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SEROPREVALENCE OF HEPATITIS E VIRUS IN FIVE HIGH-RISK POPULATIONS FROM THE REPUBLIC OF MOLDOVA: A CROSS-SECTIONAL STUDY

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SUMMARY

Introduction The study has assessed the seroprevalence of Hepatitis E virus (HEV) markers in different at-risk groups within the Republic of Moldova. The risk groups included blood donors, hemodialysed patients, medical workers, tuberculosis (TB) patients, and intravenous drug users (IDUs).

Materials and methods A cross-sectional descriptive-epidemiological study was conducted from 2019 to 2023, with participants randomly selected from different risk groups. Blood samples were collected and tested using ELISA for Anti-HEV IgG and IgM markers. Seroprevalence was calculated with 95% confidence intervals, and statistical analyses were conducted using Epi Info 7.2 software.

Rezults Among 794 tested blood donors, 9.6% (95% CI: 7.7-11.8) were positive for Anti-HEV IgG, indicating past exposure, and 8.3% (95% CI: 6.3-10.8) for Anti-HEV IgM, suggesting recent infection. Hemodialyzed patients had a significantly higher seroprevalence: 45.8% (95% CI: 34.8–57.1) for Anti-HEV IgG and 21.6% (95% CI: 9.8–38.2) for Anti-HEV IgM. Medical workers exhibited moderate IgG prevalence at 11.8% (95% CI: 9.1-15.0) and substantially higher IgM prevalence at 38.1% (95% CI: 26.1-51.2). TB patients had lower IgG (11.9%, 95% CI: 7.8-17.2) and IgM (7.8%, 95% CI: 3.6-14.3) prevalences. IDUs had a notable IgG prevalence of 20.5% (95% CI: 12.6-30.4) but no detectable IgM.

Conclusions This study highlights the significant burden of hepatitis E virus infection among at-risk populations in the Republic of Moldova.

Keywords Hepatitis E virus, Moldova, risk groups, anti-HEV antibodies, seroprevalence.

SEROPREVALENȚA VIRUSULUI HEPATITIC E ÎN CINCI POPULAȚII CU RISC RIDICAT DIN REPUBLICA MOLDOVA: UN STUDIU TRANSVERSAL

Introducere Studiul a evaluat seroprevalența markerilor virusului hepatitei E (VHE) în grupuri de risc din Republica Moldova: donatori de sânge, pacienți hemodializați, lucrători medicali, pacienți cu tuberculoză (TB) și utilizatori de droguri intravenoase (UDI).

Materiale și metode Între 2019 și 2023, s-a efectuat un studiu transversal descriptiv-epidemiologic, cu participanți selectați aleatoriu. Probele de sânge au fost analizate prin ELISA pentru Anti-HEV IgG și IgM. Seroprevalența a fost calculată cu intervale de încredere de 95%, iar analizele statistice au fost efectuate cu Epi Info 7.2.

Rezultate Dintre cei 794 de donatori de sânge, 9,6% (IC 95%: 7,7-11,8) au fost pozitivi pentru Anti-HEV IgG și 8,3% (IC 95%: 6,3-10,8) pentru Anti-HEV IgM. Pacienții hemodializați au prezentat seroprevalențe mai mari: 45,8% (IC 95%: 34,8-57,1) pentru IgG și 21,6% (IC 95%: 9,8-38,2) pentru IgM. La lucrătorii medicali, prevalența IgG a fost de 11,8% (IC 95%: 9,1-15,0), iar cea a IgM de 38,1% (IC 95%: 26,1-51,2). Pacienții cu TB au avut prevalențe de 11,9% (IC 95%: 7,8-17,2) pentru IgG și 7,8% (IC 95%: 3,6-14,3) pentru IgM. UDI au prezentat o prevalență de 20,5% (IC 95%: 12,6-30,4) pentru IgG, fără IgM detectabil.

Concluzii Studiul nostru relevă severitatea infecției cu virusul hepatitis E în grupurile de risc din Republica Moldova.

Cuvinte cheie Virusul hepatitei E, Moldova, grupuri de risc, anticorpi anti-HEV, seroprevalență.

INTRODUCTION

Hepatitis E virus (HEV) infection is a significant global public health concern, affecting both developed and developing nations, with approximately 20 million infections annually, including 3.3 million symptomatic cases (1).

Although often considered a self-limiting illness, HEV can result in severe outcomes, particularly in immunocompromised individuals, pregnant women, and those with pre-existing liver disease. Evidence also indicates transmission via blood transfusion and parenteral routes, emphasizing the need for improved surveillance and prevention (2, 3).

Data on HEV prevalence in Eastern European countries, such as the Republic of Moldova, remain sparse, despite the presence of socio-economic challenges and gaps in healthcare access that may facilitate HEV transmission (4). Certain groups face an increased risk of HEV infection because of specific vulnerabilities. Blood donors represent a critical focus due to the potential for transfusion-transmitted HEV, as asymptomatic donors with HEV viraemia pose a risk to blood safety (3). Hemodialyzed patients face an elevated risk stemming from frequent exposure to blood products, medical equipment, and their immunosuppressed status, with studies showing significantly higher HEV seroprevalence in this population (5).

Medical workers, due to occupational exposure, are at risk of HEV infection through contact with infected patients or contaminated materials (6). Tuberculosis (TB) patients may experience exacerbated liver complications if co-infected with HEV, particularly because of the hepatotoxic nature of TB treatments and their weakened immune systems (7). Intravenous drug users (IDUs) are also highly vulnerable due to unsafe injection practices, needle sharing, and behaviors that facilitate viral transmission, with studies showing higher HEV prevalence in this group compared to the general population (8).

This study aims to determine and compare the seroprevalence of hepatitis E virus (HEV) among five distinct high-risk populations in Moldova by measuring the prevalence of Anti-HEV IgG and IgM antibodies.

MATERIAL AND METHODS

This study has assessed the seroprevalence of hepatitis E virus (HEV) among five distinct high-risk populations in the Republic of Moldova: blood donors, hemodialyzed patients, medical workers, tuberculosis (TB) patients, and intravenous drug users (IDUs). This cross-sectional descriptive-epidemiological study was conducted over the 2019–2023 period, with samples collected progressively but tested at the end, enabling a reliable assessment of HEV seroprevalence.

SAMPLING AND STUDY POPULATION

Each risk group was sampled separately based on predefined stratification criteria, ensuring a representative distribution. Participants were selected through a stratified, multistage random sampling method. Selection was not based on pre-existing lists for all groups, but rather on eligibility criteria at the time of sample collection. In groups where registries were available (e.g., blood donors, hemodialyzed patients, medical workers), recruitment was facilitated through institutional databases. Stratification was performed within each group based on relevant demographic and epidemiological characteristics, such as age, sex, and geographical area.

At each stage, individuals were randomly chosen to ensure representative distribution within each group. The sample size for each at-risk population

was determined based on previously reported HEV seroprevalence rates in similar groups from various studies. The following prevalence estimates were used as reference values:

- Blood donors: Studies in Europe have reported HEV seroprevalence ranging from 4.7% to 52.5% (9), with a conservative estimate of 10% used for sample size calculation.
- Hemodialyzed patients: Seroprevalence in Bulgaria is 6.2%, with European studies generally reporting lower values (10). A reference prevalence of 5% was used.
- Medical workers: Higher HEV seroprevalence has been reported among clinical staff compared to non-clinical workers, with studies showing rates up to 23.7% among nurses (11). A prevalence estimate of 15% was applied.
- Tuberculosis (TB) patients: Limited data exist on HEV prevalence in TB patients, but studies suggest a potential link with hepatotoxicity. Based on available evidence, a 12% prevalence was used.
- Intravenous drug users (IDUs): Global reports indicate HEV seroprevalence around 6.1% and (12, 13), with 6% used as the reference value.

To determine the appropriate sample size for each high-risk population group, we used the standard formula for sample size estimation in prevalence studies:

$$n = \frac{Z^2 P(1 - P)}{d^2}$$

whereas:

n = required sample size

Z = 1.96 (Z-score for a 95% confidence level)

P = estimated prevalence for each group, based on previous studies

d = margin of error (set at 5%)

By using the formula, the following sample sizes were obtained for each high-risk group: Blood Donors – 139, Hemodialyzed Patients – 73, Medical Workers – 196, Tuberculosis (TB) Patients – 163, and Intravenous Drug Users (IDUs) – 87, resulting in a total calculated sample size of 658.

The inclusion of 1634 subjects from the five high-risk groups in the study exceeded the required calculated sample size – 658 individuals, based on a 5% margin of error, ensuring that the number of participants is statistically representative for assessing hepatitis E virus seroprevalence in these populations (tab. 1).

Table 1. Comparison of Calculated and Article Sample Sizes.

Group	Calculated Sample Size	Article Sample Size
Blood Donors	139	794
Hemodialyzed Patients	73	83
Medical Workers	196	468
TB Patients	163	201
IDUs	87	88
Total	658	1634

DATA COLLECTION AND ETHICAL CONSIDERATIONS

Samples were collected progressively over the 2019–2023 period, but all testing was conducted at the end of the study, ensuring that the results reflect a single cross-sectional analysis rather than multiple independent datasets. Seroprevalence results represent the cumulative findings from all collected samples, as all testing was performed at the end of the study. Therefore, the reported prevalence does not correspond to any specific year within the 2019–2023 period but rather reflects an overall assessment of HEV exposure across the entire timeframe. This approach allowed for a comprehensive evaluation of HEV seroprevalence while maintaining the methodological integrity of a cross-sectional study. Blood samples were collected at designated medical institutions, including hospital laboratories, dialysis centers, and TB treatment clinics across Moldova. Prior to sample collection, all participants provided written informed consent. The study was approved by the Research Ethics Committee of the National Public Health Agency (Protocol No. N2018-055, dated 24.12.2018), ensuring compliance with ethical guidelines and confidentiality standards.

LABORATORY ANALYSIS

A total of 5 mL of venous blood was collected from each participant by trained phlebotomists using standard aseptic techniques. Blood samples were stored at 2-8°C and transported within 24 hours to the National Agency for Public Health Laboratory for further analysis. Serum samples were tested for Anti-HEV IgG and IgM using ELISA kits (DIA.PRO, Milan, Italy), with: Sensitivity – 96.3%, Specificity – 98.2%. The positivity threshold was determined based on the manufacturer's optical density (OD) ratio method, where samples with an OD ratio ≥1.1 were classified as positive, <0.9 as negative, and values between 0.9-1.1 as borderline and subject to retesting. For quality control, each assay included positive and negative controls to ensure assay reliability. Additionally, 10% of the samples were retested independently for reproducibility assessment.

STATISTICAL ANALYSIS

Seroprevalence was calculated as the proportion of positive cases within each group using the following formula:

$$Seroprevalence\ (\%) = \frac{\text{Positive cases}}{\text{Total tested individuals}} \times 100$$

To estimate the precision of these proportions, 95% confidence intervals (CIs) were computed using the Wilson score method, which is more accurate than the normal approximation for small sample sizes. The CI was determined by:

$$CI = \hat{p} \pm z_{\alpha/2} \times \sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$$

where $\hat{p}$ represents the observed proportion of positive cases, $z_{\alpha/z}$ is the critical value for a 95% CI (1.96), and n is the total sample size.

For comparisons between groups, statistical significance was assessed using the Chi-square (χ^2) test, calculated as:

$$x^2 = \sum \frac{(O-E)^2}{E}$$

where O represents the observed frequency in each category and E is the expected frequency under the null hypothesis.

For comparisons involving small sample sizes (n < 5 per category), Fisher's exact test was applied to ensure statistical validity. This test is particularly useful when expected frequencies are too low for the Chi-square test to be reliable, as it calculates an exact probability rather than relying on approximations. Statistical significance was determined using a p-value threshold of 0.05, with results considered significant if $p < 0.05$, indicating a non-random association between HEV seroprevalence and the studied risk factors. Statistical analyses were performed using Epi Info 7.2 software to ensure consistency and accuracy in data interpretation.

RESULTS

Table 2 presents the seroprevalence of hepatitis E markers among the examined population groups. The analysis includes two markers – Anti-HEV IgG and Anti-HEV IgM – with the number of positive cases and their respective percentages detailed.

Table 2. Seroprevalence of hepatitis E virus markers among various risk groups in the Republic of Moldova.

Risk group	Marker					
	Anti-HEV IgG			Anti-HEV IgM		
	Total examined	Positive	% (95% CI)	Total examined	Positive	% (95% CI)
Blood donors	794	76	9.6 (7.7-11.8)	568	47	8.3 (6.3-10.8)
Hemodialysed patients	83	38	45.8 (34.8-57.1)	37	8	21.6 (9.8-38.2)
Medical workers	468	55	11.8 (9.1-15.0)	63	24	38.1(26.1-51.2)
TB patients	201	24	11.9 (7.8-17.2)	115	9	7.8 (3.6-14.3)
IDUs	88	18	20.5 (12.6-30.4)	88	0	0
Total	1634	211	12.9 (11.0-15.1)	871	88	10.1 (8.1-12.0)

Out of 794 tested blood donors, 9.6% (95% CI: 7.7-11.8) tested positive for Anti-HEV IgG, indicating past exposure to HEV. Similarly, 8.3% (95% CI: 6.3-10.8) from 568 of blood donors tested positive for Anti-HEV IgM, suggesting recent HEV infection.

The seroprevalence of HEV markers among 83 hemodialysed patients is notably higher compared to blood donors ($p<0.05$). 45.8% (95% CI: 34.8-57.1) of hemodialysed patients tested positive for Anti-HEV IgG, indicating a substantially higher rate of past exposure to HEV. Additionally, 21.6% (95% CI: 9.8-38.2) or 37 individuals of hemodialysed patients tested positive for Anti-HEV IgM, indicating a considerable proportion experiencing recent HEV infection.

Among the 468 tested medical workers, the seroprevalence of Anti-HEV IgG is 11.8% (95% CI: 9.1-15.0), this indicates a moderate level of past exposure to HEV among this group. However, the seroprevalence of Anti-HEV IgM is substantially higher at 38.1% (95% CI: 26.1-51.2).

Out of 201 tested TB patients, 11.9% (95% CI: 7.8-17.2) tested positive for Anti-HEV IgG, indicating past exposure to HEV. In contrast, only 7.8% (95% CI: 3.6-14.3) of TB patients tested positive for Anti-HEV IgM, suggesting a lower rate of recent HEV infection.

Finally, out of 88 intravenous drug users (IDUs) tested, 20.5% (95% CI: 12.6-30.4) tested positive for Anti-HEV IgG, indicating past exposure to HEV. Notably, none of the IDUs tested positive for IgM, which may reflect lower rates of recent HEV infection or underreporting caused by limited healthcare access.

Next, we will present the results of more detailed testing for each of the investigated groups. Thus, the results for the blood donors are presented in the table 3.

Table 3. Seroprevalence of HEV markers by factors among blood donors from the Republic of Moldova.

Factor	Marker					
	Anti-HEV IgG			Anti-HEV IgM		
	Total examined	Positive	% (95% CI)	Total examined	Positive	% (95% CI)
Sex						
Male	551	56	10.2 (7.9-13.0)	381	31	8.1 (5.8-11.3)
Female	243	20	8.2 (5.1-12.4)	187	16	8.6 (5.0-13.5)
Age group (years)						
≤20	44	3	6.8 (1.4-18.7)	41	3	7.3 (1.5-19.9)
21-40	434	35	8.1 (5.9-11.0)	324	19	5.9 (3.8-9.0)
41-60	309	37	12.0 (8.8-16.1)	201	25	12.4 (8.2-17.8)
≥61	7	1	14.3 (0.4-57.9)	2	0	0
Geographical zone						
North	155	16	10.3 (6.0-16.2)	77	7	9.1 (3.7-17.8)
Central	487	37	7.6 (5.6-10.3)	377	27	7.2 (5.0-10.2)
South	152	23	15.1 (9.8-21.8)	114	13	11.4 (6.2-18.7)

Among blood donors, the seroprevalence of Anti-HEV IgG was slightly higher in males (10.2%, 95% CI: 7.9–13.0) compared to females (8.2%, 95% CI: 5.1–12.4). Similarly, Anti-HEV IgM seroprevalence was 8.1% (95% CI: 5.8–11.3) in males and 8.6% (95% CI: 5.0–13.5) in females, with no statistically significant differences ($p>0.05$), indicating comparable exposure risks between sexes.

Seroprevalence rates increased with age, suggesting cumulative exposure to HEV over time. Individuals aged ≥61 years had the highest Anti-HEV IgG seroprevalence (14.3%, 95% CI: 0.4–57.9), while those aged 41–60 years exhibited the highest Anti-HEV IgM seroprevalence (12.4%, 95% CI: 8.2–17.8). In contrast, individuals aged ≤20 years had the lowest rates for Anti-HEV IgG (6.8%, 95% CI: 1.4–18.7) and Anti-HEV IgM (7.3%, 95% CI: 1.5–19.9).

Geographically, donors from the South zone had the highest Anti-HEV IgG seroprevalence (15.1%, 95% CI: 9.8–21.8), followed by the North (10.3%, 95% CI: 6.0–16.2) and Central zones (7.6%, 95% CI: 5.6–10.3). Anti-HEV IgM seroprevalence was also highest in the South (11.4%, 95% CI: 6.2–18.7), reflecting potential regional differences in HEV transmission dynamics, environmental factors, and population characteristics.

Table 4 presents the seroprevalence rates of HEV markers among hemodialysed patients from the Republic of Moldova, categorized by various factors such as sex, age group, and geographical zone.

Table 4. Seroprevalence of HEV markers by factors among hemodialysed patients from the Republic of Moldova.

Factor	Marker					
	Anti-HEV IgG			Anti-HEV IgM		
	Total examined	Positive	% (95% CI)	Total examined	Positive	% (95% CI)
Sex						
Male	46	19	41.3 (27.0-56.8)	18	6	33.3 (13.3-59.0)
Female	37	19	51.4 (34.4-68.1)	19	2	10.5 (1.3-33.1)
Age group (years)						
21-40	10	2	20.0 (2.5-55.6)	2	0	0
41-60	39	17	43.6 (27.8-60.4)	16	3	18.8 (4.0-45.6)
≥61	34	19	55.9 (37.9-72.8)	19	5	26.3 (9.1-51.2)
Geographical zone						
North	25	13	52.0 (31.3-72.2)	13	1	7.7 (0.2-36.0)
Central	25	9	36.0 (18.0-57.5)	8	3	37.5 (8.5-75.5)
South	32	15	46.9 (29.1-65.3)	15	4	26.7 (7.8-55.1)

Among hemodialyzed patients, Anti-HEV IgG seroprevalence was 41.3% (95% CI: 27.0–56.8) in males and slightly higher in females at 51.4% (95% CI: 34.4–68.1). Conversely, Anti-HEV IgM seroprevalence was higher in males (33.3%, 95% CI: 13.3–59.0) compared to females (10.5%, 95% CI: 1.3–33.1), though the differences were not statistically significant ($p>0.05$).

Patients aged ≥61 years showed the highest seroprevalence for both Anti-HEV IgG (55.9%, 95% CI: 37.9–72.8) and Anti-HEV IgM (26.3%, 95% CI: 9.1–51.2). The youngest group (21–40 years) had the lowest rates, with 20.0% (95% CI: 2.5–55.6) for IgG and no IgM positivity. Patients aged 41–60 years exhibited intermediate seroprevalence levels.

Clear geographical differences were observed, with the North zone reporting the highest Anti-HEV IgG seroprevalence (52.0%, 95%CI: 31.3–72.2), while the Central zone had the lowest (36.0%, 95%CI: 18.0–57.5). In contrast, the highest Anti-HEV IgM seroprevalence was found in the Central zone (37.5%, 95%CI: 8.5–75.5), followed by the South zone (26.7%, 95%CI: 7.8–55.1), highlighting regional variations in HEV exposure.

Furthermore, the data gathered from the testing of medical personnel are shown in Table 5.

Table 5. Seroprevalence of HEV markers by factors among medical workers from the Republic of Moldova.

Factor	Marker					
	Anti-HEV IgG			Anti-HEV IgM		
	Total examined	Positive	% (95% CI)	Total examined	Positive	% (95% CI)
Sex						
Male	57	4	7.0 (1.9-17.0)	8	3	37.5 (8.5-75.5)
Female	411	51	12.4 (9.6-15.9)	55	21	38.2 (25.4-52.3)
Age group (years)						
21-40	127	21	16.5 (10.5-24.2)	24	10	41.7 (22.1-63.4)
41-60	230	22	9.6 (6.1-14.1)	26	10	38.5 (20.2-59.4)
≥61	111	12	10.8 (5.7-18.1)	13	4	30.8 (9.1-61.4)
Geographical zone						
North	122	18	14.8 (9.0-22.3)	19	3	15.8 (3.4-39.6)
Central	179	12	6.7 (3.5-11.4)	18	3	16.7 (3.6-41.4)
South	151	20	13.2 (8.3-19.7)	20	5	25.0 (8.7-49.1)
Professional group						
Medical doctor	26	1	3.8 (0.1-19.6)	1	0	0
Nurse	59	14	23.7 (13.6-36.6)	14	3	21.4 (4.7-50.8)
Auxiliary staff	35	3	8.6 (1.8-23.1)	3	0	0

The seroprevalence rates displayed notable variation across several categories, reflecting the intricate interplay of factors influencing HEV infection among medical workers in the Republic of Moldova.

Among medical workers, Anti-HEV IgG seroprevalence was lower in males (7.0%, 95% CI: 1.9–17.0) compared to females (12.4%, 95% CI: 9.6–15.9), while Anti-HEV IgM rates were similar between males (37.5%, 95% CI: 8.5–75.5) and females (38.2%, 95% CI: 25.4–52.3). Age-related trends showed the highest seroprevalence rates in individuals aged 21–40 years for both Anti-HEV IgG (16.5%, 95% CI: 10.5–24.2) and Anti-HEV IgM (41.7%, 95% CI: 22.1–63.4), suggesting greater vulnerability due to occupational hazards. Geographically, the Central zone had the lowest Anti-HEV IgG (6.7%, 95% CI: 3.5–11.4) and Anti-HEV IgM (16.7%, 95% CI: 3.6–41.4) seroprevalence, while other regions showed higher rates, reflecting regional differences in transmission dynamics. Moreover, nurses had the highest seroprevalence of Anti-HEV IgG (23.7%, 95% CI: 13.6–36.6) and Anti-HEV IgM (21.4%, 95% CI: 4.7–50.8) among professional roles, which is likely attributed to increased occupational exposure.

Another group in the study included patients with TB, and the results of their tests are presented below (see Table 6).

Table 6. Seroprevalence of HEV markers by factors among TB patients from the Republic of Moldova.

Factor	Marker					
	Anti-HEV IgG			Anti-HEV IgM		
	Total examined	Positive	% (95% CI)	Total examined	Positive	% (95% CI)
Sex						
Male	128	18	14.1 (8.6-21.3)	93	8	8.6 (3.8-16.2)
Female	73	6	8.2 (3.1-17.0)	22	1	4.5 (0.1-22.8)
Age group (years)						
21-40	55	5	9.1 (3.0-20.0)	38	3	7.9 (1.7-21.4)
41-60	95	11	11.6 (5.9-19.8)	50	4	8.0 (2.2-19.2)
≥61	50	8	16.0 (7.2-29.1)	27	2	7.4 (0.9-24.3)

Among male TB patients, the seroprevalence of Anti-HEV IgG was 14.1% (95% CI: 8.6-21.3), while in females, it was 8.2% (95% CI: 3.1-17.0). For Anti-HEV IgM, males had a seroprevalence of 8.6% (95% CI: 3.8-16.2), and females had 4.5% (95% CI: 0.1-22.8), indicating higher rates in males ($p>0.05$).

Seroprevalence varied by age group. The ≥61 age group had the highest Anti-HEV IgG seroprevalence at 16.0% (95% CI: 7.2-29.1), followed by 41-60 years at 11.6% (95% CI: 5.9-19.8), and 21-40 years at 9.1% (95% CI: 3.0-20.0). For Anti-HEV IgM, the ≥61 group had the highest at 7.4% (95% CI: 0.9-24.3), followed by 41-60 years at 8.0% (95% CI: 2.2-19.2). These results suggest a potential link between age and HEV exposure.

Table 7 presents the results of the study regarding the testing of intravenous drug users (IDUs) for hepatitis E virus markers.

Table 7. Seroprevalence of Anti-HEV IgG marker by factors among IDUs from the Republic of Moldova.

Factor	Anti-HEV IgG		
	Total examined	Positive	% (95% CI)
Sex			
Male	46	11	23.9 (12.6-38.8)
Female	42	7	16.7 (7.0-31.4)
Age group (years)			
21-40	30	5	16.7 (5.6-34.7)
41-60	44	11	25.0 (13.2-40.3)
≥61	14	2	14.3 (1.8-42.8)

Among male IDUs, the seroprevalence of Anti-HEV IgG was 23.9% (95% CI: 12.6-38.8), and among females, it was 16.7% (95% CI: 7.0-31.4), indicating a higher prevalence in males, though not significantly different ($p>0.05$).

For age groups, the 41-60 years group had the highest seroprevalence of Anti-HEV IgG at 25.0% (95% CI: 13.2-40.3), followed by the 21-40 years group at 16.7% (95% CI: 5.6-34.7). The ≥61 years group had the lowest rate at 14.3% (95% CI: 1.8-42.8). These findings suggest a potential age-related trend in Anti-HEV IgG prevalence among IDUs, with middle-aged individuals showing higher rates.

As mentioned earlier, all IDUs tested for the acute phase marker of hepatitis E virus – Anti-HEV IgM, have tested negative.

DISCUSSION

The study established an overall seroprevalence of anti-HEV IgG at 12.9% (95% CI: 11.0-15.1) and anti-HEV IgM at 10.1% (95% CI: 8.1-12.0) among at-risk populations in the Republic of Moldova. Among blood donors, the seroprevalence of anti-HEV IgG was 9.6% (95% CI: 7.7-11.8) and anti-HEV IgM was 8.3% (95% CI: 6.3-10.8), consistent with European studies showing anti-HEV IgG rates ranging from 4.7% to 52.5% [9]. The trend of increasing seroprevalence with age aligns with other findings, such as Wong et al., where anti-HEV IgG prevalence increased from 0.6% in younger donors to 7.4% in older donors (14).

The geographical distribution of seroprevalence among blood donors revealed higher rates in the South (15.1% for anti-HEV IgG and 11.4% for anti-HEV IgM), potentially due to environmental or socio-economic factors. These regional differences align with previous studies indicating that rural areas may have a higher prevalence of HEV due to lower sanitation levels (10).

Hemodialyzed patients showed significantly higher anti-HEV IgG seroprevalence at 45.8% (95% CI: 34.8-57.1) and anti-HEV IgM at 21.6% (95% CI: 9.8-38.2). These rates exceed those reported in Bulgaria (6.2%) and Greece (10.4%) but are lower than studies in Iran showing up to 68.6% (15). The correlation between advancing age and higher seroprevalence was observed, consistent with findings from Japan and Sweden, where older patients exhibited significantly higher seroprevalence (16, 17). Gender differences in this group were minimal, though males had slightly higher anti-HEV IgM levels, potentially reflecting variations in immune response (18).

Medical workers exhibited an anti-HEV IgG seroprevalence of 11.8% (95% CI: 9.1-15.0) and anti-HEV IgM of 38.1% (95% CI: 26.1-51.2). Comparable results were reported by Lu et al., who found higher prevalence rates among clinical staff compared to non-clinical staff [19]. Interestingly, nurses demonstrated the highest anti-HEV IgG levels at 23.7% (95% CI: 13.6-36.6), likely due to frequent patient contact, while auxiliary staff also showed elevated levels (8.6%, 95% CI: 1.8-23.1) due to their roles in sanitation and cleaning (11). These findings highlight the occupational risks associated with HEV exposure.

Among TB patients, anti-HEV IgG prevalence was 11.9% (95% CI: 7.8-17.2) and anti-HEV IgM was 7.8% (95% CI: 3.6-14.3). Male patients showed higher seroprevalence than females, consistent with studies such as Sarda et al., which identified HEV as a significant factor in hepatotoxicity during TB treatment [20]. The age-related increase in seroprevalence among TB patients aligns with cumulative exposure over time and the immunosuppressive effects of TB treatment.

Intravenous drug users had an anti-HEV IgG seroprevalence of 20.5% (95% CI: 12.6-30.4), consistent with global studies reporting rates between 6.1%

and 23.0% (12, 13). Male IDUs exhibited higher seroprevalence than females (23.9% vs. 16.7%), although the difference was not statistically significant. Age-related trends indicate higher seroprevalence in middle-aged users (41-60 years), as seen in other studies (21). The absence of anti-HEV IgM among IDUs suggests either low levels of recent infections or underreporting due to limited healthcare access.

These findings emphasize the importance of targeted interventions like routine screenings, health education, and better sanitation for high-risk groups. For hemodialysis patients, it's vital to have more rigorous blood product screening and stricter hygiene practices during dialysis. Medical workers also need stronger protective measures and awareness campaigns to reduce occupational risks. For those with tuberculosis and injecting drug users, improving healthcare access and educating them about HEV transmission could help significantly lower infection rates (1).

CONCLUSIONS

1. Hepatitis E virus infection is a serious health issue among at-risk populations in the Republic of Moldova.
2. Adequate prevention and control measures must be implemented by public health authorities. Education and awareness efforts targeting vulnerable groups are essential to reduce the risk of infection.
3. Developing more efficient prevention strategies can significantly help limit the spread of the virus.
4. Implementing these measures could reduce the disease burden and improve public health outcomes.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

ETHICS APPROVAL

The study was conducted in the Laboratory of Viral Hepatitis and Bloodborne Infections at the National Agency for Public Health in the Republic of Moldova. Ethical approval was obtained from the Research Ethics Committee of the National Public Health Agency (Protocol No. N2018-055, dated 24.12.2018).

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