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Uleanya ND
Obidike EO

Prevalence and risk factors of hepatitis B virus transmission among children in Enugu, Nigeria

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Uleanya ND (✉)
Department of Pediatrics,
Enugu State University Teaching Hospital, Enugu. Nigeria.
P. O. Box 9225,
Enugu. Nigeria.
Email: nulesa2001@yahoo.com

Obidike EO
Department of Pediatrics,
University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu. Nigeria.

Abstract*: Background:* Hepatitis B Virus (HBV) infection has reached pandemic proportions all over the world with areas of highest prevalence being the sub-Saharan Africa and Southeast Asia. Most deaths related to HBV are due to complications from chronic infection. Acquisition of infection at a younger age is the most important predictor of chronicity. Eradication of HBV is an important but difficult tasks facing public health. HB immunization is the single most important factor in hepatitis B control and was commenced in 2004 in Nigeria.
Objectives: To determine the prevalence of Hepatitis B surface antigen (HBsAg) among children in the era of HB immunization, the risk factors of transmission and knowledge of mothers about their HB status.
Methods: A cross sectional study carried out on one hundred and forty children aged 18 months to 15 years at the children outpatient clinic (CHOP) of the University of Nigeria Teaching Hospital, Ituku. Hepatitis B surface antigen (HBsAg) was determined using Determine Test Kits and a structured interviewer administered questionnaire administered.
Results: Six were positive for HBsAg, giving a prevalence rate of 4.3%. HBsAg was least prevalent among children 1-5 years (2%). None of the children ≤ 5 years who received HB vaccination was positive for HBsAg though one child > 5 years who received the vaccine was positive. Sharing of toothbrushes among siblings was found to be a significantly associated risk factor. Only 6.4% of mothers knew their hepatitis B status.
Conclusion: There is a gradual fall in the prevalence of HBsAg in our environment due to HB immunization. Sharing of toothbrushes may be a potent means of transmission of HBV infection.

Keywords: HBV, Prevalence, Children, Transmission, HB immunization

Introduction

Hepatitis B Virus (HBV) is a ubiquitous partially double stranded DNA virus with areas of highest prevalence being the sub-Saharan Africa, South-East Asia, the Amazon basin, Alaska, Northern Canada, Eastern Europe, Greenland, parts of the Middle East, China, and parts of Pacific Islands[1]. The infectious virus consists of an outer envelope – HBsAg, the first seromarker and one of the most useful markers of active or chronic hepatitis B infection, and an inner core made up of Hepatitis B core Antigen (HBcAg), found in acute or chronic infections and the e-antigen (HBeAg), which serves as a marker of active viral replication[2,3,4,5]. An estimated 2 billion people have been infected with HBV, with 350-400 million of them remaining chronic carriers worldwide[6,7]. It has also been estimated that 25 - 30% of the chronic carriers will die of the sequelae[8,9]. In Africa, the number of HBV carriers is estimated to be about 50 million representing about 10-20% of the general population and as many as 12.5 million will eventually die due to complications from hepatitis B – chronic hepatitis, cirrhosis and hepatocellular carcinoma (HCC)[8,9]. Annual mortality directly related to hepatitis B liver disease and cancer worldwide has been between 600,000 -1 million[1].

Younger age at acquisition of infection continues to be the most important predictor of chronic carriage and those who develop chronic hepatitis B have a 15 - 40 % risk of developing the complications[4,6] this chronicity being due to their immature immune system. More than 95% of adults spontaneously recover from an acute HBV infection as defined by clearance of the HBsAg from the blood, an effect that reflects the host's degree of immune response[4,10]. Transmission occurs when infected blood or body fluid from an infected person enters the body of another who is not immune[1,11]. Africans who are carriers of HBV are infected in early childhood, predominantly by horizontal transmission[8,9]. Vertical

transmission contributes 5-15% - (occurring more in those with high viral load and actively replicating virus) [8]. However, for unknown reasons, probably genetic, HBeAg positivity rates are much lower in African women of childbearing age[8,9].

The eradication of HBV is one of the most important but difficult tasks facing public health in Nigeria. This maybe due to ignorance, about the infectivity (including mechanisms of transmission) and the dire consequences of HBV infection in children. This most probably, being because the infections are asymptomatic and the sequalae are long. It may also be from the poor immunization coverage in Nigeria. As at 2010, the national immunization coverage was 69% using DPT_3 coverage[12]. There are three major methods of controlling HBV infection. The first is immunization, which is the single most important factor in hepatitis B control, has the potential of eradicating hepatitis B and studies have confirmed protection following vaccination in both industrialized and non-industrialized communities[7,8,13]. It's incorporation into National immunization programme is designed to reduce the risk of early childhood acquisition of HBV thereby reducing the number of chronic carriers in endemic populations and has the advantage of accessing infants through pre-existing vaccine delivery systems and vaccinating individuals prior to their engaging in high risk behaviours[14,15]. Next is the use of antiviral drugs such as lamivudine, tenofovir, ribavirin etc. Then the immunostimulatory therapy with α-interferon and pegylated α-interferon[7]. Other adjuncts include continued screening of pregnant mothers for HBsAg to prevent vertical transmission, post exposure prophylaxis using hyperimmune globin within 24 hours or at most 7 days following exposure[14], and massive and sustained public health education on the various avoidable modes of transmission of HBV and available preventive measures.

The universal HB immunization was commenced in Nigeria in 2004 as other major modalities are almost nonexistent. Hence mass vaccination in a large scale ought to become imperative as this will decrease the reservoir of chronic carriers. HB immunization coverage in Nigeria in 2010 was 66%[12]. Some previous studies between 1983-2005 have reported prevalence rates of 6.5-7.6% in Enugu and the environs when HB immunization was nonexistent[16,17,18]. This study was therefore undertaken to determine the prevalence of HBsAg among children in this era of HB immunization, the remote risk factors of HBV transmission in our environment and knowledge of mothers about their HB status.

Methods

The study was carried out at the Children Outpatient clinic of the University of Nigeria Teaching Hospital, a tertiary medical institution in Enugu. It was cross sectional, recruiting consecutively 140 children who attended the clinic with minor illnesses such as upper respiratory tract infections, malaria etc. from July to December 2010. Inclusion criteria were ages 18 months to 15 years and those whose parent (s) gave informed consent while all children less than 18 months or above 15 years of age as well as those whose parents refused to consent despite due education on the need for the study were excluded.

Ethical clearance was obtained from the University of Nigeria Teaching Hospital Health Research and Ethics committee. Informed consent – both verbal and written, were obtained from the child and/or the parent (s). They were duly educated on the need for, and benefits of the study, the specimen to be collected and how it was to be collected. A structured interviewer administered questionnaire was designed for the study. Information sought included biodata, occupational and educational status of both parents – for the determination of socioeconomic class, risk factors for HBV infection including previous history of blood transfusion, history of scarification, tattooing, ear piercing, circumcision, use of contaminated needles and syringes for injection (either used or reused needle or syringe was considered as contaminated), intravenous drug use, histories of sex (where necessary), bites by other children, and sharing of tooth brush. Others were child immunization status and knowledge of maternal immunization status. The immunization cards of all those who received the vaccine were demanded and verified.

Assay for HBsAg was done using Abbott Determine HBsAg test kits - an enzyme immunoassay (specificity of 99.85% and a sensitivity of 94.64%). The test was then read after a waiting interval of 15 minutes to 24 hours (as specified by the manufacturer).
The data were analyzed using SPSS version 19. Measures of central tendency – the mean were used to summarize quantitative variables where applicable. Frequency tables were constructed as appropriate. Chi square analysis for non-continuous variables with *p* value at the level of < 0.05 as significant was also done. Odds ratios for the risk factors were calculated. Socioeconomic class was determined using the method proposed by Oyedeji.[19]

Results

The age and sex distribution of the study population is as shown in Table 1. The mean age of the children was 7.27 ± 3.6 years. There were 74 males and 66 females with a male to female ratio of 1.1: 1. The majority of the children 62 [44.3%] were in the age range of 6-10 years. The least represented age range was 11-15 years – 28 (20%).Their socioeconomic class is also as shown in Table 1. Most of the subjects were in the lower class.
Among the 140 children, 6 were positive for HBsAg, giving a prevalence rate of 4.3%. Of the 6 HBsAg positive children, 5 belonged to the lower socioeconomic class while one belonged to the middle class. Three of the males and 3 of the females were positive for HBsAg

giving a prevalence rate of 4.1% and 4.5% respectively. The observed differences in the prevalence rates between males and females were not of statistical significance. The least prevalence was also observed among children 1-5 years (2%) while the highest prevalence of HBsAg was observed among those aged 6-10 years (6.5%) [C2 = 1.4 $-X^2$ =1.4, p = 0.5]. Table 2.

Table 1: Socio-demographic characteristics of the study subjects

Age Range	Number (%)
1-5	50 (35.7)
6-10	62 (44.3)
11-15	28 (20.0)
Gender	
Male	74 (52.9)
Female	66 (47.1)
Social class	
Upper class	31 (22.1)
Middle class	43 (30.7)
Lower class	66 (47.1)

* The lowest age in this study was 18 months

Table 2: Showing age prevalence of HBsAg

Age range (Years)	HBsAg Positive N (%)	Status Negative N (%)
1-5	1 (2.0)	49 (98.0)
6-10	4 (6.5)	58 (93.5)
11-15	1 (3.6)	27 (96.4)

Among the 50 children who were 5 years or less, 45 (90%) received HB immunization while the remaining 5 (10%) could not recall whether or not they received the vaccine. Thirty six (40%) children out of the 90 who were more than 5 years old received the immunization, 25 (27.8%) said they did not receive the immunization, 29 (32.2%) could not recall receiving the immunization. None of the children ≤ 5 years who had received HB immunization was positive for HBsAg. However, one (2.8%) child > 5 years who claimed (immunization not verified as subject has no card) to have received HB immunization was HBsAg positive. Table 3.

Among the children studied, whether HBsAg positive or negative, none was involved with intravenous drug abuse or unprotected sex. However, all had received intramuscular injections for one reason or the other as is depicted in Table 4.

Fifteen (10.7%), used contaminated needle/syringe. Seventeen (12.1%) had a past history of blood transfusion, 20 (14.3%) had scarification marks, 1(0.7%) had a tattoo, 75 (53.6%) were circumcised, 63 (45%) had ear piercing, 37 (26.4%) shared toothbrushes at one time or the other with other siblings (C_2 = 5.22 $-X^2$ =5.22, p = 0.04) and 55 (39.3%) had been bitten by other children at one time or the other. However, the odds ratio of the risk of transmission of HBV through these risk factors is as shown in table 4.

Among the mothers of these children, only nine (6.4%) knew their hepatitis B status. Of these seven were negative for HBsAg while 2 were positive. None of the children of the positive mothers were positive for HBsAg.

Table 3: Showing the distribution of HBsAg among immunized children

Age (Years)	Number of immunized children	HBsAg Positive N (%)	Status Negative N (%)
≤ 5	45	0 (0.0)	45 (100.0)
≥ 5	36	1 (2.8)	35 (97.2)

Table 4: Risk factors of HBV and their relative risk of positivity among the subjects

Risk factor	Total sample	HBsAg positive N (%)	χ^2	p	OR
Blood transfusion					
Present	17	1 (5.9)	0.12	0.55	1.5
Absent	123	5 (4.1)			
Scarification mark					
Present	20	2 (10.0)	1.86	0.20	3.2
Absent	120	4 (3.3)			
Tattooing					
Present	1	0 (0.0)	-	-	-
Absent	139	6 (4.3)			
Circumcision					
Present	75	3 (4.0)	0.04	1.00	0.9
Absent	65	3 (4.6)			
Intravenous drug use					
Absent	140	6 (4.3)	-	-	-
Contaminated syringe/needle					
Present	15	0 (0.0)	-	-	-
Absent	125	6 (4.8)			
Ear piercing					
Present	63	3 (4.8)	0.06	1.00	1.2
Absent	77	3 (3.9)			
Sharing of toothbrush					
Present	37	4 (10.8)	5.22	0.04	6.1
Absent	103	2 (1.9)			
Bitten by playmates					
Present	55	4 (7.3)	2.04	0.21	0.3
Absent	85	2 (2.4)			
Unprotected sex					
Absent	140	6 (4.3)	-	-	-

Discussion

This study has demonstrated an HBsAg prevalence rate of 4.3%. This is lower than the 6.6% recorded in this center five years earlier[16]. It therefore demonstrates the gradual fall in HBsAg prevalence among children in our environment as a result of HB immunization. It is also lower than the 7.6% reported by Chukwuka *et al*[17] in Nnewi and 10.7% recorded by Jibrin, *et al*[2] in Sokoto at the same time as this study. Earlier studies have also documented higher prevalence of HBV in Northern Nigeria than Enugu – 9.4% by Ashir, *et al*,[20] 44.7% by Bukbuk *et al*[21]. This reduction in HBsAg rates call for strengthening of routine immunization and sustained efforts in all parts of Nigeria, to reduce significantly the hyperendemicity of HBV.

The highest prevalence of HBsAg positivity was found in those children aged 6-10 years. This high prevalence

of HBsAg positivity in this age group agrees with other studies in Enugu.[16,18]This may be because at this age most children are very active and exploring their world. However, it differs with the observations by Jibrin[2]and Alikor[22] who found highest prevalence rate among children 11-15 years. The difference in age group of prevalence may be because of increase in other high risk behaviors including unprotected sexual habits among children of this age group, Port Harcourt being a seaport and more cosmopolitan. Komas, *et al*[23]had noted higher prevalence of HBV markers among adolescents and young adults in Bangui, who did not use condom and also those having more than one sexual partner. It may also be as a result of the inability of these children to lose the surface antigen due to impaired immunity.

In this study, zero prevalence was observed in the age group 18 months -3 years, which may imply that vertical transmission of HBV has remained low in Nigerian women. This prevalence rate in this age group may further highlight the effectiveness of HB vaccine in an endemic area like ours. Considering that Emechebe[16]documented a prevalence rate of 5.6% among children 2-5 years in this centre 5 years earlier, this study's 2% among same age range may be due to vaccine efficacy. An increasing prevalence of HBsAg with age was also observed in this study. Other studies have also noted a similar trend.[2,16,22] This pattern still shows the predominance of horizontal transmission of HBV infection in our environment. A slightly higher prevalence of HBsAg was observed among the females. Though the prevalence rates observed in this study are lower, it is at variance with the finding in Enugu earlier,[16] in Port Harcourt[22] and in Borno[21] who observed a higher prevalence among males.

The social class of the parents in this study was not significantly associated with HBsAg positivity. This may be because of equal exposure to the risk factors of HBV among children of different social classes. However, in this study it was observed that the higher the social class, the lower the number of children positive to HBsAg. This could be because people in the lower socioeconomic class are more likely to indulge in activities that may promote infection with HBV such as alternative medicine, share sharp objects and toothbrushes. This is similar to the findings of Komas,[23] and Emechebe.[16]

In 2004, the universal HB immunization was commenced in Nigeria though it was incorporated into the National Programme of Immunization (NPI) in 1995. The total sum of vaccinated children in this study who were sure of their immunization was 81. Only one was positive for surface antigen. If actually this subject received complete doses of the vaccine, it may point to the fact that it is not 100% effective in preventing HBV infection. This prevalence of 1.2% is comparable to that observed by Odusanya, *et al*.[13] Not minding this finding, with such a level of vaccine efficacy it is likely to impact positively and prevent or reduce the transmission of hepatitis B infection in the community.

This study also revealed a very poor knowledge of hepatitis B among the mothers. That only 6.4% knew their HB status is worrying and reflects the poor general knowledge and attitude towards hepatitis B. The implication is the hyperendemicity of this deadly disease in Nigeria. This calls for massive public health enlightenment campaign just like in HIV/AIDS to curb this disease. In developing countries like Nigeria, intravenous drug use is not yet common among children. However, exposure to repeated injections sometimes with contaminated therapeutic injection equipment, probably due to ignorance, parental preferences, or lack of awareness of infection control practices and resources for sterilization, are very common.[24]The zero prevalence in this study among the risk factors of tattooing and contaminated needle/syringe may have been as a result of the small sample size involved. Also although not statistically significant as risk factors, but as has been documented previously blood transfusion and scarification marks have odd ratios of 1.5 and 3.2 respectively, making them potent risk factors. [24] Al-Fawaz[25]had adduced that even an HBsAg free blood obtained by the very sensitive 3rd generation screening techniques can not completely safeguard against HBV. This is true of occult hepatitis B in which there is presence of HBV DNA in the liver in the absence or undetectable serum HBsAg and measurable or immeasurable serum HBV DNA.[26]Also, it had been noted that history of blood transfusion was a sufficient risk factor for chronic hepatitis B infection, a major etiologic factor for primary hepatocellular carcinoma in Africa.[27]

Sharing of toothbrush among siblings/household members was found to be statistically significant while bite by playmates was not. The alkaline nature of the saliva may have been contributory in hindering transmission through bite. However, an intraoral trauma during brushing could be the source of transmission. Also the chance of transmitting the virus through this route is likely to be substantial given the fact that such sharing is likely to occur over prolonged periods. This finding is similar to that by Nwokediuko.[24]

Conclusion

There is a gradual fall in the prevalence of hepatitis B surface antigen in our environment possibly due to HB immunization. The vaccine may also not be 100% protective. Sharing of toothbrush was found to be a significantly associated mode of transmission of HBV infection. There is a very poor knowledge of HBV among our people.

Author's contribution
UND: Conceived the study, developed the research question, and designed the questionnaire, literature review, data collection, directed data analysis, manuscript writing and general coordination.
OEO: Co-designed the questionnaire, directed data analysis and manuscript writing
Conflict Interest: None
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