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Prevalence of hepatitis B markers seropositivity in sickle cell (SCA) children in ABUTH Shika, Kaduna State

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Abstract

Background: The study was carried out to determine the scope and pattern of hepatitis B infection among patient with sickle cell disease presenting at ABUTH Shika. Aims and objectives. This research work was conducted to determine the seropositivity of HBV infection amongst SCA patients and also to determine the associated potential risk in the acquisition of the infection.
Patients and method: In order to determine the pattern of HBV infection among children with SCA aged 6 months to 12 years and associated risk factors; a random selection of 146 children was made at the paediatric haematology clinic of Ahmadu Bello University Teaching Hospital, Shika. For each SCA patient, an age-and sex- matched control with genotype AA presenting with minor ailments were selected from the paediatric outpatient of the hospital. The children were screened for various markers of hepatitis B virus using a spot test and ELISA test.
Results: The prevalence rates of hepatitis B infection documented in the SCA and control groups were 24.66% and 28.77% respectively. The prevalence was highest in 9 - 12 year age group for both SCA patients and controls with prevalence of 42.86% and 42.11% respectively. None of the risk factors studied which included blood transfusions, parenteral injections, hospitalization, ulcers, tattooing, traditional circumcision, ear piercing, traditional scarification and contact with known hepatitis case were significantly associated with HBV infection in either the SCA or control group. There was also no association between frequency of hospitalizations, transfusions and people sleeping in the same room with HBV infection in either SCA patients or the control groups. The most frequent marker found among both the SCA and control group was anti-HBc.
Conclusion: High prevalence of HBV infection was detected in both the subjects and controls. Children with SCA were not found to be at increased risk of contracting hepatitis B infection. It is recommended that all children should benefit from early vaccination.

Keywords: Hepatitis B virus, Sickle cell anaemia, Paediatric outpatient department, Enzyme linked immunosorbent assay

Introduction

Africa is known to be hyperendemic for HBV infection, where the disease is contracted during infancy and early childhood resulting in 15-20% of its populace being chronic carriers.[1-5] In Africa, majority of the infections are acquired between 6 months and 6 years of age with other family members implicated as a source of infection

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(Horizontal transmission). [3] In areas of intermediate endemicity (2-8%: Italy, Japan, Spain, Greece, Portugal) infection occur in both children and adults.[3] In areas of low endemicity (< 1%: North West – Europe, North America, UK, and Australia), infection in infancy and childhood is uncommon.[3]

Prevalence studies on HBV infection in Nigeria have shown the disease to be highly endemic.[6-15] Variable prevalence rates documented are 5.5% – 12.6% in adults, and 0.7% – 46% in children using different methods.[6-15] This wide variability can be attributed to the differences in culture, behaviours of the various subpopulations studied and the differences in screening methods used. Pooled prevalence for Nigeria from 2000 to 2013, was 13.6% while in children it was 14.0%. This further confirms the high prevalence HBV infection in children.[16]

HBV is transmitted predominantly via the parenteral route. These include the use of contaminated blood and blood products, surgical and non-surgical procedures, mass immunization, other routes are by contact with contaminated body fluids, sexually and by vertical transmission.[1,2] Overcrowding, presence of tropical ulcers,[17] bedbugs in sleeping areas[17,18] and mosquitoes[19,20] have also been implicated in the acquisition of HBV infection. Sharing of toothbrush amongst siblings and household members has been documented to be statistically significant as a risk factor for HBV infection in SCA children.[21]

Sickle cell anaemia (SCA) is a haemoglobinopathy; with genetic predisposition resulting from the mutation of the gene coding for the β-chain of haemoglobin. The sickle cell gene is known to be widespread, reaching its highest incidence in equatorial Africa.[22] It occurs also in parts of Sicily, southern Italy, northern Greece, southern Turkey, the Middle East, Saudi Arabia, especially the eastern province and much of central India.[22] This distribution is determined by the occurrence of the sickle cell mutation and its selection by falciparum malaria.[22]

Between 10-40% of the population of the world is affected by this genetic disorder.[23] In African countries alone, estimates suggest that more than 100,000 people die each year from the disease and only 14% survive to adulthood.[23]

In Nigeria, about 0.12-1.08 million people suffered from sickle cell anaemia (1976).[23] It has been noted that Nigeria has the largest number of patients with SCA in the world,[24] with the sickle cell trait frequency varying between 15%-25%,[22,25] while the homozygous state affecting 1.6% of the population.[25] Intra country variations have been documented as evidenced by varying gene prevalence rates in north, west and eastern part of the country.[25]

Sickle cell anaemia is a major health problem in Nigeria and it is associated with considerable mortality and morbidity.[24,26-28] Hepatic crisis (hepatopathy) is a common cause of hospitalisation among children suffering from SCA,[29] and the clinical presentation may closely mimic viral hepatitis,[29-31] thus making distinction between the two difficult. Hepatic dysfunction evidenced by jaundice, hepatomegaly and deranged liver function tests are commonly attributed to SCA, with the role of HBV infection not clearly defined.[29-31]

Sickle cell patients have been thought to be more prone to HBV infection with the tendency of developing a chronic carrier state for the following reasons.

a. Majority of SCA patients come from an environment where hepatitis B infection is endemic and may come in contact with the infection at an early age.[6-15,24] Such early exposures are likely to produce mild anicteric infections which might be missed clinically. Studies have shown that these mild attacks are likely to progress to chronicity.[14,34]
b. Repeated blood transfusions and parenteral drug administrations in them may result in the contact with the agent of HBV infection early in life.
c. The presence of some degree of immunological impairment in SCA[33-36] may be responsible for their inability to effectively eliminate HBV leading to a carrier state and hence constituting to the infectious reservoirs or pool.

There are few studies on the prevalence of HBV infection among SCA children, most of which were inconclusive.[37-44] Studies in the northern part of Nigeria documented a high prevalence of HBV infection in children with SCA, with the mode of acquisition not clearly established.[42,47,49] It then becomes necessary to carry out studies that will adequately assess the scope of HBV infection in

Nigeria, to determine its mode of acquisition with a view to protecting this vulnerable group of children with SCA from this dreadful but yet preventable disease – HBV infection. It will also help in planning public health preventive programmes, particularly vaccination programmes for children with SCA.

Patients and methods

Study design: The study was cross sectional and conducted among SCA children and controls with genotype AA attending Ahmadu Bello University Teaching Hospital Shika/Zaria. Zaria is located within the Guinea Savannah belt of Nigeria, 80 kilometres north of Kaduna, at an altitude of 610 meters above sea level with an annual rainfall of about 1092mm.[48] The climate is hot and dry except during the cold dusty harmattan period between October and March.[48]

Zaria has a population of 408,198 according to the 2006 census figures. It is predominantly populated by the Hausa-Fulani indigenes, majority of who are Muslims and farmers. The indigenes mostly live within the ancient walled city. The non-indigenes come from more than 120 Nigerian ethnic groups. They are mostly civil servants, traders, crafts men and women. They live mostly in other areas of Zaria outside the city wall.[48]

The clinic serves as a referral centre for children with sickle cell disease from Kaduna State and parts of neighbouring States [Katsina, Zamfara, Niger and Kebbi]. The clinic holds once weekly, with an attendance of 35 – 50 patients per day. And the age group of patients seen in the clinic is between 6months to 12 years. Older children are been attended to by the haematologist.

Subjects: The case control study was conducted amongst children with SCA attending the paediatric haematology clinic ABUTH Shika. The controls were age-sex- matched patients with haemoglobin genotype AA presenting at the hospital's paediatric outpatient department (POPD) with minor ailments not related to liver disease.

Subject Selection: The patient selection was based on the following criteria.

Inclusion criteria: Patients with sickle cell genotype confirmed using alkaline electrophoresis were included in the study, those with SCA aged 6 months and 12 years of age were also included, and any sickle cell patient presenting in steady state was included.

Exclusion criteria: Any SCA patient who had previously received Hepatitis B vaccination was excluded, and those who denied of consent were excluded.

Sample size determination

The sample size was determined using a test for two proportion.[50]

$$n = \frac{(p_1q_1) + (p_2q_2)}{p_1 - p_2} f$$, Where p_1 = the proportion of children with SCA who are HBsAg positive, $q_1 = 1 - p_1$, p_2 = the proportion of children with Haemoglobin AA who are HBsAg Positive, $q_2 = 1 - P_2$, f (The power) = 13 obtained from the table in Appendix II using the 95%. Confidence interval at a significance level of 0.05

In this study the values of P_1 and P_2 were taken from previous study by Angyo et al.[40]

Where; $P_1 = 0.23$ (22.85%), $P_2 = 0.20$ (19.57%), $q_1 = 1 - 0.23 = 0.77$, $q_2 = 1 - 0.20 = 0.80$

$$n = \frac{(0.23 \times 0.77) + (0.20 \times 0.8) \times 13}{0.23 - 0.20}$$

$n = 146$

The minimum sample size of 146 for the case group and 146 for the control group was used.

Sample Method: A systematic sampling technique[50] was employed as follows. The sample frame was obtained from the list of record of SCA children attending paediatric haematology clinic ABUTH, Shika.

The sampling frame (f) determined by f = n/N; Where n = sample size, N = Total number of SCA children attending the clinic.

The sample interval k determined by k = 1/f

A number less than the sample interval (k) was randomly selected. Other selections were a + k, a + 2k, a + (n-1) k.[50] The controls were age and sex matched with the SCA children. They were selected from POPD of ABUTH Shika. Multistage sampling technique was used. Those with minor ailments

were selected, from which those with genotype AA were selected and they were finally age and sex matched with the subjects. One month difference was entertained for the infants while three months for other age groups.

Ethical Approval: The approval of the Ahmadu Bello University Teaching Hospital Ethical Committee was obtained before the commencement of the study.

Consent: Consent was obtained from the consultant in charge of the paediatric Haematology clinic. Written and signed informed consent was also obtained from parents/caregiver of the patients used, and from the patients where applicable.

Patient selection and analytical procedure: Sickle cell anaemia was confirmed by haemoglobin electrophoresis using cellulose acetate membrane. The children were in steady state as indicated by normal temperatures, absence of pains, liver and or spleen enlargement that were not tender and normal haematocrit values in the absence of crises.
The control consisted of children with minor ailment that is unconnected to the liver and also absence of significant pyrexia (temperature ³ 38.3^{oc}) age-sex- matched, with haemoglobin genotype HbAA confirmed by alkaline electrophoresis using alkaline cellulose acetate method attending the paediatric outpatient department (POPD) of Ahmadu Bello University Teaching Hospital, Shika. For the control group, two visits were required, the first to determine their genotype group and second to enrol the selected children into the study.
The data was collected using a fill-in protocol detailing bio data with relevant past medical history and clinical features for each subject and control. Questions about the past exposure to known risk factors to HBV infection in the past four weeks or more were enquired into for all the children.
A physical examination was carried out in each child to specifically look for the presence or absence of jaundice, hepato-splenomegaly, scarification, ear piercing, circumcision in both males and females, ulcers or tattoo marks which had been present for four weeks prior to the study. Eight millilitres of venous blood were obtained from antecubital vein on the forearm after thorough cleaning of the overlying skin with 2% povidone iodine. A new plastic syringe with a stainless needle was used for each venepuncture. The blood collected was centrifuged within 4 hours of collection at 5000rpm for 5 minutes. Serum was separated, decanted into a clean dry plain bottle and stored at –20oC until assayed.

Serological tests: The method used for detecting HBsAg was Diaspot HBsAg (one step Hepatitis B surface antigen test strip). Anti-HBc, anti-HBs, and anti-HBe were detected by the sensitive enzyme linked immmosorbent assay (ELISA) technique.
The Diaspot HBsAg is a rapid chromatographic immunoassay for the qualitative detection of Hepatitis B surface antigen in serum or plasma. The test strip is made in USA Lot: HBsAg 400005,), sensitivity > 99% and specificity >99%. it contains anti-HBsAg and anti-HBs coated on the membrane. The Elisa technique is a third generation screening technique; it is a commercial kit (Diadnostic Automation Inc. 23961 craftman Rd. Ste E/F Calabasas, Califonia 91302 USA), sensitivity 99.3% and specificity 99.7%. It detects the presence of antigen or antibodies in a system utilizing enzyme and substrates as indicator system.
Assay procedure: Just before the assay, all the samples were allowed to thaw at room temperature and the kits also allowed to stand at room temperature. All the assay steps were performed continuously as follows according to manufacturer's instructions.

Data analysis: The data obtained was analysed using a desktop computer with Epi info 7 software. The results were presented as frequency tables, lines and chart. Chi square test, Fisher's exact test and odds ratio were used to test for significant association. A p-value of less than 0.05 was considered significant.

Results

Table1 summarizes the various characteristics of both the SCA children and the controls. Majority were males, predominantly Hausa Fulani Muslims. There was no statistically significant difference in mean ages of both subjects and control. The t- test for each age group were 0.67, 0.42, 0.01, 1.04

Table I: Characteristics of children with SCA and control

Characteristics	SCA n=146	*Control n=146*
Gender		
Male	85	85
Female	61	61
Age groups		
6mo-3yrs	33	32
>3yrs-6yrs	43	48
>6yrs-9yrs	28	28
>9yrs-12yrs	42	38
Religion		
Christianity	23	10
Islam	123	136
Tribe		
Hausa	103	129
Others	43	17

Table II: Summary of HBV status of children with SCA and control group

Sex	SCA	Number positive	% positive	Controls	Number positive	% positive
Female	61	12	19.67	61	14	22.95
Male	85	24	28.24	85	28	32.94
Total	146	36	24.66	146	42	28.77

respectively.

Table II summarizes the prevalence of HBV infection among subjects and controls.

Thirty-six (12 females and 24 males) out of the 146 children with SCA were positive for the various markers of HBV (HBsAg, Anti-HBc, Anti-HBs) giving a prevalence of 24.66%. Among the control group, forty-two (14 females and 28 males) were also positive for the various markers of HBV, giving a prevalence of 28.77%. There was no significant difference between the prevalence HBV in children with SCA and control group (χ^2 = 0.44, p= 0.508). Similarly, there was no significant difference in prevalence of HBV in males compared to the females for both children with SCA and controls SCA: (χ^2 = 0.98, df 1 p = 0,323); Controls (χ^2 = 1.28, df 1, p = 0.259).

Table III shows the distribution of markers anti-HBc and anti-HBs and HBsAg among the SCA and control group. Five (3.42%) of the SCA patients with evidence of HBV infection had both HBsAg and anti-HBc present as markers in their sera while 25(17.12%) who had no HBsAg had anti-HBc marker present. The prevalence of these markers was however higher in the control group as 8(5.48%) controls with evidence of HBV had both HBsAg and anti-HBc as markers while 30(20.55%) who had no HBsAg, had anti-HBc present.

None of the SCA children with HBsAg had Anti-HBs. Eight out of these 14 had anti- HBc in their sera, while in the control group, six (4.11%) with negative HBsAg had anti-HBs. Three out of these 6

Table III: Pattern of distribution of B-markers among children with SCA and control

		SCA			Control		
		HBsAg		Total	HBsAg		Total
Markers		+(%)	-(%)		+(%)	-(%)	
Anti-HBc	+	5(3.42)	25(17.12)	30	8(5.48)	30(20.55)	38
	-	0	116(79.45)	116	1(0.68)	107(73.29)	108
Anti-HBs	+	0	14(9.59)	14	0	6(4.11)	6
	-	5(3.42)	127(86.99)	132	9(6.16)	131(89.73)	140

also had anti- HBc in their sera.

Table IV shows the history of exposure to potential risk factors associated with HBV infection among children with SCA and control group. Those exposed to the potential risk factors were considered with regard to the presence or absence of HBV marker. There was no statistically significant association between the potential risk factors and HBV infection in both children with SCA and control.

Table V shows the association between the number of blood transfusions and HBV infection in both the SCA and control group: 21.43% of the subjects who had not received blood transfusion prior to the study had evidence of HBV infection. There was no statistically significant association between number of transfusions and HBV infection among the subjects. (χ^2 (chi square for trend)= 3.11, df = 2, p value = 0.2115), but the prevalence of HBV was found to have increased with increasing number of transfusions.

None of the 42 HBV positive controls had ever received blood transfusion: none of the three who had was HBV positive. Fifty-one (17.47%) of the study children (48 SCA subjects and 3 controls) had a history of at least one transfusion. Of these, 15(29.4%) had evidence of HBV infection: Also of the 241 children who had never been transfused, 63(26.1%) were positive for HBV infection. Thus, there was no significant difference between transfused and non-transfused children with respect to HBV positivity. ($\chi^2 = 0.23$, $p = 0.63$).

Table VI shows the frequency of hospitalization in relation to HBV infection in both SCA and control group. Eighteen (20.69%) of the 87 SCA children who had never been hospitalized prior to the study had evidence of HBV infection. There was no significant difference between evidence of HBV infection and the number of previous hospitalizations in SCA patients (χ^2 (chi square for trend) =2.97 df = 2, p = 0.227). Thirty-six (30.00%) of the 120 control group who had never been hospitalized showed evidence of HBV. There was no significant association between number of hospitalization and HBV infection in the control group (χ^2 (chi square for trend) = 0.02 df 1, p = 0.894).

Table VII shows the number of people per bedroom and HBV infection in both children with SCA and control group. The prevalence of HBV infection did not differ significantly irrespective of number of people who slept in a room: (χ^2 = 1.02, df 2, p= 0.601) for SCA children and (χ^2 = 4.94, df 2, p = 0.085) for controls.

Table VIII shows the infectivity of both SCA and control group with HBV infection. Among the 5 SCA children with HBsAg present in their sera, two (40%) also had anti-HBe while 1(12.50%) of the 8 from the control group with HBsAg in their sera had anti-HBe present.

From tables III and VIII, seven groups of patients were identified among the SCA and control groups. The groups are as indicated in Table IX. The table shows the group of various markers detected in the

Table IV: Potential risk factors associated with HBV status among children with SCA and controls

Risk factors	*SCA (N = 146)*		*Control (N = 146)*			
	HBV positive number(n=36) exposed (%)	HBV negative number(n=110) exposed (%)	HBV positive number(n=42) exposed (%)	HBV negative(n=104) number exposed (%)	Odds Ratio (95% confidence interval	P-value
Blood Transfusion	15(10.27)	33(22.60)	0 (-)	3(2.05)	1.09- (0.99-1.20)	0.34*
Intravenous Infusion	10(6.84)	21(14.38)	5(3.42)	16(10.96)	1.52 (0.37-6.44)	0.51
Parenteral Injection	17(11.64)	40(27.40)	7(4.79)	19(13.01)	1.15 (0.37-3.70)	0.79
Hospitalization	18(12.33)	41(28.08)	6(4.10)	20(13.70)	1.46 (0.45-4.89)	0.48
Ulcers(skin)	6(4.11)	20(13.70)	10(6.84)	23(15.75)	0.69 (0.18-2.58)	0.54
Traditional Uvulectomy	22(15.07)	61(41.18)	32(21.92)	77(52.74)	0.87 (0.44-1.72)	0.66
Contact with known case of Hepatitis	4(2.74)	7(4.79)	7(4.79)	12(8.22)	0.98 (0.16-5.91)	0.65*
Circumcision	25(17.12)	58(39.73)	32(21.92)	61(41.78)	0.82 (0.41-1.63)	0.54
Scarification, tattooing and Blood letting	12(8.22)	20(13.70)	9(6.16)	16(10.96)	1.07 (0.13-3.63)	0.91
Surgery	3(2.05)	5(3.42)	0 (-)	3(2.05)	1.6- (0.94-2.74)	0.33*
Intramuscular injection	34(34.29)	93(63.70)	37(25.34)	95(65.07)	0.94 (0.52-1.68)	0.82

- = Relative Risk * Fisher's exact test = Not significant

Table V: Number of blood transfusions and HBV infection in children with SCA and controls

Frequency	SCA		Controls		
	Total no. of patients	Number with markers (%)	Total No. of Patients	Number with marker (%)	P-value
0	98	21(21.43)	143	42(29.37)	0.17
1	34	9(26.47)	3	0(-)	NA
2	14	6(42.9)	-	-	NA
Total	146	36	146	42	

NA – Not Applicable

Table VI: Frequency of hospitalizations and HBV infection in children with SCA and controls

Frequency	*SCA* Total no. of patients	No. With marker (%)	*Controls* Total no. of controls	No. With marker (%)	p-value
0	87	18(20.69)	120	36(30.00)	0.14
1	32	8(25.00)	21	6(28.57)	0.77
2	27	10(37.04)	5	0(-)	NA
Total	146	36	146	42	

NA – Not Applicable

Table VII Number of persons per bedroom and HBV infection in children with SCA and controls

No. Person per bedroom	SCA Total number	No. Positive (%)	Controls Total number	No. Positive (%)	p-value
<3	27	8(29.63)	26	7(26.92)	0.83
3 – 5	96	24(25.00)	105	27(25.71)	0.91
>5	23	4(17.39)	15	8(53.33)	0.02*
Total	146	36	146	42	

* - Fishers exact test - Significant

Table VIII: Infectivity of children with SCA and controls with HBV infection

	SCA HBsAg Positive (%)	Control HBsAg Positive (%)
+	2(40.00)	1(12.50)
Anti-HBe		
-	3(60.00)	7(87.50)
Total	5	8

Table IX: Distribution of markers according to groups

Groups	SCA n(%)	Control n(%)
Group I – HBsAg (+) Alone	0	1(0.68)
Group II – Anti HBc (+) Alone	17(11.64)	27(18.49)
Group III – Anti HBs (+) Alone	6(4.11)	3(2.05)
Group IV – HBsAg (+) Anti HBc (+) Anti HBe (+)	2(1.37)	1(0.68)
Group V – HBsAg (+) Anti HBc (+) Anti HBe (-)	3(2.05)	7(5.48)
Group VI – HBsAg (-) Anti HBc (+) Anti HBs (+)	8(5.48)	3(2.05)
Group VII – HBsAg (-) Anti HBc (-) Anti HBs (-)	110(75.34)	104(11.23)
	146	146

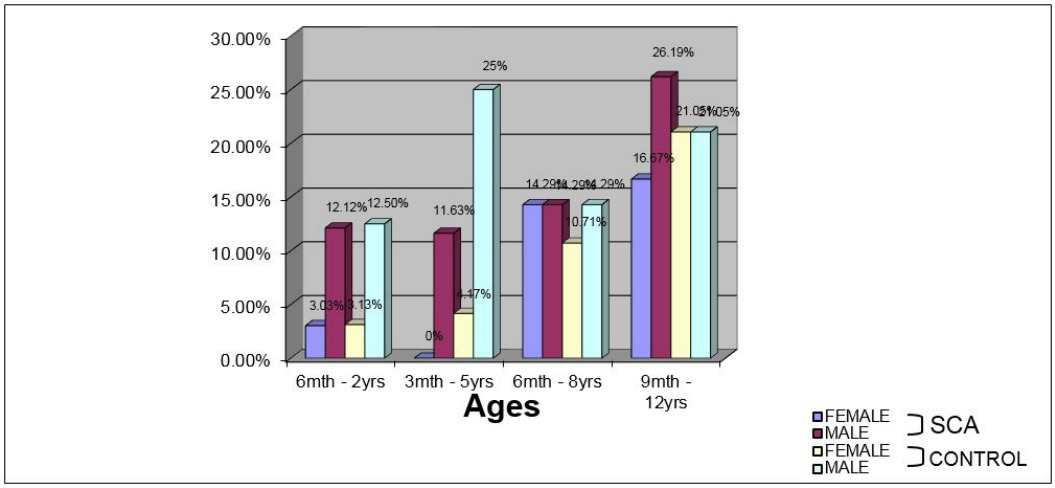

Figure 1: Bar chart showing age sex distribution of HBV infection in both SCA patients and Controls

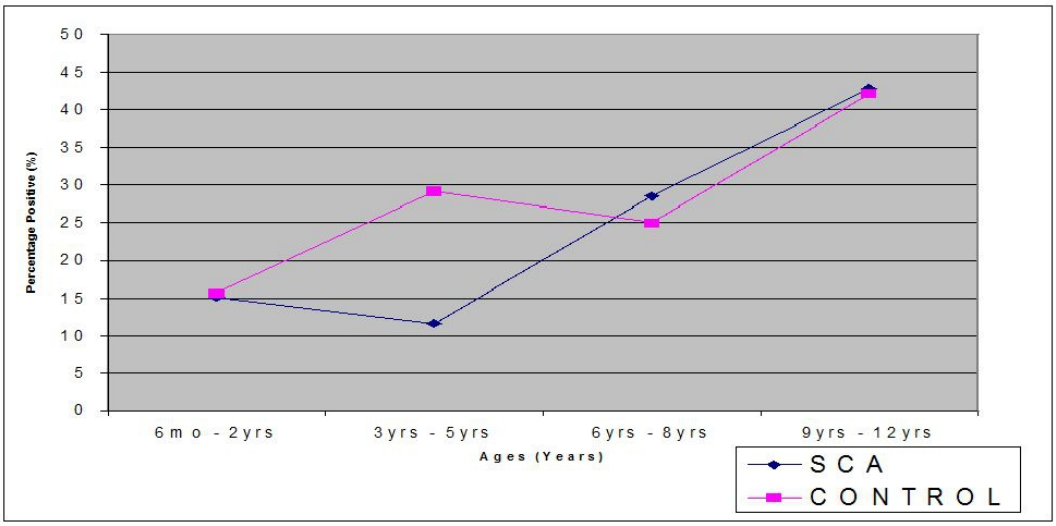

Figure 1: Bar chart showing age sex distribution of HBV infection in both SCA patients and Controls

various groups.

Figure 1 is a bar chart showing age sex distribution of HBV infection in both SCA patients and Controls. It shows the sex distribution within various age groups with evidence of HBV infection. The chart showed that more males than females have evidence of HBV infection.

Fig. 2 shows the frequency of HBV infection in various age groups of SCA patients and control. There was a linear rise in frequency except for a drop at age group >3 – 6yrs and >6 – 9yrs for the SCA patients and controls respectively.

Discussion

The prevalence of HBV infection obtained in the present study from both SCA and control groups is high and it confirms the hyperendemicity of HBV infection in Nigeria, as reported by various studies.[6-15] The use of both rapid immuno-chromatographic assay and Elisa methods showed the prevalence of HBV infection among SCA patients to be 24.66%. This is comparable to a figure of 22.85% reported by Angyo et al[40] in Jos among sickle cell anaemia patients. Jibrin et al in Sokoto also reported a prevalence of 17.3% in SCA patient.[43] Both authors used similar ELISA technique used in the current study. This similarity could be as a result of similarity in environmental factors.

Earlier reports from Enugu,[49] Lagos,[48] Zaria,[53] Ibadan[49] and ekiti[44] documented lower prevalence rates ranging from 1 - 6.5% among children with SCA. These figures did not vary significantly from the reported range in the general population.[6-11] The studies cited[38,37,42] used less sensitive screening methods (haemagglutination, complement fixation and latex agglutination test) which may be responsible for the lower values reported. Another explanation is that only one marker was employed in the definition of hepatitis B infection. In comparison, if the current study were based on HBsAg alone, a similar prevalence rate of 3.47% would have resulted. Ekiti study reported very low prevalence of 1%, reason was that most of the study group had received hepatitis B vaccination.[44] HBsAg was found only in those not vaccinated.[44]

The prevalence obtained from this study is however lower than that obtained in various studies among SCA patients from Benin.[39,41] Abiodun et al[39] documented a prevalence of 39%, Nnebe-Agumadu and Abiodun[41] reported a prevalence of 37%. They used sensitive Elisa technique to screen for both HBsAg and anti-HBc. The higher prevalence obtained from Benin could be due to the well-known variation in epidemiology of the HBV between different geographical or cultural groups.

The prevalence of 24.66% obtained among children with SCA was not significantly different from the 28.77% obtained among the age and sex-matched controls. It is striking that children with SCA do not have significantly increased prevalence of HBV infection. This finding is similar to previous studies by Kaine[38] in Enugu and Angyo[40] in Jos who found no significant difference in prevalence of HBs antigenaemia among SCA patients and their age and sex- matched controls, although the studies cited used HBsAg as sole marker, in contrast to the three markers used in the current study. It however contrasts with that by Abiodun et al[39] from Benin who found an increased prevalence of 39.2% among SCA patients as against 19.3% among their age and sex-matched controls using the same Elisa method. All the studies cited above found no association between blood transfusion and HBs antigenaemia, therefore some unidentified factor might have been responsible for the difference documented in Benin.[39]

Various studies documented a higher prevalence of HBV in males than females.[14,37] This has been explained on the basis of a more rapid decline in HBsAg in women resulting in a shorter duration of the carrier state.[51] Why this is so in children cannot be readily explained. Higher prevalence was documented among males than females in this study, but the difference was however, not statistically significant. This is similar to the finding of Kaine et al[38] from Enugu, Angyo et al[40] from Jos and Nnebe-Agumadu et al from Benin[41] who found no significant difference in HBV infection among males and females. It however contrasts with the findings from Ibadan where a significant higher prevalence in females was documented.[49]

The current study noted the prevalence of HBV to increase with advancing age in both SCA patients and controls, with the rise among the SCA patients being statistically significant. Nnebe Agumadu[41] also reported same pattern with the peak of prevalence of HBV infection within the age group 6 – 10 years among sickle cell patients. Other

wokers[11,14,48] observed similar increasing prevalence with advancing age in school children. It however contrasts with that of Angyo et al[40] and Jibrin et al[43] who documented a peak among the 3 – 5 years and 1 -5years age group in both children with SCA and controls respectively and thereafter, a progressive fall with advancing age in both groups. This contrast could be due to possible difference in the mode of transmission. The result from Jos[40] seems to suggest that; the studied group could have come in contact with HBV very early in life. The increase in prevalence with advancing age in the current study supports horizontal transmission rather than vertical.

The role of blood transfusion in the transmission of HBV in SCA patients has been speculated by many workers.[31,38-42] Transmission of HBV through blood transmission especially from unscreened commercial donors has also been established with incidence of infection increasing with number of units of transfusion.[32] In the present study, the theoretically expected pattern was not confirmed as no significant correlation was found between frequency of blood transfusions and presence of HBV markers in the sera of both SCA patients and controls. Other wokers[37,39-41,49] had reported similar findings. This observation could be a manifestation of the improvement in regular screening of donor blood before transfusion. However, 15 of 36 (41.7%) seropositive patients had received blood transfusion, implying that blood transfusion may have a role to play but other modalities of transmission are applicable in more than 50% of cases. None of the seropositive controls had received blood transfusion; this might suggest that there are definitely other means of transmission yet to be identified. Among SCA patients, there appears to be a subtle trend of increasing risk of HB with increasing number of blood transfusion, this was however not statistically significant.

History of traditional uvulectomy, contact with cases of hepatitis, circumcision in both boys and girls, ear piercing in girls, scarification, tattooing, bloodletting using horns, surgery and intramuscular injections were found not to be significantly associated with HBV infection in both SCA patients and controls. This report is similar to that of Angyo et al,[47] Jibrin et al[43] and Adeleye et al[49] who also found no association between similar risk factors studied and presence of HBs antigenemia in both sickle cell and control groups. An earlier observation by Olumide10 from Ibadan among adults and also Chukwuka et al[46] from Nnewi among school children also showed no association between risk factors studied and HBV infection. However, Jumbo et al[45] from Jos reported that tonsillectomy, tattooing, use of sharp objects as well as trading were significant risk factors associated with HBV infection among their subjects from a rural settlement. This difference might be as a result of use of non-sterile instruments for tonsillectomy, tattooing in the rural setting.[45]

Although, HBV infection is very common in children in Nigeria,[11-15] the predominant mode of transmission is unknown. Intra family spread,[17,40] mosquitoes,[19,20] blood sucking arthropods[17,18] and genetic susceptibility have all been speculated in the mode of transmission of HBV infection. There is however, no definite substantiation of the role of these factors. The data presented in the current study suggest that other factors, yet to be identified in the transmission of HBV infection may play a very important role in the spread of HBV infection among children in our environment and they could possibly fall into the 20-40% of those whose route of transmission is unknown.[2]

In the current study 36(24.66%) SCA patients and 42(28.77%) controls were positive for the various markers of HBV infection. Only one patient from the control was positive for HBsAg alone. This signifies period of incubation. Seventeen of the SCA patients and 27 of the controls were positive for anti- HBc alone. This suggests convalescent period. Six SCA patients and 3 controls were sero-positive for anti-HBs alone. It suggests recovery with loss of anti-HBc, or recovery with development of immunity. Two and one patient from the SCA and control group respectively was positive for three markers (HBsAg, anti-HBc, anti-HBe). This signifies an acute infection with a good prognosis. Three of the SCA patients and 7 of the control patients were positive for HBsAg, anti-HBc and negative for anti-HBe. This suggests that they have an acute infection and are also highly infective. Eight of the subjects and 3 of the control were sero-positive for anti-HBc, anti-HBs, and sero-negative for HBsAg. This means that they have recovered from the infection. One hundred and ten patients

from the SCA group and 104 patients from the control group were sero-negative for all the markers tested for. Since they are not vaccinated, they are at risk of contacting the infection.

All the five SCA patients with HBsAg positive had anti- HBc positive in their sera, while eight of the nine controls with HBsAg positive were anti-HBc positive. This signifies acute hepatitis B or a persistent carrier state. Liver function test could not be carried out to affirm the acute nature of the disease and carrier state can only be confirmed if HBs-antigenaemia persists for after 6 months which was not feasible in the present study.

Seventeen (14.22%) of the SCA patients with markers and 27(64.29%) of the control group had anti-HBc alone. The test method used for anti-HBc detects both IgG and IgM thus making the differentiation between acute and chronic infection difficult. Nevertheless, the result is more likely to represent a past contact with HBV (i.e. IgG since acute infection (IgM) would have been associated with positive HBsAg.

Eight (22.22%) SCA patients and 3(7.1%) controls had both anti-HBc and anti-HBs positive in their sera. The presence of these two markers to the exclusion of others signifies either recovery or convalescent phase. In this regard, there was no significant difference between the SCA patients and controls. This observation is important because the immune system of SCA patients is known to be deficient in some respect.[33,47] The theoretical expectation would be that SCA patients might be unable to clear infection effectively. However, in the light of the findings of the present study, it would appear that the deficiency does not extend to HBV. Anti-HBe was found to be present in two of the SCA patients with HBsAg and in one of the controls, this signifies possible recovery.

The most frequent marker among both SCA patients and the control group was anti-HBc which accounted for 88.33% of all SCA patients with markers and 90.48% of the control group with markers. This finding was not different from the Benin report.41 This implies that most of the children have developed recovery antibodies to HBV and are either in the recovery or convalescence phase.

Six (16.67%) of the SCA patients with markers, and 3(7.14%) of the control group with markers had only anti-HBs in their sera. None of them had prior HB vaccination. Presence of anti-HBs alone in the absence of past vaccination signifies repeated exposure without infection or recovery from infection with loss of detectable anti-HBc. It shows that children are repeatedly exposed and infected with HBV, which is commonly seen in hyper endemic region. This supports the high prevalence documented in the current study. It also emphasises the need to identify the modalities of transmission.

This study confirms the high prevalence of HBV infection in both children with SCA and control. The inability to find association between the risk factor studied and HBV infection does not underscore the need for preventive measures against exposure to be strictly observed. It also shows the urgent need for the implementation of prophylactic measures.

Limitations

1. Elisa technique which is the most sensitive test was not used to determine all the markers because of cost constraints. Rapid chromatographic immuno assay(Diaspot test) was used for the determination of HBsAg while Elisa was used for other markers.
2. We were unable to do liver function test especially in those with markers. Doing this would have improved the quality of the study.
3. HBeAg was not tested for because of financial constraints.

Conclusions

1. There is a high prevalence of HBV infection in both SCA patients and control group, thus confirming the high level of endemicity in the community.
2. The study has demonstrated that blood transfusions may have a role to play in acquisition of the infection in SCA patients.
3. The other risk factors studied were not found to be associated with the acquisition of HBV infection in both groups.
4. This study has not confirmed that SCA patients are at increased risk of HBV infection.

Recommendation

Further multicentre studies aimed at identifying the predominant mode of HBV infection in our environment need to be carried out.

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