Risk factors and seroprevalence of hepatitis B surface antigenemia in mothers and their preschool age children in Ilorin, Nigeria

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Background: The transmission of the hepatitis B virus is parenteral, sexual and perinatal. Fulminant hepatitis occurs in 1% of cases of symptomatic acute hepatitis, and the main problem of hepatitis B viral infection is its chronicity, as defined by hepatitis B surface antigen carriage for more than 6 months. **Objective:** A descriptive seroepidemiological study of hepatitis B virus and its associated risk factors has been conducted among mothers and their child of preschool age attending the WELL CHILD Clinic of the University of Ilorin Teaching Hospital and the Immunization Clinic of the Children Specialist Hospital, Ilorin, Nigeria. **Materials & methods:** Sera of 70 mother and child pairs were subjected to enzyme-linked immunosorbent assay for the detection of surface antigen of hepatitis B virus. **Results:** Prevalence rates of 5.7 and 10% were obtained for surface antigen of hepatitis B virus in mothers and children respectively. The highest surface antigen of hepatitis B virus prevalence rate recorded was 2.9% for children who were aged 2–4 years, while the lowest prevalence rate recorded was 1.4% for those aged less than 1 year. **Conclusions:** Blood transfusion and mode of delivery appeared to be the most significant risk factors contributing to the transmission of hepatitis B virus among these subjects. All four mothers who were positive for the surface antigen of hepatitis B virus had positive children for this marker.

Hepatitis B virus (HBV) infection and its chronic sequela have become significant in our environment, most importantly, owing to the higher mortality rate associated with liver cirrhosis and hepatocellular carcinoma. The WHO have estimated that more than 2 billion people have been infected with HBV (including 350 million chronically infected). Each year, approximately 1 million people die as a result of HBV infection and over 4 million new acute clinical cases occur [1]. In countries where HBV is highly endemic (hepatitis B surface antigen [HBsAg] prevalence rate of 8% or higher), most infections occur during infancy and early childhood. Infection occurs commonly in all age groups, although the high rate of chronic infection is primarily maintained by transmission during infancy and early childhood. Where endemicity is low (HBsAg prevalence rate of below 2%), infections occur in young adults, especially those belonging to known risk groups [2]. Nigeria is highly endemic. The most common circumstances that lead to HBV infection in this population have not been fully elucidated.

A preliminary survey of HBV infection in children and adults in northern Nigerian reported that the exposure rate to HBV (frequency of HBeAg and anti-HBs) ranged from 59% in children aged under 5 years to 72.5 in adults aged over 30 years, while the frequency of HBsAg alone was 40 and 10%, respectively [3].

In all epidemiological studies, age has always proved to be the most important factor. The age of acquiring infection is the major determinant of the incidence and prevalence rates [4]. In many cases, the route of transmission is obscure. The presence of HBsAg in maternal milk would suggest that breastfeeding might be an important route. Mastication of food by mothers before feeding to infants is common in some cultures and might lead to infection of infants in this population.

In areas with high HBV endemicity, perinatal is the main route of transmission. Perinatal transmission is common, especially when HBV-infected mothers are also HBeAg-positive. The rate of transmission from HBsAg-positive, HBeAg-positive mothers is more than 70%, while from HBsAg-positive, HBeAg negative mothers, it is less than 10% [5].

In the past, recipients of blood products were at high risk. In countries where pretransfusion screening of blood for HBsAg is required, and where pooled blood clotting factors (especially antihemophilic factor) are processed to destroy the virus, this risk has been virtually eliminated;

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Table 1. Relationship between age of children and hepatitis B virus transmission.

HBsAg	Age (years)						Total
	<1	*1*	*2*	*3*	*4*	*5*	
Positive	0 (0%)	1 (1.4%)	2 (2.9%)	2 (2.9%)	2 (2.9%)	0 (0%)	7 (10.0%)
Negative	3 (4.3%)	16 (22.9%)	20 (28.6%)	13 (18.6%)	9 (12.9%)	2 (2.9%)	63 (90.0%)
Total	3	17	22	15	11	2	70

df = 5; x^2 = 0.863; p < 0.05. Statistically, there is no significant difference in the ages of the children and their HBsAg-positivity status.
HBsAg: Hepatitis B virus surface antigen.

however, it is still present in many developing countries. Contaminated and inadequately sterilized syringes and needles have resulted in outbreaks of hepatitis B among patients. This has been a major mode of transmission worldwide [6]. Direct percutaneous inoculation of virus by needles can occur with contaminated blood or blood products, hemodialysis, tattoing, ear piercing, acupuncture, sharing needles during illicit drug use or accidental needle sticks by hospital personnel. Since HBV is quite stable, transmission can be expected by means of environmental surfaces that may contact mucous membranes or open skin breaks, such as tooth brushes, baby bottles, toys, eating utensils, razors, hospital equipment, such as respirators or endoscopes, or laboratory glasswares and instruments.

The most important routes of transmission in the USA are undoubtedly by percutaneous transfer and probably mucous membrane contact of blood and possibly other body fluids (e.g., saliva) and by heterosexual and homosexual sexual intercourse. The report of transmission by the bite of an infected patient is consistent with the presence of HBV in saliva [7].

Experimental infection with chimpanzees suggests that oral infection takes place through small breaks in the oral mucosa. Cases of apparent direct transmission from HBV-infected to susceptible individuals after sexual intercourse have been reported.

Even in countries with low HBV endemicity, a high proportion of chronic infections may be acquired during childhood since the development of chronic infection is age dependent. Most of these infections would be prevented by perinatal vaccination against hepatitis B of all newborns or infants [1]. Serological evidence of previous infections may vary depending on age and socioeconomic class. Exposure to HBV may be common in certain high-risk groups, including injecting drug users, heterosexuals with multiple partners, men who have sex with men, household contacts and sex partners of HBV-infected persons, healthcare and public safety workers who have exposure to blood in the workplace, clients and staff in institutions for the developmentally disabled, hemodialysis patients and prisoners [8].

Therefore, this study was aimed at finding the seroprevalence of HBV and the associated risk factors among mothers and children of preschool age attending the Well Child Clinic of the University of Ilorin Teaching Hospital and the immunization clinic of the Children Specialist Hospital, Ilorin, Nigeria.

Materials & method

Subjects & samples

In total, 70 preschool-age children aged between less than 1 and 5 years attending the WELL CHILD Clinic in the University of Ilorin Teaching

Table 2. Relationship between gender and hepatitis B virus transmission in children.

HBsAg	Male	Female	Total
Positive	5	2	7
Negative	33	30	63
Total	38	32	70

df = 1; x^2 = 0. 337; p < 0.05.
There is statistically no significant difference in child's gender and hepatitus B virus transmission.
HBsAg: Surface antigen of Hepatitis B virus.

Hospital and the Children Specialist Hospital (Centre Igboro) in Ilorin, Nigeria, West African and their mothers were randomly recruited in the company of other relatives. Those aged over 5 years were exempt from this study. All subjects were HIV-seronegative according to their clinical history and the child's gender ration used in this study was 1:1 for males and females, respectively. Serum samples were obtained from mothers and their children by venepuncture and stored frozen in aliquots at -20°C.

Epidemiological characteristic collection

Subjects were verbally informed of the study and a questionnaire was used to obtain demographic information, such as age, sex and social lifestyle, that would shed light on possible modes of transmission of HBV or risk factors, such as history of previous blood transfusion, history of circumcision, history of jaundice, history of use of unsterile needles, child's mode of delivery, history of HBV vaccination and history of scarification (tribal marks).

Assays

HBsAg was detected using third-generation enzyme linked immunosorbent assay (ELISA) kit (Orthodiagnostics Raritan). A repeat ELISA test was performed on each positive HBsAg sample, in order to eliminate false positivity after carrying out a neutralization test for each positive test sample detected. Results were finally regarded as positive after a repeat positive ELISA test.

Statistical analysis

The results were subjected to statistical analysis using EPI-Info version 6 software package. The critical level for statistical significant was set at 5% confidence level using the chi-square analysis. Results were presented in bar charts. Cross tabulations of variables were performed to determine burden of risks.

Results

The age distribution of children as a determinant in the time of exposure to HBV infection is shown in **Table 1**. Of the 70 respondents, the study revealed that children aged 1 year or less had 5.9% positivity for HBsAg, aged 2 years had 9.1% positivity, aged 3 years had 13.3% positivity, aged 4 years had 18.2% positivity, while aged 5 years had no positivity. These differences are not statistically significant ($p > 0.05$).

Of the 70 children enrolled for the study, seven (10.0%) were positive for HBsAg, while 63 (90.0%) were negative. On the basis of the sex of the children screened for HBsAg, of the seven positive respondents, five were males and two were females. This difference is not statistically significant ($p > 0.05$) (**Table 2**). It is of interest to note in this study that four mother and child pairs were found to be positive for HBsAg, while three children were positive for HBsAg despite the negative status of their mothers. The prevalences rates and the possible mode of transmission and are shown in **Tables 3 & 4**.

All of the mothers positive for HBsAg (100%) had a previous history of use of unsterile needles; 75% of them had history of circumcision; 50% of them had been previously transfused; another 50% had history of scarification and 25% of them had a history of jaundice. None of the mothers had received vaccination against HBV.

Conversely, 57.1% of children positive for HBsAg had a history of circumcision; 42.9% had been previously transfused; 14.3% had history of scarification; and 14.3% had been vaccinated against HBV. None of the children positive for HBsAg had a history of jaundice or previous use of unsterile needles.

Considering the child's mode of delivery, of the seven positive children for HBsAg, five had a normal delivery, while two were delivered by caesarian operation. The difference is statistically significant ($p < 0.05$) (**Table 5**).

Discussion

Chronic HBV infection has become the leading cause of liver cirrhosis and hepatocellular carcinoma in North America, Southern Europe and Japan [9]. In Asia and sub-Saharan Africa, HBV infection is endemic and thought to be the main etiological factor in over 75% of chronic liver disease [10]. The results from this present study in Ilorin, Nigeria, revealed that 10% of children were HBsAg positive, with children aged 5 years having the least prevalence (0%), while those children between the ages of 2 and 4 years having the highest prevalence (2.9%), and those aged 1 year having a prevalence of 1.4%. The detection of HBsAg in the serum of 10% of children aged 1–4 years is an indication of early exposure to HBV. Neonatal transmission is a possibility to be considered, especially in those aged 1 year. Neonatal transmission from chronic carrier mothers and mothers with acute hepatitis B in the third trimester or first 2 months postpartum

Table 3. Prevalence of HBsAg in relation to mother and child status.

HBsAg (n = 4)	Mother positive	Mother negative
Children positive	4 (100%)	3 (75.0%)
Children negative	0 (0%)	0 (0%)

HBsAg: Hepatitis B surface antigenemia.

have been clearly documented in the USA and highly endemic populations, and such, infected infants commonly develop persistent infections [7].

This study revealed a nonsignificant association between the sex of the children and HBV transmission. This finding has been confirmed by Lesi and colleagues, who used sex as a risk factor in chronic liver disease [11]. Four mother and child pairs were found to be positive for HBsAg in this study. The risk factors associated with these mother and child pairs are: history of previous blood transfusion, history of circumcision, previous HBV vaccination and history of scarification. Such prevalence and concordance rate in the mother and child pairs is similar to the findings of Chalkravati and colleagues, who investigated perinatal transmission of HBV [12]. There are reports that demonstrated that many infants of mothers who are chronic carriers but escape perinatal infection become infected in the first few months of life, probably by contact with their infected mothers or siblings [1]. However, three (4.1%) children were positive for HBsAg despite the negative status of their mothers. Risk factors for transmission of HBV infection in this group might possibly be via blood transfusion or from other siblings, since they all have history of exposure to other associated risk factors considered in this study. In this cohort, the ages of the mothers were not considered.

Regarding the risk factors associated with HBV transmission in this study, the highest figure of 100% was obtained from mothers with a past history of unsterile needle use for injection was quite significant. This finding agrees with the work performed by Halim and Ajayi who reported the use of unspecialized blades as a risk factor in HBV transmission [13]. Other significant risk factors identified in this study in mothers were history of circumcision (75.0%), history of previous blood transfusion (50.0%), history of jaundice (25.0%) and history of tribal marks (50.0%). These findings are not unexpected since epidemiological studies have consistently demonstrated that transfusion of unscreened blood and blood products, and sociocultural practices, such as circumcision and scarification, are important routes of transmission of HBV infection [14]. These sociocultural practices are often attended by the use of scientifically unsterilized devices. It is therefore plausible to suggest that engagement in these activities could have exposed the HBsAg-positive mothers to HBV infection initially. While the precise cause of previous jaundice was not identified in the study patients, it is possible that the initial hepatitis occurred from other organic causes. However, a flare-up of underlying hepatic inflammation may account for the history of jaundice in the subjects. However, the nonsignificant association between HBV

Table 4. Description of the various modes of hepatitis B virus transmission and prevalence rates in mother and child.

Mode	Mothers HBsAg positive (n = 4)	Children HBsAg positive (n = 7)
History of previous blood transfusion	2 (50.0%)	3 (42.9%)
History of circumcision	3 (75.0%)	4 (57.1%)
History of HBV vaccination	0 (0%)	1 (14.3%)
History of jaundice	1 (25.0%)	0 (0%)
History of used of unsterile needles	4 (100.0%)	0 (0%)
History of tribal marks	2 (50.0%)	1 (14.3%)

n = the total number HBsAg-positive.
HBsAg: Hepatitis B surface antigenemia.

Table 5. Relationship of child's mode of delivery and hepatitis B virus transmission.

HBsAg	Normal delivery	Caesarian section	Total
Positive	5	2	7
Negative	61	2	63
Total	66	4	70

Degrees of freedom: 1, x^2 = 0. 006; $p < 0.05$. There is statistically significant difference in the mode of delivery and HBV transmission. HBsAg:Hepatitis B virus surface anitgen.

seropositivity in mothers in this study and the history of previous HBV vaccination is in conformity with the findings by Alter and colleagues who reported that no recognizable risk factor could be ascribed to 30% of cases of HBV infection in adults [15].

However, history of previous blood transfusion (42.9%), history of circumcision, history of HBV vaccination and history of scarification (50.0%) have been associated with HBV transmission in children, as shown by the result of this study. This finding is in concordance with the work performed by Halim and Ajayi [13]. However, no significant association was found between HBV seropositivity in children with a history of jaundice and previous use of unsterile needles. A study by Rosenthal arrived at the same conclusion [16]. HBV infection in children is rarely observed unless there are special circumstances, such as transfusion-associated outbreak.

This study also highlights the significance of the child's mode of delivery as a plausible risk factor in HBV transmission. This finding is further supported by the results of HBsAg posititvity obtained among children aged 1–4 years in this cohort, which possibly could not have been detected before 1 year of life. Statistically, the difference between those delivered by normal delivery and cesarian operation could further explain the significance of blood transfusion and exposure to unscreened blood products as an important route of HBV transmission. A risk factor for the transmission of HBV infection in this group may possibly be via blood transfusion or from other siblings. The result also suggests that these children positive for HBsAg could have acquired it from their mother's blood during the caesarian section. This finding further confirmed vertical transmission as an important route of HBV infection.

The work by Conte and colleagues reported that cesarian section does not decrease the risk of HBV transmission and should be used only if clinically required [17]. In summary, vertical transmission or infection transmitted from mother to newborn accounts for another sizeable group of children with HBV infection. The surveillance of such children with long-term follow-up is necessary. There is already compelling evidence from this study to indicate that hepatocellular carcinoma, prevalent among young adults in our environment, may be related to hepatitis B antigenemia persisting over several years. Necessary measures provided in the universal precaution should become mandatory for those engaged in the art of ear piercing or scarification. Health education could drive the point home in order to achieve the standard required to interrupt the cycle of transmission through this route. The need for an effective vaccine against HBV infection cannot therefore be overemphasized. Thus, we suggest four main strategies in preventing HBV infection: public education in order to highlight the risk factors involved, behavior modification, passive immunoprophylaxis and active immunization.

Highlights

- A descriptive seroepidemiologic study of hepatitis B virus and its associated risk factors has been conducted among pairs of mothers and children of preschool age attending the 'Well Child' clinic of the University of Ilorin Teaching Hospital and the 'Immunization Clinic' of the Child Specialist Hospital, Ilorin, Nigeria.
- Blood transfusion and mode of delivery were the most significant risk factors that contributed to the transmission of HBV among these subjects.
- All four mothers who were positive for the surface antigen of hepatitis B virus also had positive children for this marker.

Conclusion

It is important to note that infection by HBV early in life underscores the potential of adding to the burden of viral hepatitis and its attending complication of hepatocellular carcinoma later in life.

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