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Human Immunodeficiency Virus and Hepatitis B Virus Coinfection among Sickle Cell Disease Patients in A Teaching Hospital in North-Central, Nigeria

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Abstract **Original Research**

The intersection of Sickle Cell Disease and blood-borne viral infections remains a critical public health concern in Nigeria, where the high burden of hemoglobinopathies necessitates frequent therapeutic blood transfusions and injections. These essential life-saving interventions simultaneously elevate the vulnerability of patients to unsafe injection practices and transfusion-transmissible infections, like the Human Immunodeficiency Virus and Hepatitis B Virus. This study aimed at determining the prevalence of HIV-HBV coinfection among all SCD patients, identify age variations and determines the risk factors for the coinfection in the study area. SCD status of the participants were confirmed by running an aliquot of the whole blood from the EDTA bottle for haemoglobin genotype on electrophoretic tank (Volkmann SAE 2761) with cellulose acetate paper at pH of 8.4. HIV testing was done using Nigerian National Serial algorithm for HIV testing. Hepatitis B statuses of the participants were tested using 2 chromatographic immunoassays. Three hundred and fifty Sickle cell disease (SCD) patients between 18 months and 45 years (mean age = 15.3±9.2 years) were systematically recruited for this study. Male to female ratio was 1:1.2; consisting of 160 male and 190 female participants. Twenty-four participants were HIV and HBV positive; making prevalence of HIV-HBV coinfection 6.9% among SCD in this study. The factors significantly associated with HIV-HBV coinfection in SCD patient were blood transfusion and where the blood was transfused. SCD patients with history of blood transfusion are 11 times at risk of the coinfection compared with those not transfused. Furthermore, those transfused in private hospitals are 5 times at risk of coinfection compared transfused in tertiary public hospital.

Keywords: Sickle cell Disease, HIV, HBV, Coinfection, Blood Transfusion.

INTRODUCTION

The intersection of Sickle Cell Disease and blood-borne viral infections remains a critical public health concern in Nigeria, where the high burden of hemoglobinopathies necessitates frequent therapeutic blood transfusions and injections. [1] While these life-saving interventions are essential, they simultaneously elevate the vulnerability of

patients to unsafe injection practices and transfusion-transmissible infections, like the Human Immunodeficiency Virus, Hepatitis C, Lassa fever and Hepatitis B Virus. [2] Although empirical evidence indicates that the a priori probability of HIV/HBV coinfection in these populations remains statistically low, the potential for compounded morbidity and mortality necessitates rigorous screening protocols. [3] Current investigations in South-west Nigeria suggest that while blood transfusion remains a clinical necessity, risk factors such as the sharing of sharp objects and body scarring contribute significantly to the acquisition of these pathogens in sickle cell disease populations. [4] Moreover, the correlation between the cumulative volume of transfused blood and seropositivity for viral markers highlights a direct, albeit fluctuating, dependency that mandates stricter adherence to pre-transfusion screening protocols. [5,6] Despite these risks, limited data are available regarding the precise clinical impact of HIV-HBV coinfection in sickle cell disease, where the synergy between these pathologies may exacerbate systemic complications such as splenic dysfunction, avascular necrosis, and pulmonary arterial hypertension. [7] Furthermore, emerging evidence suggests that the observed prevalence of these coinfections in stable outpatient cohorts may be underestimated due to survivorship bias, where patients with severe manifestations succumb to complications before reaching adulthood. [3,8] Consequently, systematic longitudinal surveillance is required to accurately characterize the seroprevalence of these pathogens and to evaluate the efficacy of current blood safety initiatives in high-risk hematology settings. [9,10] In this context, the implementation of more sensitive screening assays, such as fourth-generation enzyme-linked immunosorbent assays, is essential to mitigate the residual risk posed by blood donors. [11] Beyond screening advancements, it is imperative to address the interaction between antiretroviral therapy and the hematological management of sickle cell disease, as these pharmacological regimens may influence both vaso-occlusive crisis frequency and viral progression. [12] Prevalence of HIV-HBV coinfections ranges from 5-17%; a range which has not significantly changed for decades, despite increasing commitment towards safe blood transfusion and HIV control programmes in Nigeria. However, the value varies across regions and centers in the country. [13,14,15,] Most studies focused only on the paediatrics age groups while there is paucity of data for the adults SCD. This study aimed at determining the prevalence of HIV-HBV coinfection among all SCD patients, identify age variations and determines the risk factors for the coinfection among SCD patients in the study area.

STUDY DESIGN AND METHODOLOGY

Study site and design

This is a descriptive cross-sectional study conducted at the University of Ilorin Teaching Hospital, Ilorin (UITH) between February and November, 2009. The facility runs Sickle Cell Clinics for patients of all ages – paediatrics and adults. An average of 50 sickle cell disease (SCD) patients is seen weekly. The hospital provides blood transfusion and laboratory testing services for HIV, Hepatitis B and other diseases. It is a comprehensive care, treatment and support centre for HIV/AIDS. It is a referral centre serving all the senatorial districts in Kwara state and part of Kogi, Niger, Osun and Ekiti states. It offers both secondary and tertiary healthcare services to the general public.

Sample size and sample collection.

The minimum sample size was calculated using the standard formula for proportions in large populations ($N > 10,000$): $N = Z^2pq/d^2$. Using $Z = 1.96$ (95% confidence interval), $p = 0.319$ (prevalence of 31.9% for HIV-Hepatitis B coinfection in another study, used as the best available Nigerian estimate), $q = 0.681$, and $d = 0.05$ (precision), the calculation yielded $N = 333.8$. Considering attrition, it was rounded up to 350. Three hundred and fifty confirmed SCD patients who met the inclusion criteria were systematically recruited into the study. The participants' SCD statuses were confirmed by haemoglobin-electrophoresis. [16] They were patients of UITH aged 18months to sixty years who met the inclusion criteria and granted voluntary

informed consent (ascension for paediatrics age group). Excluded were patients whose SCD status were not confirmed, having SCD crisis, who had blood transfusion within past 3months, on antiviral therapy or refused to grant informed consent for the study.

An interviewer administered semi-structured questionnaire containing sociodemographic information and possible risk factors for HIV and Hepatitis B infections was used to obtained data from each participant. Five milliliters of venous blood was aseptically obtained from each subject using sterile disposable syringe and needle; dispensed as 3mls and 2mls into plain specimen and Ethylene diaminetetraacetic acid (EDTA) bottles respectively.

Laboratory Procedure

SCD status of the participants were confirmed by running an aliquot of the whole blood from the EDTA bottle for haemoglobin genotype on electrophoretic tank (Volkmann SAE 2761) with cellulose acetate paper at pH of 8.4. Sera were obtained from centrifuged clotted blood in the plain bottles for HIV and Hepatitis B tests.

Hepatitis B statuses of the participants were tested using 2 chromatographic immunoassays, namely, Rightchoice HBsAg rapid diagnostic kit manufactured in Isreal and Diastop HBsAg rapid diagnostic kit from USA. Only samples concordantly positive to both kits are considered Hepatitis B virus positive. The tests were conducted with strict adherence to manufacturer's manual. The reliability of the tests were further established by controlling each batch of the test kits with test on known positive and negative controlled blood samples.

HIV testing was done using Nigerian National Serial algorithm for HIV testing using, Determine and Unigold rapid test kits to detect antibodies to HIV1 and HIV 2. Sample tested positive for the 2 kits were considered positive; while discordant samples are tested with a third kit: the chembio HIV 1 / 2 STAT-Pak assay kit. Positivity to the third kit is considered positive for HIV. [17] The test procedure was controlled by known HIV positive and Negative samples. Manufacturer's instructions on testing procedure were strictly adhere to.

Pretest and posttest counseling were conducted for each participants and the positives were referred to appropriate clinic for care, treatment and support.

Data collection and Analysis

The test results' data and the extracts from the questionnaires were examined for completeness, validated and documented on spreadsheet and analyzed using Statistical Package for Social Sciences (SPSS) version 15-0 software. Frequency tables were generated. Statistical significance of variables was estimated using the chi-square and student 't' test for categorical variables and continuous variables respectively. A p-value of <0.05 was considered significant. Data were presented on tables and chart as simple percentages or cumulative frequencies.

Ethical Clearance

Ethical approval for the study was obtained from the institutional ethic Review committee of the University of Ilorin teaching Hospital, Ilorin. In additional, written informed consents were obtained from adult participants, and Parent/Guardian of paediatrics participants prior to enrolment into the study.

RESULTS

Three hundred and fifty Sickle cell disease (SCD) patients between 18 months and 45 years (mean age = 15.3±9.2 years) were systematically recruited for this study. Male to female ratio was 1:1.2; consisting of 160 male and 190 female participants. Two hundred and thirteen participants (60.86%) had at least secondary education, while only 27 (7.7%) had no formal education. Modal education level was secondary school education with 162 (46.3%) participants. 279 (79.7%) participants were students; others were 33 (9.4%) traders, 11 (3.1%) civil servants, and 27 (77.1%) preschool children. There were 226 (64.6%) Muslims and 124 (36.4%)

Christians among the participants. There were 321(91.7%) unmarried, 28 (%) married, one (0.3%) widow and no divorcee. (see table 1) Three hundred and forty had haemoglobin SS and ten had haemoglobin SC among the participants.

Twenty-four participants were HIV and HBV positive; making prevalence of HIV-HBV coinfection 6.9% among SCD in this study. Age distribution of HIV-HBV coinfected SCD patients is as shown in table 2. Seventeen out of Twenty-four (70.83%) of HIV-HBV coinfected SCD patients are below 20years. 17 out of the 260 under 20 years SCD had the coinfection, making the Prevalence of the coinfection in the paediatrics age group 6.64%. While 7 out of the 90 adult SCD patients had the coinfection and the prevalence among them is 7.78%. (see tables 1 &2)

All sociodemographic factors, namely gender, age, level of education, marital status, religion and occupation bore no statistically significant association with HIV-HBV coinfection in sickle cell disease patients as shown in table 3. Past history of hospitalization; previous blood transfusion; type of healthcare facility where the blood transfusion was done; exposure to multiple sexual partners; and unprotected coital exposure (inappropriate / non-use of condom were clinical risk factors which significant statistical predisposition to HIV-HBV coinfection (p-values > 0.05). (see table 3) Other possible clinical risk factors such as, Scarification marks, Tattooing, sharing of clippers, needle sharing, number of pints of blood transfused, history of sexually transmitted disease, past surgery, circumcision, and incomplete HBV vaccination were not statistically significant factors predisposing to HIV-HBV coinfection. This is different from findings of other researchers where sharing of sharps, scarification or cumulative blood pints transfusion predisposes to the coinfection in SCD patients. No participant uses illicit drugs, patronize sex worker or engaged in homosexuality. (Table 3)

Regression analysis revealed that the odd of a SCD patients being coinfected with HIV-HBV is not significantly influenced by previous hospitalization, having multiple sexual partner, improper use of condom or marital status. The only factor significantly associated with HIV-HBV coinfection in SCD patient is blood transfusion and where the blood was transfused. SCD patients with history of blood transfusion is 11 times at risk of the coinfection compared with those not transfused. Furthermore, those transfused in private hospitals have 5 times higher risk of the coinfection than those transfused in tertiary public hospital. (see table 4)

DISCUSSION

Three hundred and fifty SCD patients accessing medical care at the University of Ilorin Teaching hospital within the study period were recruited into the study. 260 (74.29%) were below 20 years old. Predominance of children with SCD at the hospital is in-keeping with Onuchukwu et al's finding in the same hospital about the same period. [18] He recruited 166 SCD patients age between 6months and 14 years within 12 months for his study. Similarly, Odaibo et al at Ibadan had 63.5% of SCD patients in their study age below 20years. [1] The children dominance may be due high health-seeking behavior for children than adults, and low life expectancy for SCD patients, making adult SCD patients' population lower. [8] Many SCD patients don't survive beyond the childhood period because of their higher susceptibility to infections, poor nutrition, complications of SCD crisis and inability to cope with incessant needs to pay medical bills. [8, 10] 91.71% of the participants were singles, reason being that they are predominantly children. Only 8% were married probably due to general population unwillingly to have SCD partners, and SCD patients too may be unwilling to compound the stress of marriage and childbearing to their medical burdens. The male to female distribution was almost equal, indicating no significant gender preponderance in SCD. The gender distribution finding is similar to that of other researchers in the center and other study centers. [1, 2, 8,19] Ilorin, being a Muslim dominated city accounted for higher number of muslims than Christians among the study population. Over 60% of the subjects had at least secondary school education and almost 80% were students revealing high level of enlightenment and commitment to learning despite their health challenges.

Prevalence of HIV-HBV coinfection among SCD patients in this study was 6.9%, as 24 out of the 350 participants tested positive for both HIV and HBV infections. This value is within the national HIV-HBV coinfection prevalence value range of 5-17% at the study period. [2] This National prevalence still remains the same now despite all the progresses made in HIV control and blood transfusion safety. There is no higher predisposition to the coinfection among SCD patients than the general population based on the findings of this study. The prevalence is within the National reference range of the coinfection for the general population. This prevalence is similar to findings of other researchers, though it contrasts a few other findings. The most remarkable risk factors to the coinfection among SCD patients are blood transfusion and being transfused at a private health facility. Higher prevalence of coinfection among SCD who survived to adulthood is likely due to cumulative exposure to risks of the infections from blood transfusion, unsafe injections and other risk of adulthood as in the general population. With increasing awareness for safe blood transfusion, non-profit driven practices among health professionals in public hospitals, and access to freely donated blood from the National Blood Service Agency (NBSA), transfusion is apparently safe in government owned health facilities. This is contrary to the practices of most private-owned hospitals which are profit-driven and having little or no access to freely donated blood from NBSA. Blood transfusion in most peripheral / private facilities are less supervised or regulated. These facilities often patronize commercial blood donors, and their HIV and viral Hepatitis status testing were often skipped on assumption of known serostatus being a familiar donor. This made transfusion in most private settings unsafe and predisposes recipients to blood-borne infections, especially HIV and HBV. [5, 6, 11] Blood transfusion as a major predisposing factor to HIV and viral hepatitis among SCD and general population had been established by many researchers. The Ministry of Health and the NBSA must intensify efforts to curb unsafe blood transfusion practices in Nigeria, especially in private health institutions.

Table 1: Sociodemographic Characteristics of the Participants

VARIABLES	FREQUENCY (N=350)	PERCENT (100%)
Age (in years)		
1-9	114	32.57
10-19	146	41.71
20-29	58	16.57
30-39	22	6.29
40-49	10	2.86
Marital status		
Single	321	91.71
Married	28	8.00
Widow/widower	1	0.29
Divorcees	0	0.0
Gender		
Male	160	45.71

Female	190	54.29
Highest Educational level		
No formal education	27	7.71
Primary	110	31.43
Secondary	162	46.29
Tertiary	51	14.57
Religion		
Christian	124	35.43
Moslem	226	64.57
Occupation		
Student	279	79.71
Trader	33	9.43
Civil servant	11	3.14
Preschool	27	7.71

Table 2: Age Distribution of Hiv-Hbv Coinfection

AGE GROUPS (years)	FREQUENCY	PERCENTAGE
1-9	8	33.33
10-19	9	37.50
20-29	1	4.17
30-39	6	25.00
40-49	0	0.00
TOTAL	24	100.00

Table 3: Relationship between Hiv-Hbv Coinfection and Some Associated Factors among Scd Patients

VARIABLES	N	X^2	P-value	Remark
Gender	**350**	**1.592**	**0.207**	**Not significant**
Age	**350**	**74.15**	**0.223**	**Not significant**
Marital status	**350**	**7.668**	**0.871**	**Not significant**
Religion	**350**	**43.84**	**2.764**	**Not significant**

Previous Hospitalization	**350**	**8.744**	**0.003**	**Significant**
Educational status	**350**	**1.302**	**0.729**	**Not significant**
Blood Transfusion	**350**	**40.06**	**0.000**	**Significant**
Number of Pints of Blood Transfused	**350**	**0.010**	**0.995**	**Not significant**
Where transfused	**350**	**227.9**	**0.000**	**Significant**
Scarification marks	**350**	**1.463**	**0.226**	**Not significant**
Tattooing	**350**	**2.085**	**0.149**	**Not significant**
Clipper sharing	**350**	**2.656**	**0.103**	**Not significant**
Needle/sharps sharing	**350**	**11.089**	**0.998**	**Not significant**
Illicit drug use	**0**	**-**	**-**	**-**
Sex worker patronage	**0**	**-**	**-**	**-**
Homosexuality	**0**	**-**	**-**	**-**
Multiple sexual partners	**350**	**5.273**	**0.022**	**Significant**
Use of condom	**350**	**8.730**	**0.013**	**Significant**
History of sexually transmitted diseases	**350**	**3.932**	**0.637**	**Not significant**
History of surgery	**350**	**6.984**	**0.786**	**Not significant**
Circumcised	**350**	**2.301**	**0.129**	**Not significant**
Incomplete HBV vaccination	**350**	**31.56**	**0.064**	**Not significant**

Table 4: Logistic Regression for Predictors of Hiv-Hbv Coinfection among Scd Patients

VARIABLES	ODDS RATIO	95% CI	P-VALUE
Hospitalization	**0.231**	**0.0875 - 3.604**	**0.219**
Marital status	**1.356**	**0.875 - 4.15**	**0.722**
Blood transfusion	**11.44**	**3.908 – 21.87**	**<0.05**
Where transfused	**5.056**	**0.045 - 6.634**	**<0.05**
Multiple sexual Partner	**1.665**	**0.147 – 3.314**	**0.563**
Condom usage	**2.783**	**0.010 – 4.342**	**0.573**

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Authors contribution

AGM – Conceptualization, Data curation, Manuscript writing (drafting and editing)

ABT – Data curation, Manuscript writing (drafting and editing)

CN – Supervision

Conflict of Interest

Authors declared no conflict of interest