

HBV, HCV and HDV infections in Albanian refugees in Southern Italy (Apulia region)

M. CHIRONNA, C. GERMINARIO, P. L. LOPALCO, M. QUARTO*
AND S. BARBUTI

Department of Internal Medicine and Public Health – Hygiene Section, University of Bari, Piazza G. Cesare 4 – Policlinico, 70124 Bari, Italy

(Accepted 25 April 2000)

SUMMARY

The seroprevalence of hepatitis B, C and D markers was assessed in a sample of 670 Albanian refugees in Southern Italy in 1997. The mean age was 25 years (s.d. = 12.3). Of study subjects 62.1% (95% CI: 58.4–65.7) were positive for anti-HBc antibodies and 13.6% (95% CI: 10.9–16.1) for HBsAg. The prevalence of anti-HBs was 47.6% (95% CI: 43.8–51.3). Among HBsAg carriers the prevalence of HBeAg was 7.7% (95% CI: 2.2–13.1). The highest carrier rate for HBsAg (25.5%; 95% CI: 16.7–34.3) was found in the age group 21–25 years. A relevant finding was a prevalence of HBsAg of 8.1% in children 10 years and under. The prevalence of anti-HCV antibodies was 0.3% (95% CI: 0.0–0.7) while only one of the HBsAg carriers was positive for anti-HDV (1.1%, 95% CI: 0–3.2). In Albania, hepatitis B infection represents a public health priority that should be addressed by a universal vaccination campaign.

INTRODUCTION

Viral hepatitis is still a major health problem throughout the world and hepatitis B virus (HBV), hepatitis C virus (HCV) and hepatitis D virus (HDV) are the most important agents responsible for parenterally and sexually transmitted diseases.

It is well known that the epidemiology of hepatitis B, C and D varies by geographical area. Low (less than 2%), intermediate (2–8%) and high prevalence (more than 8%) areas have been recognized for hepatitis B. High endemic areas are represented by large parts of Asia and Sub-Saharan Africa, but the disease is also endemic in South America [1–3]. In Eastern Europe prevalence rates for HBsAg, ranging from 1.5% in the Czech Republic to 10.7% in Moldova, have been reported [4].

The prevalence of HCV infection is low (0.2–2%) in the general population of Europe, United States,

Indonesia and Japan, but is higher (2–5%) in South America and Asia and highly endemic (> 5%) in many parts of Africa [5, 6].

Hepatitis delta infection is correlated with HBV although the epidemiology of HDV does not coincide with that of HBV. It is principally found in some areas of the Amazon basin, in tropical Africa, in the Middle East and in the Mediterranean basin [7].

In 1991, a serious political and socioeconomic crisis in Albania, a small Eastern European country, caused a massive migration of refugees to the Apulia region of Southern Italy [8]. Since little was known about the health status of the Albanian population, a surveillance system was set up by the Italian Ministry of Health in collaboration with the Institute of Hygiene of the University of Bari, to monitor health problems that were expected to have a high frequency [9]. Seroepidemiological data on the distribution of viral hepatitis among refugees indicated, preliminarily, a high endemicity of HAV and HBV infections in Albania [10]. In addition, a high prevalence of

* Author for correspondence.

hepatitis B markers was also found in a sample of pregnant Albanian refugees in Greece [11].

Following a new exodus of thousands of Albanians to Apulia in 1997, we investigated a large sample of refugees in order to assess the seroprevalence of blood-borne viral hepatitis, especially hepatitis B, and to suggest preventive strategies aiming at controlling the spread of these infections.

METHODS

Between March and May 1997 about 17605 Albanians arrived clandestinely in Apulia. They were housed in eight refugee camps but the number of refugees in the camps varied daily due to a quick turnover, (the Italian Government had decreed immediate expulsion of clandestine refugees to limit the influx). A team of physicians went to refugee camps and, after obtaining informed consent, took blood samples, on a voluntary basis, from subjects present on that day. For children, the consent to take a blood sample was obtained from parents or legal guardians. A total of 670 unselected Albanian refugees were recruited. Personal data (age, sex and place of residence) were obtained from all subjects. Blood samples were taken to the laboratory, centrifuged and kept at -20°C until testing.

The sera collected were then tested for the following hepatitis markers: HBsAg, anti-HBs, total anti-HBc (IgG and IgM), HBeAg, anti-HDV and anti-HCV. Hepatitis B markers were detected in serum samples by IMX-Microparticle Enzyme Immunoassay MEIA (Abbott Diagnostics). Antibodies to hepatitis delta virus (anti-HDV IgG) were determined on HBsAg-positive subjects by a commercial enzyme immunoassay (Abbott anti-Delta EIA, Abbott Laboratories). The presence of antibodies to hepatitis C virus (anti-HCV) was ascertained by a third generation Elisa test (HCV 3.0 Elisa, Ortho-Clinical Diagnostics). The repeatedly reactive serum samples were confirmed for the presence of anti-HCV antibodies using a recombinant immunoblot assay (Chiron RIBA HCV 3.0 SIA, Ortho Diagnostic System). The interpretation of the results was according to kit manufacturers' instructions.

Data were processed using Epi-Info (version 6.0). Confidence intervals were calculated by the quadratic method and χ^2 test was used to compare proportions. If a *P*-value was below 0.05, the difference between proportions was considered statistically significant.

RESULTS

Four hundred and twenty-five of 670 refugees were male (63%) and 245 were female (37%). Of these, 33 (5%) were 5 years and under, 56 (8%) were aged 6–10 years, 71 (10%) 11–15 years, 105 (16%) 16–20 years, 94 (14%) 21–25 years, 92 (14%) 26–30 years, 82 (12%) 31–35 years, 59 (9%) 36–40 years, 46 (7%) 41–45 years and 32 (5%) older than 45 years. Mean age was 25.0 years (s.d. = 12.3 years, range 2–72 years). They came from different areas of Albania; 39% from Vlorë and Fier districts (South Albania), 32% from Durrës and Tiranë districts (Central Albania), 24% from Lezhë and Shkodër districts (North Albania). The remaining 5% came from other rural villages of Albania.

The seroprevalence of HBV, HCV and HDV markers is shown in Table 1. Of 670 subjects 62.1% were positive for anti-HBc (95% CI: 58.4–65.7). The overall prevalence of HBsAg was 13.6% (95% CI: 10.9–16.1) while the prevalence of anti-HBs was 47.6% (95% CI: 43.8–51.3). Among HBsAg carriers the prevalence of HBeAg was 7.7% (95% CI: 2.2–13.1). No difference between males and females was observed (Table 2). Moreover, the prevalence of HBV markers showed no relation to the place of residence (North, South or Central Albania).

Table 3 shows the prevalence of HBV markers stratified by age. In the age group 2–5 years the prevalence of HBsAg was 3.0% (95% CI: 0.0–8.8), of anti-HBc 9.1% (95% CI: 0.0–18.0) and of anti-HBs 21.2% (95% CI: 7.26–35.1). Five of the ten children under 4 years of age were only anti-HBs positive, suggesting a previous history of vaccination against HBV. The prevalence of anti-HBc, HBsAg and anti-HBs in the age group 6–10 years were 30.3% (95% CI: 18.3–42.4), 10.7% (95% CI: 2.6–18.2) and 19.6% (95% CI: 9.2–30.0) respectively. Thus, the HBsAg carrier rate in children up to 10 years was 8.1%. The proportion of refugees positive for HBV markers increased with age. The highest rate of positivity for HBsAg was found in the age group 21–25 years (25.5%, 95% CI: 16.7–34.3). None of the subjects over 4 years was positive for anti-HBs alone.

A very low prevalence of anti-HCV antibodies was found. In fact, only two adult subjects were repeatedly reactive for anti-HCV and were confirmed as positive by RIBA assay, giving a prevalence of 0.3% (95% CI: 0.0–0.7).

Table 1. Seroprevalence of HBV, HCV and HDV markers in Albanian refugees

Hepatitis markers	No. tested	No. positive	% (95% CI)
Anti-HBc	670	416	62.1 (58.4–65.7)
HBsAg	670	91	13.6 (10.9–16.1)
Anti-HBs	670	319	47.6 (43.8–51.3)
HBeAg+*	91	7	7.7 (2.2–13.1)
Anti-HCV	670	2	0.3 (0.0–0.7)
Anti-HDV*	91	1	1.1 (0.0–3.2)

* The prevalence of HBeAg and anti-HDV was evaluated only on HBsAg positive subjects.

Table 2. HBV markers in the 670 Albanian refugees by sex

Markers	No. tested	No. positive	% (95% CI)	P-value
Anti-HBc				
M	425	260	61.2 (56.5–65.8)	
F	245	156	63.6 (57.6–69.7)	0.521
HBsAg				
M	425	65	15.3 (11.8–18.7)	
F	245	26	10.6 (6.7–14.4)	0.088
Anti-HBs				
M	425	192	45.2 (40.4–49.9)	
F	245	127	51.8 (45.5–58.0)	0.096
HBeAg*				
M	65	4	6.1 (0.3–12.0)	
F	26	3	11.5 (0.0–23.8)	0.66†

* Calculated on HBsAg positive subjects.

† Yate's corrected χ^2 .

Table 3. Seroprevalence of HBV markers by age groups

Age groups (years)	No. tested	Anti-HBc		HBsAg		Anti-HBs	
		No. pos.	% (95% CI)	No. pos.	% (95% CI)	No. pos.	% (95% CI)
2–5	33	3	9.1 (0.0–18.0)	1	3.0 (0.0–8.8)	7	21.2 (7.26–35.1)
6–10	56	17	30.3 (18.3–42.4)	6	10.7 (2.6–18.2)	11	19.6 (9.2–30.0)
11–15	71	44	61.9 (50.6–73.2)	9	12.6 (4.9–20.4)	31	43.6 (32.1–55.2)
16–20	105	70	66.6 (57.6–75.6)	13	12.3 (6.0–18.6)	47	44.7 (35.2–54.2)
21–25	94	67	71.2 (62.1–80.4)	24	25.5 (16.7–34.3)	42	44.6 (34.6–54.7)
26–30	92	65	70.6 (61.3–79.9)	13	14.1 (7.0–21.2)	50	54.3 (44.1–64.5)
31–35	82	56	68.2 (58.2–78.3)	12	14.6 (6.9–22.2)	44	53.6 (42.8–64.4)
36–40	59	42	71.1 (59.6–82.7)	4	6.7 (0.3–13.1)	37	62.7 (50.3–75.0)
41–45	46	32	69.5 (56.2–82.8)	6	13.0 (3.3–22.7)	25	54.3 (39.9–68.7)
> 45	32	26	81.2 (67.7–94.7)	4	12.5 (1.0–23.9)	22	68.7 (52.6–84.8)

Among 91 HBsAg carriers, only 1.1% (95% CI: 0.0–3.2) was positive for antibodies against HDV.

DISCUSSION

Following an exodus of Albanian refugees to the Apulia region of Italy in 1997, a seroepidemiological study was undertaken to evaluate the prevalence of blood-borne viral hepatitis in subjects coming from this neighbouring country.

Concerning hepatitis B, although our sample may be biased with respect to the general population it is consistent with a high prevalence of HBV in Albania. The endemicity of HBV infection is defined as high when the prevalence of HBsAg in the population is more than 5% [12, 13]. In our sample the overall prevalence of HBsAg was 13.6% and the overall prevalence of anti-HBc, which indicates the burden of HBV infection, was 62.1%. In a previous study conducted on pregnant women who had emigrated to Greece from Albania, the prevalence rates for HBsAg and anti-HBc were 13.4 and 70.8% respectively [11].

An important finding was the presence of HBsAg in 8.1% of children up to 10 years of age, suggesting that the HBV carrier state is largely acquired early in childhood by vertical transmission and by horizontal transmission from highly infectious siblings or other family members [14, 15].

Although vertical and horizontal transmission represent the main routes of transmission, an important role in the spread of HBV in Albania could also have been played by the use of non-disposable needles and syringes in medical and vaccination practice. In addition, hospitalization in Albania is associated with hepatitis B infection, due to poor medical and nursing practice [11].

In the study conducted during the previous influx in 1991, the overall prevalence of HBsAg among Albanian refugees was 19% and a prevalence of 16% was found in children up to 10 years of age [10].

Starting from 1994, newborns in Albania have been vaccinated against HBV through the economic aid given by International Rotary (Italian districts), but no precise information is available on the administration of the vaccine and the coverage. Therefore, it is probable that the difference in HBsAg prevalence in subjects aged up to 10 years, between the 1991 and 1997 studies, could be due to the vaccination of younger children. This hypothesis is supported by the fact that in our study half of the children under 4 years of age (10 subjects), negative for other HBV

markers, were found to be positive for anti-HBs. The fact that the remaining five children under 4 years did not show anti-HBs, presumably indicates that the vaccination campaign did not cover the entire population of Albanian children.

Although the sample of Albanian refugees studied may be not representative of the Albanian population, on the basis of the present findings and considering the role of hepatitis viruses in the development of chronic liver diseases, we believe that Albania needs to put in place a long-term vaccination strategy for hepatitis B. In particular, the vaccine should be administered to all newborns according to the schedule proposed in other countries [16]. In addition, vaccination against HBV in adults belonging to high-risk groups should also be recommended.

In our study a very low prevalence for HDV infection was found. In fact, only 1.1% of HBsAg (+) was positive for anti-HDV antibodies. Such finding agrees with previous studies of Albanian refugees [10, 11]. Furthermore, this prevalence rate is lower than that reported in Italy and in the Mediterranean basin [7].

HCV infection seems to be rare in Albania (0.3%) and does not represent a major public health problem. Although HCV can be transmitted in the same way as HBV, it is probable that the low prevalence found reflects low transmission efficiency by vertical and by sexual routes [17].

In conclusion, in Albania HBV infection represents a public health priority that should be addressed by a nationwide vaccination programme. Finally, a surveillance system for viral hepatitis should be set up to monitor the trend of acute viral hepatitis and to evaluate the impact of such a vaccination programme.

ACKNOWLEDGEMENTS

We thank Mr Gatti for carrying out the serological tests. We also would like to thank Pasteur–Mérieux MSD, Ortho Diagnostic Systems and Abbott for providing reagents for testing samples.

REFERENCES

1. Dusheiko G. Hepatitis B: an overview. In: Rizzetto M, Purcell RH, Gerin JL, Verme G, eds. *Viral hepatitis and liver disease*. Turin: Minerva Medica, 1997: 57–66.
2. Kew MC. Current epidemiological trends of viral hepatitis. In: Rizzetto M, Purcell RH, Gerin JL, Verme G, eds. *Viral hepatitis and liver disease*. Turin: Minerva Medica, 1997: 562–6.

3. Fay OH. Hepatitis B in Latin America: epidemiological patterns and eradication strategy. The Latin American Regional Study Group. *Vaccine* 1990; **8**: S100–6.
4. Favorov MO, Nemechek V, Yashina TL, et al. Current epidemiological trends of viral hepatitis in Eastern Europe and the former Soviet Union. In: Rizzetto M, Purcell RH, Gerin JL, Verme G, eds. *Viral hepatitis and liver disease*. Turin: Minerva Medica 1997: 555–8.
5. Maertens G, Stuyver L. Genotypes and genetic variation of hepatitis C viruses. In: Harrison TJ, Zuckerman AJ, eds. *The molecular medicine of viral hepatitis*. New York: John Wiley & Sons, 1997: 184–5.
6. Tandon BN, Tandon A. Epidemiological trends of viral hepatitis in Asia. In: Rizzetto M, Purcell RH, Gerin JL, Verme G, eds. *Viral hepatitis and liver disease*. Turin: Minerva Medica 1997: 559–61.
7. Rizzetto M, Hadziyannis S, Hansonn BG, Toukan A, Gust I. Hepatitis delta virus infection in the world: epidemiological patterns and clinical expression. *Gastroenterol Int* 1992; **5**: 18–32.
8. Donvito M, Quagliara V, Calabrese F. Emergencies in human migrations: Military Medicine in the relief activities during the Albanian exodus. *Minerva Anesthesiol* 1991; **57**: 1511–5.
9. Greco D, Squarcione S, Germinario C, Lo Caputo S, Binkin N, Panatta M. Health response to a large and rapid influx of Albanian refugees in Southern Italy, 1991. *Disasters* 1993; **16**: 347–55.
10. Santantonio T, Lo Caputo S, Germinario C, et al. Prevalence of hepatitis virus infections in Albanian refugees. *Eur J Epidemiol* 1993; **9**: 537–40.
11. Malamitsi-Pouchner A, Papacharitonos S, Sotos D, et al. Prevalence of different hepatitis markers among pregnant Albanian refugees in Greece. *Eur J Epidemiol* 1996; **12**: 297–301.
12. Maynard JE. Hepatitis B vaccine: strategies for utilization. In: Maupas P, Guesry P, eds. *Hepatitis B vaccine*. INSERM Symposium No. 18. Amsterdam: Elsevier/North Holland Biomedical Press, 1981: 13–9.
13. Sobeslavsky O. Prevalence of markers of hepatitis B infection in various countries: a WHO collaborative study. *Bull WHO* 1980; **58**: 621–8.
14. Barin F, Perrin J, Chotard J, et al. Cross sectional and longitudinal epidemiology of hepatitis B in Senegal. *Prog Med Virol* 1981; **27**: 148–62.
15. Botha JF, Ritchie MJ, Dusheiko GM, Mouton HWK, Kew MC. Hepatitis B virus carrier state in black children in Ovamboland: role of perinatal and horizontal infection. *Lancet* 1984; **ii**: 1210–2.
16. Zanetti AR, Tanzi E, Romano L, Grappasonni I. Vaccination against hepatitis B: the Italian strategy. *Vaccine* 1993; **11**: 521–4.
17. Centers for Disease Control. Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. *MMWR* 1998; **47** (N. RR-19): 1–39.