

Prevalence study of different hepatitis markers among pregnant Albanian refugees in Greece

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Accepted in revised form 16 February 1996

Abstract. Aim of the study was to record the prevalence of the various types of viral hepatitis, especially hepatitis B, in pregnant Albanian refugees in Greece. The study comprised 500 pregnant refugees of mean age 25.1 ± 4.6 years. In Albania, all women had lived in overcrowded houses and had been exposed to non throw-away needles and syringes. Various indices for all hepatitis types were determined. The prevalence of HBsAg was 13.4%, of anti-HBs 53%, of total anti-HBc 70.8%, of anti-HBc IgM 0.4%, of HBeAg 1.2%, of anti-HBe 58.6%, of anti-HAV 96.2%, of anti-HAV IgM 1%, of anti-HDV 0.4%, of anti-HCV 0.6% and of anti-HEV 2%. HBeAg was found positive in 7.5% of HBsAg carriers. Prevalence of

hepatitis B markers, as determined by HBsAg and/or anti-HBs and/or total anti-HBc was significantly higher in those with a history of previous hospitalization in Albania ($p = 0.01$) and those with previous history of hepatitis ($p = 0.02$). The high prevalence of hepatitis B markers in pregnant Albanian refugees proves that HBV infection is highly endemic in Albania and the possibility of perinatal transmission to the offsprings urges for HBV vaccination programmes. On the other hand improvements in the socioeconomic conditions and the sanitation system in Albania is anticipated to reduce the incidence of HAV and HBV infections.

Key words: Hepatitis, Pregnancy, Refugees, Albanians, HAV, HBV, HCV, HDV, HEV

Introduction

Recently Albania – a small country in the Balkans, totally isolated from the rest of Europe since the last World War, with very limited economical sources and a low standard of hygiene – was abandoned immediately after the fall of the former political regime and the opening of the borders by a large number of its citizens, who sought work and shelter in the neighbour countries, mainly Italy and Greece [1]. The massive escape to the latter was more convenient due to geographical vicinity and to the ties to the land of origin of the large Greek minority, residing ever since in the region of North Epirus, comprising now South Albania.

Unpublished data from various Greek hospitals, where Albanian refugees had been treated for various reasons, gave a high percentage of them being infected by hepatitis viruses.

The aim of this study was to record the burden of infection by the various types of hepatitis, especially hepatitis B, in pregnant women of Albanian citizenship, who live as refugees in Greece. This record would help to prevent vertical transmission to their offsprings by early vaccination and would give the baseline information to formulate a health policy

aiming at limiting the spread of viral hepatitis and its consequences.

Subjects and methods

The study comprised 500 consecutive pregnant refugees of Albanian citizenship, who had entered Greece mainly in the years 1991–1994 and were cared for their pregnancy in the 'Alexandra' Hospital. Living conditions of all women in their homeland were poor: 425/499 (85.2%) reported 5 or more persons living in the paternal house, which in 459/499 (92%) cases had 3 or less rooms altogether (kitchen and bathroom included) (persons/room: mean \pm SD: 3 ± 1 , range 1–11). The conditions in the conjugal house were similar: In 329/467 (70.4%) cases 5 or more persons resided in the same house sharing in 347/467 (74.3%) cases 3 or less rooms (persons/room: mean \pm SD: 4 ± 3 , range 1–11). All women had been vaccinated against tetanus, diphtheria and pertussis by non throw-away syringes and needles, as reported. Of the total number only 92/499 (18.4%) had been treated in a hospital in Albania and 22/497 (4.4%) of them reported a liver disease. Also 50/499 (10%) had been operated on, 35/499 (7%) had

undergone termination of pregnancy and 123/499 (24.6%) had delivered one or more children before their fled. History of clinical hepatitis in themselves, in the paternal and the conjugal family was reported in 57/493 (11.6%), 87/480 (18.1%) and 45/410 (11%) respectively.

At their admittance to the hospital, following informed consent, 10 ml of venous blood was drawn from all women and the following hepatitis indices were determined in the serum: HBsAg, anti-HBs, total anti-HBc, anti-HBc IgM, HBeAg, anti-HBe, anti-HDV, anti-HAV, anti-HAV IgM, anti-HCV. In 98 consecutive cases anti-HEV was tested. The serum markers of HBV and HAV were measured by IMx-Microparticle Enzyme Immunoassay-MEIA (Abbott Diagnostics). Anti-HCV and anti-HDV antibodies were determined with an enzyme immunosorbent assay (Abbott HCV EIA 2.0 and Abbott Anti-Delta EIA respectively). The anti-HEV were measured by an enzyme immunoassay based on two recombinant HEV antigens (Abbott Labs).

Hepatitis A (HAV) infection was defined by the presence of anti-HAV and anti-HAV IgM, Hepatitis B (HBV) by the presence of HBsAg, anti-HBs, total anti-HBc, anti-HBc IgM, HBeAg and anti-HBe, Hepatitis C (HCV) by the presence of anti-HCV, Hepatitis D (HDV) by the presence of anti-HDV and Hepatitis E (HEV) by the presence of anti-HEV.

The results were analyzed using two sample t-test for quantitative data and chi-square (χ^2) or Fischer's exact test for comparing proportions. The software used was SPSS/PC+.

Results

Mean age \pm SD of the studied women was 25.1 ± 4.6 years, range 14–42 years [age groups in years (y), n and % were respectively: 14–19 years: 37 (7.4%), 20–24 years: 212 (42.4%), 25–29 years: 176 (35.2%), 30–34 years: 53 (10.6%) and 35+ years: 22 (4.4%)]. Three hundred seventy nine (75.8%) were of Greek ethnic origin and 121 (24.2%) of Albanian. Two hundred ninety nine (59.8%) resided in the Greek minority regions of South Albania and 201 (40.2%) in the rest of the country. School education (mean \pm SD: 11.9 ± 2.5 y, range 4–18 y) lasted for 90 (18.0%) up to 9 y, for 297 (59.5%) 10–12 y and for 112 (22.4%) 13 or more years. Lastly 478 (95.6%) women were married and 22 (4.4%) unmarried. The prevalence of various markers concerning HAV, HBV, HDV, HCV and HEV are presented in Table 1. It should be noted that out of the 67 HBsAg (+) women, 5 (7.5%) were HBeAg (+) and 60 (89.6%) anti-HBe (+). Among the 2 anti-HBc IgM (+) women 1 was also HBsAg (+). Lastly among the 67 HBsAg (+) women, 1 (1.5%) was anti-HDV (+).

Subsequently we associated respectively anti-HAV and presence of any marker of HBV defined as HEPB

Table 1. Prevalence of various hepatitis serologic markers among the 500 pregnant Albanian refugees

Hepatitis marker	n (+ve)	%	95% C.I.
Anti-HAV	481	96.2	94.5–97.9
Anti-HAV IgM	5	1.0	0.1–1.9
Total anti-HBc	354	70.8	66.8–74.8
Anti-HBc IgM	2	0.4	0.0–1.0
HBsAg	67	13.4	10.4–16.4
Anti-HBs	265	53.0	49.0–57.0
HBeAg	6	1.2	0.3–2.1
Anti-HBe	293	58.6	54.6–62.6
Any HBV marker	365	73.0	69.0–77.0
Anti-HDV	2	0.4	0.0–1.0
Anti-HCV	3	0.6	0.0–1.3
Anti-HEV*	2	2	0.0–4.8

* Anti-HEV was tested in 98 Albanian refugees.

(an entity comprising HBsAg and/or anti-HBs and/or total anti-HBc) with age, number of persons per room in the paternal and conjugal home, years of school education, place of residence in Albania, ethnic origin, vaccinations performed by needle, hospitalization in Albania, operations performed in Albania, abortions and deliveries having taken place in Albania, history of hepatitis in the studied woman, in her paternal and her conjugal family. Concerning Hepatitis A the presence of anti-HAV was statistically associated (inversely) with the history of hepatitis in the paternal ($p = 0.005$) as well as in the conjugal home ($p = 0.01$) (Table 2). Concerning Hepatitis B the prevalence of the markers examined was significantly higher in those women who reported previous hospitalization in Albania ($p = 0.01$) and a history of hepatitis ($p = 0.02$) (Table 2).

Discussion

It has been reported that clinical Hepatitis A incidence in Eastern European countries varies from 50 to 300/10⁵ per year [2]. The high anti-HAV prevalence found in the studied Albanian refugees is in accordance with the knowledge that in the majority of less developed or developing countries almost all adults and older children have antibodies indicative of prior, usually asymptomatic, infection with Hepatitis A in childhood [3, 4]. As with all enterically transmitted organisms the endemicity within a specific country is related directly to sanitation and hygienic standards and inversely to socioeconomic conditions [3, 5, 6]. The high index of persons/rooms in both the paternal and conjugal house of the studied women, as well as their low socioeconomic status, proven by their fled from their homeland may be a dominant reason for the high prevalence of anti-HAV. Furthermore, we found an inverse statistically significant association of anti-HAV with the history of

Table 2. Prevalence of anti-HAV and HEPB (HBsAg and/or anti-HBs and/or total anti-HBc) by socioeconomic characteristics and other data in 500 pregnant Albanian refugees

	Anti-HAV			HEPB		
	(+) n = 481	(-) n = 19	<i>p</i>	(+) n = 365	(-) n = 135	<i>p</i>
Age (x ± SD) years	25.2 ± 4.6	23.7 ± 5.8	0.19	25.2 ± 4.6	24.8 ± 4.7	0.38
Persons/rooms in paternal home (x ± SD)	2.9 ± 1.1	3.2 ± 2.1	0.26	2.9 ± 1.1	2.9 ± 1.2	0.79
Persons/rooms in conjugal home (x ± SD)	4.0 ± 3.5	2.9 ± 2.5	0.24	3.9 ± 3.4	4.3 ± 3.7	0.29
Education (x ± SD) years	11.9 ± 2.5	12.2 ± 2.6	0.66	12.0 ± 2.4	11.8 ± 2.7	0.32
<i>Place of residence:</i>						
South Albania	290	9		220	79	
Other	191	10	0.26	145	56	0.72
<i>Ethnic origin:</i>						
Greek	367	12		278	101	
Albanian	114	7	0.19	87	34	0.75
Vaccinations by non disposable needle	481	19	1.00	365	135	1.00
Hospitalization*	Yes	91	1	77	15	0.01**
	No	389	18	287	120	
Operations*	Yes	49	1	36	14	0.87
	No	431	18	328	121	
Abortions*	Yes	35	0	24	11	0.55
	No	445	19	340	124	
Deliveries*	Yes	120	3	97	26	0.08
	No	360	16	267	109	
History of hepatitis in herself	Yes	56	1	49	8	0.02**
	No	418	18	310	126	
History of hepatitis in paternal home	Yes	79	8	59	28	0.26
	No	381	11	289	103	
History of hepatitis in conjugal home	Yes	40	5	31	14	0.48
	No	347	9	263	93	

* In Albania.

** Statistically significant.

hepatitis in the paternal and conjugal home. Although intrafamilial spread of the disease is well established [3, 4, 7] this unexpected finding is probably due to poor understanding of the term 'hepatitis', which is frequently confused with 'jaundice' and 'thalassemia' in individuals of low socioeconomic status in Greece and probably in Albania. Lastly, the low anti-HAV IgM prevalence found in the studied population was expected, as this specific response is relatively short-lived and such antibodies disappear in 2 to 12 months after acute hepatitis [8, 9].

Concerning the topic of Hepatitis B and refugees a considerable number of papers has been published [10–15]. Also, it is a common knowledge that the presence of HBsAg in the serum of an individual indicates acute or chronic HBV infection [16].

Furthermore, the endemicity of Hepatitis B infection is considered high in those areas of the world where the prevalence of HBsAg is 5–15% [4, 17, 18]. This index was found positive in 13.4% of Albanian pregnant refugees, proving thus high endemicity of HBV infection. The main routes of transmission in the developing countries are vertical and horizontal [19]. Nevertheless, a probable important parenteral exposure is the use of non-disposable needles and syringes used in medical practice and vaccination programmes [20]. Indeed, in our study all women reported being vaccinated by non disposable needles and syringes. Other indices indicative of immune response to HBV infection yielded also high prevalence: anti-HBs was found in 53% and total anti-HBc in 70.8% of cases. On the other hand, HBeAg which

is associated with HBV replication and infectivity [21, 22] was found in 1.2% of cases and in 7.5% of the HBsAg(+) women. This low prevalence of HBeAg among HBsAg carriers could be an indirect evidence that in the studied population the majority of HBV infections do not follow the pattern of vertical transmission. In addition, anti-HBe, suggesting low titer of HBV and low infectivity was positive in 58.6% of cases and in 89.6% of the HBsAg(+) women. Anti-HBc IgM, indicating recent infection with HBV and persisting for 2-6 months [23, 24] was found in 0.4% of cases and in only one woman with HBsAg(+). Our finding of the statistically significant association of Hepatitis B infection markers with previous hospitalization in Albania is highly indicative that one important route of transmission is due to poor medical or nursing practices in hospital environment.

Anti-HDV was found in a low percentage of 0.4% and in 1.5% of HBsAg(+) women. Although the transmission patterns and epidemiology of HDV closely parallel those of Hepatitis B, and HDV infection occurs with highest frequency in those parts of the world with highest HBV endemicity, low HDV prevalence has also been reported especially for some countries in Asia [25-27].

Anti-HCV was found also in a very low percentage (0.6%) posing thus no concern. The main route of Hepatitis C infection is blood transfusion, intravenous drug use, hemodialysis, history of organ transplantation as well as history of tattooing, while heterosexual transmission of HCV appears to be a rare occurrence [28-30]. The discordance of Hepatitis C and Hepatitis B prevalences in this refugee population cannot be easily explained in the present study. The frequency of high risk practices for HCV transmission is very low in the present population of relatively young female refugees. And this may explain the rarity of HCV infection in this population. An alternative explanation is that HBV infection is transmitted easily horizontally and vertically and its spread is not necessarily related to the above mentioned high risk practices in endemic populations. Lastly Hepatitis E does not seem to pose a special problem for Albanians, although it is transmitted by the fecal-oral route [31, 32]. Apparently, approximately 2% of the examined women were found to have anti-HEV.

Although HBeAg prevalence among HBsAg carriers in the studied group was low the danger of perinatal transmission of HBV exists and can be devastating for the offspring. Infants infected with HBV have a 90% chance of becoming chronic carriers at birth [24, 33, 34]. The only way of prevention is through administration of Hepatitis B immune globulin and vaccination of infants at birth in order to avoid HBV chronic carriage [24, 33, 35-37]. Our study proves that Albania urgently needs universal HBV vaccination programmes for pre-

venting perpetuation of transmission of the disease. Indeed, universal HBV vaccination in countries with high to moderate HBV endemicity has been advocated as cost-effective [38]. Moreover, recent studies [39] have concluded that broader vaccination in countries even with lower endemicity could also prove cost-effective. On the other hand, improvements in the socioeconomic conditions in Albania is expected to reduce the high HAV and HBV prevalence.

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