The decline of hepatitis B viral infection in South-Western Saudi Arabia

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ABSTRACT

Objectives: Hepatitis B virus (HBV) infection is endemic in the Kingdom of Saudi Arabia (KSA). The Jizan region in the South-Western area of the country was noted for a high prevalence of hepatitis B surface antigen (HbsAg) carrier rate. The study was carried out to determine the prevalence of HBsAg and other markers of HBV among residents of Jizan and evaluate the impact of the measures adopted in the last decade, to control HBV.

Methods: The study was carried out between 1995 and 1998. The subject were studied in 4 groups: Group A consisted of voluntary blood donors (n=14883) tested within the blood banking system during the time period June 1995 to June 1997, Group B were patients treated in the hospitals (n=4692) during the period June 1995 to June 1996, Group C consisted of volunteers recruited from the community (n=1172) and Group D children aged <10 years (n=229). Serum samples were obtained from the subjects tested for HBsAg, total antibody to hepatitis B core antigen, antibody to HBsAg and antibody to hepatitis C virus.

Results: Hepatitis B surface antigen was positive in 5.4% of 14883 voluntary blood donors (Group A) and in 5.1% of 1172 persons recruited from the community (Group C) 40.2% were positive for at least one marker of HBV. The prevalence of HBsAg in-patients in Group B was 9.7% (456 of 4692). These prevalence rates are significantly lower than the prevalence of 12% and 32% reported in 1985 and 1986. Only 2 (0.9% of 229) children in Group D were positive for HBsAg, indicating a major decline from the rate of 8.8% observed in an earlier survey.

Conclusion: The low prevalence of HBsAg in children, provides evidence for the effectiveness and efficacy of the integration of hepatitis B vaccination into the extended program of immunization in KSA. The significant decline of HBV markers among unvaccinated Saudi adults indicated an indirect effect of other factors (for example health education and socio-economic progress) on the prevalence and transmission of HBV in Jizan. In areas of high endemicity, the epidemiological characteristics HBV are modified significantly by the combination of HBV vaccination and other complimentary control strategies.

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The high prevalence of hepatitis B virus (HBV) infection in the Kingdom of Saudi Arabia (KSA) is well reported. By the age of 10 years, approximately 7% of apparently healthy children are positive for hepatitis B surface antigen (HBsAg) (HBV carriers) and 20% are positive for at least one marker of the HBV.[1] The average prevalence rate of HBsAg in the Saudi adult population is approximately 8%, and 60% have evidence of past exposure to HBV.[2,3] However, several surveys of voluntary blood donors have shown marked regional variations in the prevalence of HBV in KSA.[2,4-7] The Jizan region of KSA is a focus of hyper-endemic HBV infection and its sequelae of chronic liver diseases and hepatocellular carcinoma.[8,9] A survey carried out in 1985 demonstrated an overall HBV exposure rate of 46.5% and HBsAg prevalence of 12.7% among 724

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Saudi adults residing in the region.[4] In 1986, a comparative study of different regions of KSA, reported a rate of HBsAg to be 32.2% among 237 blood donors in Jizan, compared to a rate of 4.7% in a similar population in Riyadh in the Central region of KSA.[5,7] Similarly, a community-based national survey among Saudi children in 1990 indicated that 8.8% of 283 Jizan children were HBsAg positive and 27.9% of them were positive for at least one HBV marker.[10] These rates were higher than the corresponding national average rates of 6.7% and 19.9%.[1] Since these aforementioned surveys, the socio-economic development in the country had improved dramatically. As part of a control strategy against HBV, the Saudi government successfully integrated hepatitis B (HB) vaccination into the national expanded program of immunization (EPI) in 1989.[8] In addition, the efficient primary health care system had become more widely utilized by the population, thereby reducing the prevalence of traditional medical practices, which included skin scarifications and cauterization.

To evaluate the impact of these changes on the epidemiology of HBV in the Jizan region the prevalence rates of HBV markers were determined among apparently healthy, unvaccinated volunteers and children who had been the target population for HB vaccination within the EPI system. In addition, the prevalence of HBV was determined among patients evaluated in the Jizan hospitals during the period of study.

Methods. The population of Jizan region is approximately one million people served by 10 hospitals including the 500 beds regional referral center, the King Fahd Central Hospital (KFCH), Jizan, KSA. The screening for HBV, hepatitis C virus (HCV) and, human immunodeficiency virus (HIV) in blood donors and patients in the health care system were performed mainly in a central virology laboratory located in the KFCH and to a less extent in selected general hospitals using centrally procured kits and uniform protocols. The results of tests for markers of viral hepatitis obtained during the screening of blood donors were reported to a central registry. The subjects of the study consisted of 4 groups. Group A (14883) comprised apparently healthy voluntary male blood donors who were screened in the blood banks of all the general hospitals and the KFCH, over a period of 25 months (June 1995 to June 1997). They were all non–commercial volunteer donors and were usually relatives and friends of patients. They were tested for HBsAg, antibody to HCV (anti-HCV), HIV and venereal disease research laboratory (VDRL) as part of the routine screening for blood donation. Group B was consisted of consecutive patients (n=4692) who were tested for HBsAg, and anti-HCV, HIV and VDRL during the respective visits to the clinics or admission during the period of study. The patients had a variety of illnesses and were not categorized according to the various clinical diagnoses in this analysis. Group C consisted of 1172 apparently healthy volunteers (752 males and 420 females), recruited from the community as previously described[1] were tested for HBsAg, antibody to hepatitis B core antigen (anti-HBc) antibody to HBsAg (anti-HBs) and anti-HCV. A questionnaire was completed for each participant to obtain information on age, sex, nationality and history of previous jaundice, blood transfusion (BT), past surgical operation, past scarifications or cauterization. The socio-economic class was determined as previously described using the educational level, occupation and type of accommodation.[1,9] Group D comprised 229 children (121 males and 108 females) who were recruited as previously described.[11] The ages ranged from 1-10 years (median 6 years). Nearly all the children in the survey had been vaccinated. From each subject, 5-10 cc of venous blood was obtained serum sample by centrifugation of separation from coded and stored at -20°C until testing. Serological tests were carried out within 3 days on most of the samples, and not later than one month in any of the samples. Commercially available enzyme immunoassay (EIA) (Abbott Laboratories Chicago, Illinois.) were used for the detection of HBsAg, anti-HBc and anti-HBs. Anti-HCV

Table 1 - Hepatitis B surface antigen and anti-HCV in blood donors in Jizan region, Kingdom of Saudi Arabia [1995-1997].

Months and year	HBsAg			Anti-HCV		
	Tested	Positive n	(%)	Tested	Positive n	(%)
June 1995	611	35	(5.7)	588	12	(2)
July 1995	794	65	(8.2)	566	10	(1.8)
August 1995	912	47	(5.2)	595	9	(1.5)
September 1995	599	24	(4)	565	20	(3.5)
October 1995	384	14	(3.6)	154	11	(7.1)
November 1995	595	29	(4.9)	543	8	(1.5)
December 1995	240	7	(2.9)	181	1	(0.6)
January 1996	484	29	(6)	124	2	(1.6)
February 1996	629	14	(2.2)	613	9	(1.5)
March 1996	793	52	(6.7)	664	14	(2.1)
April 1996	176	3	(1.7)	162	2	(1.2)
May 1996	196	9	(4.6)	215	2	(0.9)
June 1996	514	26	(5.1)	487	6	(1.2)
July 1996	994	58	(5.8)	830	27	(3.3)
August 1996	873	127	(14.5)	837	16	(1.9)
September 1996	1037	45	(4.3)	933	11	(1.2)
October 1996	521	19	(3.6)	532	17	(3.2)
November 1996	770	27	(3.5)	735	25	(3.4)
December 1996	453	23	(5.1)	426	13	(3.1)
January 1997	428	23	(5.4)	428	5	(1.2)
February 1997	717	28	(3.9)	695	13	(1.9)
March 1997	612	27	(4.4)	572	5	(0.9)
April 1997	333	22	(6.6)	333	2	(0.6)
May 1997	771	14	(1.8)	771	4	(0.5)
June 1997	447	34	(7.6)	447	10	(2.2)
Total	**14883**	**801**	**(5.4)**	**12966**	**254**	**(1.9)**

HBsAg - hepatitis B surface antigen, HCV - hepatitis C virus

was detected by a third generation EIA (Murex III). Reactive samples were re-tested by supplementary immunoblot assays (HCV Blot 3.0 Genelabs Diagnostics and Ortho Diagnostics Systems Raritan, New Jersey).

Statistical analysis. Continuous variables were expressed by stating the means and the respective SD. Categorical data was stated as proportions. Proportions were compared using Chi-square or Fisher's exact test. Difference in trend was tested by Mantel Henzel test. Means were compared by the Student's t-test. Using the EPI info software (Version 6.0; Center for Disease Control, Atlanta Georgia, USA), all tests were carried out by standard statistical methods.[12]

Results. The prevalenceof HBsAg in Group A was 5.4% (835 of 14883) and 1.9% (258 of 12996) for anti-HCV. Tests for HIV and VDRL were positive in 0.2% (15 of 7916) and 0.3% (20 of 7582). The monthly rates of HBsAg varied from 1.7% ((3 of 176 persons) in April 1996 to 14.5% (127 of 873) in August 1996 (**Table 1**). A similar but less marked variation was observed in the rates of anti-HCV positivity (ranging from 0.47-7.1%). The prevalence in Group B who were tested from June 1995 to June 1996, HBsAg was detected in 9.7% (456 of 4692 patients) and 3.8% (23 of 605 patients) were positive for anti-HCV. During the period, the monthly prevalence of HBsAg varied between 4% and 14% in hospital patients, compared to the variation of 2-8% among blood donors. **Table 2** summarizes the demographic characteristics and prevalence results in Group C. Sixty percent of 1172 were Saudis and 64.2% were males. History of BT was low; occurring in only 0.7%. Combining all nationalities, the overall prevalence of HBsAg was 4.1%, with no significant difference in the rates among males (4.3%) and females (3.8%) as summarized in **Table 3**. Separate analysis of the 704 Saudi citizens (398 males and 354 females) showed that 36 (5.1%) were positive for HBsAg. In this sub-group, the prevalence in the males (5.8%) was not significantly different from that in the females (4.2%) although, the prevalence was higher in the males, compared to the females in the age group of 21-30 years (**Table 4**). Anti-HBc and anti-HBs were present in 30.4% (214 persons). The corresponding rates for isolated anti-HBc or anti-HBs were 4.7% (33 patients) and 0.6% (4 patients), giving an overall exposure rate of 40.2%. Hepatitis B surface antigen was positive in 2 (0.9%) of 229 children (Group D) age <10 years.

Discussion. The results of this survey indicate that 5.4% of 14883 blood bank donors in Jizan region were positive for HBsAg, a rate that is similar to the prevalence (6.7% of 126863 donors) reported from the Eastern region of KSA.[13] This prevalence is higher than the rates reported from Western population (0.1-0.5%) but lower than those from the Far-Eastern countries.[14,15] Comparison of the prevalence of HBsAg obtained in the

Table 2 - Prevalence of HBsAg and anti-HCV in asymptomatic residents of Jizan region, Kingdom of Saudi Arabia.

Characteristic	Males		Females		Total	
	n	(%)	n	(%)	n	(%)
Nationality						
Saudi	398	(52.9)	306	(72.9)	**704**	**(60.1)**
Non-Saudi	74	(9.8)	56	(13.3)	**130**	**(11.1)**
Asians	264	(35.1)	52	(12.4)	**316**	**(27)**
Africans	16	(2.1)	6	(1.4)	**22**	**(1.9)**
Past history						
Blood transfusion	7	(0.9)	3	(0.7)	**10**	**(0.9)**
Jaundice	15	(2)	6	(1.4)	**21**	**(1.8)**
Scarification or cautery	24	(3.1)	12	(2.9)	**36**	**(3.1)**
N of positive						
HBsAg	32	(4.3)	16	(3.8)	**48**	**(4.1)**
Anti-HCV	9	(1.2)	4	(1)	**13**	**(1.1)**
VDRL	2	(0.3)	0	(0)	**2**	**(0.2)**

HBsAg - hepatitis B surface antigen, HCV - hepatitis C virus, VDRL - venereal disease research laboratory

Table 3 - Gender-related prevalence of HBsAg and anti-HCV in 1172 residents of Jizan region, Kingdom of Saudi Arabia.

Characteristic	Males		Females		Total	
	n	(%)	n	(%)	n	(%)
HBsAg						
Saudi	23/398	(5.8)	13/306	(4.2)	**36/704**	**(5.1)**
Non-Saudi	4/74	(5.4)	2/56	(3.6)	**6/130**	**(4.6)**
Asians	4/264	(1.4)	1/52	(1.9)	**5/316**	**(1.6)**
Africans	1/16	(6.3)	0/6	(0)	**1/22**	**(4.5)**
Anti-HCV						
Saudi	6/398	(1.5)	3/306	(1)	**9/704**	**(1.3)**
Non-Saudi	2/74	(2.7)	1/56	(1.8)	**3/130**	**(2.3)**
Asians	1/264	(0.4)	0/52	(0)	**1/316**	**(0.3)**
Africans	0/16	(0)	0/6	(0)	**0/22**	**(0)**

HBsAg - hepatitis B surface antigen, HCV - hepatitis C virus

Table 4 - Age-related prevalence of HBsAg in 704 apparently healthy Saudi.

Age (years)	Males			Females		
	Tested	n	(%)	Tested	n	(%)
11-20	56	2	(3.6)	54	2	(3.7)
21-30	176	12	(6.8)	130	7	(5.4)
31-40	100	6	(6)	81	3	(3.7)
≥41	66	3	(4.5)	41	1	(2.3)

HBsAg - hepatitis B surface antigen, HCV - hepatitis C virus

volunteers recruited from the community with those reported by a survey in the same region 11 years earlier, revealed a significant decline in the prevalence of HBsAg (12.1% versus 5.1%) and to a less extent, in the exposure rate. (46.5% versus 40.2%).[4] The difference in the latter was due mainly to the decline in the prevalence of anti-HBc alone. It has been reported that persons who are positive for anti-HBc alone could be harboring undetectable levels of HBsAg and therefore are probably infectious.[6,16,17] Therefore, the decline over a period of 8-10 years in the prevalence of chronic HBV carriers (namely persons positive for HBsAg or isolated anti-HBc) in the Jizan region is very significant (from 20.2% in 1985 to 7.2% in 1996). The decline is more dramatic when the findings are compared to the results of an earlier survey of 237 Jizan residents in which 32.2% were positive for HBsAg, and 52% had evidence of past exposure to HBV.[5,7] Surveys in the Eastern region of KSA had also shown a similar fall in the prevalence of HBV among blood donors.[13-18] The factors responsible for the fall in HBV carrier rate in unvaccinated populations cannot be explained easily. The collective socio-economic state of a population has an impact on the prevalence of most transmissible infections.[5,19,20] An inverse relationship was observed between HBV prevalence and socio-economic and educational status of some populations.[21] In an earlier surveyed it was suggested that general socio-economic, under development may be a contributory factor to the higher prevalence of HBsAg in Jizan region compared to other well developed areas of the country.[5] In the last decade, the region has undergone a remarkable development with a better education and higher level of personal and public hygiene. Furthermore, traditional medical practices, including scarifications and cauterizations have become infrequent as a result of a better utilization of free and accessible medical care facilities. The significant decline in the prevalence of HBV in the population may be attributable to these factors. Hepatitis B vaccination contributed immensely to an effective control of HBV in KSA. We had shown that the overall prevalence of HBsAg among Saudi Arabian children decrease from 6.7% to 0.3 % and the prevalence of isolated anti-HBc declined from 0.46 to 0%, 10 years after the integration of HB vaccine into the national EPI.[22] The present study in which 0.9% of the Jizan children were positive for HBsAg compared to a carrier rate of 8.8% in 1989 further confirms the effectiveness of the program, especially in an area of high HBV prevalence such as Jizan region.[1] Similar reduction in HBV prevalence had been noted in other countries with similar programs of prevention.[23,24]

It is evident that there is a considerable interplay of factors in the control of HBV. Hepatitis B vaccination remains the corner stone of any effective and efficient strategy. However, other factors (for example, socio-economic development and advance in health education) may contribute significantly to the decline of HBV, particularly among unvaccinated populations.

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