Spatiotemporal Analysis of Patients With Hepatitis B in a Reference Center in the State of Amazonas

Análise Espaço Temporal de Pacientes Portadores de Hepatite em um Centro Terciário no Amazonas

Análisis Espacio-Temporal de Pacientes Portadores de Hepatitis en un Centro Terciario en el Amazonas

RESUMO

A hepatite B é uma infecção viral que afeta o fígado e pode evoluir para formas graves, como cirrose e carcinoma hepatocelular e sua transmissão ocorre principalmente por contato com sangue ou fluidos corporais contaminados, configurando um problema de saúde pública de grande relevância, já coinfecção pelo vírus Delta (HDV) representa um agravante, pois acelera a progressão da doença hepática e dificulta o manejo clínico. Este estudo transversal analisou portadores de hepatite B que realizaram teste anti-HDV entre 2017 e 2023 na Fundação de Medicina Tropical Doutor Heitor Vieira Dourado, onde foram aplicados testes estatísticos de proporção (qui-quadrado e exato de Fisher), além da avaliação de variáveis contínuas com testes paramétricos e não paramétricos, utilizando o software RStudio, assim este estudo é relevante por contribuir para a compreensão dos fatores laboratoriais e sociodemográficos relacionados à coinfecção pelo HDV, fornecendo subsídios para estratégias de prevenção, diagnóstico precoce e melhor acompanhamento clínico dos pacientes.

DESCRITORES: Hepatite B, Vírus Delta, Coinfecção, Epidemiologia, Saúde Pública

ABSTRACT

Hepatitis B is a viral infection that affects the liver and can progress to severe forms, such as cirrhosis and hepatocellular carcinoma it is transmitted primarily through contact with contaminated blood or bodily fluids, constituting a major public health problem, coinfection with the Delta virus (HDV) poses an aggravating factor, as it accelerates the progression of liver disease and complicates clinical management. This cross-sectional study analyzed hepatitis B patients who underwent anti-HDV testing between 2017 and 2023 at the Dr. Heitor Vieira Dourado Tropical Medicine Foundation. Statistical tests of proportions (chi-square and Fisher's exact) were applied, in addition to the evaluation of continuous variables with parametric and non-parametric tests using RStudio software, therefore, this study is relevant because it contributes to the understanding of laboratory and sociodemographic factors related to HDV coinfection, providing support for prevention strategies, early diagnosis, and improved clinical monitoring of patients.

DESCRIPTORS: Hepatitis B, Delta Virus, Coinfection, Epidemiology, Public Health

RESUMEN

La hepatitis B es una infección viral que afecta al hígado y puede evolucionar hacia formas graves, como cirrosis y carcinoma hepatocelular. Su transmisión ocurre principalmente por contacto con sangre o fluidos corporales contaminados, lo que la configura como un problema de salud pública de gran relevancia. La coinfección con el virus Delta (HDV) representa un agravante, ya que acelera la progresión de la enfermedad hepática y dificulta el manejo clínico. Este estudio transversal analizó a portadores de hepatitis B que se realizaron la prueba anti-HDV entre 2017 y 2023 en la Fundación de Medicina Tropical Doctor Heitor Vieira Dourado, donde se aplicaron pruebas estadísticas de proporción (chi-cuadrado y exacta de Fisher), además de la evaluación de variables continuas con pruebas paramétricas y no paramétricas, utilizando el software RStudio. De este modo, el estudio es relevante por contribuir a la comprensión de los factores laboratoriales y sociodemográficos relacionados con la coinfección por HDV, proporcionando insumos para estrategias de prevención, diagnóstico precoz y mejor seguimiento clínico de los pacientes.

DESCRIPTORES: Hepatitis B; Virus Delta; Coinfección; Epidemiología; Salud Pública.

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INTRODUCTION

According to the WHO (2025), hepatitis B is a disease caused by the hepatitis B virus (HBV). The infection can be acute (short-term) or chronic (lasting more than six months), but most people with the chronic form of the disease have no symptoms for years, making it a "silent" infection and hindering early diagnosis.

Oliveira *et al.* (2025) explain that the hepatitis B virus is found in blood and other bodily fluids, such as semen, saliva, and vaginal secretions, and its transmission occurs mainly through direct contact with these fluids, ranging from sexual intercourse (STI), sharing needles and syringes, contact with contaminated materials (razor blades, toothbrushes, nail clippers, etc.), and especially vertical transmission (the virus can be passed from mother to baby during pregnancy or childbirth).

In cases where the infection is not treated properly, the virus causes chronic infection, causing progressive damage to the liver, such as cirrhosis (difficult healing impairs organ function), liver cancer (hepatocellular carcinoma is one of the main complications of chronic hepatitis B), and ultimately liver failure (the organ loses its ability to function, which can be fatal to the individual). Therefore, there is a need for prevention and control of the disease (Brazil, 2023; Brazil, 2022).

According to data from FAPEAM (2011) and current data from the Ministry of Health (2025) in Brazil, there are marked regional disparities in the occurrence of hepatitis B. the North Region, especially Amazonas, has a high prevalence, with an estimated 250,000 people carrying the virus located in the state of Amazonas, with persistent endemic cases along the Juruá, Purus, and Madeira rivers.

Although more recent and detailed data are scarce, the Ministry of Health (2025) reported that between 2014 and 2024, Amazonas managed to reduce deaths from hepatitis B by 18.5%, from 27 to 22 per year. Even with this progress, there continues to be low adherence to treatment, with only 1,406 of the 4,849 people referred for treatment actually starting it.

To understand the spatiotemporal analysis of hepatitis B infections, which is a crucial tool for understanding its dynamics and directing control actions, Latin American studies have applied geospatial techniques to identify clusters and outbreaks, especially in vulnerable populations, such as pregnant women, highlighting the efficiency of localized interventions (Alburquerque *et al.,* 2023).

In the Amazonian context, there are alarming reports of co-infection with the Delta virus (HDV), associated with higher morbidity and mortality. In Lábrea, a municipality in Amazonas, more than 70% of samples reactive for HBV were also positive for HDV, a scenario that reinforces the need for continuous and detailed surveillance (Nunes; Júnior; Pedrosa, 2025).

Based on this bias, the spread of the virus in specific communities, such as transvestites and transgender women in highly vulnerable situations in Manaus, requires special attention, as they are at greater risk of exposure (Litaiff *et al.,* 2023). The availability of rapid testing and expanded vaccination, promoted by the SUS and local agencies such as the Dr. Heitor Vieira Dourado Tropical Medicine Foundation, constitutes an important advance, according to sources from the Amazon Agency in 2025.

According to Ribeiro *et al.* (2024), even with these efforts, gaps remain, and there is still a shortage of studies that systematically combine geographic surveillance with temporal analysis in reference units in Amazonas, as there are few analyses that map endemic foci, detect outbreaks, and correlate these events with sociodemographic and geographic determinants.

METHOD

This is a cross-sectional observa-

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tional study, conducted on a spontaneous basis at the Dr. Heitor Vieira Dourado Tropical Medicine Foundation (Manaus, Amazonas, Brazil), with retrospective collection of medical records and laboratory records of patients seen between January 1, 2017, and December 31, 2023. A total of 98 participants were included.

The target population comprised individuals with a serological diagnosis of hepatitis B treated at the service during the defined period, with a consecutive sample (census of eligible cases), including all cases that underwent testing for antibodies against the hepatitis D virus (anti-HDV) during the study period.

The inclusion criteria were: age ≥ 18 years; complete serological profile for hepatitis B in the index episode, defined by the presence of at least one of the following markers: hepatitis B virus surface antigen (HBsAg), immunoglobulin M antibody against hepatitis B virus core antigen (anti-HBc IgM), immunoglobulin G antibody against hepatitis B core antigen (anti-HBc IgG), hepatitis B virus e antigen (HBeAg), and/or antibody against hepatitis B virus e antigen (anti-HBe).

Exclusion criteria included individuals under 18 years of age; absence of anti-HDV test results, incomplete serological profile, duplicates, records with irrecoverable inconsistencies in essential variables (gender, age, origin) and clinical and laboratory definitions followed the Clinical Protocol and Therapeutic Guidelines for Hepatitis B and Coinfections and recent international guidelines on hepatitis B (WHO, 2024; Brazil, 2023).

The data were extracted from the laboratory information systems and electronic medical records of the service, with deterministic linking by institutional identifiers, such as a standardized extraction questionnaire (previously piloted data dictionary) to record: a) sociodemographic variables — per capita income (in minimum wages in force during the period), education (complete years), sex (male/female), age (complete years), origin (municipality/state); b) serological variables — HBsAg, anti-HBc IgM, anti-HBc IgG, HBeAg, anti-HBe; c) main exposure — anti-HDV result (reactive/non-reactive).

The collection included double-checking 10% of the forms for quality control, checking consistency between fields (e.g., compatibility between age and date of birth), and standardizing categories of origin according to the national registry of municipalities. The categories and cut-off points adopted complied with PCDT 2023.

The distribution of variables between groups with and without hepatitis D virus coinfection was compared. For categorical variables, *Pearson's* chi-square test or *Fisher's* exact test was applied when indicated by low expected frequency. For continuous variables, normality was assessed using the *Shapiro-Wilk* test (complemented by visual inspection of histograms and quantile-quantile plots). Approximately normal data were compared using *Student's* t-test for independent samples, and data with non-normal distribution were analyzed using the *Kruskal-Wallis* test. Hypotheses were two-tailed, with a significance level of 5% (α=0.05), effects were accompanied by effect sizes and 95% confidence intervals when applicable (phi/Cramér V for contingency tables; Cohen's d for comparisons of means, *Kruskal's* eta-squared for nonparametric comparisons). The rationale for the set of tests follows recent methodological recommendations.

The study fully complied with national guidelines for research involving human subjects, including National Health Council Resolution No. 466/2012 (in force) and complementary norms of the Research Ethics Committee/National Research Ethics Commission (CEP/Conep) System, such as Resolution No. 674/2022 and Resolution No. 706/2023. The protocol was submitted and approved via Plataforma Brasil, with registration of the Certificate of Ethical Review (CAAE) and the opinion number of the institution's Research Ethics Committee (insert: CAAE 78868717.9.0000.0005, CEP Opinion No. 2,493,796), as it involves secondary data from medical records, without nominal identification, ensuring confidentiality and security of information, with restricted access to authorized personnel and presentation of results only in aggregate form.

RESULTS

The results of this study included 98 participants, of whom 61 (62%) were male and 23 (48%) had incomplete elementary school education. In relation to laboratory variables, statistically significant differences ($p<0.05$) were observed between the groups with isolated hepatitis B and coinfection with the hepatitis D virus. The white blood cell count was 6,326 mm^3 in the group with hepatitis B and 5,096 mm^3 among those coinfected. Platelets had mean values of 196,250 mm^3 for hepatitis B and 103,500 mm^3 for delta coinfection. Regarding liver enzymes, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) had averages of 27 IU/L and 33 IU/L, respectively, in the hepatitis B group, while in those coinfected with delta they reached 42 IU/L and 45 IU/L. The mean total bilirubin value was 0.69 mg/dL for hepatitis B and 1.00 mg/dL for coinfection. The prothrombin time (PT) was 1.11 seconds for the hepatitis B group and 1.19 seconds for those coinfected.

This information is summarized in Table 1 below, presented with values arranged in a clear and legible manner.

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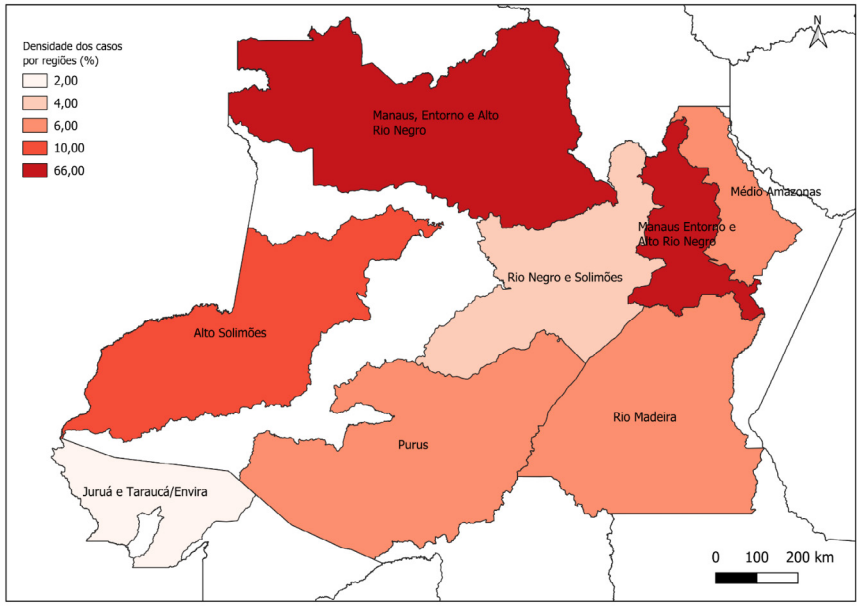
Table 1. Comparison of sociodemographic and laboratory variables between patients with hepatitis B and those coinfected with hepatitis D virus. Dr. Heitor Vieira Dourado Tropical Medicine Foundation, Manaus, Amazonas, Brazil, 2017–2023.

Characteristic	N = 100
Leukocytes (mm3)	6,018 (4,648, 7,285)
Hemoglobin (g/dl)	14.62 (13.25, 15.27)
Hematocrit (%)	44.1 (40.1, 46.2)
Platelets (mm³)	166,800 (99,900, 217,000)
Characteristic	N = 100
Aspartate aminotransferase (IU/L)	32 (22, 44)
Alanine aminotransferase (IU/L)	37 (24, 52)
Total bilirubin (mg/dL)	0.72 (0.58, 1.15)
Direct bilirubin (mg/dL)	0.18 (0.13, 0.29)
Indirect bilirubin (mg/dL)	0.57 (0.42, 0.87)
International Normalized Ratio (INR)	1.13 (1.04, 1.23)
Albumin (g/dL)	4.40 (4.10, 4.50)
Alpha-fetoprotein (IU/mL)	2.55 (1.85, 3.67)
Creatinine (mg/dL)	0.80 (0.70, 1.00)

Figure 1. Spatial distribution of hepatitis B and delta virus coinfection cases by health regions. Dr. Heitor Vieira Dourado Tropical Medicine Foundation, Manaus, Amazonas, Brazil, 2017–2023.



The spatial distribution of hepatitis B and delta virus coinfection cases in the state of Amazonas showed heterogeneous concentrations among health regions. The highest density was recorded in Manaus, Entorno, and Alto Rio Negro, with 66% of cases, the second highest concentration occurred in the Alto Solimões region, with 10% of records, followed by Rio Purus, which represented 6% of the total. The other areas had lower proportions, revealing a less significant distribution.

These findings reinforce the importance of understanding the geographical variation of the disease, since epidemiological conditions may be related to sociocultural and demographic factors and access to health services. A graphical representation of these results is shown in Figure 1.

DISCUSSION

The findings of this study, revealing a predominance of males (62%) and low educational attainment (48% with incomplete elementary school education), point to social vulnerabilities associated with hepatitis B and its coinfection with the delta virus. Such demographic characteristics have already been observed in other regions of the Amazon, where populations with lower educational levels and in contexts with less access to health services have a higher incidence of viral hepatitis, and these factors may reflect barriers to early diagnosis and adherence to treatment (Oliveira *et al.,* 2025; Colares *et al.,* 2020).

Laboratory tests showed significantly lower platelet counts (103,500 mm³ vs. 196,250 mm³) among coinfected individuals, as well as elevated liver

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enzyme levels (AST: 42 IU/L vs. 27 IU/L; ALT: 45 IU/L vs. 33 IU/L), total bilirubin (1.00 mg/dL vs. 0.69 mg/dL), and prothrombin time (1.19 s vs. 1.11 s) are indicative of greater liver impairment and probable synthetic dysfunction. These findings corroborate recent international literature, which associates HDV coinfection with more rapid progression to cirrhosis and greater liver toxicity (WHO, 2024; Nguyen, 2020).

Spatial analysis reinforces this interpretation, with the high density of cases (66%) in Manaus, Entorno, and Alto Rio Negro suggests that, in addition to larger populations and infrastructure, these locations may concentrate referral services and, consequently, greater detection of coinfections. In contrast, regions such as Alto Solimões (10%) and Rio Purus (6%) reflect lower capillarity of health services and possible underdiagnosis. Recent regional studies highlight that geographic dispersion, population isolation, and transportation difficulties aggravate the control of hepatitis B and coinfection with delta in the Amazon (Ferreira *et al.,* 2023; Costa *et al.,* 2020; FAPEAM, 2011).

It is essential to discuss that the cross-sectional and retrospective design prevents causal inference, as well as not allowing clinical evolution to be monitored or the incidence of outcomes such as cirrhosis or mortality to be estimated. Furthermore, the use of medical records as a source may lead to information bias and the exclusion of cases with incomplete data. In addition, the spontaneous demand sample may not represent vulnerable subpopulations that do not access FMT-HVD, which limits the generalization of results to indigenous or riverine populations.

However, despite these limitations, this study makes relevant contributions. First, it identified laboratory markers that suggest greater severity in coinfection and should guide more active surveillance of these patients. Second, spatial mapping identifies regions with a higher concentration of cases, which is essential for targeting testing, vaccination, and clinical intervention campaigns. For example, prioritizing the expansion of services in the Alto Solimões region may reduce underdiagnosis.

Compared to recent Brazilian literature, the observations of this study are in line with findings from fields such as Lábrea, where coinfection density was also high, and the occurrence of severe laboratory changes was associated with coinfection (Barbosa, 2025). Furthermore, other investigations confirm that HDV coinfection accelerates the progression of hepatitis B, intensifies necroinflammation, and challenges clinical treatment (Celestino, *et al,* 2023).

In terms of practical implications, the results point to the need for integrated policies, promoting systematic testing for HDV in all patients with hepatitis B, implementing educational actions in locations with low levels of education, and strengthening local surveillance structures, especially in regions with a dispersed population distribution.

To this end, the spatiotemporal analysis of patients with hepatitis B at a reference center in the state of Amazonas highlights not only the magnitude of the disease but also its heterogeneous distribution throughout the territory, marked by areas with a higher concentration of cases that constitute potential endemic foci.

This perspective broadens the understanding of the social and geographical determinants of infection, allowing us to visualize how factors such as population mobility, inequality in access to health care, and living conditions directly influence the dynamics of transmission, because by identifying critical areas, it becomes possible to anticipate outbreak scenarios and structure faster and more effective responses, directing resources and prevention strategies more equitably.

Thus, the integration of spatial analysis with clinical and epidemiological data provides support for strengthening public policies, contributing to reducing the burden of hepatitis B and HDV coinfection in the Amazon region, one of the most challenging in terms of epidemiological surveillance in the country. Future longitudinal studies are recommended to monitor the clinical evolution of coinfected individuals, assess the impact of interventions, and estimate outcomes such as cirrhosis, hepatocellular carcinoma, and mortality. Including individual variables such as HIV coinfection or substance use could deepen our understanding of the determinants of worse prognosis.

CONCLUSION

The investigation identified the spatiotemporal distribution of hepatitis B cases in a reference center in Amazonas, highlighting relevant epidemiological patterns and revealing areas of higher risk for the development of the disease. The results demonstrated that there are significant differences in the clinical and laboratory profiles of patients with isolated hepatitis B compared to those coinfected with the delta virus, with worsening hepatic parameters and greater clinical severity among the latter.

According to Colares *et al.* (2020), this differentiation points to the need for more rigorous monitoring targeted at the most vulnerable groups, as the high incidence of the disease in the Amazon region confirms its relevance as a public health problem, requiring the implementation of prophylactic measures and prevention strategies adapted to local specificities.

Spatial analysis contributed to identifying endemic foci and possible outbreaks, highlighting the importance of expanding vaccination coverage and strengthening epidemiological surveillance actions, especially in areas that are difficult to access.

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However, some gaps were evident, such as the scarcity of information on behavioral factors, vaccination history, and access to health services, which could deepen the understanding of the dynamics of infection. In addition, underreporting and the limitation of specialized tests in inland municipalities may have underestimated the real magnitude of the problem.

Future research may explore in greater detail the relationship between social determinants, environmental conditions, and the clinical evolution of hepatitis B, especially in cases of coinfection with the delta virus. Such investigations may support more effective policies for prevention, early diagnosis, and treatment. To this end, this study achieved its objective by highlighting relevant clinical differences between the groups analyzed and reinforcing the urgency of regional coping strategies. The implementation of prophylactic measures in risk areas is essential to reduce the incidence and complications of the disease, as well as paving the way for new approaches that strengthen public health in the Amazon.

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