Review

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Epidemiological Peculiarities of the Hepatitis E Virus Infection in Brazil: A Scoping Review

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Abstract

Introduction: Although Brazil has industrialized regions, such as the Southeast, it still has underdeveloped regions with poor sanitary conditions, such as the North and Northeast, similar to regions in Africa and Asia, where HEV-1 circulates. However, it is suspected that HEV occurs as a zoonosis in Brazil. Due to the wide variation in HEV prevalence across the five regions of this country, a scoping review was conducted to systematically identify any the prevalence and genotype of HEV. The following research question was formulated. **Aims**: to review the epidemiological peculiarities and genotype of HEV in the five regions of Brazil. **Methods**: This is a scoping review, conducted based on the methodological framework developed by the JBI and the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist. The searches were conducted in June and July 2025, using the following databases: MEDLINE and LILACS. A search equation was developed to map the evidence on the epidemiology of HEV infection in Brazil based on the Population, Concept, and Context (PCC) Strategy. **Results**: Of the 57 studies on the prevalence of hepatitis E virus infection in Brazil, 45 (78.9%) were in humans and 12 (21.1%) in swine. The overall prevalence of the IgG marker in Brazil ranged from 0.5% in the North region to 59.4% in the South region. On the other hand, the lowest prevalence of the IgM marker was recorded in the Northeast region (0.1%) and the highest in the North region (16.3%). Among the 12 studies involving pigs, the occurrence of HEV in these animals was identified in all regions of Brazil, with variations in the types of samples tested, husbandry methods, and prevalence detected. Exclusively hepatitis E viruses belonging to genotype 3 (HEV-3) were identified in all regions of Brazil where genotypic analysis was performed. **Conclusion**: based on the findings of this review, it can be considered that HEV infection occurs in all five regions of Brazil, with higher prevalence in the South and Southeast regions. The circulating genotype in the country is HEV-3, possibly transmitted through pig consumption and breeding interpretations.

Keywords: hepatitis E; serosurvey; prevalence; Brazil; Genotype 3; epidemiology; anti-HEV IgG

1. Introduction

Hepatitis E virus (HEV) is the main cause of acute enterically transmitted hepatitis worldwide [1]. Recent data from the World Health Organization (WHO) estimate that in 2021, there were approximately 20 million cases and 3,500 deaths from hepatitis E worldwide [2,3].

HEV belongs to the Hepeviridae family, Orthohepevirus genus, species A, classified into eight genotypes (HEV-1 to HEV-8) [4]. Of these, genotypes 1 to 4 have been isolated in humans, while genotypes 5 to 8 infect animals exclusively [5]. Contamination by genotypes 1 and 2 occurs via the

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fecal-oral route, through contaminated water, occurring in regions with poor sanitary conditions, such as Africa and Asia [6]. Sporadic cases are common, but large outbreaks also occur, affecting up to thousands of people [7]. Genotypes 3 and 4 infect humans through contaminated meat or direct contact with pigs, causing acute infections that are usually asymptomatic and self-limiting [8,9]. However, in immunocompromised patients, it can occasionally progress to chronic hepatitis and cirrhosis [10].

In recent decades, however, HEV has also been described in industrialized countries in Europe and North America through autochthonous cases. These cases are associated with genotypes 3 and 4, with epidemiological and clinical characteristics distinct from the 1 and 2 genotypes that circulate in developing countries [8,11].

In a meta-analysis conducted to assess the global prevalence of HEV, involving 287 studies and 1.099,717 patients, the percentage of anti-HEV IgG was found to be 12.47%. The data were stratified to estimate the prevalence of anti-HEV in 75 countries across six continents. The highest anti-HEV IgG positivity was found in Africa (21.76%), followed by Asia (15.80%), Europe (9.31%), North America (8.05%), South America (7.28%), and Oceania (5.99%). The data revealed that HEV-1 infection occurred mainly in India and China, and that HEV-3 was more commonly found in European countries [12].

In Latin America and the Caribbean, the overall prevalence of hepatitis E observed in a recent systematic review and meta-analysis was 9.0%, with significant heterogeneity (I^2 = 97.3%) and percentages ranging from 0% to 36% [13] (Magri et al 2025), respectively, in Brazil (kidney transplant [14] and hemodialysis patients [15]) and Cuba (occupational exposure in pigs [16]).

In Brazil, particularly, in a systematic review with meta-analysis conducted a few years ago, a general prevalence of anti-HEV of 6% (95% CI: 5.0–7.0) was observed, but with great heterogeneity (I^2 = 86.7%) between studies, ranging from 0% (95% CI: 0.0–3.0) in the state of Amazonas, in the northern region of the country [17], to 10.0% (95% CI: 7.0–15.0) in the state of Santa Catarina, in the southern region [18], confirming that HEV infection in Brazil occurs with wide variation in prevalence [19].

As a result of the short period of HEV viremia and the fact that most studies are cross-sectional, there is little data on the HEV genotype circulating in Brazil. However, the absence of descriptions of epidemic outbreaks and data evaluated in pigs suggest that HEV-3 is the circulating genotype in our environment [9]. Although Brazil has industrialized regions, such as the Southeast, it still has underdeveloped regions with poor sanitary conditions, such as the North and Northeast, similar to regions in Africa and Asia, where HEV-1 circulates [20]. However, it is suspected that HEV occurs as a zoonosis in Brazil.

Due to the wide variation in HEV prevalence across the five regions of Brazil, a scoping review was conducted to systematically map the research carried out in this area and identify any gaps in knowledge. The following research question was formulated: What are the epidemiological characteristics of HEV infection in the regions of Brazil?

2. Materials and Methods

This is a scoping review, conducted based on the methodological framework developed by the JBI [21] and the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist [22].

Eligility criteria

The eligibility criteria for this scoping review were established as follows: publications on the epidemiology of hepatitis E virus (HEV) infection in Brazil since 1995, when the first reports of the disease appeared in the country, with no language restrictions. Regarding the type of study, primary and secondary, empirical, quantitative research was selected, with preference given to cohort, case-control, and cross-sectional studies. Letters to the editor, validation studies, review articles, case reports, abstracts in event proceedings, incomplete articles, studies in the project phase, or studies without results were excluded. Articles related to HEV epidemiology in other countries

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and those involving the contamination of mollusks or other animals, such as horses, capybaras, and wild boars, were also excluded.

Information sources

The searches were conducted in June and July 2025, using the following databases: Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed, MEDLINE via the Virtual Health Library (VHL), and Latin American and Caribbean Health Sciences Literature (LILACS). The gray literature was retrieved from Google Scholar, the Brazilian Digital Library of Theses and Dissertations (BDTD), and the Thesis and Dissertation Catalog (CTD) of the Coordination for the Improvement of Higher Education Personnel (CAPES).

Search

A search equation was developed to map the evidence on the epidemiology of HEV infection in Brazil. The equation is presented in Figure 1.

Objective/ Problem	to verify the epidemiological characteristics of HEV in Brazil, including its mode of transmission, by searching for genotyping studies in humans and pigs/ What are the epidemiological peculiarities of HEV infection in the regions of Brazil?		
	P	**C**	**C**
Extraction	Epidemiology	Hepatitis E	Brazil
Combination	epidemiology; epidemiologia	hepatitis E; hepatitis E virus; Hepatite E; vírus da hepatite E	brazil; brasil
Construction	(“epidemiology” **OR** “epidemiologia”)	(“hepatitis E” **OR** “hepatitis E vírus” **OR** “hepatite E” **OR** “vírus da hepatite E”)	(“Brazil” **OR** “Brasil”)
Use	(“epidemiology” **OR** “epidemiologia”) **AND** (“hepatitis E” **OR** “hepatitis E vírus” **OR** “Hepatite E” **OR** “hepatite E” **OR** “vírus da hepatite E”) **AND** (“Brazil” **OR** “Brasil”); (“hepatitis E” **OR** “hepatitis E vírus”) **AND** (“Brazil” **OR** “Brasil”); (“hepatitis E/epidemiology” **OR** “hepatitis E vírus”) **AND** (“Brazil”)		

* P = population; C = Concept; C = Context.

Figure 1. Population, Concept, and Context (PCC) Strategy. Pernambuco, Brazil, 2025.

Selection of sources of evidence

The results obtained from the databases were exported to a Microsoft Excel® spreadsheet for independent study selection and screening by two researchers, with disagreements resolved by a third examiner. The first phase involved reading titles and abstracts. Studies that met the inclusion criteria were analyzed in the second phase by reading the full manuscripts. Finally, manual searches of the references of the included studies were performed.

Data charting process and Data itens

First, data were extracted independently by two reviewers using Microsoft Excel® spreadsheets. The information was confirmed by the third reviewer, and disagreements and doubts were resolved through discussion until consensus was reached among the authors. Data mapping was based on the JBI tool for characterizing the studies [21]. The extraction table included authorship, journal of publication, country of origin, year of publication, objectives, design, sample size, and main results regarding the identification of HEV seroprevalence in the five regions of Brazil.

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3. Results

Initially, we identified 309 publications in the MEDLINE and LILACS databases. Another source was obtained through citation searching (Figure 2).

After excluding duplicates (170), we analyzed 140 references by reading the abstracts. Of these, 83 publications were subsequently excluded, leaving 57 references selected for full-text reading, which were included in the final review. Of the 57 studies on the prevalence of hepatitis E virus infection in Brazil, 45 (78.9%) were in humans and 12 (21.1%) in swine.

The distribution of the 45 studies involving HEV and humans is presented in Table 1. It was found that most studies were conducted in the Southeast region (35.5%), particularly in the state of São Paulo (87.5%), followed by the Northeast (20%) and Central West (20%). The lowest number of studies was observed in the North region (11.1%), with 3 (60%) in the state of Pará, 1 (20%) in Acre, and the other in the states of Amazonas and Rondônia (20%).

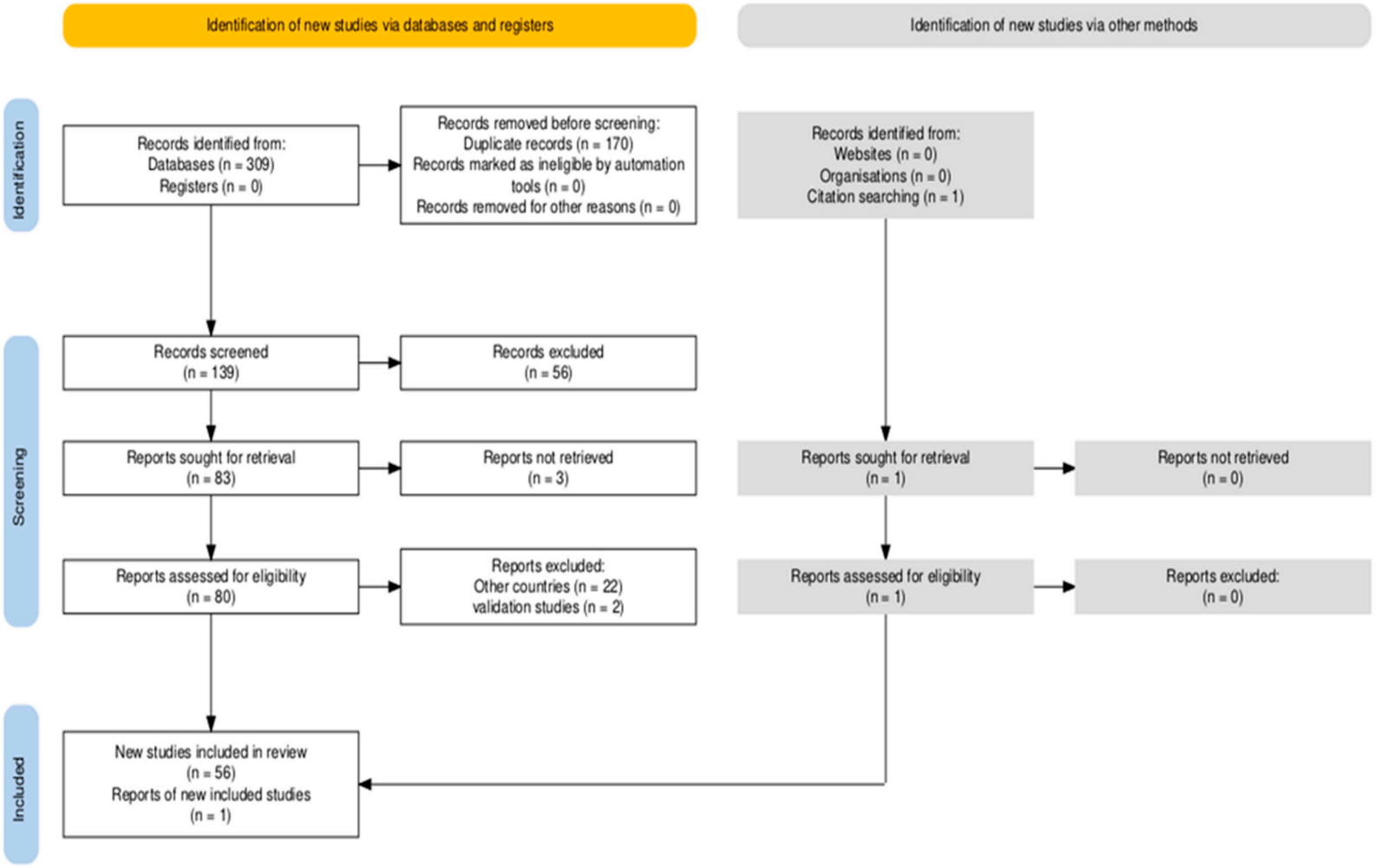

Figure 2. PRISMA Flow Diagram, generated with the PRISMA Flow Diagram tool [23], schematically visualizing the article selection process.

Table 1. Articles published between 1995 and 2025 describing the prevalence and epidemiological peculiarities of HEV markers in Brazil, according to the five major regions of the country.

Brazil Region	Author/Year	Type of study	Selected population	Epidemiological Peculiarities	Sample size	Anti-HEV prevalence	RNA	Genotype

						IgG n (%)	IgM n (%)		
North									
Acre	Vitral CL et al., 2014 [24]	Retrospective cross-sectional	Residents of an agricultural settlement in 2004	Age > 21 years	388	50 12,8%	7 16,3%	n/a	n/a
Amazônia/ Rondônia	Vasconcelos MP et al., 2024 [25]	Cross-sectional	Yanomani Indians Urban and rural areas	HEV in urban areas (2.97%), rural areas (14.2%) and village areas (2.8%)	811	55 6,8%	n/a	n/a	n/a
Pará	Souza AJS *et al*., 2018 [26]	Cross-sectional	Afro-descendant community	Young men reported eating bushmeat	535	3 0,5%	6 1,1%	negative	n/a
	Souza AJS *et al*., 2019 [27]	Cross-sectional	Suspected cases of acute hepatitis	Male gender (55.2%)	318	29 9,1%	16 5,0%	Negative	n/a
	Nascimento RS *et al*., 2021 [28]	Cross-sectional	Crack cocaine users	Poorer and homeless; longer use of crack cocaine	437	79 18,1%	6 1,4%	Positive	3c
Northeast									
Bahia	Paraná R *et al*., 1997 [15]	Retrospective cross-sectional	200 Blood donors 392 hemodialyzed	Blood donors	200	4 2%	n/a	n/a	n/a
	Paraná R *et al*. 1999 [29]	Cross-sectional	Acute sporadic non-A, non-B (NANB)	Aminotransferses elevation.	43	5 12%	negative	n/a	n/a
	Lyra AC *et al*., 2005 [30]	Cross-sectional	Patients with acute viral hepatitis	Higher prevalence of HEV in patients with acute hepatitis	73	21 28,8%	5 6.8%	n/a	n/a
Pernambuco	Passos-Castilho AM *et al*., 2016 [31]	Retrospective cross-sectional	Patients with schistosomiasis mansoni	Patients treated at a referral hospital with advanced forms of the disease	80	15 18,8%	negative	negative	n/a
	Bezerra LA *et al*., 2019 [32]	Cross-sectional	People living with HIV/AIDS	Higher HIV infection time	366	15 4,1%	n/a	Negative	n/a

	Cunha GG *et al.*, 2022 [33]	Cross-sectional	Blood candidates and donors	All male gender, consumption of pork and chicken	996	9 0,9%	n/a	n/a	n/a
	Araújo LRMG *et al.*, 2024 [34]	Cross-sectional	Patients with chronic liver disease	Contact with pigs and more advanced liver disease	227	7 3,08%	n/a	negative	n/a
	Gomes CTO *et al.*, 2024 [35]	Retrospective cross-sectional	Patients with schistosomiasis mansoni	More advanced periportal fibrosis (Niamey D/E/F)	286	15 5.24%	Negative	Negative	n/a
Piaui	Silva-Sampaio JP *et al.*, 2025 [36]	Cross-sectional	Blood donors	66.7% male gender, 75% age ≥ 30 years	890	12 1,35%	1 0,1%	negative	n/a
Central West									
Goiás	Martins RM *et al.*, 2014 [37]	Prevalence survey	Recyclable material collectors	Contact with human feces (87.5%) and animal feces (75%)	431	22 5,1%	3 0,7%	negative	n/a
	Freitas NR *et al.*, 2016 [38]	Cross-sectional	Patients with acute viral hepatitis	Consumo carne de porco (95%) e animais selvagens (75%)	379	20 5,3%	1 0,3%	negative	n/a
	Freitas NR et al., 2017 [39]	Cross-sectional	Rural settlement	75% male gender, Time in rural settlement > 5 years	464	16 3,4%	n/a	negative	n/a
	Oliveira JMNS *et al.*, 2018 [40]	Cohort	kidney transplant recipients	100% Previous hemodialysis, Consumption of wild animal meat (87.5%)	316	8 2,5%	1 0,3%	negative	n/a
	Teles AS *et al.* 2023 [41]	Cross-sectional	Recyclers, immigrants, refugees, and homeless people	Homeless; Recyclers	459	4 0,87%	1 0,2%	negative	
Mato Grosso	Assis SB *et al.*, 2002 [42]	Prevalence survey	School children	Absence of sanitary sewage.	487	22 4,5%	n/a	n/a	n/a

	Silva SM *et al.*, 2022 [43]	Cross-sectional	Pig handlers	age ≥ 50 years, Longer exposure to pigs	310	26 8,4%	n/a	n/a	n/a
Mato Grosso do Sul	Castro VOL *et al.*, 2018 [44]	Cross-sectional	Crack users	Low education level (73.7%), unprotected sexual intercourse	698	99 14,2%	2 0,28%	negative	n/a
	Weis-Torres SMDS *et al.*, 2022 [45]	Retrospective cross-sectional	Blood donors	75% male, 70% age ≥ 30 years; Lack of sewage system	250	16 6.4%	Negative	n/a	n/a
Southeast									
São Paulo	Focaccia R *et al.*,1998 [46]	Prevalence survey	General population		1,059	1.68%	n/a	n/a	n/a
	Gonçales NS *et al.*, 2000 [47]	Cross-sectional	Blood donors and staff at a university hospital,	blood donors with elevated ALT, and cleaning staff	375	18 4,8%	n/a	n/a	n/a
	Hering T *et al.*, 2014 [48]	Cross-sectional	Kidney transplant	Transplant patients with elevated aminotransferases	192	28 15%	n/a	20 10%	n/a
	Passos-Castilho AM *et al.*, 2015 [49]	Retrospective cross-sectional	Patients with clinical suspicion of HEV	age ≥ 40 years	2,271	47 2,1%	27 4,9%	1	3b
	Passos-Castilho AM et al., 2017 [50]	Cross-sectional	Blood donors	age ≥45 years	500	49 9,8%	1	negative	n/a
	Bricks G et al., 2018 [51]	Cross-sectional	Chronic HCV patients	contact with pigs and consumption of pork	618	63 10,2%	negative	n/a	n/a
	Ferreira AC et al., 2018 [52]	Cross-sectional	People living with HIV	age ≥40 years	354	38 10,7%	5 1,4%	negative	n/a

	Bricks G *et al.*, 2019 [53]	Cross-sectional	Chronic HCV patients	age ≥60 years; contact with pigs	618	63 10,2%	negative	n/a	n/a
	Araújo DCA *et al.*, 2020 [54]	Cross-sectional	Residents of a small municipality in São Paulo	consumption of raw meat	248	50 20,7%	negative	n/a	n/a
	Conte DD *et al.*, 2021 [55]	Cross-sectional	Patients in the Emergency Room with altered levels of Alanine aminotransferases	Altered levels of Alanine aminotransferases	401	n/a	2 of 90 2.2%	16of 311 5.1%	n/a
	Moraes ACP *et al.*, 2021 [56]	Cohort	Liver transplants	HBV/HCV coinfected	294	24 8.2%	6 2%	17 5,8%	n/a
	Zitelli PMY et al., 2021 [57]	Cross-sectional	Chronic HCV patients	More advanced liver disease; more Type-2DM,	181	22 12%	3 1,6%	9 4,9%	n/a
	Ribeiro LB *et al.*, 2024 [58]	Cross-sectional	Patients with acute viral hepatitis	Elevated aminotransferases	91	12 13.2%	4 4.4%	1	3f
	Zicker M *et al.*, 2024 [59]	Prospective	Liver transplanted and donors	n/a	190	19 10%	1 0.53%	negative	n/a
Rio de Janeiro	Trinta KS *et al.*, 2001 [60]	Retrospective cross-sectional	acute viral hepatitis; hemodialysis; intravenous drug users; blood donors;	n/a	1,115	2.1% acute viral hepatitis 6.2% hemodialysis; 11.8% UDIVs; 4,.3% blood donors	n/a	n/a	n/a
	Santos DC *et al.*, 2002 [61]	Cross-sectional	Manguinhos Community	age ≥40 years	699	17 2.4%	n/a	n/a	n/a
South									
Paraná	Bortoliero AL et al., 2006 [62]	Cross-sectional	Blood donors	There was no association with sociodemographic variables	996	23 2.3%	n/a	n/a	n/a

	Hardtke S et al., 2018 [63]	Cross-sectional	209 pregnant women; 199 female blood donor	age ≥40 years; >3 number of pregnancies	408	91 22,5%	n/a	negative	n/a
Santa Catarina	Passos-Castilho AM et al., 2016 [18]	Cross-sectional	Blood donors		300	30 10%	1 0,3%	negative	n/a
Rio Grande do Sul	Moss da Silva SC et al., 2019 [64]	Cross-sectional	PVHIV; Blood donors	age ≥40 years; poor sanitation; alcohol use	601	42 6,98%	n/a	8 1,33%	3
	Costa *et al.*, 2021 [65]	Cross-sectional	cirrhosis; crack users; liver transplanted; blood donors	higher in cirrhosis; crack users; liver transplanted patients and blood donors	400	78 19,5%	6 1,5%	negative	n/a
	Zorzeto R *et al.*, 2021 [66]	Cross-sectional	Blood samples were from laboratories	age ≥40 years	3,000	1,783 59,4%	n/a	negative	n/a

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The variations in the prevalence of Hepatitis E, according to the regions of Brazil, are presented in Figure 3. The overall prevalence of the IgG marker in Brazil ranged from 0.5% in the North region to 59.4% in the South region. On the other hand, the lowest prevalence of the IgM marker was recorded in the Northeast region (0.1%) and the highest in the North region (16.3%).

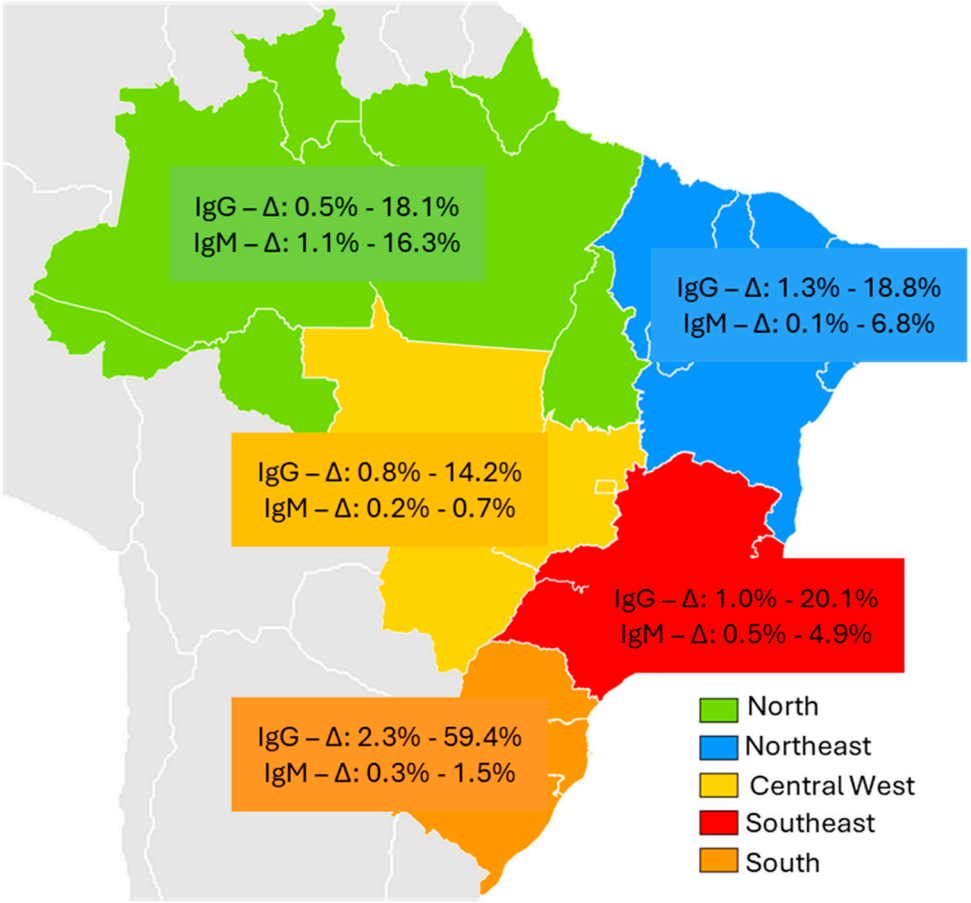

Figure 3. Prevalence of HEV infection markers (IgG and IgM) in the Brazilian population, according to the five major regions of the country, 1995–2025.

Among the 12 studies involving pigs, the occurrence of hepatitis E virus (HEV) in these animals was identified in all regions of Brazil, with variations in the types of samples tested, husbandry methods, and prevalence detected. The data are presented in Table 2.

Table 2. Prevalence and genotypic characteristics of HEV infection in pigs, according to the five major regions of the country, 1995–2025.

Brazil Region	State	Author/Year	Herd Characteristics	Biological sample tested	Total (n=)	Prevalence HEV		RNA	Genotype
						IgG n(%)	IgM n(%)		
North	Pará	Souza AJ *et al*, 2012 [67]	Six-month-old pigs from a licensed slaughterhouse (60%) and a slaughterhouse not registered with health regulatory agencies (40%). Samples collected during slaughter.	Serum, feces and liver	151	13 8.6%	0	15* 9.9%	3c; 3f
Northeast	Pernambuco	Oliveira-Filho EF *et al*., 2017 [68]	Coming from a slaughterhouse located in the metropolitan region of Recife (30%) and farms in the rural region of the state (70%)	Serum	325	266 82%	-	n/a	n/a
	Pernambuco	Oliveira-Filho EF *et al*., 2019 [69]	Animals aged two to six months, from farms that use intensive and extensive production systems.	Feces	119	-	-	2 (1.68%)	3f
Central West	Mato Grosso	Costa Lana *et al*., 2014 [70]	Four-month-old animals from large-scale farms (50%) and family farms (50%). Overall, 18 (72%) of the 25 pigs presented microscopic liver lesions, characterized by fibrosis and portal inflammation.	Bile, liver and feces	25	-	-	15** 83,3%	3b;3f
	Mato Grosso	Campos CG *et al*., 2018 [71]	Growing piglets of both sexes, between three and four months of age, and breeding females, between eight and twenty-four months of age, from subsistence farms.	Serum and feces	150	-	-	12 8%	3d; 3h;3i
Southeast	Rio de Janeiro	Vitral CL *et al*., 2005 [72]	Pigs ranging in age from 1 to > 25 weeks in four commercial herds	Serum	357	227 63.6%	-	n/a	n/a
	Rio de janeiro	dos Santos DR et al., 2011 [73]	Healthy animals aged > five months, from three legal slaughterhouses.	Bile	115	-	-	11*** 9.6%	3b

	Minas Gerais	Amorim AR *et al*., 2018 [74]	Healthy animals for slaughter at a state slaughterhouse. No macroscopic lesions were observed in the livers of slaughtered pigs during bile collection.	Bile	335	-	-	51 15.2%	3c;3i
	São Paulo	Cortez A et al., 2021 [75]	Samples from a state swine biobank.	Feces	89	-	-	7 7.86%	3b; 3h; 3j
South	Paraná	Gardinali NR et al., 2012 [76]	Samples came from maturation cycle farms (58.3%) and grow-to-slaughter farms (41.7%). All pigs were asymptomatic.	Feces	170	-	-	26 15.3%	3b
	Paraná	Passos-Castilho AM *et al*., 2017 [77]	Animals aged between four and 16 weeks old from a small rural property in the region.	Feces	170	-	-	34 20%	3b
	Rio Grande do Sul	da Silva MS *et al*., 2018 [78]	Animals from farms located near peri-urban areas or landfills, indigenous reservations, and farms that feed pigs with food scraps. Samples from two different periods were analyzed: 2012 (50.6%) and 2014 (49.4%)	Serum	1444	1034 71.6%	-	6**** 0.8%	3b; 3c; 3h

* Authors report that, interestingly, in the present study, HEV RNA was detected more frequently among pigs without serological evidence of HEV infection: among fifteen pigs with positive PCR, only one had detectable anti-HEV IgG. The samples analyzed in the present study were obtained from pigs at slaughter age (approximately six months), which may have led to the failure to detect IgM antibodies. ** Among the 18 animals with microscopic liver lesions, HEV RNA was detected in eight (32%) of the pigs by nested PCR and in seven (28%) of the pigs by IHC in at least one of the samples analyzed from each animal. *** Viral loads observed for bile samples ranged from 101 to 105 genome copies/mL. **** 6/713 samples analyzed for the year 2014.

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Exclusively hepatitis E viruses belonging to genotype 3 (HEV-3) were identified in all regions of Brazil where genotypic analysis was performed. Intra-genotypic diversity was evidenced by the distribution of different phylogenetic subtypes among the states and is presented in Figure 4.

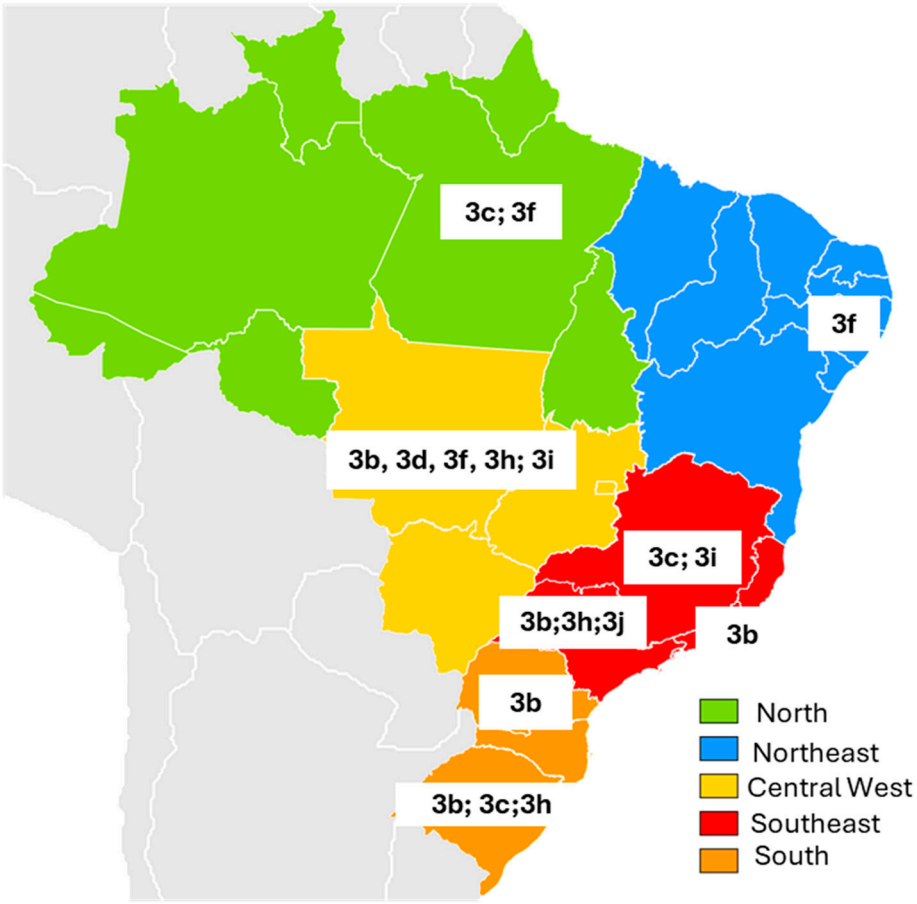

Figure 4. Distribution of the different phylogenetic subtypes of HEV genotype 3, according to the five major regions of Brazil, 1995–2025.

In the North Region, in the state of Pará, subtypes 3c and 3f were identified. In the Northeast, in the state of Pernambuco, the isolated viruses were classified as subtype 3f. In the Central-West Region, in the state of Mato Grosso, multiple subtypes were detected: 3b and 3f in one study, and 3d, 3h, and 3i in another, demonstrating genetic diversity of HEV in the region. In the Southeast Region, in the state of Rio de Janeiro, subtype 3b was identified. In Minas Gerais, the viruses were grouped into subtypes 3c and 3i. In the state of São Paulo, subtypes 3b, 3h, and 3j were detected. In the southern region, in the state of Paraná, the isolated viruses belonged to subtype 3b. In Rio Grande do Sul, subtypes 3b, 3c, and 3h were identified.

4. Discussion

Recent estimates regarding hepatitis B and C viruses suggest a downward trend in the incidence and prevalence of these infections in Brazil, possibly as a consequence of vaccination and antiviral treatment in recent years [79,80]. However, data on the occurrence of HEV infection in this country are very scarce, which may be due to the unavailability of the anti-HEV test for patients from the Brazilian Public Unified Health System.

Brazil has a vast territorial extension and a significant population with considerable ethnic and cultural miscegenation. The Brazilian people have experienced cultural influences from indigenous peoples (the original people), which persists mainly in the North and Central West regions; from the Portuguese in the Northeast, and from Italians and Germans in the Southeast and South.

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Additionally, the influence of the African people is present in practically all regions of the country, brought over during the 17th and 19th centuries. Certainly, this aspect is of great importance for the wide variation in the prevalence and peculiarities of HEV in Brazil.

Due to the heterogeneity of studies conducted in Brazil, stemming from the large number of articles found—about 48 papers in the last 30 years—assessing different groups across the five different regions of the country, as well as the use of different tests, obtaining more robust data from across the territory is challenging. Nevertheless, when evaluating the data in general, there is a trend of increasing prevalence from North to South regions, with intermediate numbers in the Central West and Northeast (Table 1). Socio-demographic data also reveal a trend of higher education levels, greater purchasing power, and increased industrialization in the Southeast and South regions of Brazil.

Indeed, when observing the epidemiological data on HEV, variation among the different regions of Brazil becomes evident, particularly with a higher occurrence of this virus in the Southeast and South regions of the country. It is noteworthy, however, that some authors have suggested that differences in prevalence in the country could be attributed to the sensitivity issues of ELISA tests for detecting anti-HEV from different manufacturers [19, 81]. Nonetheless, more recent data using modern tests suggest that differences in the accuracies of anti-HEV IgG tests may not be as significant [12, 54, 82].

There is a scarcity of studies in the general population of Brazil, with the vast majority conducted on blood donors or specific groups. Initial studies particularly evaluated the occurrence of anti-HEV in patients with acute hepatitis of undetermined etiology (non-A, non-E hepatitis), in addition to blood donors. Therefore, these data were obtained using older ELISA tests. More recent studies assessed specific high-risk groups, such as drug users, hemodialysis patients, HIV soropositive individuals, transplant recipients, and patients with underlying chronic liver disease, among others (Table 1).

One of the first well-designed epidemiological studies conducted in Brazil took place in the city of São Paulo, where active searches were conducted in randomly selected households across all neighborhoods and social strata. A total of 1,059 individuals were evaluated, estimating the prevalence of anti-HEV IgG at 1.68% of the population, with a tendency to increase in older individuals and residents of the West and downtown areas of the city [46]. Shortly thereafter, similar data was observed in the city of Rio de Janeiro, also in the Southeast, in the Manguinhos Community, where an anti-HEV prevalence of 2.4% was found among 699 individuals [61]. More recently, in a small municipality in the state of São Paulo, a prevalence of 20% of anti-HEV was found among 248 individuals, with an association of the marker with the consumption of raw meat [54]. This is also indicated in Table 1.

Among blood donors, an increase in prevalence is observed in the South region of Brazil. In fact, the first article published in this country in 1997 involved 200 blood donors from Salvador, in the Northeast region, where an anti-HEV prevalence of 2% was noted [15]. Subsequently, in another two studies in this region, prevalences of 0.9% among 996 donors in Recife and 1.35% among 890 donors in Teresina were observed, both in the Brazilian Northeast [33, 36]. On the other hand, in Santa Catarina, an anti-HEV prevalence of 10% was observed among 300 blood donors [18]. Furthermore, in the neighboring state of Rio Grande do Sul, prevalences of 7.1% among 281 blood donors and 18.7% among 80 blood donors were found [65].

In general, in practically all studies, an increase in the prevalence of anti-HEV is observed with increasing age of the evaluated individuals [43, 50,53]. This aspect has already been described in a meta-analysis of European studies and is likely due to a longer duration of exposure to HEV [83]. Indeed, some studies have revealed higher anti-HEV prevalence associated with longer exposure to the virus, such as longer crack cocaine use, longer HIV infection duration, or longer residence in rural settlements [28, 32, 39].

Another interesting aspect in Brazilian studies regards the higher prevalence of HEV in patients with more advanced liver disease. In fact, some articles have documented a higher prevalence of anti-

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HEV in cirrhotic patients with advanced fibrosis and diabetes mellitus [57, 65]. Two articles involving patients from the Brazilian Northeast, where Schistosomiasis mansoni is endemic, revealed high prevalence of anti-HEV in patients with this parasitosis. Moreover, associations of the HEV marker with more advanced forms of schistosomiasis were also observed, raising the possibility that the virus may have worsened the evolution of the parasitosis or that more severe patients had a higher risk of contamination [31,35].

The increased risk of HEV contamination in patients with schistosomiasis may be due to a lack of sanitation and treated water in endemic regions. Indeed, some studies in Brazil reveal a higher risk of HEV contamination in areas with inadequate sewage systems, such as in rural settlements [39, 42, 45].

These findings may suggest that genotypes 1 or 2 of HEV circulate in Brazil, which present transmission via the fecal-oral route, as occurs in regions of Africa and Asia [7, 8]. However, in these regions lacking adequate sanitation infrastructure, in rural areas, domestic pig farming and consumption of game meat also occur, which is strongly related to genotypes 3 or 4 of HEV, considered zoonotic transmission [7, 8,68].

In fact, research on Brazilian studies regarding the prevalence of HEV markers in pigs reveals quite high percentages in four regions of the country, except for the North region, ranging between 60 and 80% of swine. Additionally, in virtually all studies that researched the genotype, HEV-3 was found (Table 2). Moreover, in the four studies in humans where HEV genotype research was conducted, variants of HEV-3 were found in all [28, 49, 58, 64].

Supporting these findings, in Brazil there are studies revealing a higher occurrence of anti-HEV associated with pig farming and consumption of pork and game meat [26, 34, 38, 40, 51]. It is noteworthy that in the Southeast and South regions of Brazil, where there was greater influence from Italian and German cultures, the climate is temperate and there is a habit of raising pigs for consumption of meat and its smoked derivatives during winter. Often, these farms are domestic and not very well-regulated by health surveillance agencies.

The main limitation of this review refers to the scarcity of robust studies involving significant samples of the Brazilian population across the five regions of the country, in large cities of the industrialized regions and in small municipalities in rural areas. Moreover, the heterogeneity of the studies regarding sample size, differences in ELISA kits used, and peculiarities of the various groups evaluated also pose challenges.

In conclusion, based on the findings of this review, it can be considered that HEV infection occurs in all five regions of Brazil, with higher prevalence in the South and Southeast regions. The circulating genotype in the country is HEV-3, possibly transmitted through pig consumption and breeding.

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Abbreviations

The following abbreviations are used in this manuscript:

ELISA	Enzyme-Linked Immunosorbent Assay
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HEV	Hepatitis E virus
JBI	Joanna Briggs Institute
PCC	Population, Concept, and Context
PRISMA-ScR	Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews
WHO	World Health Organization

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