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Brief Original Article

Seroprevalence and risk assessment of viral hepatitis E infection in a group of exposed persons from Republic of Moldova

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Abstract

Introduction: Viral hepatitis E is considered to be an important issue for public health in developing countries. The aim of the present study is to evaluate morbidity and risk factors in occupationally exposed groups such as people working on sausage production.
Methodology: Seroprevalence of HEV (hepatitis E virus) and risk factors to infection were determined in a cross-sectional study of two groups of populations: people working on sausage production (n = 70) and persons without occupational exposure (people working in the textile industry n = 70) in Moldova, a country without reported cases of hepatitis E.
Results: The seroprevalence of HEV was 14.3% (CI 95%, 13.1-15.5%) in the group of exposed, compared with no cases in the non-exposed group that indicates on no previous infectious contact with hepatitis E virus.
Conclusions: The increased seroprevalence of HEV among persons with occupational exposure to swine meat suggest animal-to-human transmission of this infection.

Key words: hepatitis E virus; Moldova; occupational exposure; anti-HEV IgG antibodies.

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Introduction

Hepatitis E virus (HEV) is one of the leading causes of acute viral hepatitis worldwide, due to this is an important public-health concern [1]. Hepatitis E (HEV) virus infection is more importantly when occurs as zoonotic spread from animals to humans, despite cases of spreading occurring from human to human or between animals. Foodborne transmission of hepatitis E virus (HEV) to humans from consumption of undercooked pig liver and deer meat [2-4] has been reported in Japan [5] and in France [6]. Also, it has been shown that either people in contact with animals (such as workers from swine farms and slaughter-houses presented) have a higher risk for anti-HEV immunoglobulin G (IgG) positivity, demonstrating that these present risk factors for occupational contact with HEV [7]. Other sources of infection such as blood transfusion cannot be excluded [8].

In Poland, sera from 182 patients were tested for anti-HEV IgG, positivity was found in 15.9% [9]. In Russian Federation the presence of hepatitis E markers ranged from 2.1 up to 7.5% [10]. In Turkey a study established that the anti-HEV IgG seroprevalence was 34.8% in the agricultural farm workers, and 4.4% in the control subjects. The risk of acquiring hepatitis E was 11.5 fold higher in farm workers than in the controls [11]. In Romania a study conducted in 2014 had shown that the anti-HEV IgG seroprevalence was 14.9% (22 positive sera from 148 tested) [12]. In Republic of Moldova, the true impact of hepatitis E virus on public health is unknown. No studies have been conducted to establish the seroprevalence of HEV in the general population. In the population with occupational exposure - swine farmers, only one study was conducted in 1998 [13].

Emerging from the exposed ones the aim of the present study was to establish the seroprevalence of HEV in professional exposed persons and to determine the risk of infection depending on gender, age and professional group.

Methodology

To determine the risk of hepatitis E virus infection, a cross-sectional study was performed. The exposed group consisted of 70 people working on sausage production and the non-exposed group consisted of 70

people working in the textile industry, both groups from the city of Soroca, Republic of Moldova. All the people included in the study gave informed consent for participation in it, they were asked to provide five milliliters of venous blood, collected by a trained phlebotomist. The Ethics Committee of the State University of Medicine and Pharmacy "Nicolae Testemitanu" approved these tests (protocol num. 86 from 21.06.2017).

Serum samples extracted from the blood of persons from both groups were tested for the anti-HEV IgG antibodies for detection of hepatitis E virus infectious contact. The test was performed by ELISA with approved diagnostic kits with 96,3% sensitivity and 98,2% specificity (HEV IgG, Enzyme Immunoassay, DIA.PRO, Milan, Italy). Also, in parallel, these sera were tested by an original method, patented by us, for the determination and evaluation of the anti-HEV IgG antibodies in the blood serum, which excludes the appearance of equivocal results [14]. Anti-HEV IgG antibodies in subjects without clinical signs of hepatitis, was used as an epidemiological tool to measure exposure to this virus. To determine the risk ratio, odds ratio and 95% Confidence Intervals (CI) by gender, age group, professional category, results were statistically processed using the Epi Info 7.2 and MedCalc software.

The study was conducted in the Laboratory of Viral hepatitis and bloodborne infections of the National Agency for Public Health from the Republic of Moldova during the first half of 2018 year.

Description of groups

Among the subjects included in the exposed group, 52.9% were men (CI 95%, 40.6 - 64.9%) and 47.1% (CI 95%, 35.1-59.4%) were women. In the non-exposed group the proportion of men to women was 31.4% vs. 68.6%. The mean age in the exposed group was 48.7 years (95% CI, 45.8 to 51.7), in the non-exposed group – 44.7 years (95% CI, 41.8 to 47.6). In both groups most people were part of the age group 30-39 years: in exposed group – 24.3% (CI 95%, 14.8-36.0%), in the non-exposed group – 30.0% (CI 95%, 19.6-42.1%). Regarding to professional appurtenance in the exposed group the majority of persons were from the auxiliary staff – 52.8% (CI 95%, 40.5-64.9%), in the non-exposed group the majority were workers 60.0% (CI 95%, 47.6-71.5%) (Table 1).

Results

In the exposed group 14.3% (CI 95%, 13.1-15.5%) or 10 persons from 70 were positive to anti-HEV IgG antibodies. In the non-exposed group no one was positive to anti-HEV IgG antibodies, it means that these persons had no previous exposure to HEV.

From those 10 patients positive to anti-HEV IgG antibodies, 5 were men and 5 were women, or 13.5% (CI 95%, 4.5-28.7%) positive from the total number of men in exposed group, and respectively 15.1% (CI 95%, 5.1-31.9%) positive from the total number of women in this group.

Compared to the non-exposed group that means a RR of 6.7 (CI 95%, 0.4-114.9) for men and RR 15.9 (CI 95%, 0.9-277.3) for women from the exposed group.

In the age group of 16-29 years from the exposed group the weight of patients positive to anti-HEV IgG antibodies was 33.3% (CI 95%, 0.8-90.6%), in persons aged 30-39 from the same group this index was 5.9% (CI 95%, 0.2-28.7%), in persons aged 40-49 this index was 21.4% (4.7-50.8), in persons aged 50-59 - 5.9% (CI 95%, 0.2-28.7%) and finally in persons aged 60-69 -

Table 1. General characteristics of study subjects.

Factor	Group			
	Exposed (n = 70)		Control (n = 70)	
	Abs.	% (CI 95%)	Abs.	% (CI 95%)
Sex				
Male	37	52.9% (40.6-64.9)	22	31.4% (20.9-43.6)
Female	33	47.1% (35.1-59.4)	48	68.6% (56.4-79.2)
Age group (years)				
16-29	3	4.3% (0.9-12.0)	7	10.0% (4.1-19.5)
30-39	17	24.3% (14.8-36.0)	21	30.0% (19.6-42.1)
40-49	14	20.0% (11.4-31.3)	15	21.4% (12.5-32.9)
50-59	17	24.3% (14.8-36.0)	16	22.9% (13.7-34.4)
60-69	19	27.1% (17.2-39.1)	11	15.7% (8.1-26.4)
Professional group				
Chief	10	14.3% (7.1-24.7)	3	4.3% (0.9-12.0)
Worker	23	32.9% (22.1-45.1)	42	60.0% (47.6-71.5)
Auxiliary staff	37	52.8% (40.5-64.9)	25	35.7% (24.6-48.1)

21.0% (CI 95%, 6.1-45.6%). Compared to the same age groups from the non-exposed (were all are negative to anti-HEV IgG antibodies) the age groups from the exposed have the following Risk Ratio (RR): persons aged 16-29 – RR 6.0 (CI 95%, 0.3-116.6), persons aged 30-39 – RR 3.7 (CI 95%, 0.2-84.7), persons aged 40-49 – RR 7.5 (CI 95%, 0.4-132.8), persons aged 50-59 – RR 2.8 (CI 95%, 0.1-64.9), persons aged 60-69 – RR 5.4 (CI 95%, 0.3-91.8).

Depending on the professional group in exposed persons 1 from the senior staff was positive to the anti-HEV IgG antibodies, or 10.0% (CI 95%, 0.3-44.5). Also 7 exposed workers from a total of 23 were positive, or 30.4% (CI 95%, 13.2-52.9). From auxiliary staff in exposed group 2 patients were positive or 5.4% (CI 95%, 0.7-18.2). We remind that no person in the non-exposed group was positive to the anti-HEV IgG antibodies. This means that the RR depending on professional group is the following in for the exposed persons: for the group of senior staff RR = 1.1 (CI 95%, 0.1-21.7), for the workers group RR = 26.9 (CI 95%, 1.6-450.4) and for the auxiliary staff RR = 3.4 (CI 95%, 0.2-68.4) (Table 2).

Discussion

According to the aim of the present study we established that the seroprevalence of HEV in professional exposed persons was 14.3% (compared to the non-exposed group where no cases were recorded). This is in full consistency with past studies in the field, thus Drobeniuc et al. also indicates higher values compared to the general population of HEV seroprevalence in exposed populations from 8.37% to 28.51% [7,13]. This phenomenon can be explained by the more frequent and intense contact of these people with potential infection factors such as pork and products derived from them. In this context, the group of workers in pig farms, slaughterhouses and sausage workers are considered as high risk groups of infection [4,13].

Our study found that there is practically no difference between the level of HEV seroprevalence in males (13.5%) and females (15.1%) in the exposed group. What is to be expected, thus Hartl et al. do not talk about any gender difference in the risk of hepatitis E virus infection [7].

When analyzing the level of HEV seroprevalence by age groups, it was established that this is not a uniform one as we would expect, with an increase in this index with age. The highest level of infection was found in those aged 40-49 years - 21.4%. The irregular distribution in our perception can have two explanations: the first - relatively small sample of the study and the second - high migration of workers/employees that reduces the exposure time of those with more work experience. Some sources in the field like Wenzel et al. confirm our expectations that the seroprevalence of HEV is increasing with age, which is due to a longer period of exposure to risk factors [15].

Regarding on occupational category as expected in the group of workers, who contacted directly with pork meat and sausage production, they had the highest level

Table 2. Number and weight of positive and negative to anti-HEV IgG persons in the exposed and control group, with odds and risk ratio.

	Anti-HVE+				Anti-HVE -				95% CI	
	Exposed group		Control group		Exposed group		Control group		Odds ratio (CI 95%)	Risk ratio (CI 95%)
	Abs.	Prevalence (CI 95%)	Abs.	Prevalence (CI 95%)	Abs.	Prevalence (CI 95%)	Abs.	Prevalence (CI 95%)		
Sex										
Male	5	13.5% (4.5-28.7)	0	0	32	86.5% (71.2-95.5)	22	100% (84.6-100)	7.6 (0.4-144.7)	6.7 (0.4-114.9)
Female	5	15.1% (5.1-31.9)	0	0	28	84.9 % (68.1-94.9)	48	100% (92.6-100)	18.7 (1.0-351.2)	15.9 (0.9-277.3)
Age group (years)										
16-29	1	33,.3% (0.8-90.6)	0	0	2	66.7% (9.4-99.1)	7	100% (59.0-100)	9.0 (0.3 299.9)	6.0 (0.3-116.6)
30-39	1	5.9% (0.2-28.7)	0	0	16	94.1% (71.3-99.9)	21	100% (83.9-100)	3.9 (0.2-102.3)	3.7 (0.2- 84.7)
40-49	3	21.4% (4.7-50.8)	0	0	11	78.6% (49.2-95.3)	15	100% (78.2-100)	9.4 (0.4- 201.2)	7.5 (0.4- 132.8)
50-59	1	5.9% (0.2-28.7)	0	0	16	94.1% (71.3-99.9)	16	100% (79.4-100)	3.0 (0.1-79.1)	2.8 (0.1-64.9)
60-69	4	21.0% (6.1-45.6)	0	0	15	79.0% (54.4-93.9)	11	100% (71.5-100)	6.7 (0.3- 136.8)	5.4 (0.3- 91.8)
Professional group										
Chief	1	10.0% (0.3-44.5)	0	0	9	90.0% (55.5-99.9)	3	100% (29.2-100)	1.1 (0.1-34.0)	1.1 (0.1-21.7)
Worker	7	30.4% (13.2-52.9)	0	0	16	69.6% (47.1-86.8)	42	100% (91.6-100)	38.6 (2.1-715.4)	26.9 (1.6-450.4)
Auxiliary staff	2	5.4% (0.7-18.2)	0	0	35	94.6% (81.8-99.3)	25	100% (86.3-100)	3.6 (0.2-78.0)	3.4 (0.2-68.4)

of HEV seroprevalence - 30.4%, due to the continuous and intense exposure to this risk factors associated with the transmission of HEV, phenomenon confirmed also by other studies in the field [13]. The other two groups had lower levels of detection of this marker, however, with positive individuals in those groups, leading us to the idea that the infection was due to possible interhuman transmission or accidental exposure to hepatitis E virus.

Conclusion

In conclusion, it is important to note that the present study needs to be expanded in the future with the inclusion of blood donors, as the Republic of Moldova is a country with moderate endemic morbidity in parenteral viral hepatitis (including B, C and D). The obtained data will be used to upgrade some positions of the National Program for the Control of Viral Hepatitis B, C and D for the years 2017-2021 and the National Blood Transfusion and Blood Safety Self-Guarantee Program for the years 2017-2021.

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