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Original Article

Seroprevalence of HBsAg among adolescents and adults in the Muhayil Aseer region of KSA: 25 years after the introduction of national vaccination



Suliman M. Al Humayed, ABIM

Department of Internal Medicine, College of Medicine, King Khalid University, Abha, KSA

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المخلص

أهداف البحث: تهدف هذه الدراسة للتعرف على مدى الانتشار المصلي وعوامل الخطورة ذات الصلة للمستضد السطحي لفيروس التهاب الكبد "ب" بين المراهقين والبالغين في منطقة محایل عسير بالمملكة العربية السعودية.

طرق البحث: أجريت هذه الدراسة المقطعية لعينة مختارة من المراهقين والبالغين في منطقة محایل عسير بالمملكة العربية السعودية. تم تعبئة استبانة شاملة من خلال المقابلة الشخصية لجميع المشاركين، كما تم أخذ عينات من الدم، وأجري الاختبار المصلي للمستضد السطحي لفيروس التهاب الكبد "ب".

النتائج: ضمت الدراسة ١٣٣ مراهقا و ٩٣٨ بالغاً. وأظهرت الدراسة أن الانتشار المصلي بلغ ١.٥% و ٦.١% بين المراهقين والبالغين، على التوالي. كما أظهرت الدراسة أن الأفراد الذين لم يحصلوا على التطعيم ضد التهاب الكبد "ب" يحملون بشكل ملحوظ خطورة أعلى للتعرض للمستضد السطحي لالتهاب الكبد الفيروسي "ب".

الاستنتاجات: أبرزت هذه الدراسة مدى فاعلية التطعيم في الوقاية من التهاب الكبد الفيروسي "ب". لذا ينبغي تعزيز تدابير وقائية صارمة ضد التهاب الكبد الفيروسي "ب" في منطقة الدراسة.

الكلمات المفتاحية: الانتشار المصلي للمستضد السطحي لالتهاب الكبد الفيروسي ب؛ التهاب الكبد الفيروسي؛ المراهقين؛ محایل؛ عسير، التطعيم

Abstract

Objective: The objective of this work was to investigate the seroprevalence and associated risk factors of HBsAg

among adolescents and adults in the Muhayil Aseer region of KSA.

Methods: A cross-sectional study was conducted on a selected sample of adolescents and adults in the Muhayil Aseer region of KSA. A comprehensive questionnaire-based interview was performed for all participants, blood samples were taken, and sera were tested for HBsAg.

Results: The study included 133 adolescents and 938 adults. A seroprevalence of 1.5% and 6.1% were recorded among adolescents and adults, respectively. The study showed that persons without the hepatitis B vaccination carried a significantly higher risk for developing sero-positivity for HBsAg.

Conclusion: The present study further endorsed the effectiveness of vaccination in preventing hepatitis B virus (HBV) infection. Strict preventive measures against HBV infection need to be fostered in the study area.

Keywords: Adolescents; HBsAg seroprevalence; HBV; Muhayil Aseer; Vaccination

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Corresponding address: Department of Internal Medicine, College of Medicine, King Khalid University, Abha, P.O. Box 641, KSA.

E-mail: s_humayed@yahoo.com

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Introduction

Earlier studies and reports dating back to 1980 on the seroprevalence of hepatitis B virus (HBV) infection in KSA

that were compiled and further analysed by Al-Faleh in 2003¹ have documented a high endemicity of HBV infection: 5–10% of the population were infected. The highest rate of infection was in the southern region of KSA. By 1989, a year prior to the addition of the HBV vaccine to the Extended Program of Immunization (EPI), the prevalence of HBV infection among children was 7%. Consequently a mass vaccination program was launched in that year.² Eventually, a steady significant decline of HBV infection among children was observed.^{1,3} In 2008, a sero-survey was conducted in regions of different HBV endemicity and Al-Faleh et al. documented a zero prevalence of HBsAg among students (16–18 years of age) in Almadinah Almunawwarah and Al-Qaseem both of which are located in the Aseer region, the region with the highest endemicity, thus documenting the efficacy of the HBV vaccine and its long-term protection.⁴ According to the Ministry of Health, new cases of HBV infection (4259) reported in 2013 amounted to 70% of all reported cases (6106) of viral hepatitis.⁵

Previously in KSA, the HBV vaccine was given in three doses (0, 1 and 5 months).⁶ However, as of January 2013, the schedule has been revised and re-adjusted: commencing at birth and continuing at 2-month intervals for a total of four doses. Strict measures are undertaken by the authorities to ensure that all children complete their EPI. Since the introduction of the HBV vaccination in 1990, it is expected that all children and adults of 25 years of age or younger have been vaccinated against HBV.

The objective of this work was to investigate the seroprevalence of HBsAg among adolescents and adults utilizing a sensitive enzyme immunoassay capable of detecting less than 0.1 WHO IU/ml HBsAg in Muhayil Aseer, located in southwest KSA. In addition, relevant risk factors were studied in the selected area.

Materials and Methods

Settings

The study was a cross-sectional study on a representative sample of adolescents and adults in the Muhayil Aseer region of KSA.

The study area

The Aseer region is located in the southwest of KSA and covers an area of more than 80,000 km². It borders Jizan and is located to its northeast. The region is divided into 11 Governorates. The Muhayil Governorate is the location of the current study (Figure 1) and has a total population of 214,758 (Saudi Central Department of Statistics and Information, 2013). Health care is provided through a network of 36 primary health care centres and a general hospital, the Muhayil General Hospital.

Sampling procedures

During late 2014, patients and their relatives who were aged 10 years or older and attended the outpatients' clinics of

Muhayil General Hospital for any reason (attending clinics, doing any laboratory investigation, blood donation and pre-marital screening) were included in the sample.

Questionnaire interview

A comprehensive questionnaire interview was offered to all participants. The questionnaire included socio-demographic data and history of relevant exposures. History of blood transfusion was also enquired about. Similarly, the following data were collected: history of any surgical operations, tooth extraction, wet cupping and hepatitis B vaccination.

Ethical approval

The study was reviewed and approved by the ethical committee of King Khalid University. Informed consent was obtained from each individual.

Blood sampling

Approximately 5- to 10-ml venous blood samples in plain tubes were taken from each participant and were allowed to clot at room temperature (range 18 °C–20 °C). Samples were then centrifuged at 10,000 rpm for 10 min, and the separated sera were aliquoted into two portions and stored at –20 °C until transported in ice boxes to the Virus Lab of the Abha College of Medicine, where they were grouped by collection area and stored in classified boxes in similar conditions as described above.

Serologic tests for HBsAg

HBsAg was tested by a fourth generation enzyme immunoassay (ELISA) obtained from DIA.PRO Diagnostic Bioprobes Srl via G. Carducci, Milano, Italy. Briefly, the sold phase was pre-coated with mouse monoclonal antibodies specific to the sub determinants a, d and y. Test sera were reacted with these antibodies, incubated and washed. The captured HBsAg was further reacted with conjugated mouse monoclonal antibodies against those sub determinants. Test plates were subsequently washed and reacted with a substrate. The resulting colour was read by a double beam multi-scan ELISA reader at 450 nm. The manufacturer's protocols were strictly followed in testing and interpreting the results.

Statistical analysis

Data were coded, validated and analysed using the Statistical Package for the Social Sciences (SPSS), version 13.0 (SPSS Inc., Chicago, IL, USA). The frequency, percentage, arithmetic mean, and mode are used to present the data. The chi-square test and Fishers' exact test were used as tests of significance at a 5% level of significance. Binary logistic multivariate analysis, adjusted odds ratio and antecedent 95% CIs were used to identify potential risk factors for HBsAg seropositivity.

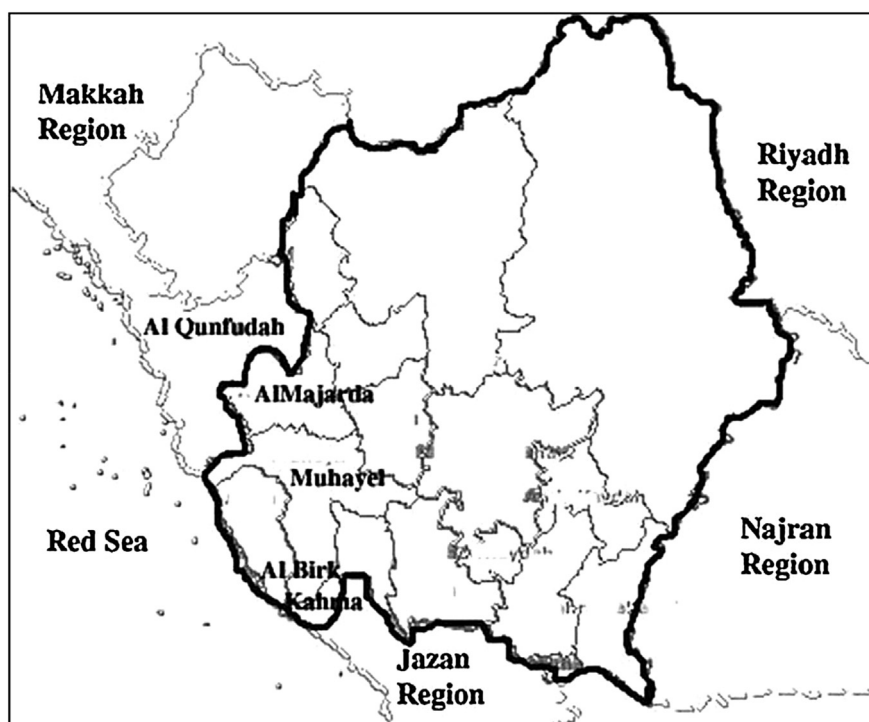


Figure 1: Map showing the Aseer region and Muhayil area.

Results

Description of the study sample

The present study included 1071 persons in the Muhayil Aseer region of KSA. Participant's ages ranged from 10 to 72 years with an average age of 35.4 ± 17.8 years and a median of 30 years. The presents study included 133 (12.4%) adolescents (aged 11–19 years) and 938 adults (20 years and older). Regarding sex distribution, 50.4% (67) of adolescents and 51.1% (479) of adults were males. The gender difference was not statistically significant ($\chi^2 = 0.222$, $P = 0.882$). Regarding the marital status among adults, 75.2% were married, 20.1% were widowed or divorced, and the rest were single. The majority of adolescents (96.3%) were single. The majority of adult females (95.1%) were housewives. The highest proportion of adult males (45.3%) were either farmers or shepherds. As for the level of education of adults, 24.5% were illiterate. Very few (2.3%) were university educated.

History of relevant exposures

History of blood transfusion among adolescents (1.5%, 2) was not significantly different ($\chi^2 = 0.153$, $P = 0.283$) from that of adults (3.1%, 3.0). Similarly, history of surgical operations and history of wet cupping were not significantly different among adolescents and adults. However, history of hepatitis B vaccination was significantly higher among adolescents (64.7%, 86) compared to adults (24.9%, 234).

Sero-prevalence of hepatitis B (HBsAg)

Two adolescents tested positive for the hepatitis B surface antigen, giving a sero-prevalence of 1.5%. Among the adults, 57 tested positive for the hepatitis B surface antigen, giving a sero-prevalence of 6.1% (Figure 2). The age difference was statistically significant ($\chi^2 = 4.681$, $P = 0.015$) (see Table 1).

Determinants of HBsAg sero-positivity

Multivariate binary logistic regression analysis was used to identify potential risk factors associated with HBsAg sero-positivity (Table 2). After adjusting for other potential risk

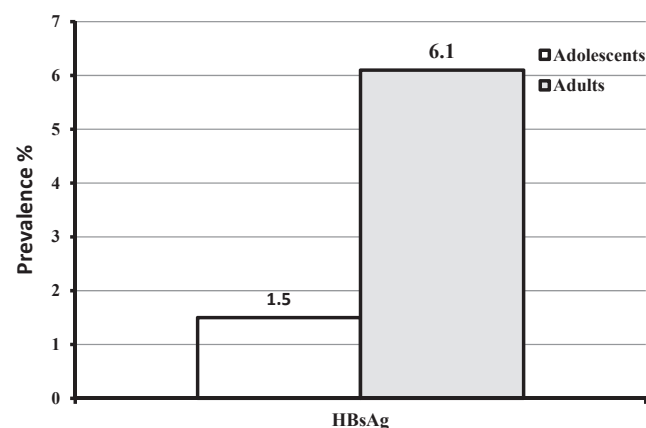


Figure 2: Seroprevalence of Hepatitis B (HBsAg) Viral Infections among the study sample of adolescents and adults in the Muhayil Aseer region of KSA.

Table 1: Distribution of the study sample of adolescents (aged 10–19 years) and adults (aged 20 years and older) in the Muhayil Aseer region, by relevant exposures and seropositivity.

Variable	Adolescents (N = 133)		Adults (N = 938)		P value
	Number	%	Number	%	
History of blood transfusion	2	1.5	30	3.2	0.283
History of surgical operations	2	1.5	43	4.6	0.109
History of tooth extraction	4	3.0	88	9.4	0.012
History of wet cupping	0	0.0	22	2.3	0.098
History of hepatitis B vaccination	86	64.7	234	24.9	0.001
HBsAg seropositive	2	1.5	57	6.1	0.015

Table 2: Multivariate analysis, adjusted Odds ratio (aOR) and antecedent 95% confidence intervals (CI) of potential risk factors determining sero-positive HBsAg in the Muhayil Aseer region of KSA.

Variable	aOR	95% CI	
		Lower	Upper
Gender: Males vs. Females	1.024	0.591	1.776
History of blood transfusion ^a : Yes vs. No	2.704	0.909	8.048
History of any surgical operation: Yes vs. No	1.652	0.605	4.514
History of tooth extraction: Yes vs. No	1.811	0.847	3.871
History of wet cupping: Yes vs. No	1.125	0.236	5.378
History of yellow eye in adulthood: Yes vs. No	1.076	0.279	4.149
History of hepatitis B vaccination^a: No vs. Yes	2.792	1.182	6.623

^a Significant (P < 0.05).

factors, the study showed that persons without the hepatitis B vaccination had more than two times the risk to become sero-positive for HBsAg (aOR = 2.792, 95% CI: 1.182–6.623). Conversely, gender, and history of other exposures were found to be of no significance in developing sero-positive HBsAg.

Discussion

Hepatitis B virus infection (HBV) is a major cause of chronic liver disease worldwide.⁷ Data from the World Health Organization (WHO) estimates the burden of HBV infection to be approximately 2 billion cases with more than 240 million known to be chronically infected.⁸ In addition, more than half a million patients worldwide die annually as a result of HBV-related liver diseases, such as decompensated liver cirrhosis, end-stage liver disease or hepatocellular carcinomas.⁹

HBV infection is endemic in KSA. A plethora of studies have been published since 1984 addressing various aspects of

the disease: its prevalence among the general population and the different age groups in the Kingdom,^{1,4,10–13} blood donors,^{14–17} health care workers,¹⁸ pregnant women,^{19–21} disease patterns,^{22,23} virus genotypes and its relation to hepatocellular carcinoma.^{24,25}

Although the general trend of HBV infection in KSA is declining,³ this infection remains a significant challenge. The Saudi Ministry of Health Statistics Year Book of 2013 reported a total of 6106 new cases of viral hepatitis of which 70% (4259) were due to HBV infection.⁵ The present study showed that there were only two adolescents (1.5%) infected with HBV, in contradistinction to 57 adults (6.1%). It is expected that adolescents would have received the HBV vaccination as part of the Saudi EPI. However, only 64.7% of adolescents in the present study reported that they were vaccinated. The two adolescents who were found to be sero-positive were among the one third who gave no history of vaccination and likely acquired their infection from either tooth extraction or surgical operations.

The low seroprevalence of HBV infection among adolescents in this study confirms the previous findings of others^{3,4} and highlights the effectiveness of vaccination in preventing HBV infection. Furthermore, the effectiveness of vaccination was also reflected in the relative high rate of HBV infection among adults (6.1%), most of who were not vaccinated and were exposed to the risk factors of acquiring the infection investigated in this study. This rate of infection among adults is higher than the range of 1.5%–2.6% reported by Memish et al., in 2010.²⁶ The assay employed in this study is capable of detecting very low quantities of HBsAg (<0.1 WHO IU/ml HbsAg), thus the sensitivity of this assay may be higher than that of earlier assays employed in previous studies and might explain the higher rate found in this study.

Although wet cupping, a common practice in KSA, was not implicated in the transmission of HBV infection in this study, it was found by Alothman and Al Ghamdi to be the only plausible risk factor for transmission of HIV to a Saudi citizen.²⁷ The equipment used for wet cupping is available as disposable off-the-shelf items in local pharmacies. Therefore, health education in such remote areas must take into consideration the local habits and practices that may play a role in HBV transmission.

Prevention of HBV infection can be achieved through a variety of actions. Advocacy and continuous efforts to raise awareness of HBV infections among the general population will help to reduce transmission in the general community and in remote areas such as Muhayil, the focus region of the present study. Strengthening efforts to keep coverage of the HBV vaccine in the EPI programs of the affected areas is also important. Implementation of strict blood safety strategies that include keeping high quality-assured screening of all donated blood and blood components used for transfusion will also help. Additionally, infection control precautions in health care settings will significantly help prevent the transmission of the infection. Similarly, safe injection practices can protect against HBV transmission.

In conclusion, the present study further highlights the effectiveness of vaccination in preventing HBV infection. However, in addition to vaccination, strict preventive measures need to be encouraged in the study area.

Study limitations

- The study was based entirely on the recall of the interviewees, and thus, there is an inherent recall bias.
- No further investigations were performed regarding other markers of HBV infection.

Author's contribution

SMA is the sole author of the article, who perceived and designed the study, while Roche Saudi Arabia provided the required funds. The author conducted the research, interpreted the results of the study and analyzed the data. He drafted the manuscript and critically revised its content and approved its final version and is responsible for the content.

Conflict of interest

The author has no conflict of interest to declare.

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References

1. Al-Faleh FZ. Changing pattern of hepatitis viral infection in Saudi Arabia in the last two decades. *Ann Saudi Med* 2003; 23(6): 367–371.
2. Al-Faleh FZ, Ayoola EA, Al-Jeffry M, Arif M, Al-Rashed RS, Ramia S. Integration of hepatitis B vaccine into the expanded program on immunization: the Saudi Arabian experience. *Ann Saudi Med* 1993; 13: 231–236.
3. Ayoola AE, Tobaigy MS, Gadour MO, Ahmed BS, Hamza MK. The decline of HBV viral infection in South-Western Saudi Arabia. *Saudi Med J* 2003; 24: 991–995.
4. Al-Faleh F, Al-Shehri B, Al-Ansai B, Al-Jaefri C, Al Mazrou Y, Shaffi A, et al. Long-term protection of hepatitis B vaccine 18 years after vaccination. *J Infect* 2008; 57: 404–409.
5. The Saudi Ministry of Health. *Health statistic year book*; 2013. Ministry of Health, Riyadh, Saudi Arabia ISSN: 1319-3229.
6. Abdo AA, Sanai FM, Al-Faleh FZ. Epidemiology of viral hepatitis in Saudi Arabia: are we off the hook? *Saudi J Gastroenterol* 2012 Nov–Dec; 18(6): 349–357.
7. Harkisoen S, Arends JE, Van Erpecum KJ, Van den Hoek A, Hoepelman AI. Hepatitis B viral load and risk of HBV-related liver disease: from East to West? *Ann Hepatol* 2012; 11: 164–171.
8. World Health Organization. *Prevention and control of viral hepatitis infection: framework for global action. WHO/HSE/PED/HIP/GHP*; 2012.
9. Ott JJ, Stevens GA, Groeger J, Wiersma ST. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. *Vaccine* 2012; 30: 2212–2219.
10. Arya SC, Ashraf SJ, Parande CM, Elsayed M, Sahay R, Ageel AR, et al. HBV virus in Jizan, Saudi Arabia. *J Med Virol* 1985; 17: 267–274.
11. El Hazmi MA. HBV markers in Saudi Arabia: a comparative study in different regions. *Ann Saudi Med* 1986; 6: 185–190.
12. Al-Faleh FZ, Ayoola EA, Arif M, Ramia S, Al-Rashed R, Al-Jeffry M, et al. Seroepidemiology of hepatitis B virus infection in Saudi Arabian children: a baseline survey for mass vaccination against hepatitis B. *J Infect* 1992; 24: 197–206.
13. Al-Faleh FZ, Al-Jeffri M, Ramia S, Al-Rashed R, Arif M, Rezeig M, et al. Seroepidemiology of hepatitis B virus infection in Saudi children 8 years after a mass hepatitis B vaccination programme. *J Infect* 1999; 38: 167–170.
14. Altamimi W, Altraif I, Elsheikh M, Alkshan A, Qasem I, et al. Prevalence of HbsAg and anti-HCV in Saudi blood donors. *Ann Saudi Med* 1988; 18(1): 60–62.
15. Shatoor AS, Zafer MH. Hepatitis B virus markers in male blood donors. *Bahrain Med Bull* 2002; 24(4): 1–17.
16. Al-Hazmi MM. Prevalence of HBV, HCV, HIV-1,2 and HTLV-I/II infections among blood donors in a teaching hospital in the Central region of Saudi Arabia. *Saudi Med J* 2004; 25(1): 26–33.
17. Bashawri LA, Fawaz NA, Ahmed MS, Qadi AA, Almawi WY. Prevalence of seromarkers of HBV and HCV among blood donors in eastern Saudi Arabia, 1998–2001. *Clin Lab Haematol* 2004; 26(3): 225–228.
18. Almuneef MA, Memish ZA, Balkhy HH, Otaibi B, Helmi M. Seroprevalence survey of varicella, measles, rubella, and hepatitis A and B viruses in a multinational healthcare workforce in Saudi Arabia. *Infect Control Hosp Epidemiol* 2006; 27(11): 1178–1183.
19. Ramia S, Abdul-Jabbar F, Bakir TM, Hossain A. Vertical transmission of hepatitis B surface antigen in Saudi Arabia. *Ann Trop Pediatr* 1984; 4: 213–216.
20. Al-Mazrou YY, Al-Jeffri M, Khalili MK, Al Ghamdi YS, Mishkhas A, Bakhsh M, et al. Screening of pregnant Saudi women for hepatitis B surface antigen. *Ann Saudi Med* 2004; 24: 265–269.
21. Alrowaily MA, Abolfotouh MA, Ferwanah MS. Hepatitis B virus sero-prevalence among pregnant females in Saudi Arabia. *Saudi J Gastroenterol* 2008; 14(2): 70–73.
22. Memish Z, Qasim L, Abed E, AlBasheer A, Aldraihim A, Alknawy B, et al. Pattern of viral hepatitis infection in a selected population from Saudi Arabia. *Mil Med* 2003; 168(7): 565–568.
23. Al-Tawfiq JA, Anani A. Profile of viral hepatitis A, B, and C in a Saudi Arabian hospital. *Med Sci Monit* 2008; 14(1): 52–56.
24. Ayoola EA, Gadour MO. Hepatocellular carcinoma in Saudi Arabia: role of hepatitis B and C infection. *J Gastroenterol Hepatol* 2004; 19(6): 665–669.
25. Abdo AA, Al Jarallah BM, Sanai FM, Hersi AS, Al Swat K, Azzam NA, et al. Hepatitis B genotypes: relation to clinical outcome in patients with chronic hepatitis B in Saudi Arabia. *World J Gastroenterol* 2006; 12: 7019–7024.
26. Memish ZA, Knawy BA, El-Saed A. Incidence trends of viral hepatitis A, B, and C seropositivity over eight years of surveillance in Saudi Arabia. *Int J Infect Dis* 2010; 14: e20–e115.
27. Allothman A, Al Ghamdi G. *Wet cupping associated with transmission of HIV infection: case report*. 16th European Congress of Clinical Microbiology and Infectious Diseases; 2006. Nice, France, April 1–4.

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