ESCOLA BAHIANA DE MEDICINA E SAÚDE PÚBLICA
CURSO BIOMEDICINA

FERNANDA SOUZA NOVAIS

ANALYSIS OF HEPATITIS E VIRUS (HEV) INFECTION PREVALENCE IN TRANSPLANT PATIENTS

SALVADOR – BA
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Trabalho de Conclusão de Curso apresentado à Escola Bahiana de Medicina e Saúde Pública, como parte dos requisitos para obtenção do título de Bacharel em Biomedicina.

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Este Trabalho de Conclusão de Curso foi julgado adequado à obtenção do grau de Bacharel em Biomedicina e aprovada em sua forma final pelo Curso de Biomedicina da Escola Bahiana de Medicina e Saúde Pública.

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RESUMO

A hepatite E, causada pelo vírus da hepatite E (HEV), é uma preocupação crescente, especialmente, devido ao potencial de cronificação em pacientes imunocomprimidos. O objetivo deste estudo foi determinar a prevalência de infecção pelo HEV em pacientes imunocomprometidos que realizaram transplante de órgãos sólidos e medula óssea. Estudo de corte–transversal realizado no Complexo Hospitalar Universitário Professor Edgard Santos (Complexo HUPES-UFBA) e no Hospital Ana Nery (HAN). Participaram do estudo 275 pacientes imunocomprometidos, sendo 18 pacientes transplantados de fígado (TF), 153 transplantados de rim (TR), e 105 transplantados de medula óssea (TMO). Todos os participantes assinaram o TCLE/TA e responderam a um questionário sociodemográfico e epidemiológico. Dados secundários foram obtidos através da revisão de prontuários médicos. Uma amostra de sangue foi colhida para pesquisa sérica dos anticorpos anti-HEV IgG e anti-HEV IgM pelo método de ELISA (Wantai) e detecção do HEV-RNA pelo método de RT-qPCR (Realstar HEV RT-qPCR kit 2.0, Altona Diagnostics). A coleta de amostras de soro foi realizada para a detecção de anticorpos anti-HEV (IgM e IgG) e do RNA viral, utilizando métodos sorológicos e moleculares. Os resultados mostraram uma soroprevalência de 5,5% para anti-HEV, com 4,7% dos pacientes reagentes para IgG e 0,7% reagentes para IgM. Nenhum paciente apresentou RNA viral detectável, indicando a ausência de infecção ativa. A prevalência foi maior entre os TR (7,8%), seguido pelos TF (5,6%) e TMO (2,9%). Não houve associação significativa entre a soroprevalência e os fatores de risco, exceto para o sexo masculino. Conclui-se que, a baixa soroprevalência do anti-HEV IgG/IgM Total e ausência de viremia revelam uma baixa exposição ao HEV em pacientes transplantados de órgãos sólidos e TMO. O rastreio do HEV-RNA pode prevenir doença crônica de fígados em pacientes imunocomprometidos. Novos estudos com uma casuística maior serão necessários para identificar riscos de exposição.

Palavras-chave: Hepatite E; Imunocomprometidos; Transplante.

ABSTRACT

Hepatitis E, caused by the hepatitis E virus (HEV), is a growing concern, especially due to its potential for chronicity in immunocompromised patients. The aim of this study was to determine the prevalence of HEV infection in immunocompromised patients undergoing solid organ and bone marrow transplantation. This was a cross-sectional study conducted at the Professor Edgard Santos University Hospital Complex (HUPES-UFBA Complex) and the Ana Nery Hospital (HAN). The study included 275 immunocompromised patients, including 18 liver transplant (LT) patients, 153 kidney transplant (KT) patients, and 105 bone marrow transplant (BMT) patients. All participants signed the informed consent form and answered a sociodemographic and epidemiological questionnaire. Secondary data were obtained through review of medical records. A blood sample was collected for serum testing of anti-HEV IgG and anti-HEV IgM antibodies by ELISA (Wantai) and detection of HEV RNA by RT-qPCR (Realstar HEV RT-qPCR kit 2.0, Altona Diagnostics). Serum samples were collected for detection of anti-HEV antibodies (IgM and IgG) and viral RNA using serological and molecular methods. The results showed a seroprevalence of 5.5% for anti-HEV, with 4.7% of patients reactive for IgG and 0.7% reactive for IgM. No patient had detectable viral RNA, indicating the absence of active infection. The prevalence was higher among KT (7.8%), followed by LT (5.6%) and BMT (2.9%). There was no significant association between seroprevalence and risk factors, except for male gender. It is concluded that the low seroprevalence of anti-HEV IgG/Total IgM and absence of viremia reveal a low exposure to HEV in solid organ transplant and BMT patients. HEV-RNA screening can prevent chronic liver disease in immunocompromised patients. Further studies with a larger sample will be necessary to identify exposure risks.

Keywords: Hepatitis E; Immunocompromised; Transplants.

SUMÁRIO

1 INTRODUCTION

Hepatitis E (HEV) is a significant disease in developing countries, yet it is underestimated in Brazil. According to the WHO, around 20 million people may be exposed to the virus annually, resulting in 3.3 million symptomatic cases and 44,000 deaths [1]. Its transmission occurs through person-to-person contact, from mother to fetus, and through the consumption of contaminated water and food, especially pork and wild game meat [2]. HEV infection is generally self-limited in immunocompetent individuals; however, it becomes a serious concern in pregnant women, immunocompromised individuals, and users of immunosuppressants [3].

Among the immunosuppressed, HEV can lead to chronic hepatitis and cirrhosis, with viral RNA being detected in patients who exhibited elevated aminotransferases and progression to liver disease [4]. Studies also show the presence of antibodies and viral RNA in blood and organ donors and recipients, demonstrating exposure to the virus [5]. The risks of infection are linked to factors such as age, comorbidities, immunosuppressive therapies, and the presence of immunomodulatory infections such as HIV and cytomegalovirus [6].

Cases of HEV infection following bone marrow transplants have also been reported, with some even suggesting viral replication in the bone marrow [7, 8]. Other reports associate HEV with increased aminotransferases and the development of cirrhosis in transplant recipients [9]. Although transplants are effective in treating various diseases, failures in screening for infections can occur, leading to the chronicity of hepatitis E in transplanted and/or transfused patients. At Fiocruz/Ba, studies have already been conducted on HEV, estimating the prevalence in various groups, including blood donors (7.1%), HIV-positive individuals (9.2%), patients with chronic parenchymal liver disease (14%), and, lastly, patients with Guillain-Barré Syndrome (10.5%) [10, 11].

HEV remains under-investigated in Brazil, with few laboratories offering specific tests. The identification of HEV-RNA is crucial for appropriate interventions, particularly in immunosuppressed individuals, to prevent more severe outcomes [12, 13]. These findings reinforce the need for effective surveillance, aiming to mitigate the impacts of chronic infection in vulnerable populations. The aim of this study was to investigate the burden of hepatitis E among solid organ and bone marrow transplant patients.

2 METHODS

2.1 STUDY DESIGN

The design of this study was observational, cross-sectional, aimed at determining the prevalence of HEV infection in immunocompromised patients who had undergone liver (LT), kidney (KT), and/or bone marrow transplantation (BMT).

2.2 STUDY LOCATION AND PERIOD

The study was conducted at the Professor Edgard Santos University Hospital from Federal University of Bahia (HUPES-UFBA Complex), and Hospital Ana Nery (HAN), both located in Salvador, Bahia, between 2021 and 2023. These hospitals are reference healthcare units in Bahia, offering various medical specialties, ranging from outpatient care for infectious, genetic, and autoimmune diseases, to performing complex surgical procedures such as organ and tissue transplants. Data and samples were analyzed at the Pathology and Molecular Biology Laboratory from Gonçalo Moniz Institute, Fiocruz-BA.

2.3 PARTICIPANTS

Immunocompromised patients who had undergone BMT and LT at the HUPES-UFBA Complex, and KT recipients from HAN participated in the study. This project was approved by the Fiocruz Ethics Committee (CEP-Fiocruz) and the ethics committees of the collaborating institutions under approval number 4.408.759. All adult patients signed an informed consent form (TCLE) agreeing to participate in the study. Adolescent participants signed the corresponding informed assent term (TALE) while their parents or legal guardians signed the TCLE on their behalf. In cases where the participant was illiterate, consent was obtained using a fingerprint on the TCLE/TALE.

2.3.1 Criteria

Inclusion: Both genders; aged 16 years or older; presenting some degree of immunocompromise due to an underlying disease or post-BMT, LT, or KT care, regardless of the transplant duration

Exclusion: Individuals who voluntarily chose to withdraw from the study, those who did

not participate in the data collection interview, or did not provide a blood sample for testing were excluded from the study without any detriment to their medical follow-up at the respective health units.

2.4 SAMPLE SIZE CALCULATION

The sample universe for this study included immunocompromised patients treated at the HUPES-UFBA Complex and HAN: 200 LT recipients, 400 KT recipients, and 400 BMT recipients per year. Assuming an HEV infection prevalence of 5%, a confidence interval of 95%, and a margin of error of 5%, the minimum sample size for a cross-sectional study from a population of 200 individuals should be 53 participants, and from a population of 400 individuals, 62 participants.

2.5 DATA COLLECTION

All participants were recruited by the research team. Primary data were obtained from participants through interviews using individual sociodemographic and epidemiological questionnaires. The interviews were conducted in a suitable location to ensure the confidentiality of the information. Secondary data, such as clinical-laboratory and follow-up data, were obtained by reviewing medical records. All data was collected using offline mobile devices. Later, the data were transferred and managed in a REDCap database system (version 13.1.26-2024 Vanderbilt University), hosted at FIOCRUZ-BA at http://bdp.bahia.fiocruz.br/.

2.6 SERUM SAMPLE COLLECTION

A 10 mL venous blood sample was collected in a non-additive vacuum tube by venipuncture by trained professionals from the collaborating institutions. After clot retraction, the serum was aliquoted into three different cryotubes: one was stored in -20ºC freezers and two were stored in -70ºCuntil use. The -20ºC aliquot was used for serological tests, one -70ºC aliquot was used for molecular diagnosis and HEV-RNA sequencing in positive case and the other for safeguard.

2.7 SEROLOGICAL DIAGNOSIS

Anti-HEV IgM and IgG antibodies were determined by capture ELISA and indirect ELISA, respectively, according to the manufacturer's instructions (Wantai Biopharm, Beijing, China). A pre-coated plate with an antigen was used to test the participants' serum

along with controls. The protocol included: adding 100uL of diluent solution and 10uL of controls and samples; incubation at 37ºC for 30 minutes; 5 washes with diluted washing solution; adding 100uL of HRP-conjugated anti-human antibody with incubation at 37ºC for 30 minutes, followed by 5 washes with washing solution. Subsequently, 50uL of each chromogenic solution (A and B) was added, incubated at 37ºC for 15 minutes, avoiding light. Finally, 50uL of the stop solution was added, and the plate was read on the RT 6000 spectrophotometer (RAYTO brand) at 450nm. The washes were performed using an RT 3000 plate washer (RAYTO brand).

2.8 BIOCHEMICAL ASSAY OF ALANINE AMINOTRANSFERASES (ALT)

Serum ALT levels were obtained through medical record reviews. The activity of these enzymes is often measured using a colorimetric method (e.g., ab105134, Abcam). For all participants, the determination of serum transaminases, alanine aminotransferase (ALT), and aspartate aminotransferase (AST), was performed by a kinetic, oxidative-reductive method at ultraviolet wavelength, in the invisible range, using ready-to-use reagents.

2.9 MOLECULAR DIAGNOSIS

HEV-RNA was extracted from 140uL of serum using the QIAmp Viral RNA Mini kit (Qiagen, Venlo, Netherlands) following the manufacturer's instructions. HEV-RNA detection was performed using 25uL of total RNA by RT-qPCR, with a commercial kit according to the manufacturer's instructions (Realstar HEV RT-PCR kit 2.0, Altona Diagnostics Hamburg, Germany). The kit includes an internal control, which was used in all samples before HEV-RNA extraction to ensure experiment quality. In addition to internal controls, all experiments were conducted with a positive control from the kit and a positive HEV-RNA control. The external positive control corresponded to a standard plasma prepared with genotype 3a and/or a plasma from a reference panel containing 11 different HEV genotypes (1a, 1e, 3b, 3c, 3e, 3f, 4c, 4g, and 2a) distributed by the World Health Organization for diagnostic kit validation (Paul-Ehrlich-Institute, PEI codes 6329/10 and 8578/13, respectively).

2.10 DATA ANALYSIS

Descriptive data were analyzed in REDCap (version 13.1.26-2024 Vanderbilt University) and comparisons were performed using Epi Info 7.2.6 software. Results were

presented as descriptive data in the form of case numbers, mean ± standard deviation (SD), and range (minimum and maximum), whenever possible. The prevalence of outcome among the exposed was divided by the prevalence of the outcome non-exposed, and obtained the prevalence ratio (RP), which was used as a measure of association. Comparisons between categorical variables were performed using Yates' corrected chi-square method or Fisher's exact test when appropriate. Comparisons between continuous variables and HEV infection outcomes were performed using the Kruskal-Wallis or Mann-Whitney method. A two-tailed p-value < 0.05 was considered significant for all analyses.

3 RESULTS AND DISCUSSION

A total of 275 patients were included in the study, of which 105 underwent BMT, 18 LT, and 153 KT. One participant receiving both LT and KT. The seroprevalence was 5.5%, which will be further detailed in Table 5. As for the causes of transplants among patients, in HCTs the most frequent causes observed were acute leukemia (36%), myeloma (22%), and non-Hodgkin lymphoma (4.5%) (Figure 1). In kidney transplants, the most common cause was hypertension (32%), followed by indeterminate causes (31%), glomerulonephritis (11%), and diabetes (5%). Other causes include cytomegalovirus, nephrotic syndrome, chronic renal failure, lupus, drug abuse, polycystic kidneys, meningitis, atrophic kidneys, and kidney stones (Figure 2). Among liver transplant patients, there were multiple causes, with hepatitis C alone being the most frequent (35.3%), followed by hepatitis B (23.5%), autoimmune hepatitis (17.6%), and alcoholic liver disease (17.6%). Other causes include hepatocellular carcinoma, Caroli disease, biliary atresia, drug-induced hepatitis, and cytomegalovirus (Figure 3).

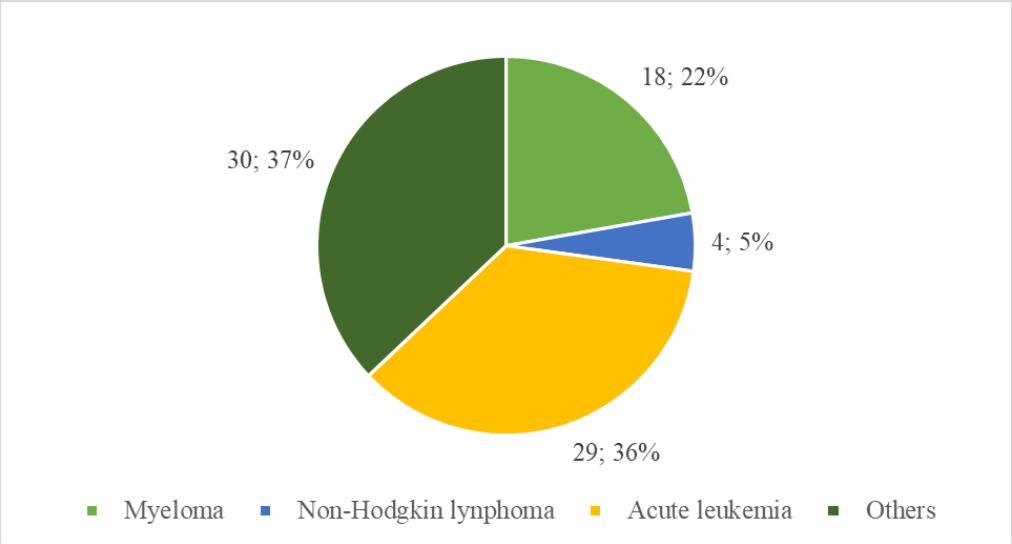

Figure 1. Cause of bone marrow transplants (BMT), HUPES-UFBA Complex, 2021-2023.

Source: Author

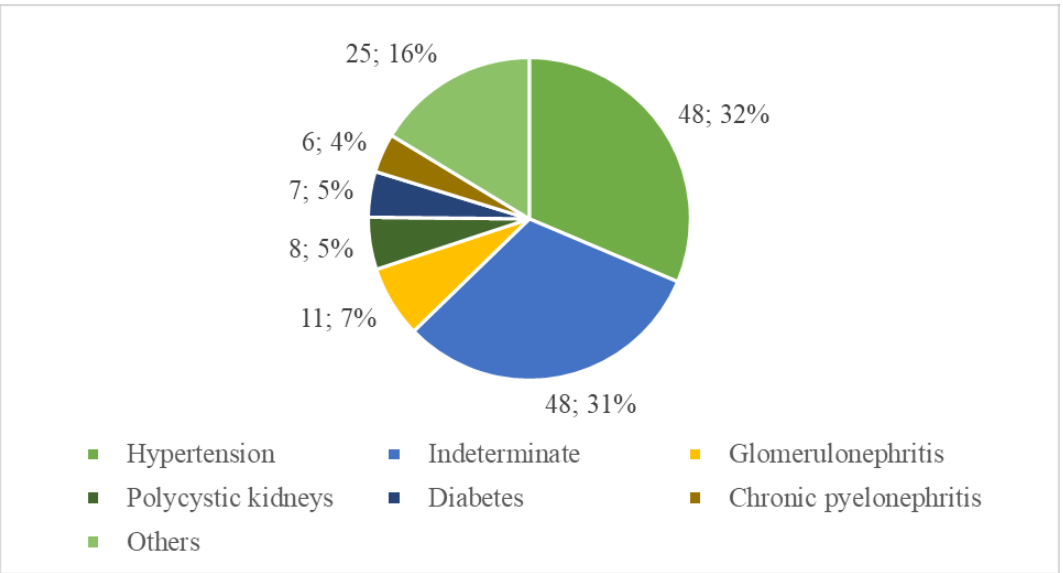

Figure 2. Cause of kidney transplant (KT), HAN 2021-2023.

Source: Author

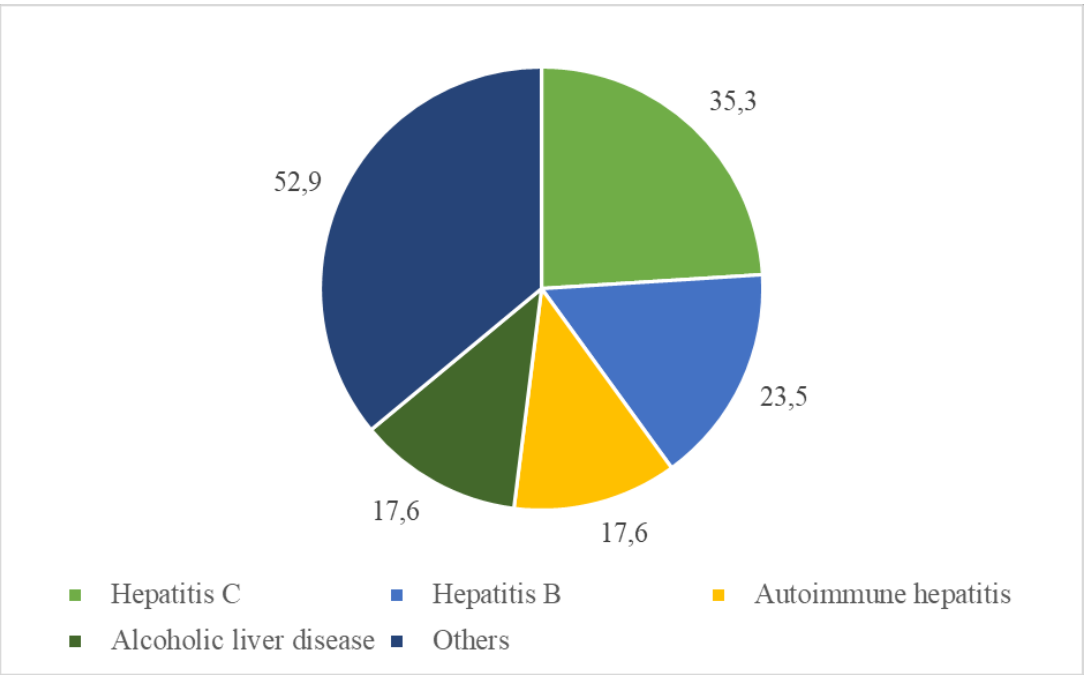

Figure 3. Cause of liver transplant (LT), HUPES-UFBA Complex 2021-2023.

Source: Author

Regarding the sociodemographic characteristics, most patients were male (56.7%), with this predominance being particularly higher among LT recipients (84.2%), likely due to the higher prevalence of underlying liver diseases in men [14], often linked to excessive alcohol consumption and delayed medical care (Table 1). Most patients were not originally from Salvador (67.5%) and resided in the Metropolitan Region of Salvador

(58.5%). The remaining patients who lived in rural areas often migrated to the capital due to the lack of specialized medical services for follow-up. In terms of racial distribution, many participants self-identified as Black or mixed race (83.3%), which aligns with the profile of users of the Brazilian unified public health system (SUS), as reported annually by the Brazilian Institute of Geography and Statistics (IBGE). Regarding educational levels, the most common category was high school graduates or those with incomplete higher education (44.0%), with only 8.4% having completed higher education. We found no significant differences between the data from our participants and official IBGE data (Table 1).

Table 1. Socio-demographic characteristics of immunocompromised patients who underwent bone marrow (BMT), kidney (KT), and liver transplants (LT), HUPES-HAN, 2021-2023.

	BMT				KT				LT				Total			
Characteristics	n*	%	mean	±SD	n*	%	mean	±SD	n*	%	mean	±SD	n**	%	mean	±SD
Total	105	100,0			153	100,0			18	100,0			275	100,0		
Sexo																
Male	54	51,4			88	57,5			15	83,3			156	56,7		
Female	51	48,6			65	42,5			3	16,7			119	43,3		
Age (years)			41.3	14.03			47.2	13.2			51.3	18.2			45.2	14.2
Born in Salvador																
Yes	24	22,9			59	38,8			6	33,3			89	32,5		
No	81	77,1			93	61,2			12	66,7			185	67,5		
City of residence																
Great Salvador	57	54,3			93	60,8			12	66,7			161	58,5		
Other cities in the interior of the state	48	45,7			60	39,2			6	33,3			114	41,5		
Skin color																
White	18	16,7			10	6,5			3	16,7			31	11,2		
Brown	57	52,8			84	54,9			11	61,1			151	54,3		
Black	27	25,0			58	37,9			4	22,2			89	32,0		
Yellow	3	2,8			1	0,7			0	0,0			4	1,4		
Schooling																
Illiterate / Fundamental I Incomplete	11	10,5			20	13,1			1	5,6			32	11,6		
Fundamental I Complete/ Fundamental II Incomplete	23	21,9			35	22,9			3	16,7			60	21,8		
Fundamental II Complete/ Medium Incomplete	14	13,3			22	14,4			3	16,7			39	14,2		
Medium Complete/ Superior Incomplete	51	48,6			61	39,9			9	50,0			121	44,0		
Superior Complete	6	5,7			15	9,8			2	11,1			23	8,4		

* Total varies according to data availability. ** One participant underwent both KT and LT. SD = standard deviation.

Source: Author

Although HEV is primarily transmitted via the fecal-oral route, through the ingestion of contaminated water or food, there is also the possibility of bloodborne transmission [15,16]. Considering that HEV infection is not routinely screened in hospitals and blood banks, there is a risk for these immunocompromised patients, as the majority reported having received blood transfusions (83%). All KT and LT patients had already undergone surgical procedures, where as this finding was less common among bone marrow transplant patients (54.8%), as this type of transplant does not require surgical preparation, unlike solid organ transplants (Table 2).

Table 2. Percutaneous risks of immunocompromised patients who underwent bone marrow transplant (BMT), kidney transplant (KT), and liver transplant (LT), HUPES-HAN, 2021-2023**.**

Caracteristics	BMT		KT		LT		Total	
	n*	%	n*	%	n*	%	n**	%
Total	105	100,0	153	100,0	18	100,0	275	100,0
Received blood/blood product donation								
Yes	98	93,3	117	77,5	11	68,8	225	83,0
No	7	6,7	34	22,5	5	31,3	46	17,0
Underwent surgical procedure								
Yes	57	54,8	153	100,0	18	100,0	227	82,8
No	47	45,2	0	0,0	0	0,0	47	17,2

* Total varies according to data availability. ** One participant underwent both KT and LT. SD = standard deviation.

Source: Author

Regarding lifestyle habits, a significant portion of the patients revealed to be alcoholics (46.2%). Among the LT, 27.8% reported consuming alcoholic beverages, which represents a risk, even for occasional consumers, given the synergy between alcoholism and liver infections, especially in individuals undergoing this type of transplant. Most participants have an active sexual life, with oral sex (52.7%) more frequent than anal sex (36.0%). Condom use is irregular, with only 18.8% confirming consistent use. Although HEV is not classified as a sexually transmitted infection (STI), there is a risk of fecal-oral transmission during anal-oral sex. Although the reference is to the hepatitis A virus in men who have sex with men [17], both viruses share the same transmission route (Table 3).

Table 3. Lifestyle habits of immunocompromised patients who underwent bone marrow transplant (BMT), kidney transplant (KT), and liver transplant (LT), HUPES-HAN, 2021-2023.

Caracteristics	BMT		KT		LT		Total	
	n*	%	n*	%	n*	%	n**	%
Total	105	100,0	153	100,0	18	100,0	275	100,0
Alcohol								
Yes	45	43,3	76	50,0	5	27,8	126	46,2
No	59	56,7	76	50,0	13	72,2	147	53,8
Oral sex								
Yes	44	43,6	84	57,1	11	64,7	139	52,7
No	57	56,4	63	42,9	6	35,3	125	47,3
Anal sex								
Yes	21	20,8	65	44,2	9	52,9	95	36,0
No	80	79,2	82	55,8	8	47,1	169	64,0
Condom use								
Never	34	40,5	75	65,2	7	70,0	115	55,3
Sometimes	21	25,0	23	20,0	1	10,0	45	21,6
Always	20	23,8	17	14,8	2	20,0	39	18,8

* Total varies according to data availability. ** One participant underwent both KT and LT. SD = standard deviation.

Source: Author

Regarding environmental and hygiene risks, most participants reported having access to piped water (96.0%), with 86.2% sourced from the public distribution network (data not present). Despite most living in urban areas, a significant portion reported lacking a sewage system (25.6%), highlighting deficiencies in basic sanitation that facilitate HEV contraction, as substantial epidemiological evidence suggests waterborne transmission, especially in South/Southeast/Central Asia and Northwest Africa. Additionally, 27.7% reported experiencing floods, increasing HEV exposure risk. Zoonotic HEV transmission is primarily linked to the consumption of processed meats, pork, and artisanal sausages. A considerable portion of patients reported contact with livestock (45.6%); some studies suggest that not only pork consumption but also exposure to these animals may be a significant transmission route, given the identification of specific swine strains capable of infecting humans (Table 4).

Table 4. Environmental and hygiene risks of immunocompromised patients who underwent bone marrow transplant (BMT), kidney transplant (KT) and liver transplant (LT), HUPES-HAN, 2021-2023.

Caracteristics	BMT		KT		LT		Total	
	n*	%	n*	%	n*	%	n**	%
Total	105	100,0	153	100,0	18	100,0	275	100,0
Piped water								
Yes	98	93,3	149	97,4	18	100,0	264	96,0
No	7	6,7	4	2,6	0	0,0	11	4,0
Sewage								
Yes	58	57,4	128	84,2	16	88,9	201	74,4
No	43	42,6	24	15,8	2	11,1	69	25,6
Floods/inudation								
Yes	36	38,3	33	21,6	4	22,2	73	27,7
No	58	61,7	120	78,4	14	77,8	191	72,3
Neighborhood with pig farming								
Yes	17	16,7	41	26,8	1	5,6	59	21,7
No	85	83,3	112	73,2	17	94,4	213	78,3
Raise herd animals								
Yes	52	51,0	65	43,0	7	38,9	123	45,6
No	50	49,0	86	57,0	11	61,1	147	54,4

* Total varies according to data availability. ** One participant underwent both KT and LT. SD = standard deviation.

Source: Author

Serological tests for anti-HEV IgG and IgM antibodies, as well as RT-qPCR, were conducted on all samples. Among these, thirteen (4.7%) were reactive for anti-HEV IgG, and 2 (0.7%) were reactive for anti-HEV IgM, resulting in a total anti-HEV seroprevalence of 5.5%, which is lower than other studies conducted in Brazil where seroprevalence ranges from 2.3% to 20% [21]. The seroprevalence varied by group: 2.9% in BMT, 5.6% in LT, and 7.8% in KT. No case presented detectable HEV-RNA, and most participants had liver transaminases within reference values. These results indicate that all groups have been exposed to HEV at some point in their lives (Table 5).

Table 5. Laboratory characteristics of immunocompromised patients who underwent bone marrow (BMT), kidney (KT), and liver transplant (LT), HUPES-HAN, 2021-2023

Caracteristics	BMT				KT				LT				Total			
	n*	%	mean	SD	n*	%	mean	SD	n*	%	mean	SD	n**	%	mean	SD
Total	105	100,0			153	100,0			18	100,0			275	100,0		
Liver profile	104				146				17				266			
Men ALT (NR: 40 UI/dL)	54		33,2	29,3	84		26,6	13,2	14		31,7	20,9	151		28,6	21,4
≤ NR	41	75,9			74	88,1			11	78,6			125	82,8		
Women ALT (NR: 32 UI/dL)	50		34,4	44,1	62		23,5	11,9	3		31,3	9,1	115		27,5	30,6
≤ NR	38	76,0			51	82,3			1	33,3			90	78,3		
HEV Serology	105				153				18				275			
Anti-HEV IgG reactive	3	2,9			10	6,5			0	0,0			13	4,7		
No reactive	102	97,1			143	93,5			18	100,0			262	95,3		
Anti-HEV IgM reactive	0	0,0			2	1,3			1	5,6			2	0,7		
No reactive	105	100,0			151	98,7			17	94,4			273	99,3		
Total Anti-HEV reactive	3	2,9			12	7,8			1	5,6			15	5,5		
No reactive	102	97,1			141	92,2			17	94,4			260	94,5		
Molecular Diagnosis	105				153				18				275			
HEV-RNA detectable	0	0,0			0	0,0			0	0,0			0	0,0		
Undetectable	105	0,0			153	100,0			18	100,0			275	100,0		

* Total varies according to data availability. ** One participant underwent both kidney and liver transplants.

Source: Author

The analysis of total anti-HEV positivity distribution by age range revealed a cumulative increase up to the fifth decade of life, followed by a decrease in the fifth decade, and then a new increase from the sixth decade of life, particularly among BMT patients. This suggests a potential re-exposure of these patients to HEV (Chi-square trend $p > 0.05$) (Figure 1). The group of KT patients showed an apparently higher seroprevalence than other groups, especially when compared to BMT patients. The literature review did not identify references indicating the reason for this.

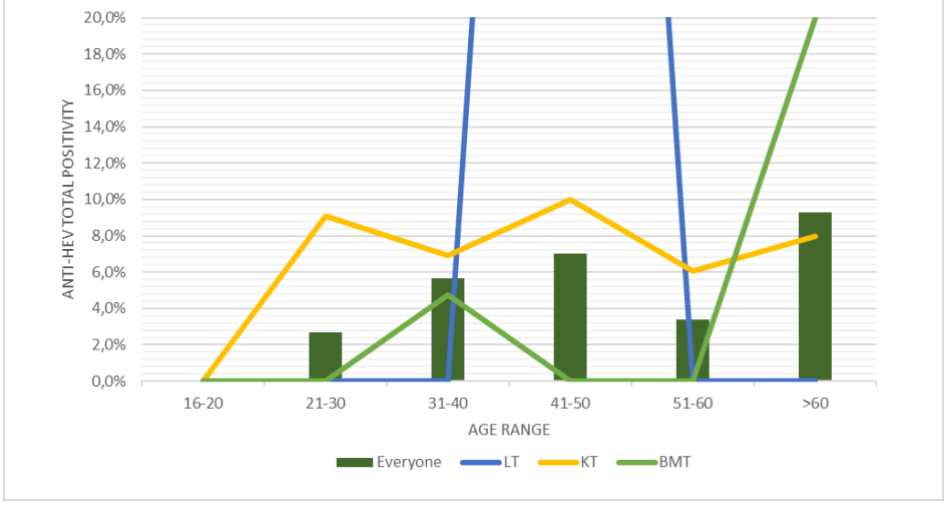

Figure 4. Distribution of Total anti-HEV positivity by age group of immunocompromised patients who underwent bone marrow transplantation (BMT), kidney (KT) and liver transplantation (LT), HUPES-HAN, 2021-2023.

Finally, the analysis of risk factors for exposure to HEV, based on the seroprevalence of anti-HEV, revealed a significant association only with males, the reason for which is still unclear, however activities carried out in the field, meat consumption Hunting and animal husbandry are traditionally more closely linked to men. The other variables did not demonstrate an association, possibly due to the limited number of participants in the study (Table 6).

Table 6. Factors associated with exposure to HEV in immunocompromised patients who underwent bone marrow (BMT), kidney (KT) and liver (LT) transplantation, HUPES-HAN, 2021-2023

Caracteristics	N*	n	Prev.	PR	95% CI	p-value
Total**	275	15	5,5%	-	3,08 - 8,84	-
Study group***						
KT	153	12	7,8%	2,75	0,79 - 9,49	ns
LT	18	1	5,6%	1,94	0,21 - 17,68	ns
BMT	105	3	2,9%	1,00		
Gender						
Male	156	13	8,3%	4,96	1,14 - 21,55	0,02
Female	119	2	1,7%	1,00		

* Total varies depending on data availability.

** 95% CI calculated at https://sample-size.net/confidence-interval-proportion/.

*** One participant received a double transplant of TR and TF.

Source: Author

4 CONCLUSIONS

Despite the low seroprevalence found, immunocompromised patients might be mor e susceptible to infections in general. The data indicates that HEV is circulating within t he studied populations and could potentially compromise their lives upon exposure. Ad ditionally, inadequate sanitary conditions and the lack of screening capable of tracking f or HEV may influence this risk.

5 CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

6 FINANCING STATEMENT

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ANEXO

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