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SHORT COMMUNICATION

Comparative Seroprevalence of Hepatitis A And E Viruses in Blood Donors from Wielkopolska Region, West-Central Poland

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Abstract

The objective of the present study was to investigate the seroprevalence of HAV and HEV in Polish blood donors (BDs). One hundred and ten randomly selected healthy BDs, living in Wielkopolska Region were tested for anti-HAV IgG and anti-HEV IgG with commercial assays. The seroprevalence of anti-HAV was 11.8%; anti-HEV were detected in 60.9% of BDs ($p < 0.0001$). Consumption of risky food was more common in anti-HEV-positive BDs (59.1% vs. 33.3%; $p = 0.01$). Twelve out of 20 BDs (60%) with no history of travel abroad were exposed to HEV. Wielkopolska Region, Poland should be regarded as a new HEV infection-hyperendemic area in Europe.

Key words: blood donors, HAV, HEV, Poland, seroprevalence

The prevalence of hepatitis E virus (HEV) infections in Central Europe has been described only partially and few studies report such data for this part of the European continent (Lapa *et al.*, 2015). The knowledge of this subject in Poland is limited to two reports discussing the seroprevalence of IgG antibodies in 182 patients from Poznan center (anti-HEV-positivity in 15.9% patients, EIA-gen HEV IgG kits; Adaltis, Milano, Italy) (Bura *et al.*, 2015) and in 1016 hunters from all 16 Polish provinces (anti-HEV detected in 20.3% participants with ELISA recomWell HEV IgG kits; Microgen, Neuried, Germany) (Sadkowska-Todys *et al.*, 2015).

For another primary hepatotropic virus transmitted by the fecal-oral route, that is, hepatitis A virus (HAV), in the 21st century, Poland has experienced a shift toward very low endemicity (Magdzik and Czarkowski, 2004) and is currently one of the countries with the lowest hepatitis A incidence among the European Union member states (European Centre for Disease Prevention and Control, 2014).

A comparative study of HAV and HEV exposure markers (the presence of IgG antibodies against respective viruses) in 110 randomly selected healthy (HBV, HCV, HIV and syphilis-negative; no jaundice in the past) unpaid voluntary blood donors (BDs; 75 men and 35 women) living in Wielkopolska Region (Greater Poland; one of the largest regions in Poland, located in the west-central part of our country) was performed. The BDs were 19–58 years of age (38.4 ± 9.6; median age – 40 years).

Anti-HAV IgG (anti-HAV) seroprevalence was determined by a chemiluminescent microparticle immunoassay (CMIA; ARCHITECT HAV Ab-IgG kits; Abbott Laboratories, Wiesbaden, Germany) whereas for anti-HEV IgG (anti-HEV) WANTAI HEV-IgG ELISA kits (Wantai Biological Pharmacy Enterprise, Beijing, China) were used, both according to the manufacturers' instructions. These tests are accepted diagnostic tools for the assessment of exposure to HAV and HEV, respectively.

The serum samples were collected at the Regional Blood Center in Poznan, Poland, during the first 6 months of 2015 and were stored at –20°C prior to testing.

All the BDs gave their written informed consent. The study was approved by the local Bioethics Committee (reference number: 263/15) and was funded by Poznan University of Medical Sciences (number of funds: 502-01-02205314-04519).

Numerical data were presented as mean and standard deviation. The comparison of age was performed by t-Student test. The assumption if data follow normal

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distribution was checked by Shapiro-Wilk's test. The homogeneity of variances was checked by Levene's test. Nominal data were compared by Chi-square test of independence. For the factors that might influence the HEV seroprevalence odds ratios (OR) and 95% confidence intervals (CI) were calculated. Statistical analysis was performed with Statistica 12 (Statsoft, Inc.) software.

All tests were considered significant at $p < 0.05$.

The seroprevalence of anti-HAV was 11.8% (13/110), whereas anti-HEV were detected in 60.9% of BDs (67/110) ($p < 0.0001$); in 2 cases a borderline HEV antibodies testing result was found and included as negative in further analysis.

The distribution of combined HAV and HEV IgG assessment results was as follows: double (anti-HAV/anti-HEV) positive – 5 persons (4.5%), only anti-HAV-positive – 8 BDs (7.3%), double negatives – 35 participants (31.8%) and only anti-HEV-positive – 62 persons (56.4%).

Anti-HAV-positive BDs were older (46.7 ± 6.8 years, range 38–58) than seronegatives (37.2 ± 9.4 years, range 19–58) ($p = 0.0006$).

For anti-HAV positive samples the mean ±SD relative light units (RLU) signal/cut off (s/co) ratio value was 11.03 ± 3.16 (range 4.12–14.47; the positive result was defined as RLU s/co > 1.00) and for anti-HEV positive samples the mean optical density/cut off (OD/co) ratio value was 5.932 ± 3.454 (range 1.221–14.458; the positive result was defined as OD/co > 1.100; values between 0.9 and 1.100 were considered borderline); it is worth to know that in only 9 HEV seropositive persons (13.4% out of all HEV-positive BDs) the OD/co ratio was lower than 2.000. The prevalence of some variables in relation to anti-HEV IgG status is shown in the Table I.

The main conclusion from the above analysis is that the culinary habits indicating the consumption of some risky food (raw / undercooked meat or seafood) were more common in the BDs exposed to HEV. This factor has been recognized as the source of infections with the zoonotic genotypes of the virus (Said *et al.*, 2009; Mansuy *et al.*, 2011; Guillois *et al.*, 2013; Meng, 2013). In addition, a trend toward a more frequent prevalence of anti-HAV in HEV-seronegative (*vs* HEV-seropositive) BDs in conjunction with a significantly less common presence of HAV exposure marker among the study participants suggest that the main modes of transmission for these viruses in our region are different.

Although there was no mean age difference between the study participants exposed to HEV and anti-HEV-negatives (in our opinion, it was only because the group of BDs was small), the number of HEV-seropositive BDs aged > 30 tended to be higher than the prevalence of these antibodies in younger persons (see Table I). An evident relationship between the seroprevalence of HEV and age is reported in most available studies among BDs (Dreier and Juhl, 2014).

It should be stressed that in case of 20 persons with no history of travel abroad anti-HEV positivity was found in 60% of them (n = 12). It supports some previous suggestions (Bura *et al.*, 2015) that autochthonous (locally acquired) HEV infections do occur also in Poland.

Despite an obvious limitation of this study, that is, a small number of participants, its results are surprising because they indicate that Wielkopolska Region is a hyperendemic area for HEV infections. In Europe, similar seroprevalence of anti-HEV (52.5%) was found only in the Toulouse region, southwestern France (Mansuy *et al.*, 2011). Such a high frequency of HEV-seropositivity, significantly more important than found in previous surveys from our country in specific populations (patients of Infectious Diseases Department

Table I
Status of anti-HEV and selected variables in 110 BDs from western Poland.

Variable	Anti-HEV+ (n = 67)	Anti-HEV – (n = 43)	OR [95% CI]	p
Mean age ± SD [years] Median age (IQR[a])	39.5 ± 8.9 41 (34 – 46)	36.6 ± 10.3 37 (27 – 45)	NA[b]	0.1198
BDs aged > 30	56 (83.6%)	29 (67.4%)	2.46 [0.99–6.09]	0.0523
Men	45 (67.2%)	30 (69.8%)	0.89 [0.39–2.02]	0.7749
Current place of residence – city	55 (82.1%)	35 (81.4%)	1.05 [0.35–3.29]	0.9233
Childhood place of residence – city	46 (69.7%)	29 (67.4%)	0.90 [0.37–2.25]	0.8038
Travel abroad during lifetime	55 (82.1%)	35 (81.4%)	1.05 [0.39–2.82]	0.9266
Contact with swine	12 (17.9%)	8 (19.1%)	0.93 [0.34–2.50]	0.8814
Anti-HAV positivity	5 (7.5%)	8 (18.6%)	2.83 [0.86–9.33]	0.0866
Consumption of raw / undercooked meat or seafood	39 (59.1%)	14 (33.3%)	2.89 [1.29–6.48]	0.0100

[a]IQR – interquartile range; [b]NA – not assessed.

and hunters) (Bura *et al.*, 2015; Sadkowska-Todys *et al.*, 2015), can be explained by a very good sensitivity of the Wantai assay. Some seroprevalence assessments across Europe have shown that the use of these tests can result in several times higher ratios of anti-HEV in comparison to other manufacturers' assays (Bendall *et al.*, 2010; Mansuy *et al.*, 2011; Wenzel *et al.*, 2013).

Faced with such unexpected data, at least one question of fundamental importance must be asked: what is the practical significance of such a common occurrence of HEV infections in Wielkopolska Region?

The answer is difficult because to the best of our knowledge none of the Polish hepatology centers has been performing tests for hepatitis E to date and there are no data on the prevalence of acute hepatitis of unknown etiology neither in our region nor Poland-wide. Due to a very common subclinical exposure to HEV revealed by this study, a potential danger of HEV-infected blood transfusions, particularly to immunocompromised recipients, should also be taken into account (Matsubayashi *et al.*, 2004; Hewitt *et al.*, 2014; Huzly *et al.*, 2014). This issue should be rapidly clarified.

In conclusion, the results of the current report suggest that Wielkopolska Region, west-central Poland, should be regarded as a new HEV infection-hyperendemic area in Europe.

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