyses were performed in the software SPSS, version 20.1, adopting the statistical significance of 5% ($p \leq 0.05$).

In line with the research ethics guidelines recommended by resolution No. 466, 2012 of the Brazilian National Health Council, this study, which is part of an institutional research project of the authors, was approved by the Research Ethics Committee (REC), under opinion No. 5.721.740, 2022, and certificate of presentation for ethical assessment (CAAE) No. 63981922.6.0000.0104; since we used secondary data, this study was exempted from the informed consent form.

RESULTS

Between 2010 and 2019, 124,966 cases of hepatitis B were reported in Brazil, with an average detection coefficient of 6.20/100,000 inhab. The South (14.40/100,000 inhab.), North (11.31/100,000 inhab.), and Midwest (6.83/100,000 inhab.) regions presented coefficients above the country. The Southeast and Northeast regions showed average rates of, respectively, 4.74/100,000 inhab. and 2.41/100,000 inhab.

There was a decreasing trend in the detection of hepatitis B in Brazil, with a deceleration at the end of the series ($–0.23x–0.03x^2$). The North and Northeast regions showed stationarity, while Southeast (–0.31x), South ($–0.41x–0.14x^2$), and Midwest (–0.38x) showed decline. In Acre (62.14/100,000 inhab.) and in Rondônia (35.39/100,000 inhab.) the highest coefficients were observed (Table 1).

Among the FUs, 11 had a decreasing trend of HBV detection, especially those belonging to the South, Southeast, and Midwest regions. The highest falls were in Mato Grosso (–0.93x) and Santa Catarina ($–1.20x–0.25x^2$). Nine FUs showed a stationary trend and seven showed increased detection of hepatitis B, of which Acre (+0.74x) and Pará (+0.18x) stood out (Table 1).

Additionally, in the period analyzed, 4,589 deaths were recorded with hepatitis B as the cause, with an average mortality rate of 0.23/100,000 inhab. The regions North (0.45/100,000 inhab.), South (0.32/100,000 inhab.), and Midwest (0.36/100,000 inhab.) presented the highest values. The Southeast and Northeast regions showed coefficients of, respectively, 0.21/100,000 inhab. and 0.13/100,000 inhab.

There was a decreasing trend in hepatitis B mortality in Brazil ($r^2=0.89$) and in Southeast ($r^2=0.87$), South ($r^2=0.92$), and Midwest ($r^2=0.91$) regions, while North and Northeast showed stationarity. Among the FUs, eight had a decreasing trend in hepatitis

B mortality. The highest falls were in Paraná (r^2=0.95) and Tocantins (r^2=0.85). In addition, 16 FUs showed a stationary trend and three showed increased mortality rates, of which the state of Acre (r^2=0.93) stood out (Figure 1).

Between 2010 and 2019, 168,205 cases of hepatitis C were reported in Brazil, with an average detection coefficient of 8.33/100,000 inhab. The South and Southeast regions presented average coefficients above the country, with, respectively, 19.83/100,000 inhab. and 9.63/100,000 inhab. The North and Midwest regions had a coefficient of 4.71/100,000 inhab. and the Northeast region of 2.48/100,000 inhab.

There was a decreasing trend in the detection of hepatitis C in Brazil, with a deceleration of the decrease at the end of the series ($–0.13x–0.04x^2$). The North, Northeast, and Midwest regions showed stationarity, while Southeast (–0.39x) and South (–0.21x) showed decline. In Rio Grande do Sul (35.68/100,000 inhab.) and Acre (29.22/100,000 inhab.) the highest coefficients were noted (Table 2).

Among the FUs, 13 showed a decreasing trend in the detection coefficient of hepatitis C, especially those located in the South and Southeast regions. The largest falls were observed in Rio de Janeiro (–0.68x) and São Paulo (–0.55x). Six states showed a stationary trend and eight showed increased detection, of which Acre (+0.55x) and Pará (+0.30x) stood out (Table 2).

In addition, in the period analyzed, 18,861 deaths were recorded with hepatitis C as the underlying cause, with a mean mortality rate of 0.94/100,000 inhab. The South (1.58/100,000 inhab.) and Southeast (1.21/100,000 inhab.) presented values above the country. The North and Midwest regions had an average coefficient of 0.60/100,000 inhab. and the Northeast region of 0.38/100,000 inhab.

There was a decreasing trend in hepatitis C mortality in Brazil, with a deceleration of the decrease at the end of the series (r^2=0.98). All regions showed a decline in mortality, especially in the South (r^2=0.96) and Southeast (r^2=0.96). Among the FUs, 15 had a decreasing trend. The largest falls were observed in Acre (r^2=0.51) and Santa Catarina (r^2=0.88). In addition, 11 units showed a stationary trend and only Alagoas showed a slight increase at the end of the series (r^2=0.95) (Figure 2).

There was a weak inverse correlation between the hepatitis B detection coefficient and illiteracy rate among people aged 18 years or older (p=0.04). Regarding the diagnosis of hepatitis C, there was a weak direct correlation with HDI (p=0.01) and life expectancy at birth (p=0.01), moderate direct correlation with *per capita* income (p<0.01), and moderate inverse correlation with illiteracy rate (p<0.01) (Table 3).

DISCUSSION

Brazil, as a whole, showed a decreasing trend of detection and mortality from hepatitis B and C in the period from 2010 to 2019. The South and North regions presented the highest rates of diagnosis and deaths from HBV, with a decreasing and stationary trend, respectively. Regarding hepatitis C, the highest rates were for the South and Southeast regions, both decreasing in the series. In Acre and Pará, there was increased detection of both viral infections.

The decreasing trend of detection and mortality of hepatitis B and C, as well as national and international disparities around spatial distribution, were observed in other studies[9-12,20,21]. Sousa and collaborators pointed to the expansion of screening through more effective rapid tests—including in hemotherapy services, the universalization of the

HBV vaccine, and the offer of new anti-HCV therapeutic regimes as possible explainers for such fact[22].

Specifically with regard to hepatitis B, a retrospective cohort study developed in Iran identified that the rate of HBV infection among the vaccinated group was significantly lower than in the non-vaccinated group, providing a protection of approximately 29% in the occurrence of cases[23]. This situation could explain the decreasing trends in detection and mortality observed for hepatitis B, when considering the potential impact of vaccination in Brazilian states.

Regarding hepatitis C, the decreasing trend of mortality, for example, may be associated with therapy with direct-acting antivirals, established by the Ministry of Health in SUS in 2015[8]. These drugs are more effective in treating the infection and, in contrast, are associated with a lower occurrence of adverse drug effects[24]. This context could promote better adherence to the therapeutic regime, leading, as a consequence, to a reduction in the number of deaths.

On the other hand, there was a growing trend in the detection of HBV and HCV in some states of the North and Northeast regions, possibly due to greater access to rapid testing actions[25-27]. The expansion of diagnostic actions and campaigns aimed at priority regions and populations may lead to substantial increases in the number of reported cases of viral hepatitis[13]. This would explain, in part, the growing trends observed in some localities of the country.

The WHO estimates that, worldwide, about 80% of the population living with HBV or HCV remains without access to diagnosis and/or adequate treatment[28]. Thus, it is understood that, in the short term, health education strategies, encouraging vaccination, testing of the population, and use of treatment can cause increases in cases of viral hepatitis, as a possible consequence of the discovery of serological status among people who, until then, were not aware.

However, these actions, in the medium and long term, may be responsible for reducing detection and mortality from viral hepatitis[20]. Therefore, such initiatives should guide the organization of health services at different levels of care, from the perspective of comprehensiveness. In addition, it is relevant to consider the intra and inter-region health articulation within the care network, in order to encourage rearrangements to favor access and follow-up to care for affected people.

In Brazil, despite the role of primary health care (PHC) in the promotion of health to people with chronic conditions[29], there is still a timid performance in viral hepatitis. In the North region, for example, Almeida and collaborators showed that 90% of PHC units have rapid testing for infections; however, treatment remains centralized in outpatient clinics and hospitals, which may compromise access to medicines and monitoring of affected people[25].

It is essential that PHC strengthen its role in the detection of cases, especially focusing on early diagnosis. Additionally, it is necessary to increase vaccination coverage rates for hepatitis B through actions in PHC. Nevertheless, only the decentralization of diagnosis and the development of preventive strategies may not be sufficient for the elimination of hepatitis, since difficulty in access and follow-up of treatment impairs the effective control of these infections[30,31].

In this perspective, the Ministry of Health, through ordinance No. 1,537 of June 12, 2020, promoted the reformulation of the strategy of dispensing medicines, hitherto centralized at the secondary level; this document aims to encourage the role of PHC in actions of promotion and prevention, screening and universal access to the treatment of viral hepatitis[32]. This decentralization is expected to accelerate the elimination of infections, as agreed in the 2030 agenda.

In this study, high rates of hepatitis diagnosis were associated with localities with lower illiteracy rates in the adult population. In addition, the increased detection rate of hepatitis C was linked to states with higher values of human development, life expectancy at birth and *per capita* income. These findings confirm the factors already described in the literature[9-13], prompting reflections about the aspects that cause and sustain the occurrence of infections in the country.

The better organization and accessibility of health services, with the possibility of offering diagnostic tests, can boost the highest detection rates, whether by active or passive search for cases. This possibly more favored scenario may be responsible for the higher burden of viral hepatitis in states with better socioeconomic indicators[27]. These conditions shape the local elimination responses and imply the different epidemiological behaviors evidenced.

Thus, it is essential to face the programmatic disparities, combined with the strengthening of permanent and continuing education actions in health, with a view to overcoming cultural and stigmatizing barriers and qualifying the performance of health professionals[20,31]. This response may provide opportunities for the dissemination of vaccination and prevention strategies, the early access to diagnosis, and the provision of antiviral therapies in a timely manner to the population at all points of the care network[33].

Finally, it should be noted that the interruption of health services due to the COVID-19 pandemic affected the diagnosis and treatment of hepatitis B and C in Latin American and Caribbean countries[34], resulting in a decline of the detection and the notification of infections between 2020 and 2021[15,16]. Thus, it is suggested the strengthening of actions aimed at combating the burden of viral hepatitis in Brazil, with a focus on increasing testing and ensuring access to referral services[35].

Still, some limitations of this research are listed: (i) secondary data may include filling errors, duplication and/or underreporting of cases; (ii) the non-adjustment in trends for interventions, such as implementation of tests or therapies; (iii) the impossibility of distinguishing whether there was an increase/decrease in the occurrence or notification of injuries; (iv) the exclusion of cases from the COVID-19 pandemic period; and (v) the grouping of data at the state level for the analyses.

In short, this study revealed disparities in the spatial and temporal behavior of hepatitis B and C in Brazil from 2010 to 2019. The South, Southeast, and Midwest regions presented decreases, while the North and Northeast regions presented stationarity of detection and decline of mortality, with some states on the rise. It was also visualized that locations (states) with better socioeconomic and development indexes had higher rates of viral hepatitis detection.

These findings may support the development and/or implementation of assertive strategies that aim to break the transmission chain and promote linkage to care. In addition, it is necessary to emphasize the role of PHC, which needs to be instrumentalized to act in the perspective of integrality along with secondary and tertiary services—specially the early testing of cases, the provision and referral to treatment, and the vaccination of the adjacent population.

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TABLES AND FIGURES

Table 1: Polynomial regression models of the temporal trend of hepatitis B detection coefficients (per 100,000 inhabitants), according to Federative Units and regions of Brazil, from 2010 to 2019.

Location	Initial coefficient	Annual evolution	r^2[a]	p-value[b]	Trend
North region	**y=11.47**	**–0.26x**	**0.27**	**0.18**	**Stationary**
Rondônia	y=35.39	$-2.10x-0.61x^2+0.14x^3$	0.98	<0.01	Increasing
Acre	y=62.14	$-12.71x-1.02x^2+0.74x^3$	0.97	<0.01	Increasing
Amazonas	y=13.96	+0.04x	0.00	0.90	Stationary
Roraima	y=18.11	–0.19x	0.16	0.31	Stationary
Pará	y=2.83	+0.18x	0.95	<0.01	Increasing
Amapá	y=3.53	+0.24x	0.46	0.06	Stationary
Tocantins	y=5.41	$-0.32x+0.06x^2$	0.92	<0.01	Increasing
Northeast region	**y=2.42**	**+0.01x**	**0.14**	**0.35**	**Stationary**
Maranhão	y=2.34	$-0.05x+0.04x^2$	0.87	<0.01	Increasing
Piauí	y=1.38	+0.05x	0.31	0.15	Stationary
Ceará	y=1.52	+0.01x	0.26	0.18	Stationary
Rio Grande do Norte	y=1.36	–0.03x	0.31	0.14	Stationary
Paraíba	y=2.32	$-0.72x+0.04x^2+0.04x^3$	0.95	<0.01	Increasing
Pernambuco	y=1.91	+0.04x	0.17	0.30	Stationary
Alagoas	y=2.38	$+0.24x+0.10x^2$	0.97	<0.01	Increasing
Sergipe	y=4.91	+0.01x	0.20	0.73	Stationary
Bahia	y=3.40	$+0.05x-0.04x^2$	0.89	<0.01	Decreasing
Southeast region	**y=4.83**	**–0.31x**	**0.97**	**<0.01**	**Decreasing**
Minas Gerais	y=3.31	–0.05x	0.24	0.21	Stationary
Espírito Santo	y=9.63	–0.89x	0.86	<0.01	Decreasing
Rio de Janeiro	y=2.98	–0.35x	0.87	<0.01	Decreasing
São Paulo	y=5.83	–0.37x	0.96	<0.01	Decreasing
South region	**y=15.40**	**$-0.41x-0.14x^2$**	**0.95**	**<0.01**	**Decreasing**
Paraná	y=15.96	$-0.38x-0.11x^2$	0.96	<0.01	Decreasing
Santa Catarina	y=21.19	$-1.20x-0.25x^2$	0.96	<0.01	Decreasing
Rio Grande do Sul	y=11.33	$+0.01x-0.10x^2$	0.84	<0.01	Decreasing
Midwest region	**y=6.91**	**–0.38x**	**0.95**	**<0.01**	**Decreasing**
Mato Grosso do Sul	y=4.50	–0.48x	0.93	<0.01	Decreasing
Mato Grosso	y=15.38	–0.93x	0.94	<0.01	Decreasing
Goiás	y=4.24	–0.14x	0.76	<0.01	Decreasing
Federal District	y=6.30	$+0.25x-0.15x^2-0.04x^3$	0.92	0.01	Decreasing
Brazil	**y=6.50**	**$-0.23x-0.03x^2$**	**0.96**	**<0.01**	**Decreasing**

a) determination coefficient; b) regarding the *F* test.

Figure 1: Spatial distribution of the initial coefficients (per 100,000 inhabitants) (A) and the temporal trend (B) of mortality from hepatitis B, according to Brazilian Federative Units, in the period from 2010 to 2019.

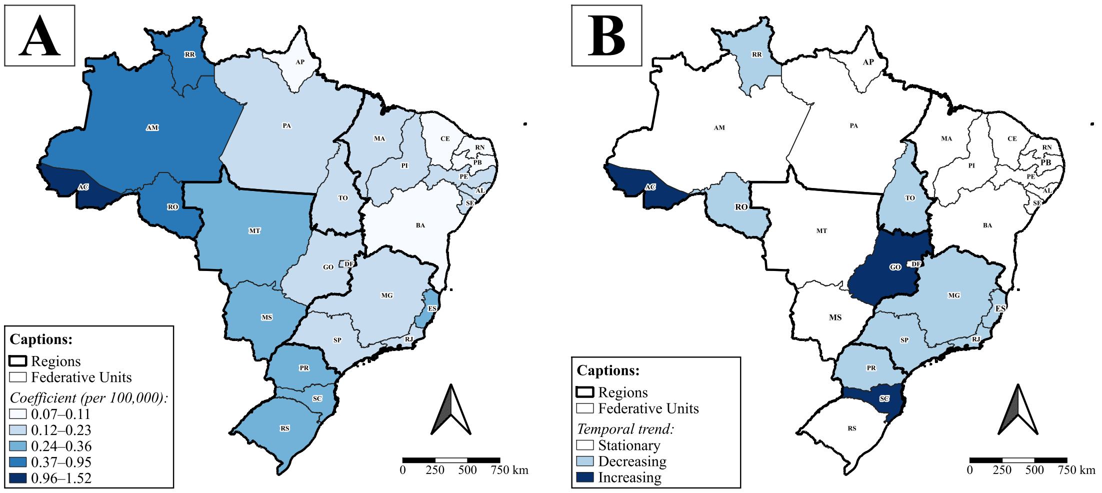

Table 2: Polynomial regression models of the temporal trend of hepatitis C detection coefficients (per 100,000 inhabitants), according to Federative Units and regions of Brazil, from 2010 to 2019.

Location	Initial coefficient	Annual evolution	r^{2a}	p-value^{b}	Trend
North region	**$y=4.87$**	**$+0.05x$**	**0.06**	**0.55**	**Stationary**
Rondônia	$y=9.36$	$+0.14x-0.18x^2$	0.99	<0.01	Decreasing
Acre	$y=29.22$	$-7.15x-1.10x^2+0.55x^3$	0.94	<0.01	Increasing
Amazonas	$y=6.96$	$-0.52x-0.08x^2+0.04x^3$	0.88	0.02	Increasing
Roraima	$y=2.40$	$-0.03x$	0.05	0.57	Stationary
Pará	$y=2.22$	$+0.30x$	0.93	<0.01	Increasing
Amapá	$y=3.41$	$+0.04x$	0.13	0.37	Stationary
Tocantins	$y=2.54$	$+0.02x$	0.08	0.48	Stationary
Northeast region	**$y=2.52$**	**$+0.00x$**	**0.00**	**0.95**	**Stationary**
Maranhão	$y=1.52$	$-0.15x+0.06x^2$	0.95	<0.01	Increasing
Piauí	$y=1.55$	$-0.05x-0.02x^2$	0.86	<0.01	Decreasing
Ceará	$y=2.01$	$+0.08x-0.01x^2-0.00x^3$	0.92	0.01	Decreasing
Rio Grande do Norte	$y=2.29$	$-0.04x$	0.53	0.03	Decreasing
Paraíba	$y=2.12$	$+0.03x$	0.15	0.33	Stationary
Pernambuco	$y=2.61$	$-0.54x-0.02x^2+0.04x^3$	0.96	<0.01	Increasing
Alagoas	$y=2.12$	$+0.26x$	0.87	<0.01	Increasing
Sergipe	$y=3.12$	$-0.00x$	0.00	0.83	Stationary
Bahia	$y=3.60$	$+0.11x$	0.60	0.02	Increasing
Southeast region	**$y=9.79$**	**$-0.39x$**	**0.89**	**<0.01**	**Decreasing**
Minas Gerais	$y=4.87$	$+0.06x$	0.16	0.32	Stationary
Espírito Santo	$y=5.43$	$+0.10x-0.10x^2$	0.91	<0.01	Decreasing
Rio de Janeiro	$y=8.61$	$-0.68x$	0.94	<0.01	Decreasing
São Paulo	$y=12.97$	$-0.55x$	0.87	<0.01	Decreasing
South region	**$y=21.35$**	**$+0.19x-0.21x^2$**	**0.94**	**<0.01**	**Decreasing**
Paraná	$y=10.49$	$+0.51x-0.11x^2-0.04x^3$	0.92	0.01	Decreasing
Santa Catarina	$y=15.45$	$-0.37x-0.10x^2$	0.96	<0.01	Decreasing
Rio Grande do Sul	$y=35.68$	$+0.69x-0.38x^2$	0.96	<0.01	Decreasing
Midwest region	**$y=4.85$**	**$-0.03x$**	**0.07**	**0.51**	**Stationary**
Mato Grosso do Sul	$y=6.30$	$-0.43x$	0.78	<0.01	Decreasing
Mato Grosso	$y=5.71$	$-0.39x-0.04x^2+0.02x^3$	0.92	0.01	Increasing
Goiás	$y=3.44$	$+0.54x-0.05x^2-0.03x^3$	0.99	<0.01	Decreasing
Federal District	$y=7.25$	$+0.57-0.12x^2-0.08x^3$	0.87	0.02	Decreasing
Brazil	**$y=8.73$**	**$-0.13x-0.04x^2$**	**0.88**	**<0.01**	**Decreasing**

a) determination coefficient; b) regarding the *F* test.

Figure 2: Spatial distribution of the initial coefficients (per 100,000 inhabitants) (A) and the temporal trend (B) of mortality from hepatitis C, according to Brazilian Federative Units, in the period from 2010 to 2019.

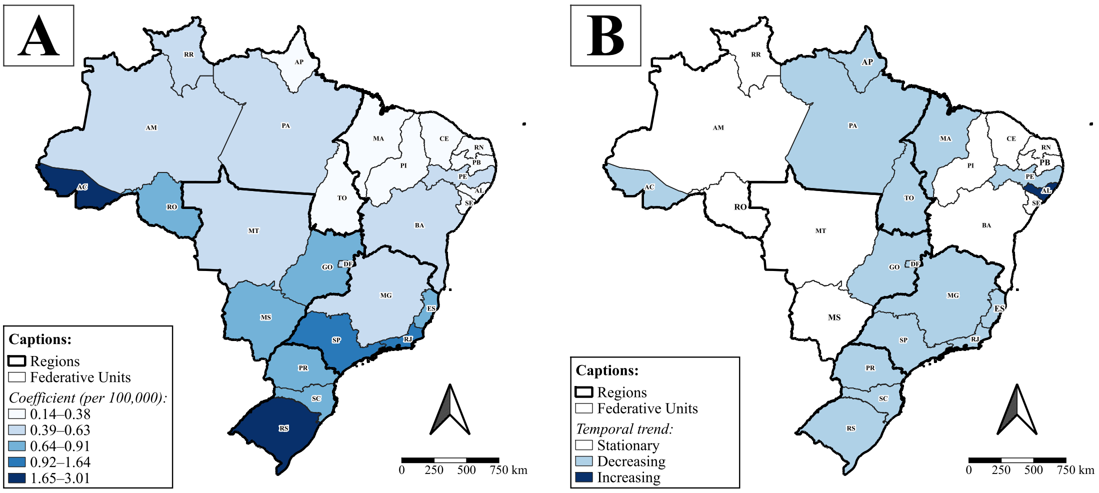

Table 3: Correlation between the average detection and mortality coefficients of hepatitis B and C (per 100,000 inhabitants) with the development indicators of the Brazilian Federative Units, in the period from 2010 to 2019.

Indicator		**Hepatitis B**		**Hepatitis C**	
		ρ[a]	**p-value**[b]	**ρ**[a]	**p-value**[b]
Detection	HDI[c]	0.19	0.32	0.46	0.01
	Illiteracy rate	–0.38	0.04	–0.64	<0.01
	Gini index	–0.23	0.24	–0.22	0.25
	Child mortality rate	–0.02	0.89	–0.32	0.10
	Life expectancy at birth	0.02	0.90	0.47	0.01
	Per capita income	0.27	0.17	0.50	<0.01
	Percentage of hospitalizations due to PCSC[d]	0.04	0.82	–0.19	0.32
Mortality	HDI[c]	0.09	0.65	–0.15	0.43
	Illiteracy rate	–0.16	0.40	0.04	0.81
	Gini index	0.15	0.43	–0.07	0.72
	Child mortality rate	0.07	0.71	0.21	0.28
	Life expectancy at birth	0.01	0.92	–0.11	0.57
	Per capita income	0.09	0.40	–0.12	0.54
	Percentage of hospitalizations due to PCSC[d]	–0.34	0.07	–0.21	0.28

a) Spearman correlation coefficient; b) referring to the Spearman correlation test; c) Human Development Index; d) primary care sensitive conditions.