Original

Low HIV, HBV, HCV Seroprevalence and inadequate HBV Vaccination in Sickle Cell Patients in Abakaliki, Nigeria: Urgent Need for Surveillance and Adult Vaccination

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Abstract

Background: Frequent hospitalization, blood transfusion, unsafe care seeking practices, and self-administration of injectable opioid analgesics could pose significant risk of Hepatitis B, C and HIV infections for patients with Sickle Cell Disease (SCD) due to chronic anaemia and bone pains. Study evaluated the prevalence of hepatitis B, C, HIV, and HBV vaccination status among SCD patients in Abakaliki.

Method: A case-control study of 244 SCD and non-SCD patients was performed. Blood samples were collected and tested for anti-HBV, HIVand HBsAg. Socio-demographic data, knowledge of HBV infection and self-reported HBV vaccination status were ascertained with pre-tested questionnaires. Data were analysed with descriptive statistics, Chi-square/Fishers exact test.

Result: Seroprevalence rates of hepatitis B, C and HIV among patients with SCD and controls were 3.3%, 0.8% and 1.6% vs 21.1%, 0.8% and 2.4% respectively. Blood transfusion posed the highest risk of acquiring HBV infection. Two patients that tested positive to HIV had history of sexual intercourse without blood transfusion. Awareness of HBV infection and vaccination were low among the patients with SCD. Only 8.2% of the SCD patients had received HBV vaccination. The commonest reason for not receiving HBV vaccination was not being aware of it.

Conclusion: The seroprevalence of hepatitis B, C, HIV infections in SCD patients is low and there are other routes of infection aside blood transfusion. Knowledge of HBV infection and vaccination coverage is low among patients with SCD. Surveillance, patient education, and HBV vaccination are highly needed for this at-risk group of patients.

Keywords: Hepatitis B, Hepatitis C, HIV, Sickle cell disease, Vaccination.

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Introduction

The impact of sickle cell disease on public health is significant and is expanding worldwide. In 2021, more than 500,000 newborns were diagnosed with sickle cell disease, with more than 75% of those cases occurring in sub-Saharan African nations.[1] SCD is an inherited haemoglobinopathy characterised by debilitating bone pain, chronic anaemia and end organ damage. Patients with SCD requires frequent hospitalization and blood transfusion which puts them at increased risk of transmission of infectious diseases. Some of the indications for blood transfusion in SCD include symptomatic anaemia, aplastic crises, splenic sequestration, prevention of stroke, recurrent stroke and pregnancy. Even though blood transfusion is indispensable and beneficial in the management of SCD, it has its complications including transmission of infections. Notable among the transfusion transmissible infections in developing countries are viral hepatitis B and C and Human Immunodeficiency Virus.[2]

Hepatitis B infection is a worldwide healthcare problem, especially in developing countries.[3] The hepatitis viruses (B and C) cause acute and chronic diseases leading to hepatitis, cirrhosis and hepatocellular.[4] Human Immunodeficiency Virus (HIV) takes advantage of surface proteins on white cells, resulting in lytic destruction and consequent CD4+ lymphopenia and immunosuppression. Infection with HBV, HCB and HIV complicates the clinical course of SCD patients.

The burden of transfusion transmissible infections (TTIs) is high among blood donors and even in the general population. Reports from literature show that Nigeria is hyper-endemic for HBV infection with a pooled prevalence of 9.8%, while recent survey puts HCV and HIV prevalence range from 2.2-1.1% and 1.4% respectively.[5-6] Among blood donors in south-south Nigeria, Okoroiwu et al, reported the Prevalence of HBV, HCV and HIV among blood donors to be 4.1%, 3.6% and 4.2% while Ogbenna et al in a recent study in south-west reported a prevalence of 1.34% for HIV, 5.79% for HBV and 2.23% for HCV.[2,7] Some studies have reported blood transfusion as a risk factor for contracting HIV, HBV and HCV in patients with SCD, while others suggest that frequency of blood transfusion does not influence infection transmission in SCD patients.[8-12] Patients with SCD are also at increased risk of contracting HIV, HCV and HBV through unsafe practices like needle sharing due to parenteral opioid misuse.[13]

Hepatitis B vaccination is effective in prevention of HBV infection and could affect prevalence of HBV in SCD cohort.[14] In 2004, Nigeria included HBV vaccine in the national programme on immunization (NPI) for coverage of children between 0-5years.[15] There is currently no national programme for HBV vaccine for adults or at-risk population in Nigeria.[16] Individuals at risk of HBV infection can however access HBV vaccine in primary, secondary and tertiary healthcare centres where they are required to pay for it.

Studies on the prevalence of HIV, HCV and HBV in adult SCD patients and HBV vaccination coverage in our environment are scanty. 10 The aim of this study is to determine the prevalence of HIV, HBV and HCV among adult patients with SCD attending a tertiary health center and ascertain their reported HBV vaccination status. This will guide initiation of interventions to prevent these infections in this group of patients.

Method

Study Area

This study was carried out at the sickle cell centre (SCC) and general outpatient clinic (GOPC)of Alex Ekwueme Federal University Teaching Hospital Abakaliki, (AEFUTHA) Ebonyi southeast Nigeria. It is a tertiary care facility where the Federal government Millenium Development Goal centre for sickle cell disease for the southeast region is domiciled.

Study Design

This was a case-control study conducted between July 2022 and December 2022. SCD patients who attends routine clinic visits at the SCC and had confirmed diagnosis of SCD using HPLC were consecutively enrolled for the study after their informed written consent was obtained. Likewise, 122 age and sex-matched controls without SCD (verbally expressed their genotype to be haemoglobin AA) were consecutively recruited from the GOPC. A matching algorithm was used to match controls to cases based on age and sex with data monitoring and verification to ensure proper matching.

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Ethical Approval

Ethical approval was obtained from the Research and Ethical Committee of AEFTHA. Written informed consent was obtained from all the participants. A proforma was used to capture their sociodemographic data, awareness of HBV infection and risks of exposure and vaccination status. The Hb phenotypes of the controls were performed with Hb electrophoresis. Ethical standards of the Declaration of Helsinki were maintained throughout the process of the study. Participants were counseled before and after the blood testing. Those who tested positive to HBV, HCV or HIV were referred to the gastrointestinal and infectious disease clinics of the hospital.

Sample Size Determination

The minimum sample size for the study was calculated with formula for case-control study

$$n = \frac{(Z^2 \times [P1(1-P1) + P2(1-P2)]}{(P1-P2)^2}$$

n= minimum sample size for each group

Z = Z score corresponding to 95% confidence level = 1.96

P1= proportion of SCD patients with HBV infection in a previous study= 2.1% [17]

P2= proportion of non SCD with hepatitis B infection in a previous study= 0.3 % [17]

Plugging in the values, we get;

$$n = \frac{(1.962 \times (0.021x(1-0.021) + 0.003x (1-0.003)}{(0.021-0.003)^2}$$

n= 56. Calculated minimum sample size for each group was 56 however 122 participants were recruited in each group.

Sampling Technique

Study participants were included in the study by using systematic random sampling. Respondents were selected at interval of two from one another. The process began by randomly selecting the third name on the list, and subsequent names were chosen at intervals of two until the available respondents were exhausted among mothers with children who were less two years of age. Although, 206 were selected but only 200 working-class nursing mothers gave a complete data.

Sample collection and laboratory analysis

A pretested interviewer-administered questionnaire was Five millilitres of blood collected from study participants were dispensed into EDTA (ethylenediaminetetraacetic acid) specimen bottle in two aliquots for hemoglobin electrophoresis analysis using the cellulose acetate method to determine their hemoglobin phenotype and serological testing for HBsAg, HIV and HCV antibodies.[18,19] Laboratory analysis was done at the research laboratory, AEFUTHA.

Data Analysis

Data was analyzed using SPSS version 23. Data were summarized as mean, frequencies and percentages where appropriate. Chi square and Fishers' test were used to compare difference in proportion between categorical variables. P value≤ 0.05 was considered significant.

Results

Table 1: Demographic profile of Study participants

	SCD	Control	Statistical test	P value
Age group				
20 – 25	83 (68.0)	80 (65.6)		
25 – 29	20 (16.4)	22 (18.0)	Fishers exact	0.312
30 – 34	7 (5.7)	9 (7.3)		
35 – 39	9 (7.4)	11 (9.0)		
≥ 40	3 (2.5)	0 (0.0)		
Mean ± SD (Range)	24.1 ± 7.2	25.3 ± 5.2	t = -1.450	0.148
	16 – 53	18 – 38		
Sex				
Male	54 (44.3)	61 (50.0)	χ^2 = 0.699	0.403
Female	68 (55.7)	61 (50.0)		
Marital status				
Single	111 (91.0)	77 (63.1)	χ^2 = 26.401	<0.001

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	SCD	Control	Statistical test	P value
Married	11 (9.0)	45 (36.9)		
Occupation				
Student/Corp member	89 (73.0)	50 (39.8)		
Trader	10 (8.2)	27 (22.0)		
Civil servant	9 (7.4)	30 (24.4)	$\chi^2 = 30.388$	<0.001
Artisan	7 (5.7)	9 (7.3)		
Unemployed/ Housewife	7 (5.7)	6 (4.9)		
Educational status				
Primary	2 (1.6)	3 (2.5)		
Secondary	49 (40.2)	30 (24.6)	Fishers exact	0.022
Tertiary	71 (58.2)	89 (72.9)		

A total of 244 participants were enrolled for the study. Table 1 depicts the demographic profile of the study participants. There was no difference between the age and sex of both groups (p=0.312 and p=0.403) respectively. The ratio of females to males was 1.3:1 in the SCD group and 1:1 in the control group. There was a significant difference in the marital status (p< 0.001with 36.9% of the control group being married while only 9% of the SCD group were married. Majority of the participants were educated, with 71 (58.2%) of the SCD participants and 89 (72.9%) of the controls haven attained tertiary level of education.

Table 2: Seroprevalence of Human Immunodeficiency virus, Hepatitis B and C virus Infections in study participants

Seroprevalence	SCD	Controls		
HBV	4 (3.3)	26 (21.1)	Fishers exact	<0.001
HCV	1 (0.8)	1 (0.8)	Fishers exact	1.000
HIV	2 (1.6)	3 (2.4)	Fishers exact	1.000

The prevalence of HBV and HIV among the patients with SCD and controls were 3.3% vs 21.1% and 1.6% vs 2.4% while similar HCV rate of 0.8% were seen in both groups. (Table 2). The prevalence of HBV and HIV was higher among the control group with a statistically significant difference in the HBV prevalence rate (p<0.001). HCV prevalence was similar in both groups.

Table 3: Awareness of HBV Infection and self-reported HBV Vaccination Status among study participants

Variable	SCD	Control	Statistical test	P value
Heard of HBV infection	17 (13.9)	70 (56.9)	$\chi^2 = 49.196$	<0.001
Source of information on HBV				
Hospital	3(17.6)	32 (45.7)		
School	9 (52.9)	8(11.4)		
Radio/TV	3 (17.6)	19 (27.1)		
Family member/Friends	2 (11.8)	11 (15.7)		
Received HBV vaccine	10 (8.2)	20 (16.4)	$\chi^2 = 3.706$	0.054
Reasons for non-vaccination status				
I am reactive	0 (0.0)	1 (1.3)		
I think it is not safe	1 (0.9)	0 (0.0)		
I didn't know I should take it	1 (0.9)	7 (9.3)		
Not necessary	2 (1.8)	6 (8.0)		
Not aware	104 (92.9)	55 (73.3)		
No reason	1 (0.9)	1 (1.3)		

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Variable	SCD	Control	Statistical test	P value
Lack of funds	3 (2.7)	5 (4.1)		
Risk exposure				
Blood transfusion	74(60.6)	14(11.4)		
Sexual exposure	42 (34.4)	29 (23.7)		
Incision marks	9 (7.4)	5 (4.1)		
Sharp needles	7 (5.7)	5(4.1)		

Table 3 shows statistically significant difference in the awareness of HBV infection among the study groups (<0.001) with more participants in the control group 70(56.9%) having heard about HBV infection than 17(13.9%) in the SCD group. Majority of the control group heard about HBV infection from the hospital while those from the SCD group heard it from the school. Thirty (24.6%) out of the 244 study participants have received at least one dose of HBV vaccination out of which only 10(8.2%) were among the SCD participants. The major reason for not getting HBV vaccination was that participants were not aware of the vaccine. Blood transfusion accounted for the highest risk of exposure to HBV among the study participants who had received blood transfusion and 74(60.6%) SCD participants have received blood transfusion.

Discussion

Blood transfusion may increase the risk of transfusion transmissible infections especially with the daunting blood transfusion safety concerns in our environment due to infrastructural, technical, logistics and personnel challenges.

We found a low seroprevalence of HCV (0.8%) among the groups studied while the controls had a much higher HBV prevalence when compared with the patients with SCD. Our study finding of HCV prevalence is comparable to that documented by Odaibo et al, in southwest Nigeria and Diarra et al in Mali.[10,20] However, another study in Nigeria reported a higher HCV seroprevalence rate among patients with SCD.[12] Also, the seroprevalence of HBsAg in SCD patients in our study is similar to the finding of Diarra et al but lower than that reported by Bolarinwa et al. [20-21] Other studies have reported higher HBV seroprevalence rates in children and adults with SCD [22-25]. We found a low seroprevalence of HIV (1.6%) in our SCD participants while the controls had a percentage of 2.4. In a meta-analysis of 16 studies, Owusu et al showed that the Seroprevalence rates of HIV in SCD patients varied between 0% and 11.5%.[26] Their study opined that variations in interactions between HIV endemicity and SCD disease burden could account influence HIV prevalence in the SCD population.

HIV, HBV and HCV infections are contracted through the similar routes. The differences in the seroprevalence rates of anti-HCV and HBsAg in our study population and other studies with higher rates could be attributable to differences in blood transfusion safety practices, demographic factors like age of the study participants and other population differences. The lower prevalence of TTIS in the SCD patients in the center of current study could be explained partly by the development and deployment of a system of documentation which enables revolving of regular or repeat blood donors in the donor sourcing pool of the blood bank dedicated for patients with SCD. Regular or repeat blood donors have low TTI risk.[27] The frequency of blood transfusion may also influence the infectivity rate as multiply transfused SCD patients will be expected to be more exposed. As per the influence of demographics, most of the studies that reported high seroprevalence of anti-HCV in SCD patients were carried out in both adults and children unlike our study which involved only adults. Sickle cell disease is associated with high mortality rates in childhood and as such a number of those infected may not survive into adulthood thereby reducing the prevalence in adulthood. Likewise, prevailing exposure risks differences in the general population could affect the prevalence of hepatitis B can C infections. Two recent studies in our locality have put the prevalence of HCV and HBV among students in the tertiary institution and the general populace in Ebonyi state at 5.2% and 6.9% respectively. [28-29] It is interesting that SCD

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patients in this study had a lower HCV and HBsAg seroprevalence when compared with the general populace and controls in our study. This further buttress the position that blood transfusion when performed under safety standards may not impose additional risks of TTIs for our chronically transfused patients with SCD. Other routes of infection including sexual exposure and mother-to-child transmission may be significant for infection transmission in the general populace. Evidence of previous exposure other than blood transfusion was responsible for HIV infection in our patients. The only 2 patients with SCD who tested positive to HIV had no history of previous blood transfusion but rather had history of sexual exposure. The low prevalence of HIV in patients with SCD may reflect Nigeria's gradually declining infectivity rate, likely due to increased public awareness and improvements in healthcare. For instance, the current HIV prevalence in Nigeria is 1.4%, a significant decrease from previous estimates of 2.8%. [30] Additionally, the low incidence of HIV infection in individuals with sickle cell disease (SCD) aligns with the hypothesis that SCD may provide some genetic protection against HIV. [31] This protection is thought to involve modifications in the CXCR4 and CCR5 receptors on CD4+ cells, which could potentially prevent the virus from entering and infecting these cells. [32]

Although this hypothesis is intriguing, more research is needed to fully understand the risk and pathogenesis of HIV in people with SCD. Exploring this potential protective mechanism could offer new insights into HIV prevention strategies and contribute to our understanding of how genetic factors influence disease susceptibility. Therefore, continued investigation is essential to validate these findings and uncover the underlying biological processes involved.

Hepatitis B vaccine became widely available in Nigeria in 2004 after its inclusion in the National Program on Immunization in 1995. Despite having attained tertiary level of education and engaging in constant visits to sickle cell clinic where health talks are provided, a good number of the SCD participants reported that they have not heard about hepatitis B infection and majority have not received HBV Vaccination. This is unlike some other studies among undergraduate students which reported higher awareness level and vaccination rates. [33-34] HBV vaccination rates as high as 95% and 86% have been reported among students in developed countries and health workers (70.2%) in Nigeria.[35-37] This disparity in the findings is attributable to the poor awareness of HBV infection and benefits of vaccination in preventing the disease. The studies that recorded high vaccination rates were among students studying health related courses and health workers who may have been sensitized adequately of the risks of HBV infections which is a prominent hazard in the workplace. Even our study alluded to this fact since most of the participants who have heard about HBV infection got their information from the hospital during their clinic visits. Public health campaigns and commemoration of health days are commonly done in the schools and hospitals to provide awareness. Education about HBV infection and the availability of vaccines may improve coverage. The frequent clinic visits of patients with SCD should afford the opportunity of giving them adequate health education. The healthcare providers for our SCD patients should make effort to include providing knowledge and sensitization about these infections and prevention of HBV with vaccination. Also, the higher rates of HBV vaccination recorded in developed countries could also be due to healthcare policies which support vaccination.[38] Target risk group vaccination of SCD population may be needed to improve the vaccination status of these at-risk populations.

Implications of the findings of this study

The findings of this study suggest that the prevalence of HIV, HCV and HBV infections among our adult SCD patients is not higher than the prevalence in the general population.

Limitations of the Study

More sensitive disease detection methods like Enzyme Linked Immunosorbent Assay were not employed in the study. The sample size of the study may be small to generalize our findings.

Conclusion

The findings of this study suggest that the prevalence of HIV, HCV and HBV infections among our adult SCD patients is not higher than the prevalence in the general population. TTIs risk may be reduced in patients with SCD when

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standard protocols are adhered to in blood transfusion services. There is paucity of awareness of HBV infection and poor vaccination coverage among patients with SCD. This calls for action by health care providers, health planners and policy makers to prioritize health interventions in this population especially around HBV education and vaccination.

Declarations

Ethical Consideration: Ethical approval was obtained from the Research and Ethical Committee of AEFTHA. Written informed consent was obtained from all the participants. A proforma was used to capture their sociodemographic data, awareness of HBV infection and risks of exposure and vaccination status. The Hb phenotypes of the controls were performed with Hb electrophoresis. Ethical standards of the Declaration of Helsinki were maintained throughout the process of the study. Participants were counseled before and after the blood testing. Those who tested positive to HBV, HCV or HIV were referred to the gastrointestinal and infectious disease clinics of the hospital.

Authors' Contribution: OCN conceptualized, designed and interpreted data of the study. FON, COA, JCA, IPE, and FEN contributed equally to data collection and the manuscript writing. All the authors gave approval of the final manuscript.

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