

Changes in the seroepidemiology of hepatitis B infection in Catalonia 1989–1996

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Abstract

The objective of this study was to investigate the prevalence of hepatitis B markers in a representative sample of 2142 subjects in Catalonia, Spain, and to compare it with previous studies. Multiple logistical regression analysis was carried out to determine variables associated with the markers studied. The prevalence of anti-HBc and HBsAg was 9.1% and 1.2%, respectively. Male gender, urban habitat, birth place outside Catalonia and lower social class were associated with the presence of anti-HBc. Carrier status was only associated with male gender. Between 1989 and 1996 there was a decrease of 46% in the prevalence of serum HBV markers mainly in the 25–44 ($P < 0.0001$) and 35–64 year ($P = 0.0002$) age groups, in those born in Catalonia ($P = 0.003$) and in those in the higher social classes ($P < 0.0001$). These decreases can be explained by the improved socioeconomic conditions and, partially, by the routine pre-adolescent and risk group programmes of immunization. © 2000 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Hepatitis B is a candidate disease for eradication, given that its reservoir is exclusively human and that there exists a highly efficacious preventive vaccine [1,2].

The European Office of the WHO estimates that one million people in Europe are still infected with the hepatitis B virus (HBV) each year. Of these, 90,000 evolve to a chronic state and more than 20,000 will die of cirrhosis or hepatocellular carcinoma [3]. It is therefore evident that the medium and long-term damage to health caused by HBV is substantial. Although some studies have shown that the prevalence of chronic HBV carriers has diminished considerably in countries which have initiated programmes of mass vaccination

[4] and that the incidence of liver cancer in children has decreased after the introduction of these programmes [5,6], the long period between infection and the appearance of the most severe clinical manifestations of the disease mean that it is difficult for HBV vaccination programmes to have a priority [7]. The elimination of hepatitis B from large areas such as countries or regions, although theoretically possible, requires good vaccination programmes which are maintained for decades [2]. Some countries where the prevalence of carriers is low are trying to move towards the control of HBV by a policy of selective vaccination of risk groups only, while other countries where the problem is of greater magnitude have opted for mass vaccination [1,6–8].

Whatever the strategy selected, in order to advance towards the elimination of HBV infection in defined areas it is essential to dispose of adequate knowledge of its extent and trend [9]. In Catalonia, a seropreva-

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lence survey was carried out in 1989 and has been of great use in establishing a policy of mass vaccination against HBV in 12-year-old schoolchildren which started in 1991 and has been continued until the present day with a coverage higher than 90% of all adolescents [10]. In this article we present the results of the seroprevalence survey on hepatitis B infection in the child and adult population of Catalonia in 1996. The objective of the survey was to investigate the current situation with regard to HBV infection and compare it with that existing in Catalonia in 1989.

2. Subjects and methods

2.1. Sample

The study was carried out among representative samples of schoolchildren and adults in Catalonia, an autonomous community of six million inhabitants in the North-East of Spain. For adults, 97 municipal areas of Catalonia were randomly selected after being stratified into urban habitat (>10,000 inhabitants) and rural (\leq 10,000 inhabitants); individuals were randomly selected using the municipal voting roll, after stratification according to the age and gender of the Catalan population. For schoolchildren, 30 schools were selected at random and all children between 6–7, 10–11 and 13–14 years from the selected schools were included in the study. The sample size was calculated on the basis of an alpha error of 5%, an expected prevalence of antibodies of 50% and a precision of ± 0.025 for the adult sample and of ± 0.055 for the schoolchild sample. In accordance with these data, the sample size necessary was 1600 individuals for the adult sample and 330 individuals for each of the school years included in the study. The final total of individuals included in the study was 2142 which represented a participation of 83%.

2.2. Laboratory analyses

The serum obtained from the study subjects was frozen at -29°C until the serologic analysis was carried out. An ELISA test was used to determine the presence of anti-HBc antibodies and HBsAg in the samples obtained (Auszyme, Abbott Laboratories and AB-AUK, Sorin Biomedica).

2.3. Sociodemographic variables

Data were obtained on age, gender, place of birth, place of residence, educational level (of the father in the case of schoolchildren) and occupation (also of the father in the case of schoolchildren). The socioeconomic level was determined on the basis of occupation

and classified according to the British system of five social classes [11]: professionals (I), intermediate (II), skilled (III), semiskilled (IV) and unskilled (V).

2.4. Comparison with the 1989 seroprevalence survey

The prevalence of markers of natural infection (anti-HBc and HBsAg) in the present study were compared with those obtained in an investigation carried out in 1989 in which a total of 1678 subjects were studied [10]. In this survey carried out before the programme of mass vaccination of pre-adolescents was started, prevalence of anti-HBs and HBsAg was investigated. Comparison of the results from the two surveys makes apparent temporal changes in the extent of infection, thus avoiding the influence of mass vaccination on the prevalence of markers of HBV infection.

2.5. Statistical analysis

The prevalence of antibodies and the 95% confidence intervals (CI) were calculated. The overall prevalence of the markers studied was obtained using the technique of direct standardization, with the 1991 population of Catalonia as the standard population. The χ^2 test was used to compare the differences between prevalences. A level of $P < 0.05$ was considered as statistically significant. To determine the association between the sociodemographic variables studied and the prevalence of markers of natural HBV infection, the odds ratio and the 95% CI were calculated. The statistically significant odds ratios were adjusted by means of a multiple logistic regression analysis [12].

3. Results

3.1. Sample

The sample obtained was of 2142 individuals of 5 years of age or over. The sample of schoolchildren was 884 children and the adult sample was of 1258 subjects. The distribution of both the child and adult samples was similar to that of the Catalan population [13].

3.2. Laboratory analysis

The overall prevalence of anti-HBc antibodies was 9.1%, and was higher in males (11.4%) than in females (6.9%), a difference which was statistically significant ($P < 0.001$) (Table 1). Prevalence increased with age, rising from $< 1\%$ in the 5–14 years age group to $> 15\%$ in subjects over 54 years ($P < 0.001$).

The overall prevalence of HBsAg was 1.2% and the

distribution according to age and gender is shown in Table 1. Again, the prevalence was higher in males (1.7%) than in females (0.7%) although this difference was not statistically significant ($P = 0.07$).

3.3. Sociodemographic variables

Table 2 shows the analysis of the association between the sociodemographic variables and the prevalence of anti-HBc in the adult population. In the raw analysis the variables associated with the infection were male gender, urban habitat, educational level below primary studies (14 years), place of birth and social classes IV–V, with odds ratios of 1.87; 2.04; 1.87; 2.04 and 2.22 respectively. All the variables except educational level were independently associated with hepatitis B markers in the multiple logistic regression analysis. An adjusted odds ratio of 2.13 was obtained for male gender, 2.01 for urban habitat, 1.66 for place of birth and 1.88 for social classes IV–V.

The only variable associated with the prevalence of

HBsAg positive serology was male gender, with a raw odds ratio of 3.23 and an adjusted one of 3.34.

3.4. Comparison with the 1989 seroprevalence survey

Comparison of the prevalences obtained in 1989 and 1996 showed that the overall prevalence of any HBV marker has decreased from 16.9 to 9.1% ($P < 0.0001$). In males the prevalence has diminished from 16.1 to 11.4% ($P = 0.0002$) and in women from 17.8 to 6.9% ($P < 0.0001$). In 1996, a lower prevalence of infection was observed in all age groups with the differences being statistically significant in the 45–64 ($P = 0.0001$) and 25–44 years ($P = 0.002$) age groups. There were also statistically significant decreases in the prevalence among those born in Catalonia ($P = 0.003$) and those belonging to the higher social classes ($P < 0.0001$) (Table 3). The overall prevalence of HBsAg carriers was 1.2% in the present study, while in the 1989 study the figure was 1%, although the differences were not statistically significant ($P = 0.07$).

Table 1
Prevalence^a of HBsAg and anti-HBc according to age and gender Catalonia, 1996

Age (yr)	n	Prevalence of anti-HBc(+)		Prevalence of HBsAg(+)	
		%	95% CI	%	95% CI
Males					
5–9	151	0.0	–	0.0	–
10–14	304	0.6	0.0–1.5	0.3	0.0–0.9
15–24	60	3.3	0.0–7.8	1.7	0.0–5.0
25–34	120	8.3	3.4–13.2	0.0	–
35–44	104	16.3	9.2–23.4	3.8	0.4–7.2
45–54	96	9.4	3.6–15.2	2.1	0.0–5.0
66–64	103	18.4	10.9–25.9	2.9	0.0–6.1
> 64	127	26.0	18.4–33.6	1.6	0.0–3.8
Total	1065	11.4	9.5–13.3	1.7	0.9–2.5
Females					
5–9	111	0.9	0.0–2.7	0.0	–
10–14	318	0.9	0.0–1.9	0.0	–
15–24	58	3.4	0.0–8.1	1.7	0.0–5.0
25–34	96	2.1	0.0–5.0	0.0	–
35–44	118	5.9	1.7–10.1	0.8	0.0–2.4
45–54	126	7.1	2.6–11.6	0.0	–
55–64	121	14.9	8.6–21.2	0.0	–
> 64	129	13.2	7.4–19.0	1.6	0.0–3.8
Total	1077	6.9	5.4–8.4	0.7	0.2–1.2
Both genders					
5–9	262	0.4	0.0–1.2	0.0	–
10–14	622	0.8	0.1–1.5	0.3	0.0–0.7
15–24	118	3.4	0.1–6.7	1.7	0.0–3.5
25–34	216	5.6	2.7–8.5	0.0	–
35–44	222	10.8	6.7–14.9	2.3	0.0–4.3
45–54	222	8.1	4.5–11.7	0.9	0.0–2.1
55–64	224	16.5	11.6–21.4	1.3	0.0–2.8
> 64	257	19.5	14.7–24.3	1.6	0.1–3.1
Total	2142	9.1	7.9–10.3	1.2	0.7–1.7

^a Standardized by age and gender.

Table 2
Results of the association between the prevalence of anti-HBc and the variables studied in the adult population

	Prevalence %	n	OR ^a (95% CI)	OR _a (95% CI)
Gender				
Male	14.8	610	1.87 (1.31–2.66)	2.13 (1.47–3.08)
Female	8.5	646		
Habitat				
Urban	12.5	1059	2.04 (1.13–3.68)	2.01 (1.08–3.77)
Rural	6.5	199		
Educational level				
≤ Primary studies	14.9	591	1.87 (1.31–2.67)	NS
> Primary studies	3.5	667		
Place of Birth				
Catalonia	9.5	953		
Other	17.7	305	2.04 (1.41–2.93)	1.66 (1.13–2.45)
Social class				
I–III	6.7	463		
IV–V	13.8	516	2.22 (1.43–3.46)	1.88 (1.20–2.96)

^a OR, odds ratio; CI, confidence interval; OR_a, odds ratio adjusted by multiple logistic regression analysis for age, gender, habitat, educational level, place of birth and social class. NS, not significant ($P > 0.05$).

4. Discussion

The results obtained in this study show that the prevalence of HBV markers is decreasing noticeably in the Catalan population. Between 1989 and 1996, the overall prevalence of past and present infection has diminished from 16.9 to 9.1%, a reduction of 46%.

Table 3
Comparison of the prevalences obtained in the seroepidemiological surveys of 1989 and 1996

	Any hepatitis B marker positive ^a						
	1989			1996			
	%	95% CI ^b	n	%	95% CI	[n]	[P]
Gender							
Male	16.1	14.2–18.0	848	11.4	9.5–13.3	1065	0.002
Female	17.8	15.8–19.8	830	6.9	5.4–8.4	1077	< 0.0001
Age (yr)							
5–9	1.6	0.0–3.2	248	0.4	0.0–1.2	262	NS
10–14	2.2	1.2–3.2	769	0.8	0.2–1.5	622	NS
15–24	10.5	4.0–17.0	86	3.4	0.2–6.7	118	NS
25–44	19.1	13.3–24.9	252	8.2	5.6–10.8	438	0.0001
45–64	21.8	16.2–27.4	211	12.3	9.3–15.3	446	0.002
> 64	23.2	15.4–31.0	112	19.5	14.6–24.3	257	NS
Place of birth ^c							
Catalonia	15.3	11.6–19.0	359	9.5	7.6–11.4	953	0.003
Other	24.5	19.7–29.3	302	17.7	13.4–22.0	305	NS
Social class ^c							
I–III	19.5	13.1–25.9	149	6.7	4.4–9.0	463	< 0.0001
IV–V	16.9	15.0–21.8	225	13.8	10.8–16.8	516	NS

^a Cases with anti-HBs as a unique positive marker are not investigated in the 1996 sample study because this marker may reflect vaccine immunization rather than past infection.

^b CI, confidence interval; NS, not significant ($P > 0.05$).

^c Variables studied only in the adult population.

Decreases have been observed in all age groups, although only those in the 25–44 (a decrease of 57%) and the 45–64 years (43.6%) age groups are statistically significant.

In the 15–24 years age group the difference was not statistically significant, probably because of the small sample size (86 in 1989 and 108 in 1996) but the decrease was 68%. Noguchi et al. [14] in a study carried out in a Japanese district found that over a period of 9 years (1980–1988) the prevalence of markers of HBV infection in the 10–19 years age group decreased from 56.4 to 5.4%. Although the authors recognize the part that improved social conditions played in this decrease, they attribute part of the reduction to vaccination. Other authors [15,16] have also indicated that improvements in social conditions may play a role in the reduction of HBV infection. In fact, in the present study, the variable of lower social class (classes IV–V) was associated to HBV infection (OR = 1.88; 95% CI = 1.2; 2.96) unlike the 1989 study. It may be thought that the improvement in living conditions has contributed to the decrease in the prevalence of HBV markers, given that in the higher social classes the prevalence has been reduced from 19.5% in 1989 to 6.7% in 1996, a reduction of 66%, which was statistically significant. However, in the lower social classes, the decrease has been more limited, decreasing from 16.9% in 1989 to 13.8% in 1996, which was not statistically significant.

The decreases in the prevalence of markers of HBV infection in the other two age groups (25–44 and 45–64 years) probably are, at least partly, a result of the policy of risk-group vaccination (health workers, intravenous drug users, prisoners, male homosexuals, travellers and those living with chronic carriers, among

others) which was introduced into Catalonia in 1985 [17–19].

The present study also shows that male gender, urban habitat, and being born outside Catalonia are associated to a higher prevalence of HBV markers. All these variables have been repeatedly associated to HBV markers in previous studies, probably as surrogate markers of risk-associated behaviour [20,21].

It is worth highlighting the association found between HBV markers and being born outside Catalonia. One limitation of our study is that we did not study the origin of those born outside Catalonia, and thus is not possible to precisely determine the reason why those born outside Catalonia have a higher prevalence of markers of infection. It is noteworthy that although in those born in Catalonia the prevalence has diminished by 37% (from 15.3% in 1989 to 9.5% in 1996), in those born outside Catalonia the decrease was significantly lower: only 27% (24.5 vs 17.7%). It is likely that these results are due to the higher prevalence of infection in the regions of origin and also to the social and environmental conditions of this population group.

The size of the population of African and Asian origin illegally residing in Catalonia should also be taken into account, as in these groups the prevalence of HBV markers is high [22]. According to emigration data, which probably underestimate the problem, the number of persons of African and Asian origin has tripled and doubled respectively between 1989 and 1996 [23].

There are few population-based studies with which to compare the precise results of the present study. In Spain, Gil et al. [24], in a study carried out in 571 young people between 16–19 years of age, showed a prevalence of anti-HBc of 3%, very similar to that obtained in the 15–24 year age group in our study (3.4%). D'Amelio et al. [25] in a study of 18–24 year old Italian soldiers in 1990 found a prevalence of 4.6%, only slightly higher than the figure of 3.3% found in the 15–24 years age group in Catalonia in 1996.

In a French study, which used samples from donors, pregnant women, and voluntary screening of healthy subjects, the prevalence of anti-HBc in 1991 was 2.8% [26]. The inclusion of blood donors, who are normally less infected, partly accounts for the fact that the prevalence was lower than that found in Catalonia, although the different socioeconomic levels of the two countries may also have an influence. In Belgium, in a study [27] carried out in 1994 using a sample of the general population the results were very similar to ours: the prevalence of anti-HBc was 9.9% compared with 9.1% in Catalonia.

In the United States, McQuillan et al. [21] in a population-based study (National Health and Nutri-

tion Examination Survey, NHNES) obtained a prevalence of markers of HBV infection of 4.9% in the period 1988–1994, only slightly inferior to that obtained in the period 1976–1980 (5.5%). However, in Catalonia, in a shorter time period, we have seen a reduction in prevalence of 46%. Although the influence of improvements in social health conditions cannot be discarded, it seems reasonable to attribute the decrease observed largely to the effectiveness of vaccination programmes.

The prevalence of carriers of HBsAg has slightly increased in the period studied, passing from 1% in 1989 to 1.2% in 1996, although the difference is not statistically significant. It is noteworthy that in children under 15 years of age the prevalence was very low (0.1%) in 1996, five times lower than the figure obtained in this age group in 1989 (0.5%). This suggests that the carrier detection programme among pregnant women and the passive–active immunization of newborn babies from HBsAg-positive mothers introduced in 1984 is working adequately. It also confirms that horizontal transmission during infancy is negligible in Catalonia and that the decision taken in 1990 not to vaccinate all newborns and to concentrate efforts on mass vaccination of pre-adolescents was right. Some European studies have found HBsAg prevalences lower than those found in Catalonia in 1996, although this information does not come from representative samples. Thus, Lindh et al. [28] in Sweden, studying the chronic hepatitis register reported a prevalence of 0.1%, which is ten times smaller than ours. In the United Kingdom, the prevalence is also lower than ours, oscillating between 0.15% in adolescents and 0.03% in pregnant women [29].

Although the overall prevalence of carriers in men (1.7%) and in women (0.7%) shows no significant differences ($P = 0.07$) the prevalence of carriers detected in the adult population was significantly higher in men (2%) than in women (0.6%), which coincides with other reports [30,31]. In countries with a high prevalence of HBsAg, this condition has not been seen to be more frequent in males at birth or in early years, but only in adulthood. This can be explained by the greater propensity for the infection to persist in males and by their higher risk of exposure [32,33].

The conclusion that may be drawn from this study is that the prevalence of HBV infection has substantially decreased in Catalonia, and this is due both to improvements in socioeconomic conditions and to the effect of vaccination programmes.

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