Volume 19 Issue 25
Originally issued as C1



Global Journal of Medical Research: C
Microbiology and Pathology
Volume 19 Issue 1 Version 1.0 Year 2019
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

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Abstract- The global epidemic of hepatitis B is a significant public health problem. The endemicity of HBV infection used to be believed high in Yemen. Data for prevalence of HBsAg among children in rural and urban areas in Yemen is scarce and incompetent. The study was made to determine the prevalence of HB surface antigen among children in 2 selected areas in Yemen. Eight hundred ad forty and 212 children were randomly selected from Sana'a city and Shabowah governorate respectively. Sera were tested for HBs antigen by ELISA technique and HB genome was tested for positive HB surface antigen specimens to confirm positivity using polymerase chain reaction (PCR) -based test. Each individual's data was collected in a pre-designed questionnaire including: sex, age and risk factors of HBV and prior vaccine of HBV.

Keywords: *hepatitis B virus, epidemiology, children, risk factors, yemen.*

GJMR-C Classification: *NLMC Code: QW 170*



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Prevalence and Potential Risk Factors of Hepatitis B Virus in a Sample of Children in Two Selected Areas in Yemen

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Abstract- The global epidemic of hepatitis B is a significant public health problem. The endemicity of HBV infection used to be believed high in Yemen. Data for prevalence of HBsAg among children in rural and urban areas in Yemen is scarce and incompetent. The study was made to determine the prevalence of HB surface antigen among children in 2 selected areas in Yemen. Eight hundred ad forty and 212 children were randomly selected from Sana'a city and Shabowah governorate respectively. Sera were tested for HBs antigen by ELISA technique and HB genome was tested for positive HB surface antigen specimens to confirm positivity using polymerase chain reaction (PCR) -based test. Each individual's data was collected in a pre-designed questionnaire including: sex, age and risk factors of HBV and prior vaccine of HBV.

The prevalence of HB surface antigen among children in Sana'a city was only 1.8%, and in Shabowah governorate was 3.8%. There was a significant association of non-vaccinated children, birth by cesarean, and with history of parental exposure with contracting HBV infection. Evidence from these studies in Yemen suggests that there is a steady increase in exposure to HBV over a lifetime. Hospital-acquired HBV infection is very common in Yemen, and high vaccination coverage rate should be achieved particularly in rural areas, in parallel with health education.

Keywords: hepatitis B virus, epidemiology, children, risk factors, yemen.

I. Introduction

Hepatitis B virus (HBV) infection is an important global health problem, with 2 billion people infected worldwide, and 350 million suffering from chronic HBV infection. The 10th leading cause of death worldwide, HBV infections result in 500 000 to 1.2 million deaths per year caused by chronic hepatitis, cirrhosis, and hepatocellular carcinoma; the last accounts for 320 000 deaths per year[1, 2, 3]. In developed countries, the disease is relatively rare and gained primarily in adulthood in which injection drug abuse and unprotected sex are the primary methods, whereas in Asia and most of Africa including Yemen, chronic HBV infection is common and usually acquired perinatally or in childhood[4-8]. The endemicity of infection was considered high in Yemen, where prevalence of positive HBsAg among adult's ranges from 8 % to 20 %, among infants was 4.1%, and up to 50 % of the populations generally have serological evidence of previous HBV infection in old reports[9-15]. However, recent studies reported a lower rate of HBsAg in which it ranges from 0.7-2% among general population including children [16, 17, 18]. More efficacious treatments, mass immunization programs, and safe injection techniques are essential for eliminating HBV infection and reducing global HBV-related morbidity and mortality [19]. Safe and effective vaccines against HBV infection have been available since 1982. The implementations of mass immunization programs, which have been recommended by the World Health Organization since 1991, have dramatically decreased the incidence of HBV infection among infants, children, and adolescents in many countries [1, 2]. However, not all countries have adopted these recommendations and there remains a large number of persons that were infected with HBV which including Yemen in which the coverage rate of HBV vaccine in urban was only 69.9%, [3, 17]. The main aim of this study is determine the prevalence of HB surface antigen among sample of children in 2 selected areas in Yemen and analysis potential risk factors of HBV transmission among the selected children.

II. Subjects and Methods

a) Study area

This cross-sectional sero-epidemiological study was conducted in healthy children less than 11 years of age in Sana'a city and in healthy children less than 16 years of age in Shabwah governorate Yemen. The Yemen is located on the Arabian Peninsula in Southwest Asia. It is bordered by Saudi Arabia to the north, the Red Sea to the west, the Sultanate of Oman to the east and the Arabian Sea to the south. The

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population in 2008 was estimated at 21,843,554, living in 3,058,299 households. Population structure is typical of a developing country, with the rural population comprising about 71% of the total population. The majority of the population is young, with nearly half (45%) below age 15 years, while the elderly age group (over 64 years) represents only about 3.4%. The literacy rate is about 47% among those 15 years and older (males 63%, females 31%), the total fertility rate 6.2, the average household size 7.1 persons, the poverty rate about 47%, and the annual growth rate of population 2.9%. Life expectancy at birth male/female is about 63/67 years, and the probability of dying under five years in 2012 was 160/1000 live births. These and other factors contribute to Yemen's low ranking in the Development Index cited in the World Human Development Report - 160 among the 162 countries that were rated in the year 2013[20].

Yemen introduced universal immunization against HBV for infants and high risk groups in early 2000, but feed-back on the coverage rate of vaccination and its efficacy in the community have been ignored for a long period. In addition, there has been inadequate information on the prevalence and risk determinants of viral hepatitis as well as on vaccination coverage rate among children in Yemen. The vaccines are provided by the UNICEF from different reliable sources.

b) Study populations and Sample size

This cross sectional study was carried out during 3 months, starting in January 2016 and ending in March 2016, after the approval of the Department of Medical Microbiology, in the Faculty of Medicine and Health Sciences, Sana'a University to the study proposal. A consent form was filled by the parents for each participant. The sample sizes for or study was calculated as follow: First we considered the rate of HBV in Sana'a city, difference (worst acceptable result higher or lower the true rate) and confidence interval as 2%, 0.5% and 95% respectively. According to our calculations, a sample size of at least 752 subjects was required from the population of children under 11 years in Sana'a city (639358 children) [20] which the sample will be selected; this was selected by systematic random method. All health centers and primary schools in Sana'a were listed (27 centers, 33 schools), then by simple random selection 4 of these centers and 4 of these schools were selected; finally, every 5th child admitted to these health centers for normal check and vaccination was selected (about 17% of male children and 13% of female children who refused to donate blood were excluded), and, every 5th child in the selected classes was selected (about 7% of male children and 6% of female children who refused to donate blood were excluded). Second, we considered the rate of HBV in Shabwah governorate, difference (worst acceptable result higher or lower the true rate) and confidence interval as 3%, 0.5% and 95% respectively. According to our calculations, a sample size of at least 178 subjects was required from the population of children under 16 years in Shabwah governorate (255600 children) [20] which the sample will be selected; this was selected by systematic random method. All health centers and primary schools in Atag, Bayhan and Mayfa'a in Shabwah governorate were selected (3 centers, 4 schools), then every 5th child admitted to these health centers for normal check and vaccination was selected (about 36% of male children and 39% of female children who refused to donate blood were excluded), and, every 5th child in the selected classes was selected (about 14% of male children and 9% of female children who refused to donate blood were excluded).

c) Data collection

A full history was taken from each studied individual or from parents; and the findings were recorded in a predesigned questionnaire. The data collected included name, age at the time of the study, sex, residence, status and risk factors of HBV contracting; and laboratory results.

d) Laboratory tests

Capillary blood or vein puncture of whole blood was collected; then sera were separated and tested for HB surface antigen by an Enzyme-linked Immunosorbant assay (ELISA) using a commercially available kit provided by Biokit, Spain. Specimens which proved repeatedly reactive by EIA in two separate tests were considered positive for hepatitis B surface antigen. In addition HB genome was tested for positive HB surface antigen specimens to confirm positivity using a commercial polymerase chain reaction (PCR) -based test (Taqman amplicor, Roche, USA) and all were positive.

e) Statistical analysis

Personal and clinical data were obtained from each subject and recorded into a pre- designed questionnaire, then the data were statistically analyzed by a software version for statistical significance (Epi Info version 6, CDC, Atlanta, USA). From two-by-two tables, the odds ratios were calculated and *P*-value was determined using the uncorrected chi square test. Fisher's exact test was used for the small expected cell sizes with a two-tailed probability value.

III. Results

Tables 1 and 2 outline prevalence and the odds ratio (OR) estimates by their 95% confidence intervals (95% CI), and by Fisher's exact test for cell value less than 5, for positive serological tests of hepatitis B virus and expected risk factors of contracting Hepatitis B virus, and with statistically significant *P*-value using uncorrected chi-square test. The crude seroprevalence

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among children in Sana'a city was 1.8% and it was 3.8% for children from Shabowah governorate. When the age of children was considered, the highest rate of HBV among children in Sana'a city was in age group 9-10 years (2.3%), with associated OR equal to 2.7, CI=0.3 - 25, but this result was not statistic significance (p=0.3). The lowest rate of HBV among children in Sana'a city was in age group 1-2 years (0.85%) (Table 1).

The highest rate of HBV among children in Shabwah governorate was in age group 11-15 years (5.1%), with associated OR equal to 2.4, CI=0.29-21, but this result was not statistic significance (p=0.39). The rates of HBV in Shabwah in age groups 1-5 years and 6-10 years were similar (2.1%). In conclusion there was non-significant effect of older age on contracting hepatitis B virus in both selected area children (Table 1, 2).

In the case of risk factors of hepatitis B virus infection for children in Sana'a city, there was a significant association of non vaccination to HBV vaccine (OR=4.2, CI=1.23-15.9, p=0.007), and with history of parental exposure (OR=4.05, CI=1.1-14.3, p=0.01). Also there was not significant association of birth by cesarean in which OR=3.3, CI=0.0-16, p=0.1) and birth in hospital (OR=1.27, CI=0.41-3.9, p=0.64) (Table 1). In the case of risk factors of hepatitis B virus infection for children in Shabwah governorate, it was found that there was a highly significant association of contracting HBV infection with non vaccination to HBV vaccine with significant rate equal to 5.5% (OR and CI=undefined, p=0.045), birth in hospital (OR=5.8, CI=1.01- 31.4, p=0.01) and birth by cesarean (OR=5.6, CI=0.7-38.7, p=0.02), but not significant with history of parental exposure (OR=2.24, CI=0.5 -11, p=0.25) (Table 2).

Table 1: Prevalence of HB surface antigen in different age groups and risk factor analysis of HBV in a sample of children under 10 years old, in Sana'a city, Yemen Factors

Age groups	HB S Ag positive		*OR*	*CI*	*P value*
	No.	%			
1-2 years (n=119) Reference	1	0.85			
3-5 years (n=274)	5	1.8	2.1	0.25-18.9	0.46
6-8 years (n=273)	5	1.8	2.2	0.25-19	0.46
9-10 years (n=174)	4	2.3	2.7	0.3- 25	0.3
Total (n=840)	15	1.8			
Factors					
Vaccinated to HBV Yes (n=504) Reference	4	0.79			
No (n=336)	11	3.3	4.2	1.23-15.9	0.007
Birth in hospital (n=334)	7	2	1.27	0.41-3.9	0.64
No (n= 506) Reference	8	1.6			
Birth by cesarean Yes (n=39)	2	5.1	3.3	0-16	0.1
No (n= 801) Reference	13	1.6			
Parental exposure Yes (n=72)	4	5.6	4.05	1.1-14.3	0.01
No (n= 768) Reference	11	1.4			

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Table 2: Prevalence of HB surface antigen in different age groups and risk factor analysis of HBV in a sample of children under 15 years old, in Shabowah governorate, Yemen Factors

Age groups	HB S Ag positive		*OR*	*CI*	*P value*
	No.	%			
1-5 years (n=47) Reference	1	2.1			
6-10 years (n=48)	1	2.1	0.97	0.05-16.1	0.98
11-15 years (n=117)	6	5.1	2.4	0.29- 21	0.39
Total (n=212)	8	3.8			
Factors					
Vaccinated to HBV Yes (n=69) Reference	0	0			
No (n=143)	8	5.5	Undefined		0.045
Birth in hospital Yes (n=22)	3	13.6	5.8	1.01-31.4	0.01
No (n=190) Reference	5	2.6			
Birth by cesarean Yes (n=13)	2	15.4	5.6	0.7-38.7	0.02
No (n= 199) Reference	6	3			
Parental exposure Yes (n=67)	4	6	2.24	0.5-11	0.25
No (n= 145) Reference	4	2.8			

IV. Discussion

The prevalence rate of HB surface antigen in our study was variants among selected healthy children in the two selected areas these differences in the prevalence rates might be the geographical differences and the national immunization programmes vaccination coverage in the capital city of Sana'a (high) and urban area of Shabowah (low) and or related to the differences in the classification of age groups. The prevalence rate in our study in Sana'a city was 1.8%, is lower than that reported among infants in Sana'a city previously where the rate was 4.1% but the rate in Shabwah (3.8%) is roughly similar to that reported previously in Sana'a city among infants [10]. Although it is difficult to compare the prevalence rates reported in our study (among children), with that reported by Al-Shamahy *et al*. [10, 11] (among children and mothers and among blood donors etc), it seems that the rate of HBsAg has decreased dramatically. Introducing hepatitis B vaccine within the national immunization programmes improvement of the people's knowledge about hepatitis risk factors through educational programmes, and the availability of measures to diagnose hepatitis in health centers and blood banks might explain this decrease [16,18, 21].

The rates of HBV in our study was higher than that reported in Northern, Western, and central Europe, North America, and Australia, children and general population where the rates of HBV surface antigen was ranged from 0.2-0.5%, [22]. In other hand the crude rate of HBV surface antigen in our study was similar to that reported in Eastern Europe, the Mediterranean, Russia and the Russian Federation, Southwest Asia, Central and South America among children general population where the rates of HBV surface antigen was ranged from 2 -7 %, [23], but lower than that reported in Parts of China, Southeast Asia, and tropical Africa among general population where the rates of HBV surface antigen was ranged from 8-20%[22]. These differences in the prevalence rates might be explained by the geographical differences in the availability of services and vaccination programmers.

Many other studies in nearby countries have shown a lower prevalence of hepatitis B among children, as Saudi Arabia (0.05%) [24], This may be because the good availability of services and vaccination programmers in Saudi Arabia and there is insufficient protection for patient children admitted to hospitals in Yemen, since sterilization, disinfection and general standards of training and proficiency are generally lacking in most hospitals in Yemen.

HBV infection effects all ages everywhere[22-26]. There was slightly trend toward increased levels of HB surface antigen with the older children where prevalence rate is ranged from 0.84% in 1-2 years group to 2.3% in 6-8 years group in Sana'a city and this trend toward increased levels of HB surface antigen with the older children is more clear in Shabowah governorate where the rate is ranged from 2.1% in 1-5 years old to 5.1% in 11-15 years group (tables 1, 2). The increasing of prevalence rate with increasing age in our study could indicate an accumulation risk of infection over time. In addition, the results indicated that horizontal spread of HBV may be of greater importance than vertical transmission.

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The study illustrates that children in Yemen mainly in rural areas as Shabowah governorate are at a high risk of becoming infected in their early years. The first risk for infection occurs in the first few days spent in hospitals during normal delivery (OR=5.84, p=0.01) or by cesarean section (OR=5.6, p=0.02), and this confirms that use of unsterilized or inadequately sterilized contaminated instruments are a possible route of infection. It is possible that there was insufficient protection for children admitted to hospitals in Yemen. Sterilization, disinfection and general standards of training and proficiency are generally deficient in most hospitals in Yemen particularly in rural areas.

The rate of HBV infection was higher in Shabowah area (3.8%) than in Sana'a city this regional variation might be due to non-uniformities in immunization and engagement in risky behaviors across different sites. Also our study shows the important of HBV vaccine in prevent infections (table 1,2) in which higher risk of contracting HBV infection among non-vaccinated children and more HBs Ag-positive cases were from unvaccinated children and rural area suggesting of poorer vaccination coverage of the rural population.

Evidence from these studies in Yemen suggests that there is a steady increase in exposure to HBV over a lifetime. Hospital-acquired HBV infection is very common in Yemen, and prevention is eventually possible by applying standard policies of sterilization, disinfection and personal training to implement this policy and guarantee refinements in the screening of blood donors. In Yemen, vaccination should be considered for all children and programs to immunize all newborn Babies with a goal of 80% coverage or more should be performed in the next 2 to 4 years particularly in rural areas, in the same with health education.

V. Conclusion

There was a significant association of non-vaccinated children, birth by cesarean, and with history of parental exposure with contracting HBV infection. Evidence from these studies in Yemen suggests that there is a steady increase in exposure to HBV over a lifetime. Hospital-acquired HBV infection is very common in Yemen, and high vaccination coverage rate should be achieved particularly in rural areas, in parallel with health education.

Acknowledgments

The authors would like to acknowledge, Sana'a University and the National Center of Public Health Laboratories (NCPHL) Sana'a, Yemen for support and provided working space and materials.

Conflict of Interest

"No conflict of interest associated with this work".

Author's Contribution

This research work is part of 2 M.Sc. thesis. The candidates are the fourth and fifth authors (BBMA) who conducted the field works and the experiments and wrote up the thesis. The corresponding author (HAA) supervised the experimental work, revised and edited the thesis draft and the manuscript. (BMJ) and (AGA) were co-advisor of the works, and helped in supervised the experimental work, revised and edited the thesis draft and the manuscript.

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