

Prevalence Rates of Viral Hepatitis Infections in Refugee Kurds from Iraq and Turkey

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Abstract

Background: Since little is known about the burden of viral hepatitis in Kurds, the prevalence of infection with hepatitis A virus (HAV), hepatitis E virus (HEV), hepatitis B virus (HBV) and hepatitis C virus (HCV) was investigated in a sample of refugee Kurds from Iraq and Turkey.

Patients and Methods: A cross-sectional study was carried out. Serological markers to hepatitis viruses were determined for 1,005 subjects from all age-groups of which 36.6% were from Turkey and 63.4% from Iraq.

Results: Overall seroprevalence for anti-HAV was 94.4% and 14.8% for anti-HEV. A significantly higher prevalence for anti-HEV was found among Iraqis (17.5%) compared to Turkish immigrants (10.0%). The prevalence of hepatitis B surface antigen (HBsAg) and total anti-HBc (core) was 6.8% and 35.6% in Turkish Kurds and 2.2% and 12.7% in Iraqis, respectively. Only 10% of children aged up to 10 years and 2.8% of subjects aged 11–20 years had been vaccinated against HBV, the majority of them coming from Iraq. One subject was confirmed as positive for anti-HCV (0.1%) and HCV-RNA and analysis showed a 4c/4d genotype.

Conclusion: This survey shows a high prevalence of enterically transmitted viral hepatitis in Kurds. HBV infection is moderately endemic, while the prevalence of HCV infection is low. There is a need for a universal immunization strategy for HBV in the Kurd population.

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Introduction

Viral hepatitis still represents a major health problem throughout the world. Hepatitis viruses spread through fecal-oral route (hepatitis viruses A and E, HAV and HEV) and blood-borne transmitted hepatitis viruses (hepatitis viruses B and C, HBV and HCV) are the most important agents responsible for enterically and parenterally transmitted disease worldwide.

In developed countries the prevalence of anti-HAV has steadily declined due to improvements in the standard of hygiene, although wide differences among countries still

persist [1, 2]. In developing countries the infection is acquired early in life and a large proportion of the population has anti-HAV antibodies [3, 4]. HEV is the causative agent of both water-borne epidemics and sporadic cases of viral hepatitis in tropical and subtropical countries with inadequate sanitation and low socioeconomic condition [5]. In developed countries HEV infection is infrequent and generally restricted to persons who have traveled to disease-endemic areas [6].

The epidemiology of HBV and HCV infection varies according to geographical area. The global prevalence of chronic HBV infection varies widely, from high ($\geq 8\%$, e.g. Africa, Asia and Western Pacific) to intermediate (2–7%, e.g. Southern and Eastern Europe) and low (less than 2%, e.g. Western Europe, North America and Australia) [7].

The prevalence of HCV infection is low (0.2–2%) in the general population of Europe, USA, Indonesia and Japan, but is higher (2–5%) in South America and Asia and highly endemic ($> 5\%$) in many parts of Africa [8–10].

Since the early 1990's thousands of refugees have arrived in southern Italy (Puglia region) mainly coming from Albania and more recently from areas of the Balkans (Kosovo) involved in wars and ethnic conflicts. Survey studies were carried out on these refugees aimed at evaluating the prevalence of hepatitis virus infections, since little or nothing was known about these populations [11–14]. Following this massive immigration, Puglia has also experienced the arrival of thousands of refugees from the Kurdistan area. During the year 2000 about 8,000 Kurdish refugees arrived in Puglia and the influx still continues. As a result of this influx seroepidemiological studies were planned to obtain information on the prevalence of some infectious diseases. Little is known about the burden of enterically and blood-borne transmitted viral

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hepatitis in the Kurdish population. Therefore, a cross-sectional study was carried out to investigate the prevalence of viral hepatitis infections (HAV, HEV, HBV and HCV) in a large refugee population from Kurdistan.

Patients and Methods

During the year 2000 about 8,000 Kurdish refugees (more than 60% from Iraq and the remaining from Turkey) arrived in Puglia in an uninterrupted flow. After identification controls, the refugees were housed in refugee camps in Puglia. For the purpose of this study, a team of physicians and nurses went to the Puglian refugee camps and every subject present in the camps on that day was asked to participate in the seroepidemiological survey. After obtaining informed consent, a blood sample was taken on a voluntary basis. The consent to take a blood sample from children was obtained from their parents or legal guardians. In addition, data such as age, sex and origin were obtained from each subject. The blood samples were then taken to the laboratory, centrifuged and stored at -20°C until testing.

The sera collected were tested for the following hepatitis markers: total anti-HAV (IgG and IgM), anti-HEV (IgG), HBsAg, anti-HBs, total anti-HBc (IgG and IgM), anti-HCV and HCV-RNA. HBV markers and antibodies to HAV and to HCV were detected in serum samples by AxSYM-Microparticle Enzyme Immunoassay MEIA (Abbott Diagnostics). Antibodies to HEV were detected by EIA (HEV IgG, Nuclear Laser Medicine). 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 carried out according to manufacturer's instructions. The repeatedly reactive samples for anti-HEV were confirmed by an immunoblot assay (RecomBlot HEV IgG/IgM, Mikrogen GmbH). Antibodies to O2-N, O2-C, O2-M and O3 proteins were detected. The results were interpreted ac-

ording to the manufacturer's instructions. Serum HCV-RNA was detected by PCR (Cobas Amplicor HCV, Roche Diagnostics) and HCV genotype determined by line probe assay (Inno-Lipa HCV II, Innogenetics).

Data were processed using the software package EPIINFO 6.04c (CDC, Atlanta, GA, USA). 95% CI was calculated by Fleiss quadratic method and χ^2 -test was used to compare proportions. For small samples, Fisher's exact test was used. If a p-value was below 0.05, the difference between proportions was considered to be statistically significant. χ^2 -test for linear trend was used to evaluate differences in the prevalence of hepatitis markers with increasing age.

Results

About 1,115 refugees present in the camps were approached and more than 90% gave their consent. A total of 1,005 Kurds, mainly male young adults, were recruited for sampling. 894 (89.0%) were males and 111 (11.0%) were females. 98 refugees (9.7%) were children aged up to 10 years, 171 (17.1%) were aged 11–20 years, 546 (54.3%) were aged 21–30 years and 186 (18.5%) were older than 30 years. The refugees were divided according to the country of provenience (Iraq or Turkey); 637 (63.4%) were from Iraq and 368 (36.6%) from Turkey. Of the 637 Iraqi subjects, 566 (88.8%) were males and 71 (11.2%) were females, while of the 368 Turkish refugees, 328 (89.1%) were males and 40 (11.9%) were females. The mean ages of the subjects from Turkey and from Iraq were both 24 years (SD 9.1 years, range 10 months to 50 years and SD 8.4 years, range 6 months to 55 years, respectively).

Table 1 shows the prevalence of anti-HAV and anti-HEV antibodies in Kurdish refugees by age-group and

Table 1
Age-specific prevalence of anti-HAV and anti-HEV in Kurdish refugees according to provenience.

Age (years)	No. of subjects	Total anti-HAV+			Anti-HEV IgG+				
		No.	% (95% CI)	P-value	ELISA+		Confirmed by WB		P-value
		No.	% (95% CI)		No.	% (95% CI)	No.	% (95% CI)	
0–10	98	59	60.2 (49.7–69.8)		0	0.0 (0.0–4.7)	0	0.0 (0.0–4.7)	
Turkey	36	21	58.3 (40.8–74.0)		0	0.0 (0.0–12.0)	0	0.0 (0.0–12.0)	
Iraq	62	38	61.2 (48.0–73.1)	0.773	0	0.0 (0.0–7.2)	0	0.0 (0.0–7.2)	-
11–20	171	161	94.1 (89.2–97.0)		18	10.5 (6.5–16.3)	18	10.5 (6.5–16.3)	
Turkey	87	80	91.9 (83.5–96.4)		2	2.3 (0.3–8.8)	2	2.3 (0.3–8.8)	
Iraq	84	81	96.4 (89.1–99.0)	0.357	16	19.0 (11.6–29.3)	16	19.0 (11.6–29.3)	< 0.001
21–30	546	543	99.4 (98.2–99.8)		98	17.9 (14.8–21.4)	95	17.4 (14.3–20.9)	
Turkey	155	153	98.7 (94.9–99.7)		17	11.0 (6.7–17.2)	17	11.0 (6.7–17.2)	
Iraq	391	390	99.7 (98.3–99.9)	0.195 ^a	81	20.7 (16.8–25.1)	78	19.9 (16.1–24.3)	0.012
> 30	186	186	100.0 (97.4–100.0)		38	20.4 (15.0–27.0)	38	20.4 (15.0–27.0)	
Turkey	90	90	100.0 (94.8–100.0)		19	21.1 (13.4–31.2)	18	20.0 (12.5–30.0)	
Iraq	96	96	100.0 (95.2–100.0)	-	19	19.8 (12.6–29.4)	18	18.7 (11.7–28.2)	0.829
Total	1,005	949	94.4 (92.7–95.7)		154	15.3 (13.1–17.7)	149	14.8 (12.7–17.2)	
Turkey	368	344	93.4 (90.3–95.6)		38	10.3 (7.4–14.0)	37	10.0 (7.2–13.7)	
Iraq	637	605	94.9 (92.9–96.4)	0.318	116	18.2 (15.3–21.4)	112	17.5 (14.7–20.8)	0.001

χ^2 -test for linear trend (anti-HAV+): 174.9, $p < 0.001$; χ^2 -test for linear trend (confirmed anti-HEV+): 24.4, $p < 0.001$; ^a Fisher's exact test; WB: Western blot

Table 2
Prevalence of HBV markers in Kurdish refugees according to age-groups and provenience.

Age (years)	No. of subjects	HBsAg+		P-value	Anti-HBc+		P-value
		No.	% (95% CI)		No.	% (95% CI)	
0–10	98	1	1.0 (0.0–6.3)		3	3.1 (0.7–9.3)	
Turkey	36	0	0.0 (0.0–12.0)	1.000 ^a	0	0.0 (0.0–12.0)	0.463
Iraq	62	1	1.6 (0.0–9.8)		3	4.8 (1.2–14.3)	
11–20	171	4	2.3 (0.7–6.2)		27	15.8 (10.8–22.3)	
Turkey	87	4	4.6 (1.4–12.0)	0.385 ^b	24	27.6 (18.8–38.3)	< 0.001
Iraq	84	1	1.2 (0.0–7.3)		3	3.6 (0.9–10.8)	
21–30	546	16	2.9 (1.7–4.8)		110	20.1 (16.9–23.8)	
Turkey	155	8	5.2 (2.4–10.2)	0.095 ^b	61	39.3 (31.7–47.5)	< 0.001
Iraq	391	8	2.0 (0.9–4.1)		49	12.5 (9.4–16.3)	
> 30	186	17	9.1 (5.5–14.4)		72	38.7 (31.7–46.1)	
Turkey	90	13	14.4 (8.2–23.7)	0.015	46	51.1 (40.4–61.7)	< 0.001
Iraq	96	4	4.2 (1.3–10.9)		26	27.1 (18.7–37.2)	
Total	1,005	39	3.9 (2.8–5.3)		212	21.1 (18.6–23.7)	
Turkey	368	25	6.8 (4.5–9.9)	< 0.001	131	35.6 (30.7–40.7)	< 0.001
Iraq	637	14	2.2 (1.2–3.7)		81	12.7 (10.2–15.6)	

^a Fisher's exact test; ^b Yates's corrected χ^2 -test; χ^2 -test for trend (HBsAg+): 12.2, $p < 0.001$; χ^2 -test for trend (anti-HBc+): 49.9, $p < 0.001$

provenience. The overall prevalence of total anti-HAV was 94.4%. A relevant finding was the presence of anti-HAV antibodies in 58.3% and 61.2% of the Kurdish children aged 0–10 years from Turkey and from Iraq, respectively. No significant differences in the rates of anti-HAV antibodies were found among refugees according to provenience (Turkey or Iraq) in all age-groups ($p > 0.05$). In addition, no significant difference in the prevalence of anti-HAV antibodies was found between males and females (94.5% vs 93.7%, $p > 0.05$).

Analyses showed that 154 subjects (15.3%) were repeatedly positive for anti-HEV by EIA and 14.8% were confirmed to be seropositive by immunoblot assay. The > 30 years age-group demonstrated the highest prevalence of

anti-HEV (20.4%). None of the children aged up to 10 years tested seropositive for HEV. When analyzing the prevalence rates by sex, no significant difference emerged between males and females (14.5% vs 10.0%, $p = 0.185$) although a higher rate of seropositivity was found among males.

A significantly higher prevalence of anti-HEV antibodies was found in Kurds from Iraq compared to that found in Kurds from Turkey (17.5% vs 10.0%, $p < 0.01$). In the 11–20 and 21–30 year age-groups the rates of seropositivity were considerably higher in subjects from Iraq ($p < 0.001$ and $p = 0.012$, respectively) compared to those in Kurds from Turkey, whereas

no significant difference emerged in subjects older than 30 years ($p = 0.829$).

The age-specific prevalence rates of HBV markers between the two groups of Kurds are reported in table 2. The prevalence of HBsAg was 6.8% in Turkish Kurds and 2.2% in Iraqis. 35.6% of Turkish Kurds and 12.7% of Iraqi Kurds were found positive for total anti-HBc. The proportion of refugees positive for HBV markers increased with age ($p < 0.001$). Subjects aged over 30 years, both Turks and Iraqis, showed the highest rate of HBsAg carriage (14.4% and 4.2%, respectively) and of anti-HBc (51.1% and 27.1%, respectively). A significantly higher rate of anti-HBc, which indicates the burden of HBV infection, was revealed in Turkish refugees compared to Iraqis in all age-groups except 0–10 years. However, a significant difference in the prevalence of chronic HBV infection was found only in refugees aged over 30 years ($p = 0.015$). In addition, no significant difference in the prevalence of anti-HBc was found between male and female Kurds from Iraq (14.1% vs 8.4%, $p = 0.186$), whereas a significant difference emerged between male and female Kurds from Turkey, particularly in refugees aged over 10 years (41.1% vs 16.7%, $p < 0.01$).

Table 3 shows the prevalence of solely anti-HBs-positives among anti-HBc-negative Kurdish refugees. About 10% of children up to 10 years had been vaccinated against HBV, the majority of them coming from Iraq. Only 2.8% of subjects aged 11–20 years tested positive for anti-HBs, while none of the adults older than 20 years had been vaccinated.

A low prevalence of anti-HCV antibodies was found in Kurdish refugees. Among 1,005 subjects tested, only one proved reactive by screening assay and was confirmed by

Table 3
Prevalence of solely anti-HBs-positive among anti-HBc-negative Kurdish refugees according to age and provenience.

Age (years)	No. of subjects	Anti-HBsAg+ ^a	% (95% CI)	P-value ^b
0–10	93	10	10.7 (5.5–19.3)	
Turkey	36	1	2.8 (0.1–16.2)	0.103
Iraq	57	9	15.8 (7.9–28.3)	
11–20	144	4	2.8 (0.8–7.4)	
Turkey	63	1	1.6 (0.0–9.6)	0.798
Iraq	81	3	3.7 (0.9–11.1)	
> 20	550	0	0.0 (0.0–0.8)	
Turkey	138	0	0.0 (0.0–3.3)	–
Iraq	412	0	0.0 (0.0–1.1)	
Total	787	14	1.8 (1.0–3.0)	

^a titer ≥ 10 mIU/ml; ^b Yates's corrected χ^2 -test

HCV RIBA (0.1%, CI: 0.0–0.6). The subject was a male Iraqi aged 38 years who tested positive for HCV-RNA revealing a 4c/4d genotype by line probe assay. No information was available on the possible risk factors.

Discussion

This study reports the results of a cross-sectional study on the prevalence of viral hepatitis infections in a large sample of Kurds who arrived in southern Italy (Puglia region) as a consequence of ethnic conflict and repression in the countries of origin.

The data is restricted to the refugee population and cannot be generalized for the whole population of the region. In addition, it is likely that the presence of maternal immunity could have influenced the prevalence rates of antibodies to HBV and to HAV in the 0–10 years age-group, although only few children were aged less than 2 years.

Nevertheless, some epidemiological evidence emerges from the present report. Although Kurdish people are a well-characterized ethnic group, the burden of viral hepatitis infections varies depending on the origin of refugees (Turkey or Iraq) and should be considered separately.

HAV infection seems to be clearly hyperendemic in Kurds from Turkey or from Iraq, since over 90% of the whole population tested was positive for anti-HAV antibodies and about 60% of seropositives were children aged up to 10 years. These data indicate past infection since none of the refugees in the camps showed clear symptoms of acute viral hepatitis on arrival. Poor hygienic, sanitary and socioeconomic conditions could be the basis of this finding, as reported previously [3, 4, 9]. In addition, a similar pattern of HAV infection was observed in other immigrant populations coming into southern Italy [13, 14]. However, the prevalence rate found in Kurdish refugee children from Turkey is higher than that recently reported in indigenous Turkish children [15], thus reflecting possible differences in socioeconomic, sanitary and hygienic conditions among ethnic groups of the same country.

The survey also shows an endemic circulation of HEV in the Kurdish population, although prevalence rates significantly differ between Kurds living in Iraq and Turkey, respectively. In particular, none of the children aged 0–10 years tested positive for anti-HEV. The absence or the low prevalence of HEV infection in children, suggesting the lack of exposure to or replication of the virus, remains an intriguing question considering the modality of transmission of the virus, as also outlined by other authors [4, 16, 17].

In the other age-groups, except that of over 30 years, a significantly higher prevalence of confirmed anti-HEV-positive subjects was found in Kurds from Iraq compared to Turkish Kurds. Moreover, the prevalence of anti-HEV detected in Kurds from Turkey seems to be higher than that previously reported in other indigenous Turkish populations [18], thus further indicating an increased risk of exposure to hepatitis viruses transmitted through the fecal-oral route for ethnic Kurds in Turkey.

The seroprevalence data obtained in the current study indicate an intermediate level of endemicity of HBV infection in Kurdish refugees since about 4% of all refugees were found to be HBsAg carriers and that more than 20% had been exposed to the virus. Nevertheless, when comparing the prevalence figures of HBV markers in the two groups of refugees, Kurds from Turkey had higher rates for HBV markers, with almost 7% of the subjects having chronic HBV infection and 36% being positive for anti-HBc. On the contrary, only 2.2% of Iraqis were positive for HBsAg and 12.7% for anti-HBc. These findings agree with those previously reported on Kurdish refugees coming from eastern Turkey [19] and with those reported on the Iraqi population [20, 21]. In addition, the level of endemicity of HBV infection in the refugee population studied is in accordance with that found in a small sample of Kurdish refugees in Greece [22], although no distinction was made in the latter study regarding the country of provenience of refugees. The low prevalence of HBsAg carriers in children seems to indicate that vertical transmission is not a main route of transmission of HBV infection. On the other hand, the increasing prevalence of HBV markers with rising age seems to suggest that HBV infection is principally acquired by sexual or parenteral exposure and by horizontal transmission, probably due to poor socioeconomic and overcrowded conditions, although no specific information was available on the possible risk factors of the subjects. No vaccination policy against HBV existed in Turkey until the end of 1998 when a universal HBV immunization program was introduced [23, 24]. In addition, data on the status of the vaccination program against HBV and the vaccination coverage in Iraq are lacking, although infant HBV immunization is included in the vaccination schedule [25]. We found that only one Kurdish child from Turkey and about 16% of Iraqi children up to 10 years of age were vaccinated against HBV as confirmed by the sole presence of anti-HBs and that only few subjects aged 11–20 years were positive for anti-HBs. Considering the very poor coverage rate found, it is necessary to highlight the importance of a universal immunization strategy against HBV in reducing the incidence of the disease and the related mortality. HBV vaccination is considered cost-effective even in countries with moderate to low HBV endemicity [23, 26–28]. Nevertheless, the enormous difficulties in implementing immunization programs in areas of the world afflicted by ethnic conflicts should be mentioned. Only international cooperation on a global scale could economically support areas like Kurdistan to procure the vaccine and maintain effective vaccination coverage. From a public health view, all refugees staying in refugee camps are vaccinated against HBV, as recommended by the Italian Ministry of Health [29].

A main finding of this survey was the very low prevalence of HCV infection found. In fact, only one adult subject from Iraq tested positive for HCV (0.1%). This data supports the evidence of a very low circulation of HCV in Turkey [30, 31], whereas further studies are necessary to confirm the

findings in the Iraqi population. The presence of a genotype 4c/4d might indicate a prevalence of genotype 4 in areas of the Middle East, as reported previously [8, 32].

In conclusion, this serosurvey shows a high prevalence of enterically transmitted viral hepatitis in the Kurdish population with a significantly higher rate of anti-HEV seropositivity in refugees from Iraq compared to that found in Turks. HBV infection seems to be moderately endemic in Kurds, although a remarkably high burden of HBV infection was found in Turkish Kurds. Finally, HCV infection is at a low level of endemicity and the adoption of general preventive measures could avoid the potential spread of HCV infection.

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