Original Article

Hepatitis B and C Infections among Children with Sickle Cell Anaemia in a Tertiary Hospital in Calabar, Nigeria

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Abstract

Background: Hepatitis B and C are hepatotropic viruses capable of causing chronic liver disease in infected individuals. Children with sickle cell anaemia are at higher risk of infection from these viruses due to their increased risk of repeated blood transfusion. No study has been done on the prevalence of hepatitis B and C in children with HBSS within this region of Nigeria. **Aim:** This study aimed to determine the prevalence and associated risk factors of serologic markers of hepatitis B virus (HBV) and anti-hepatitis C virus (HCV) in children with confirmed HBSS in a steady state. **Patients, Materials and Methods:** This was a cross-sectional study. One hundred and two children with confirmed sickle cell anaemia aged 1–17 years in the steady state attending the Paediatric Haematology Clinic of a University Teaching Hospital were consecutively recruited into the study. Blood samples were screened for HBV markers and HCV antibodies using immunochromatographic technique. A $P < 0.05$ was considered significant. **Results:** The mean age of the study participant was 8.45 ± 4.47 years. Seroprevalence of HBV markers were hepatitis B surface antigen was 1%, hepatitis B e antigen (HBeAg) 1% and hepatitis B core antibody (HBcAb) was 3.1%, hepatitis B surface antibody was 26.8%, and HBeAg 1.0%. Those positive for HBcAb were from the middle and low social classes ($P = 0.041$). Most of the patients (97.8%) received ≥3 doses of HBV vaccination. None of the children was positive for HCV antibody (0%). **Conclusion:** The seroprevalence rate of HBV infection was low and none of the study participants was positive for HCV infection. The low prevalence of HBV infection and absence of HCV infection may suggest a low prevalence of these blood-borne hepatotropic viruses among the study participants. However, the introduction of the HBV vaccination into the National Programme of immunisation is still justifiable due to its public health significance.

Keywords: Hepatitis B virus serologic markers, hepatitis C virus, Nigerian children, seroprevalence, sickle cell anaemia

Introduction

Sickle cell disease is an autosomal recessive disorder caused by a point mutation leading to a structurally abnormal hemoglobin, sickle cell hemoglobin (HBS).[1] Approximately 0.15% of African Americans are homozygous for hemoglobin S (HBSS) and about 8% are heterozygous for hemoglobin S (HBAS).[1,2]

In Nigeria, about 25% of adults have the sickle cell trait and 1%–3% have the sickle cell disease.[3-5] Sickle cell disease affects about 1%–2% of infants annually in Africa.[6]

This disorder leads to chronic hemolytic anaemia and to other clinical manifestations. Due to chronic hemolytic anaemia, children with sickle cell anaemia are prone to recurrent blood transfusion with the attendant risk of blood-borne diseases.[7,8] Although the incidence of transfusion-acquired infection has decreased over the years, the risk of viral hepatitis B and C infection in these children remains higher than in the normal population, with factors such as no vaccination or incomplete vaccination leading to increased risk of infection.[9]

In Nigeria, the prevalence of viral hepatitis B and C in children with HBSS ranges from 1.6% to 17.3%.[10-14] To our knowledge, no study has been done on the prevalence of viral hepatitis B and C in children and adolescents with HBSS within this region in Nigeria. This study aimed to determine the prevalence

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and associated risk factors of serologic markers of hepatitis B virus (HBV) and anti-hepatitis C virus (HCV) in children with confirmed HBSS in steady state.

Patients, Materials and Methods

Study setting

The study was conducted in the Paediatric Haematology outpatient clinic of the Department of Paediatrics, University of Calabar Teaching Hospital (UCTH), Calabar, Cross River State, south-south Nigeria. Cross River State has a population of 3.16million people.[15] The paediatric haematology outpatient clinic sees about 5–15 sickle cell anaemic children weekly. It has a registry comprising 184 sickle cell anaemic children (123 males and 61 females), of which some are not compliant with follow-up visits.

Study design

This was a cross-sectional study.

Study population

These involved children aged 1–17 years known with confirmed sickle cell anaemia in a steady state attending the paediatric haematology outpatient clinic. Patients meeting inclusion criteria were recruited purposively into the study until the minimum sample size was reached.

Sample size determination

The minimum sample size was calculated using Fisher's formula for determining sample size studies for population sized <10,000.[16]

The minimum sample size calculated was 92. To account for nonresponse, the calculated sample size was divided by a nonresponse rate of 0.9. Thus, the approximate minimum sample size was 102.

Ethical approval

Ethical approval for the conduct of this study was obtained from the hospital research ethics committee. Informed consent was obtained from parents of eligible participants before enrolment into the study.

Data collection

Data were collected using a semi-structured interviewer-administered questionnaire. Information obtained included biodata of study participants, family sociodemographic characteristics, clinical history relating to HBSS, viral hepatitis B and C, history of vaccination with HBV vaccine, and anthropometric measurements of study participants were obtained. The social class of parents/guardians was determined using the social classification proposed by Olusanya *et al*.,[17] this classification considered the parents/guardian's occupation and educational qualifications. The questions asked were simple, clear, and easy for the participants to understand, with little explanation.

Laboratory investigations

Two millilitres of venous blood was obtained from each child under aseptic procedure into a clean, plain labelled bottle, and allowed to clot. The serum was separated and used for the analysis. Serologic markers of HBV and HCV-antibodies (HCV-Ab) were detected using different commercially available rapid chromatographic immunoassays for the qualitative detection of serologic markers to HBV, which includes hepatitis B surface antigen (HBsAg), hepatitis B e antigen (HBeAg), hepatitis B e antibody (HBeAb), hepatitis B surface antibody (HBsAb), Hepatitis B core antibody (HBcAb) and HCV-Ab, both manufactured by ABON™ (Acro Biotech, Inc., 9500 Seventh Street, Unit M, Rancho Cucamonga, CA 91730, U. S. A). The qualitative assays were performed using one-step test strips for the detection of HBsAg and HCV-Ab in serum samples. The test was performed within 1 h of specimen collection and separation. Only clear, nonhaemolysed serum samples were used. The test strip and quality control sera were allowed to equilibrate to room temperature (15°C–30°C) before testing. Test strip was immersed vertically in the serum for 10–15 s with arrows pointing toward the serum sample as indicated on the test strip. Test-strip was placed on a nonabsorbent flat surface, and the timer started. The immunochromatographic reaction was allowed to take place within minutes, and the result read off at exactly 15 min after. The presence of two distinct coloured lines indicated a positive result, while a negative result was indicated by one coloured line in the control region and no apparent line appeared in the test region. To serve as a procedural control, a coloured line always appeared in the control line region, indicating that the proper volume of membrane wicking has occurred. The invalid result was read off when there was failure to have a control line appearing. Results with invalid responses were repeated. The HBsAg assay has manufacturer-reported specificity, sensitivity, and accuracy of >99.0%, 97.0%, and 98.5%, respectively, while the HCV-Ab antibody assay has a reported specificity, sensitivity, and accuracy of >99.0%, 98.6%, and 99.3%, respectively.

Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) for Windows, Software Version 22.1. (SPSS Inc., Chicago, IL, USA). Quantitative variables were summarised as mean and categorical data were summarised as frequency (percentage). Chi-square test was used to test for association between categorical variables. A $P \leq 0.05$ was considered statistically significant.

Results

General characteristics of study participants

A total of 102 children aged between 1 and 17 years with a mean age of 8.45 ± 4.47 years participated in the study. Most of the children recruited (38.2%) were within the age group of 6–10 years, followed by children within the age group 1–5 years (26.5%), 11–15 years (23.5%), >15 years (12.0%), respectively. Half of the children were females (50.0%), while 50.0% were males; two of the study participants had missing data on sex and were excluded from

the analysis. Most of the children (62.0%) were from high social-class family backgrounds followed by those from the middle (21.0%) and low (13.0%) social-class family backgrounds, respectively. The predominant ethnic group represented in the study was Efik (21.0%), Ibibio (17.0%), and Igbo (13.0%). This is shown in Table 1.

As shown in Table 2, half of the patients had a blood transfusion, but only 5.0% of them had undergone surgery in the past and 8.0% of the patients were stunted, with most of them (86.0%) having normal height for age.

Most of the HBSS patients (97.8%) received complete (≥3) doses of HBV vaccination, as shown in Figure 1.

Seroprevalence of hepatitis C infection in HBSS patients

None of the children studied tested positive to HCV antibody, giving a 0% prevalence of HCV infection.

Table 1: Sociodemographic characteristics

Variables	Frequency (n=102), n (%)
Age group (years)	
1–5	27 (26.5)
6–10	39 (38.2)
11–15	24 (23.5)
>15	12 (11.8)
Sex	
Male	50 (50.0)
Female	50 (50.0)
Social class	
High	63 (62.0)
Middle	22 (21.0)
Low	13 (13.0)
Missing	4 (4.0)
Tribe	
Efik	22 (21.6)
Ibibio	18 (17.7)
Ejagham	4 (4.0)
Anang	3 (3.0)
Igbo	13 (13.0)
Others	42 (41.2)

Table 2: Clinical and nutritional characteristics

Variables	Frequency (n=102), n (%)
Blood transfusion	
Yes	50 (49.0)
No	50 (49.0)
Missing	2 (2.0)
Past surgery	
Yes	5 (4.9)
No	94 (92.2)
Missing	3 (2.9)
Stunting	
Yes	8 (7.8)
No	88 (86.3)
Missing	6 (5.9)

Serological profile of hepatitis B markers in HBSS patients

The seroprevalence of the various hepatitis B markers of hepatitis B was evaluated in 97 out of the 102 HBSS patients recruited, as shown in Table 3. HBsAg has a seroprevalence of 1.0%, HBsAb was positive in 26.8%, HBeAg in 1.0%, HBeAb in 1.0% and HBcAb in 3.1%.

Relationship between sociodemographic/clinical factors and hepatitis B core antibody positivity

The relationship between important sociodemographic/clinical factors (age group, age at vaccination, sex, social class of caregivers, blood transfusion history, past surgical history, sharing of sharps, and the number of doses of HBV vaccine) and evidence of exposure to HBV infection measured by the HBcAb levels in the children managed for HBSS was explored using the Chi-square test of independence. As shown in Table 4, none of the explored factors was significantly associated with evidence of exposure to hepatitis B infection except the social class of the parents/caregivers of the children managed for HBSS. The proportions of those whose caregivers were in the low and middle social class with HBcAb positivity were relatively higher than those whose parents/caregivers were in the high social class (i.e., 7.7% and 9.5%, respectively, vs. 0.0%, $P = 0.041$).

Discussion

The result of this study showed that the prevalence of HBsAg among children with HBSS attending the paediatric paematology clinic in this low-resource setting was 1%. This shows a low endemic risk in this region among the study population.[18] The low prevalence of HBsAg in this study population is similar to the study in Saudi Arabia, with a prevalence of 1%.[19] Studies in Nigeria have shown HBsAg prevalence rates ranging from 2.45% to 14.9% in children with HBSS. The low prevalence in this study may be attributed to improved screening of blood for transfusion, about half of the study population (49%) received a blood transfusion and possibly the effect of the HBV vaccine, which is now administered routinely since its introduction into the National Program on Immunisation (NPI) in 2004, though the detectable level of HBsAb was low among the

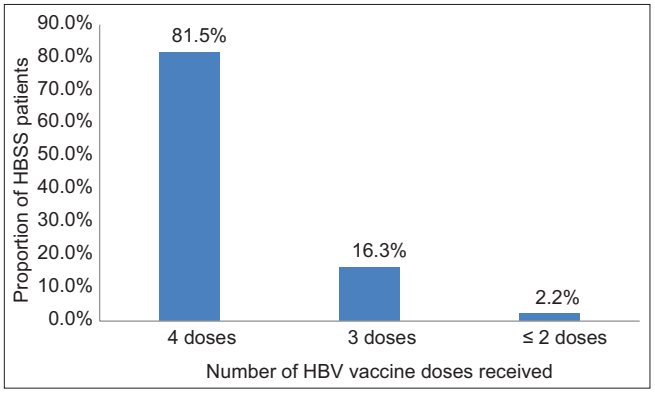

Figure 1: Number of HBV vaccine doses received. HBV: Hepatitis B virus

Table 3: Seroprevalence of hepatitis B markers in homozygous for hemoglobin S patients (*n*=97)

Hepatitis B markers	Qualitative assay result	
	Positive, *n* (%)	Negative, *n* (%)
HBsAg	1 (1.0)	96 (99.0)
HBsAb	26 (26.8)	71 (73.2)
HBeAg	1 (1.0)	96 (99.0)
HBeAb	2 (2.0)	95 (98.0)
HBcAb	3 (3.1)	94 (96.9)

HBsAg: Hepatitis B surface antigen, HBeAg: Hepatitis B e antigen, HBeAb: Hepatitis B e antibody, HBsAb: Hepatitis B surface antibody, HBcAb: Hepatitis B core antibody

Table 4: Relationship between sociodemographic/clinical factors and the presence of Hepatitis B core antibody

Sociodemographic factors	HBcAb		χ^2	*P*
	Positive (%)	Negative (%)		
Age group (years)				
1–5	1 (3.7)	27 (96.3)	2.97	0.463
6–10	1 (2.8)	36 (97.2)		
11–15	0	24 (100.0)		
>15	1 (10.0)	9 (90.0)		
Age at diagnosis (years)				
0–4	2 (2.8)	69 (97.2)	0.19**	0.545
5–9	1 (4.8)	20 (95.2)		
Sex				
Male	0	48 (100.0)	3.03**	0.242
Female	3 (6.1)	46 (93.9)		
Social class				
High	0	61 (100.0)	6.38	0.041*
Middle	2 (9.5)	19 (90.5)		
Low	1 (7.7)	12 (92.3)		
Blood transfusion				
Yes	1	48 (100.0)	0.36**	0.617
No	2 (4.2)	46 (95.8)		
Past surgery				
Yes	0	5 (100.0)	0.17**	1.000
No	3 (3.3)	88 (96.7)		
Sharing of sharps				
Yes	0	14 (100.0)	0.52**	1.000
No	3 (3.6)	80 (96.4)		
Number of vaccine doses				
4	1 (1.3)	74 (98.7)	5.83	0.054
3	0	14 (100.0)		
<3	1 (50.0)	1 (50.0)		

*Significant *P* value, **Fisher's exact test. HBcAb: Hepatitis B core antibody

study participant;[20] however, all participants in this study received the vaccine against HBV and about 97.8% received three doses or more. A study carried out among adolescents delivered before the introduction of the HBV vaccine into the NPI schedule in Nigeria gave a prevalence of 1.2%.[20] This may also mean that the prevalence of HBV among children and adolescents in this region may be generally low; however, due to the public importance of this infection, the need for the vaccine cannot be over-emphasised.

The prevalence rate of HBeAg in this study was 1%, this is similar to the 1.1% recorded in a study in Sokoto among children with HBSS.[14] The presence of HBeAg in the serological markers of HBV-infected individuals indicates a high infectivity rate. Therefore, one of the study participants had an active infection with a high risk of infectivity. It is, however, beyond the scope of this study to discuss treatment outcomes. The seroprevalence rate of HBeAb in this study was 2%. This was lower than in other studies, with a prevalence rate ranging from 6% to 13.6%. HBeAb positivity is an indication of either spontaneous seroconversion from HBeAg to HBeAb in infected individuals or in those with a precore mutant who did not develop the HBeAg at all.[14,21,22]

The prevalence of HBcAb in this study was 3.1%. The presence of HBcAb in individuals tested for serologic markers of HBV implies a previous or ongoing HBV infection. The higher HBcAb among the study population than the HBsAg prevalence may mean that some study participants may have seroconversion from HBsAg to HBsAb. The prevalence of HBcAb in this study is lower than that obtained in Sokoto (5%).[14]

Only one patient tested positive for HBsAg; because of the very low prevalence, it was difficult to subject this to any further statistical analysis. Following further analysis for those positive for HBcAb, proven risk factors for acquisition of HBV infection, such as history of blood transfusion, past surgery, and sharing of sharps, were not statistically significant in the binary regression. However, this may have been influenced by the relatively small sample size. Although not statistically significant, each of the children positive for HBcAb was in the age group of 1–5 years, 6–10 years, and greater 15 years. There was a significant association between the social class of the children and being positive for HBcAb. Positive children were from the middle and low socioeconomic class ($P = 0.041$). This is in keeping with the study by Jibrin *et al.*,[14] where all positive children were from the low and middle social classes.

The prevalence of hepatitis C infection in this study was 0% as none of the study participants tested positive to the virus. A study carried out also in the same region as the present study involving 744 secondary school adolescents showed a prevalence of 0.3%.[23] This may imply that HCV infection is low in the study region. HCV infection in HBSS children has been linked to frequent blood transfusions. This may also imply that the blood transfusion screening process in this region may be optimum, thereby not exposing the study participants to the risk of acquisition of this infection following transfusion. Studies in other regions involving HBSS children have a prevalence rate ranging from 1.7% to 7.3%.[10,13,14]

The limitation of the present study is the hospital-based nature of the study, which may not be a true reflection of the prevalence of the infection in the community. Second, this was

a cross-sectional study which limits the ability to conclude the outcome of the infections.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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