

Prevalence of hepatitis B infection markers in Lebanese children: the need for an expanded programme on immunization

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SUMMARY

This multi-centre, cross-sectional study was designed to reveal the present status of hepatitis B infection markers among Lebanese children, and provide recommendations regarding childhood immunization policies. A total of 841 children, aged between 6 months and 6·5 years, were enrolled from Lebanon's five districts. Their sera were tested for hepatitis B surface antigen and hepatitis B core IgG. The overall prevalence of hepatitis B virus infection markers was 0·8% with increasing age-specific rates from 0% at 6 months to 1·3% at > 5 years. There was no statistically significant association between the presence of hepatitis B markers and family characteristics or risk factors for infection. The highest prevalence rates were among children from Beirut suburbs (2·9%) and South Lebanon (1·6%). The risk of horizontal transmission of hepatitis B to uninfected children increased substantially after the age of 2 years. An expanded programme on immunization that integrates hepatitis B vaccine during the first year of life is needed.

INTRODUCTION

Despite all efforts made by the World Health Organization (WHO) to control hepatitis B virus (HBV), it was projected that the number of individuals carrying this virus worldwide will rise from 350 million in 1990, to around 400 million by the year 2000 [1]. This increase is believed to be a consequence to the failure of many countries to integrate hepatitis B vaccine into their national immunization programmes, as recommended by WHO in 1992 [2]. Lebanon, a country with moderate (2–3% carrier rate) endemicity for HBV [3, 4], lacks an expanded programme on immunization (EPI) that includes hepatitis B vaccine. In addition, the current status of HBV epidemiology in children is unknown. We

therefore conducted this multi-centre, cross-sectional investigation to study the prevalence of HBV infection markers in Lebanese children in the first 7 years of life.

METHODS

This multi-centre, cross-sectional study was carried out on children from 6 hospitals, covering Lebanon's 5 districts, between August 1997 and May 1999. The participating hospitals were: the American University of Beirut Medical Center, AUBMC (located in the capital city Beirut); Ghassan Hammoud Hospital (located in Saidon, the main city of South Lebanon); Orange Nasso Hospital (located in Tripoli, the main city of North Lebanon); Khoury Hospital (located in Zahleh, the main city of Bekaa, East Lebanon); Hôpital de Nôtre-Dame, located in Jbeil, and Baakleen Hospital, located in Baakleen, both in Mount Lebanon.

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Table 1. *Distribution of HBV infection markers by age and geographic location*

Variable	Number	Positive HBV markers		
		HBsAg number	Anti-HBcIgG number	Total number (%)
Age				
≤ 1 yr	107	0	0	0 (0.0)
> 1–2 yrs	173	0	0	0 (0.0)
> 2–3 yrs	141	1	2	2 (1.4)
> 3–4 yrs	146	0	1	1 (0.7)
> 4–5 yrs	118	0	2	2 (1.7)
> 5 yrs	156	0	2	2 (1.3)
Total	841	1	7	7 (0.8)
Geographic distribution				
Beirut	260	0	0	0 (0.0)
North Lebanon	115	0	0	0 (0.0)
South Lebanon	63	0	1	1 (1.6)
Bekaa	52	0	0	0 (0.0)
Mount Lebanon	118	0	0	0 (0.0)
Beirut suburbs	215	1	6	6 (2.9)
Unspecified	18	0	0	7 (0.0)
Total	841	1	7	7 (0.8)

Samples

Serum samples were collected from children between the ages of 6 months and 6.5 years (unvaccinated for hepatitis B), upon presentation to any of the participating hospitals. Subjects were included if they were coming for their routine check-up visits, vaccinations, admissions for elective surgeries or treatment of minor childhood diseases, such as respiratory infections or gastroenteritis. Children known to have a chronic liver disease, acute or chronic hepatitis, blood dyscrasias, malignancies or hemoglobinopathies were excluded.

Parents were interviewed before enrolment, and a questionnaire was filled in for each child. The questionnaire assessed family characteristics such as monthly income, highest educational level attained by either parent, paternal career, housing conditions, number of siblings, religion, and area of residence. Risk factors for hepatitis B infection such as blood transfusions, chronic illness, history of jaundice or hepatitis in the child or family, previous surgery, hospitalization, day-care or institution attendance were also assessed.

Serological assays

After obtaining parental consent, blood was withdrawn from each child and serum tested by ELISA for

hepatitis B surface antigen (HBsAg) (ETI-MAK-3, Dia Sorin s.r.l., Saluggia, Italy) and hepatitis B core IgG antibody (anti-HBcIgG) (ETI-AB-COREK-2, Dia Sorin). Additional testings were carried out for hepatitis B core IgM antibody (anti-HBcIgM), (ETI-CORE-IGMK-2, Dia Sorin), hepatitis B e-antigen (HBeAg), (ETI-EBK-2, Dia Sorin) and hepatitis B e-antibody (anti-HBe), (ETI-AB-EBK, Dia Sorin) for those samples positive for HBsAg. Samples that were positive for anti-HBcIgG were also tested for anti-HBe antibody and hepatitis B surface antibody (anti-HBs), (ETI-EB-AUK-3, Dia Sorin). All testing and interpretation of results were done at AUBMC according to the manufacturer's instructions.

Statistical analysis

The χ^2 test was used to examine the strength of the association between the independent variables (risk factors for HBV infection, family characteristics) and the dependent variable (positive HBV markers). Statistical significance was set at $P < 0.05$.

RESULTS

A total of 943 subjects were eligible for enrolment, but consent was not given for blood sampling in 60 (6.3%) children. Analysis of family characteristics and risk factors for HBV infection failed to reveal any

Table 2. Family characteristics and HBV risk factors for 841 children

Variable	HBV positive markers (n = 7)	HBV negative (n = 834)	Total (n = 841)	P value
Monthly income				
< \$400	6	376	382	
≥ \$400	1	434	435	0.06
Unspecified	0	24	24	
Parental education				
< Intermediate	6	612	618	
≥ Intermediate	1	207	208	0.68
Unknown	0	15	15	
Paternal career				
Manual	6	534	540	
Professional	1	234	235	0.68
Unknown	0	66	66	
Blood transfusion				
Yes	0	47	47	
No	7	786	793	1.0
Unknown	0	1	1	
History of jaundice				
Yes	0	17	17	
No	7	816	823	1.0
Unknown	0	1	1	
Sex				
Male	2	384	386	0.46
Female	5	450	455	
Hospitalization				
Yes	1	297	298	0.43
No	6	537	543	
Chronic illness				
Yes	0	124	124	
No	7	709	716	0.60
Unknown	0	1	1	
Region				
South Lebanon and Beirut suburbs	7	271	278	0.006
All Others	0	563	563	

significant difference between those who consented to blood withdrawal and those who refused. For the 883 children from whom blood samples were taken, there were 42 questionnaires with missing information that were excluded from analysis. The data presented hereafter are those of the 841 children with complete information. Their mean (\pm S.D.) and median ages were 3.5 (\pm 1.68) years and 3 years respectively. Males represented 54% (455) of the subjects. The majority of children were from Beirut and its suburbs (58%).

There were seven children whose serum samples contained HBV infection markers, making an overall prevalence rate of 0.8%. Only one child was positive for HBsAg, HBcIgG and HBeAg. All the other six children had positive anti-HBcIgG and anti-HBs antibodies. The age-specific rates were as follows:

1.4% between 2 and 3 years, 0.7% between 3 and 4 years, 1.7% between 4 and 5 years and 1.3% above age 5 years (Table 1). There were no children with HBV infection markers below the age of 2 years. Region-specific rates were: Beirut Suburbs 2.9%, South Lebanon 1.6%, and 0% for each of Beirut, North Lebanon, Bekaa and Mount Lebanon respectively (Table 1). Analysis of family characteristics revealed that only low family income (less than \$400 per month) was associated with a trend for increased prevalence of HBV infection markers, but this did not reach statistical significance ($P = 0.06$). None of the potential risk factors for HBV infection were found to be associated with HBV infection markers (Table 2).

Since all children with HBV infection markers were from Beirut suburbs and South Lebanon, and because

most people who are currently residing in the suburbs had migrated from South Lebanon during or before the civil war, we elected to further analyse their data as one subgroup. When age-specific prevalence rates were calculated for this new subgroup, they were as follows: 3.5% between 2 and 3 years, 1.9% between 3 and 4 years, 4.9% between 4 and 5 years, and 3.9% in those above 5 years making an overall prevalence rate of 2.5%. Comparison of this new subgroup's characteristics with those of the other districts revealed less parental lower education (70% *vs.* 77%), less crowding at home (28% *vs.* 37%), but a higher reporting of previous hospitalizations (41% *vs.* 33%), and history of jaundice in a family member (31% *vs.* 23%), all being statistically significant ($P < 0.05$).

DISCUSSION

Our study reveals that the prevalence of HBV infection markers increases substantially by the second year of life and remains at this level during the following 4 years. We had only one child whose serological profile suggested a persistent infection. In the absence of screening of his family members, we cannot exclude the possibility of either perinatal infection, or a recently acquired horizontal infection. The other 6 children with hepatitis markers had serological profiles consistent with previous exposure and natural immunity.

Our findings strongly suggest that in Lebanon, the risk of horizontal transmission of HBV to children is greatest during the first 2 years of life. Similar findings from the Middle East have been reported by Toukan [5], where the prevalence of HBV carriage was found to rise from the age of 1 year, to reach near-adult values by the age of 5 years. This led to the conclusion that horizontal transmission of HBV is the major factor contributing to HBV endemicity in the region [5].

An unexpected finding in our study was that all the children with HBV infection markers were from Beirut suburbs and South Lebanon. This finding is in agreement with the observation that most adults with HBV infection, who were followed-up at AUBMC, came from the same two regions (Shamma'a M, personal communications, May 2000). In addition, 50% of pregnant women who were positive for HBV markers in a previous study also came from South Lebanon or Beirut suburbs [4]. The exact reasons for the increased prevalence of HBV infection markers among the residents of these two regions are un-

known. The higher prevalence of family history of jaundice, and of previous hospitalizations, may be risk factors for possible hepatitis B transmission to children. However, exposure of this subgroup to a common risk factor cannot be ruled out. It is also possible that certain cultural or other unidentified habits, specific for the populations of Beirut suburbs and South Lebanon, may perpetuate the spread of HBV in these two regions. Further study on a larger sample size from both regions is needed to confirm, or exclude our findings.

The prevalence of HBV carriers in apparently healthy adult populations from Lebanon has increased from 1.4–1.6% in 1976 [3], to 2.9% in 1995 [4]. Recently, a policy of pre-marital hepatitis B screen has been adopted in this country. However, universal antenatal screening for HBsAg is not yet implemented. These data, together with the results of the present study, confirm the need for integration of hepatitis B vaccine into the national immunization schedule. Integration of HBV vaccine into the expanded programme on immunization (EPI), has proven to be a successful strategy in eradicating HBV in endemic areas of the Middle East, such as Saudi Arabia [6]. For Lebanon, we propose that hepatitis B vaccine be given at 2, 4 and 10 months of age, along with the routine administration of oral polio, diphtheria-tetanus-pertussis (DTP) and measles vaccines. Except for the price of the hepatitis B vaccine, such an EPI entails neither additional health visits to physicians, nor additional costs.

In conclusion, the finding that children over 2 years of age are at increased risk of acquiring HBV, necessitates recommending the administration of hepatitis B vaccine as an integral part of the EPI, in order to prevent horizontal transmission in Lebanon. Moreover, adherence to the universal antenatal HBsAg screening, and vaccination and immunoprophylaxis of newborns of HBsAg positive mothers within 12 h of age remains an effective policy for controlling the vertical transmission of HBV. Further studies with larger numbers of individuals from the two most prevalent districts are needed to reveal the exact epidemiology of HBV infection among children.

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