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Prevalence of HIV, HBV and HCV Infections among Sickle Cell Disease Patients in Southwestern Nigeria: A Case-Control Study

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Abstract

Aim: This study was designed to determine the prevalence of HBV, HCV and HIV infections among individuals with Sickle Cell Disease (SCD) in Ibadan, southwestern Nigeria. **Methodology:** In this case-control study, 1017 patients with SCD and 1017 age and gender matched controls were enrolled from 6 health facilities and some communities in Ibadan, southwestern Nigeria. Blood samples were tested for the presence of HIV, HBV and HCV infections. Structured questionnaire was used to capture participants' information and data analyzed using descriptive statistics, McNemar Chi-square/Fishers exact test. **Results:** Blood transfusion was significantly more common among SCD cases [566 (55.7%)] than controls [54 (5.3%)], while history of vaccination was higher in the control group (p = 0.001). The overall prevalence of HIV [2 (0.2%) vs 11 (1.1%)], HBV [58 (5.7) vs 66 (6.5%)] and HCV [10 (1.0) vs 22 (2.2%)] was lower among SCD cases than controls, respectively, although significantly different only in HCV infection (p = 0.048). All three infections were significantly higher in adults than in children. Co-infection was found only in four of the participants, all of whom were SCD patients. **Conclusion:** The prevalence of HIV, HBV and HCV infection among SCD patients indicates an improvement in the transfusion safety measures in the region. The prevalence of HBV and HCV found in this study is still relatively high when compared with reports from some other regions. There is a need for continued surveillance

and subsidized cost of drugs for treatment of these infections, especially for SCD patients who already have a compromised immunity.

Keywords

Hepatitis B, Hepatitis C, Human Immunodeficiency Virus, Sickle Cell Disease, Prevalence

1. Introduction

Sickle cell disease (SCD) is defined as the condition resulting from the inheritance of sickle hemoglobin from both parents or sickle hemoglobin from one parent and another pathological variant hemoglobin from the other parent [1]. It is one of the most common inherited anaemias globally and the most prevalent genetic disease in Nigeria [2]. Nigeria has the highest burden of SCD in the world with a prevalence of 2% to 3% [2] [3]. Over 4 million individuals have homozygous HbS, while another 40 million have sickle cell trait [4]. Some of the major complications of SCD in most patients are chronic anaemia and infection, which are major causes of death and disability, although increased susceptibility to these infections is still poorly understood [3] [5]. Due to the chronic anaemia, blood transfusion is a major therapeutic and prophylactic intervention in the management of patients with SCD. Frequent transfusion exposes SCD patients to blood borne pathogens [5] [6] most of which are viruses such as hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV) and other transfusion transmitted viruses (TTV). These infections are major health problems in developing and resource limited countries including Nigeria [7] [8].

Human immunodeficiency virus, an RNA virus is a member of the genus *lentivirus* of the family retroviridae while hepatitis B virus is a DNA virus belonging to the family hepadnaviridae and hepatitis C virus also an RNA virus is of the genus *hepacivirus*, a member of the family flaviviridae. HIV and HBV utilises the enzyme reverse transcriptase for their replication to convert RNA to DNA. These viruses share common routes of transmission [5] [9] that include: parenteral (through unscreened blood), sexual (horizontal), mother to infant (vertical) and intra-familial spread (horizontal transmission). Due to shared routes of transmission, coinfection with HIV and viral hepatitis is common [8] [9] [10] [11]. Interestingly the rates of these three infections are high, if not highest in Sub-Saharan Africa where SCD is also prevalent. According to UNAIDS 2018 estimates, the prevalence of HIV infection varies from 0.3% to 23% in Madagascar and Lesotho, respectively, with Nigeria (2,600,000) and South Africa (7,700,000) having the largest number of people living with the infection globally [12]. WHO estimates that over 257 million people are living with chronic hepatitis B globally, although only 10.5% of these infected individuals know their HBV status [13]. In Africa about 6.1% of the adult population are infected with HBV, with Nigeria being one of the countries classified as being highly endemic (*i.e.* HBV preva-

lence > 8%) [14]. Worldwide more than 170 million persons have HCV infection, of whom 71 million have chronic infection [15] [16]. The eastern Mediterranean countries have the highest prevalence of 2.3%, with other regions having an estimated prevalence of 0.5% - 1.5%. In Nigeria previous studies on HCV have reported a prevalence of 0.5% - 15%, from different parts of and various population groups in the country [17] [18] [19] [20].

There is no approved vaccine currently available against HCV and HIV infection, while highly effective vaccines are available to prevent HBV infection. In Nigeria HBV vaccine was included in the National Programme on Immunization (NPI) in 2004 [21], implying that a large proportion of children born after 2004 have been vaccinated against HBV infection. Although effective drugs for the treatment of HBV and HCV are available, they are still relatively expensive and not within the reach of a large percentage of the patients in Nigeria and other resource limited countries [22] [23]. On the other hand, although there is increasing access to antiretroviral therapy (ART) even in the developing countries due to donor support, treatment for HIV is not curative [12]. Hence the most effective way of controlling these infections is through prevention. Information on the prevalence of these viruses is important for planning of health control measures in primary and secondary prevention, particularly as HBV and HCV could result in chronic liver disease with long term risk of liver cirrhosis and hepatocellular cancer [24] [25]. Also, HIV infection could further compromise the already deficient immune status of the SCD population [26]. This study was therefore designed to determine the rate of HBV, HCV and HIV infections among individuals with and without SCD in Ibadan, southwestern Nigeria.

2. Materials and Methods

2.1. Study Area

The study was carried out in Ibadan, a metropolitan city, and the capital of Oyo State, Nigeria [https://www.britannica.com/place/Ibadan]. Ibadan has over 3 million inhabitants. Being one of the most populous cities in Nigeria, Ibadan is the largest geographical municipal area in Nigeria with a high population density of 985.13/km^2 (2551.5/sq mi). The study was conducted in the tertiary, secondary and other recognized health facilities that serve as referral centers for SCD in Oyo State as well as other States within the Southwestern region of Nigeria.

2.2. Study Design and Data Collection

This was a case control, cross-sectional study. Participants with SCD (cases) were enrolled after obtaining their consent during their routine visit to the SCD clinic in some health facilities. Cases were only enrolled in health facilities that have well-established SCD clinics and are reputed referral centers in Oyo State. These facilities include the University College Hospital, Ibadan; Adeoyo Maternity Teaching Hospital, Ibadan; State Hospital Ring Road, Oni Memorial Hospital, Ibadan Sickle Cell Foundation, Adeoyo Maternity Centre, University of Ibadan Jaja Clinic, Ibadan. Participants without SCD (controls) were recruited

during outreach programs at community levels from schools and communities using these referral hospitals and around the hospitals and clinics where cases were sourced within the Ibadan Metropolis. The same questionnaire that captured information on sociodemographic and behavioral characteristics and medical history was administered to both cases and controls by trained interviewers. Ethical approval for the study was obtained from UI/UCH Institutional Review Board **(approval # UI/EC/17/0400, 28-12-17, 28-12-18, 28-12-19, 26-12-2020) and** all aspects of the study were carried out in accordance with the ethical standards of the Declaration of Helsinki. Group pre-test counseling was offered to participants before sample collection. Their test results were given to them in a one-on-one post-test counseling session during which positive individuals were referred to the appropriate clinics. HIV positive individuals were referred to the ART clinic, while HBV/HCV positive individuals were referred to the gastroenterology clinic.

Inclusion Criteria

- Only those who had been diagnosed with SCD and were tested using the phenotypically accurate HPLC diagnostic system to confirm the presence of either haemoglobin SS or SC at the Genetics Research Unit.
- Controls were individuals with HPLC confirmed phenotypes indicating no who do not have SCD, and are community or hospital-based and from the same communities within the catchment areas of the hospital where cases were recruited.
- Hospital-based controls were patients at general outpatients (GOP), medical outpatient (MOP) and children outpatient (CHOP) clinics of the participating health centres.

Eligible cases or controls must have given written informed consent, assent or parental/caregiver consent (for children who cannot give assent) before enrolment into the study.

Exclusion Criteria

- Individuals who were pregnant at the point of recruitment were excluded from the study.

2.3. Sample Collection, Processing and Storage

Five milliliters of venous blood were collected into 2 ml and 3 ml aliquot bottles containing EDTA from each participant after obtaining their informed consent or assent (for minors) and a pre-test counseling. Both aliquots of blood were transported in a cold box from the site of collection to the University College Hospital. The 2 ml aliquot was delivered to the Genetics Research Laboratory at the Institute for Advanced Medical Research & Training (IAMRAT) for haemoglobin phenotype confirmation using the Biorad Variant 2 High Performance Liquid Chromatography (HPLC). The 3 ml aliquot was delivered to the Department of Virology, College of Medicine, both at the UCH, University of Ibadan. At the Virology Department, the 3 ml aliquot was centrifuged at 3000 rpm for 15 mins, plasma separated and stored in aliquots in −20˚C until analysed. A total of

1017 blood samples were collected from SCD Cases and 1017 samples from Non-SCD Controls. A structured questionnaire was used to capture demographic and some medical information.

2.4. Laboratory Analysis

Stored plasma samples were tested for the presence of HIV, HBV and HCV using commercially available 3rd and 4th generation ELISA kits in an internationally accredited ISO 15189 (SANAS) laboratory in the Department of Virology. Heamoglobin confirmation, analyses and quantification of study samples into Cases and Controls were carried out using the SweLab Alpha 3 Cell Counter and the Bio-Rad HLPC at the Genetics Research lab also an accredited laboratory at the College of Medicine, University of Ibadan.

2.4.1. Diagnosis of HIV Infections

Plasma samples were tested for the presence of HIV-1/2 infection using a fourth generation ELISA (GenScreen Ultra HIV Ag-Ab, Bio-Rad, Paris) that has the ability of detecting both HIV antigen and antibodies. Initially reactive samples were repeated using the same assay, and repeatedly reactive samples were further analysed by Western blot technique to confirm infection. The bands on the Western blot strips were identified by comparing them to the bands on the positive control strip and results interpreted as follows: No band present: HIV-1 and HIV-2 negative; any two or more bands including any of the glycoproteins and a gag protein band: HIV positive; any band pattern not matching the criteria for positive HIV result: indeterminate.

2.4.2. Diagnosis of HBV Infections

HBV diagnosis was made using ELISA that detects surface antigen (Monolisa, Bio-Rad, Paris) or IgM antibodies to the core antigen (HBcIgM, Dia.PRO, Italy). All assays were performed according to manufacturer recommendation. Samples that were positive for either HBsAg or HBcIgM were considered positive for hepatitis B virus infection.

2.4.3. Diagnosis of HCV Infections

A third generation ELISA (HCV-Ab, Dia.PRO, Italy) that detects HCV antibodies was used for diagnosis of HCV infection.

2.5. Data Analysis

Data were analysed using descriptive statistics, McNemar Chi-square/Fishers exact test with IBM SPSS statistics version 25.

3. Results

A total of 2034 participants were enrolled for the study, including 1017 cases and 1017 controls. Table 1 shows the demographic and some medical history of the study participants. There was no difference in the sex ($p = 0.99$) and age ($p = 0.50$) distribution between the two groups. There was, however, a significant dif-

ference in the history of blood transfusion ($p < 0.001$) and history of HBV vaccination ($p = 0.001$), with a higher rate of blood transfusion (55.7%) among individuals with SCD. On the other hand, the proportion of individuals who had HBV vaccination was higher ($p = 0.001$) among those without SCD. The male to female ratio for both groups was approximately 1.1:1.

Table 1. Characteristics of study population.

CHARACTERISTICS	CASES	CONTROL	TOTAL	p
Sex				
Male	527 (51.8)	528 (51.9)	1055 (51.9)	##
Female	490 (48.2)	489 (48.1)	979 (48.1)	
Total	**1017**	**1017**	**2034**	
Age				
0 - 9 yrs	305 (30.0)	344 (33.8)	649 (31.9)	**0.50**
10 - 19 yrs	346 (34.0)	330 (32.4)	676 (33.2)	
20 - 29 yrs	207 (20.4)	201 (19.8)	408 (20.1)	
30 - 39 yrs	99 (9.7)	84 (8.3)	183 (9.0)	
40 - 49 yrs	37 (3.6)	33 (3.2)	70 (3.4)	
50 years+	23 (2.3)	25 (2.5)	48 (2.4)	
Total	**1017**	**1017**	**2034**	
Study Centre				
CHOP	274 (26.9)	63 (6.2)	337 (16.6)	**<0.001**
RRSH	171 (16.8)	6 (0.6)	177 (8.7)	
HAEMATOLOGY	247 (24.3)	118 (11.6)	365 (17.9)	
OMCH	173 (17.0)	4 (0.4)	177 (8.7)	
IBSCF	105 (10.3)	36 (3.5)	141 (6.9)	
AMTH	19 (1.9)	41 (4.0)	60 (2.9)	
COMMUNITY	13 (1.3)	747 (73.5)	760 (37.4)	
JAJA CLINIC UI	15 (1.5)	2 (0.2)	17 (0.8)	
TOTAL	**1017**	**1017**	**2034**	
History of blood transfusion				
Yes	566 (55.7)	54 (5.3)	620 (30.5)	**<0.001**
No	451 (44.3)	963 (94.7)	1414 (69.5)	
Total	**1017**	**1017**	**2034**	
History of HBV Vaccination				
Yes	229 (22.5)	296 (29.1)	525 (25.8)	**0.001**
No	778 (76.5)	715 (70.3)	1493 (73.4)	
I don't Know	4 (0.4)	0 (0.0)	4 (0.2)	
Not Applicable	6 (0.6)	6 (0.6)	12 (0.6)	
Total	**1017**	**1017**	**2034**	

- No p-value because the cases and controls were matched exact sex.

The overall prevalence of HIV, HBV and HCV infections was 0.6%, 6.1% and 1.6%, respectively (Figure 1). The prevalence of HIV and HCV infections were higher among the controls (p = 0.12 & 0.03 respectively), while there was no significant difference in the prevalence of HBV (p = 0.52) infection between the cases and controls.

Table 2 shows the distribution of HIV infection by gender and age of the participants. Out of the 2034 participants tested 13 were positive for HIV giving an overall prevalence of 0.6%. Although there was no difference in prevalence among males and females within each of the groups, the prevalence of infection was

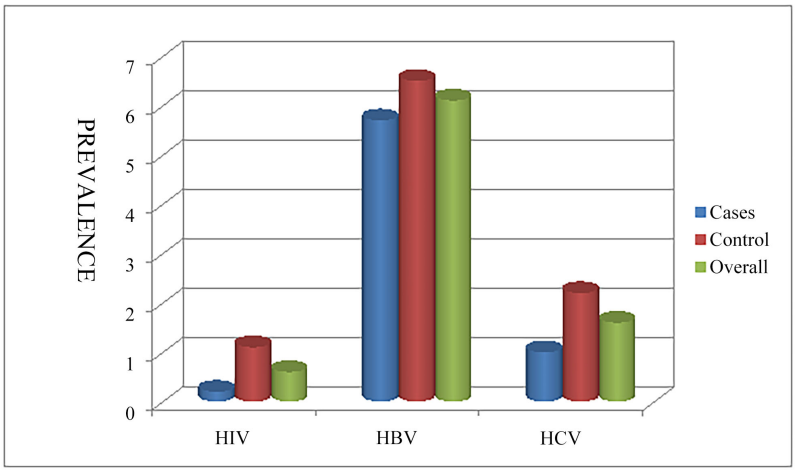

Figure 1. Prevalence of HIV, HBV and HCV among individuals with and without Sickle Cell Disorder.

Table 2. Distribution of HIV by gender and age group among individuals with or without SCD in Southwestern Nigeria.

		CASES		CONTROL		TOTAL		p value
		No Tested	No (%) positive	No Tested	No (%) positive	No Tested	No (%) positive	
Gender	Male	527	0 (0.0)	528	7 (1.3)	1055	7 (0.7)	**0.02**
	Female	490	2 (0.4)	489	4 (0.8)	979	6 (0.6)	**0.45**
	Total	**1017**	**2 (0.2)** p = 0.23	**1017**	**11 (1.1)** p = 0.55	**2034**	**13 (0.6)** p = 0.99	**0.02**
Age group	0 - 9	305	1 (0.3)	344	2 (0.6)	649	3 (0.5)	**0.99**
	10 - 19	346	0 (0.0)	330	3 (0.9)	676	3 (0.4)	**0.12**
	20 - 29	207	0 (0.0)	201	2 (1.0)	408	2 (0.5)	**0.24**
	30 - 39	99	1 (1.0)	84	1 (1.2)	183	2 (1.1)	**0.99**
	40 - 49	37	0 (0.0)	33	2 (6.1)	70	2 (2.9)	**0.22**
	≥50	23	0 (0.0)	25	1 (4.0)	48	1 (2.1)	**0.99**
	Total	**1017**	**2 (0.2)** p = 0.26	**1017**	**11 (1.1)** p = 0.07	**2034**	**13 (0.6)** p = 0.96	**0.02**

higher (p = 0.02) among the male controls compared to cases. The prevalence was highest among those in the 30 - 39 (1%) age group in the SCD population and the 40 - 49 age group (6.2%) in the control group. Overall, the rate of HIV increased with age. Similarly, there was no difference in the rate of HCV infection between by gender within the two groups, but there was a non-significant trend toward higher prevalence among the female controls (0.8%) compared to the cases (0.4%). The overall rate of HCV infection among the 2034 participants was 1.6% (Table 3). The 20 - 29 age group had the highest HCV prevalence (2.4%) among those with SCD, while among those without SCD the prevalence was highest among those ≥50 (4.0%) and 20 - 29 (3.5%) of age.

The overall prevalence of HBV infection was 6.1% however, there was no significant difference in the prevalence of HBV infection by gender both within (p = 0.32, p = 0.99 and between (p = 0.41) the groups. Table 4 shows the distribution of HBV among study participants by gender and age. Although the prevalence was higher among males (7.4%) than females (5.5%) in the control group, the difference was not significant. However, there was a significant difference in the prevalence of HBV by age within the two groups (p = 0.001). The prevalence of HBV infection was highest among controls (13.1%) and cases (11.1%) in the 30 - 39 age group. Overall, the prevalence of all three infections was higher in the adult population compared with the pediatric population (Figure 2), although this difference was not significant for HIV infection. Figure 3 shows the overall distribution of HIV, HBV and HCV infection by age. The age groups with the highest prevalence were 20 - 29, 30 - 39 and 40 - 49 for HCV, HBV and HIV, respectively.

Table 3. Distribution of HCV among individuals with or without SCD in Southwestern Nigeria by gender and age group.

		CASES		CONTROL		TOTAL		p value
		No Tested	No (%) positive	No Tested	No (%) positive	No Tested	No (%) positive	
Gender	Male	527	6 (1.1)	528	12 (2.3)	1055	18 (1.7)	**0.23**
	Female	490	4 (0.8)	489	10 (2.0)	979	14 (1.4)	**0.12**
	Total	**1017**	**10 (1.0)** p = 0.75	**1017**	**22 (2.2)** p = 0.83	**2034**	**32 (1.6)** p = 0.72	**0.048**
Age group	0 - 9	305	2 (0.7)	344	3 (0.9)	649	5 (0.8)	**0.99**
	10 - 19	346	2 (0.6)	330	9 (2.7)	676	11 (1.6)	**0.03**
	20 - 29	207	5 (2.4)	201	7 (3.5)	408	12 (2.9)	**0.57**
	30 - 39	99	1 (1.0)	84	1 (1.2)	183	2 (1.1)	**0.99**
	40 - 49	37	0 (0.0)	33	1 (3.0)	70	1 (1.4)	**0.47**
	≥50	23	0 (0.0)	25	1 (4.0)	48	1 (2.1)	**0.99**
	Total	**1017**	**10 (1.0)** p = 0.39	**1017**	**22 (2.2)** p = 0.16	**2034**	**32 (1.6)** p = 0.12	**0.048**

Table 4. Distribution of HBV infection among individuals with or without SCD in South-western Nigeria by gender and age group.

		CASES		CONTROL		TOTAL		p value
		No Tested	No (%) positive	No Tested	No (%) positive	No Tested	No (%) positive	
Gender	Male	527	30 (5.7)	528	39 (7.4)	1055	69 (6.5)	***0.32***
	Female	490	28 (5.7)	489	27 (5.5)	979	55 (5.6)	***0.99***
	Total	**1017**	**58 (5.7)** p = 0.99	**1017**	**66 (6.5)** p = 0.25	**2034**	**124 (6.1)** p = 0.41	***0.52***
Age group	0 - 9	305	9 (3.0)	344	12 (3.5)	649	21 (3.2)	**0.83**
	10 - 19	346	14 (4.0)	330	17 (5.2)	676	31 (4.6)	**0.58**
	20 - 29	207	18 (8.7)	201	23 (11.4)	408	41 (10.0)	**0.41**
	30 - 39	99	11 (11.1)	84	11 (13.1)	183	22 (12.0)	**0.82**
	40 - 49	37	4 (10.8)	33	3 (9.1)	70	7 (10.0)	**0.99**
	≥50	23	2 (8.7)	25	0 (0.0)	48	2 (4.2)	**0.22**
	Total	**1017**	**58 (5.7)** p = 0.003	**1017**	**66 (6.5)** p = 0.001	**2034**	**124 (6.1)** p ≤ 0.001	**0.52**

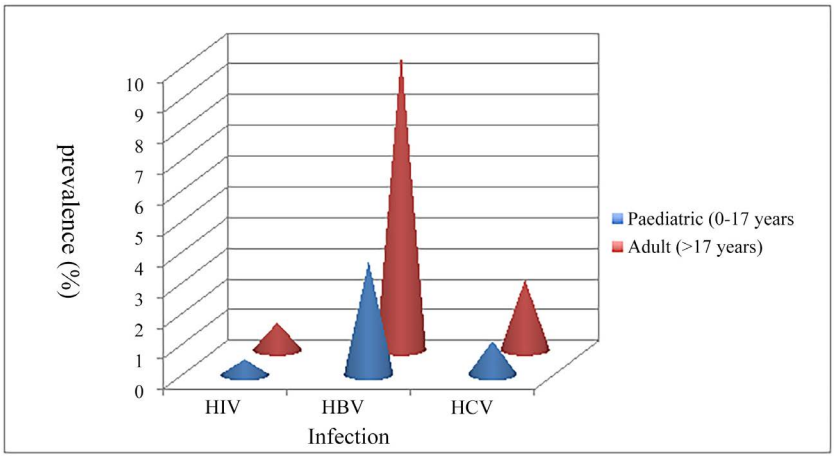

Figure 2. Distribution of HIV, HBV & HCV Infection among the adult and pediatric participants.

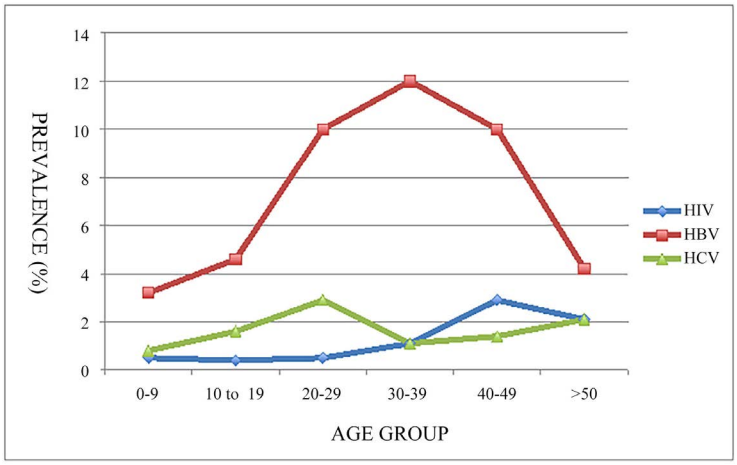

Figure 3. Prevalence of HIV, HBV & HCV by age of study participants (cases & controls).

Although there was a trend toward higher prevalence of HIV, HBV and HCV in those with a history of blood transfusion among the SCD population, these differences were not significant. About 30% (620/2034) of the study participants had history of blood transfusion. Table 5 shows the relationship between HIV, HBV and HCV and history of blood transfusion among the study population. In the control group the prevalence of infection was slightly higher among those with no history of blood transfusion, although the difference was also not significant. The prevalence of HBV and HCV infection was higher in those who received blood transfusion among the SCD cases, while the reverse was true among controls, although not statistically significant. Only 28.6% of the study population reported history of receiving hepatitis B vaccine. Figure 4 shows the distribution of HBV infection by HBV vaccination status. Overall, the prevalence of

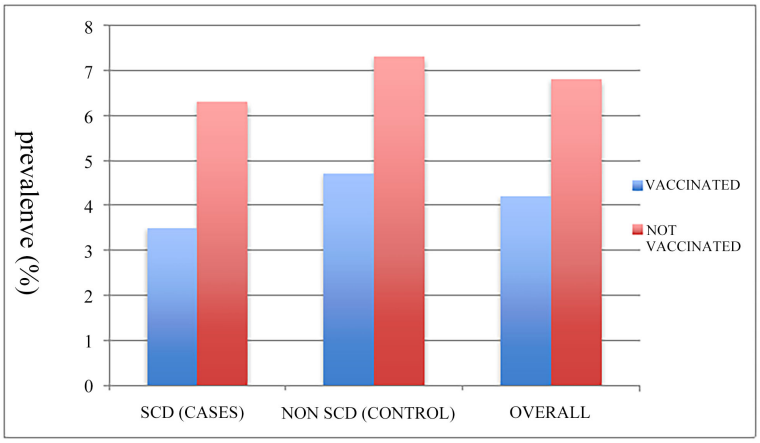

Figure 4. Distribution of HBV infection by Vaccination status in Cases and Controls.

Table 5. Distribution of HIV, HBV and HCV by history of blood transfusion among individuals with or without SCD in Southwestern Nigeria.

Infection	Transfusion Status	CASES		CONTROL		TOTAL		p value
		No Tested	No (%) positive	No Tested	No (%) positive	No Tested	No (%) positive	
HIV	Transfused	566	1 (0.2)	54	0 (0.0)	620	1 (0.2)	**0.99**
	Not transfused	451	1 (0.2)	963	11 (1.1)	1414	12 (0.8)	**0.12**
	Total	**1017**	**2 (0.2)** p = 0.99	**1017**	**11 (1.1)** p = 0.99	**2034**	**13 (0.6)** p = 0.13	**0.02**
HBV	Transfused	566	34 (6.0)	54	3 (5.6)	620	37 (6.0)	**0.99**
	Not transfused	451	24 (5.3)	963	63 (6.5)	1414	87 (6.2)	**0.41**
	Total	**1017**	**58 (5.7)** p = 0.69	**1017**	**66 (6.5)** p = 0.99	**2034**	**124 (6.1)** p = 0.92	**0.52**
HCV	Transfused	566	6 (1.1)	54	0 (0.0)	620	6 (1.0)	**0.99**
	Not transfused	451	4 (0.9)	963	22 (2.3)	1414	26 (1.8)	**0.09**
	Total	**1017**	**10 (1.0)** p = 0.99	**1017**	**22 (2.2)** p = 0.63	**2034**	**32 (1.6)** p = 0.18	**0.048**

HBV infection was significantly higher (p = 0.03) among the non-vaccinated participants when compared with those who had history of HBV vaccination. Although the difference was not significant when considered as individual groups (*i.e.* cases or control), the prevalence was still higher among non-vaccinated cases (6.3% vs 3.5%) and control (7.3% vs 4.7%).

Overall, the rate of co-infection found in this study was 0.2% (4/2034). Three of these individuals were positive for both HBV and HCV, giving an HBV/HCV co-infection rate of 0.15%, while one was positive for both HBV and HIV, for an HIV/HBV co-infection rate of 0.05%. HIV-HCV coinfection or triple infection were not found in any of the participants. All coinfections were found among those with SCD, and 3 (75%) had history of blood transfusion.

4. Discussion

Based on our review of the literature, this is the only case control study on HIV, HBV and HCV involving a large number of individuals with SCD, from Sub-Saharan Africa. Nigeria has the highest burden of SCD in the world with a prevalence of 2% - 3% in the general population [2]. In a study carried out among a similar population in Ile-Ife, Nigeria, only 82 SCD and 90 sex and gender-matched controls were enrolled in the study [27]. The large sample size in this study increases the quality, accuracy, reliability of the data generated, and reduces the margin of error, making extrapolation into the larger population more representative.

The overall prevalence of HIV infection in this study was 0.6%. This is lower than the prevalence among the general population in Nigeria [28]. This could be relevant to a higher preponderance of infection from some other states. However, it is within the range of HIV infection rates previously reported in Oyo state. According to the result of National HIV Sentinel Survey, the prevalence of HIV infection in Oyo State ranged from 0.2% - 2.1% in the 2012 survey and a mean of 0.9% in the recent Nigeria HIV/AIDS Indicator and Impact Survey (NAIIS) [29]. This is also lower than reported among some other population groups in Ibadan [30] [31]. Although the rate of blood transfusion was significantly higher among the SCD patients than the control group in this study, the prevalence of HIV was significantly lower in the SCD patients than those without SCD, similar to the results from the National Programme on Immunization. This finding is also similar to the finding of a study in the US where the prevalence of HIV infection among SCD patients was 1.5% compared to 3.3% among those without SCD [32].

Recent studies have shown that SCD is associated with decreased HIV infection [32] [33]. This could be attributed to the enhanced immune defense in SCD [32] [33] or up regulation of inflammation, iron metabolism and immunologic changes in SCD that are not favorable for HIV replication [34] in association with expected precaution by SCD patients on sexual issues. The CCR5D32 mutant allele has been shown to confer resistance against HIV infection [35]. Al-

though we did not investigate the presence of this allele in our study population, a study in Brazil [36] showed a higher rate of the CCR5D32 mutant allele among SCD patients (5.1%) than healthy controls (1.3%). However, the difference observed for SCD may be partly explained by the fact that SCD individuals have significantly less risky exposures for acquisition of HIV.

The HBV prevalence of 6.1% obtained in this study is lower than that previously reported in different populations in various parts of Nigeria [37] [38] [39]. In a study conducted among hospital patients in Lagos, the prevalence was 28.4% [40], while a higher prevalence was found in another study carried out among blood donors and hairdressers in Ibadan, Oyo state [8] [41]. One of the reasons for the difference in the HBV rate between these studies and ours is the number of participants enrolled for the studies. While the sample sizes of those studies ranged from 100 to 500, the sample size for our study was 2034. The prevalence of HBV among the SCD patients (5.7%) was lower than the prevalence of HBV among the controls (6.5%), but the difference was not statistically significant. The prevalence of HBV in the SCD population in our study is lower than previously reported among SCD patients in Nigeria [5] [27]. The lower prevalence of HBV infection found in our study may be due to the preventive effect of HBV vaccine introduced into the National Programme on Immunization (NPI) in 2004, *i.e.*, 15 years before this study [21]. This explanation is further supported by the fact that the prevalence of HBV infection was significantly lower in children younger than 18 years (3.7%) compared with adults (9.7%). The prevalence of HBV infection was also lower among vaccinated SCD patients and controls than in the unvaccinated participants.

In a review article on the status of HBV control in Africa region, Breakwell *et al.* [42] reported HBV vaccination coverage among children in Nigeria of 56% in 2015. This coverage is expected to have increased by the time of our study. Also, a study conducted using samples collected in the pre- and post-HBV vaccination era showed a reduction in the prevalence of HBV infection from 4.6% to 2.0% [43] among residents in a rural community in Nigeria. Breakwell *et al.* [42] reviewed 26 publications on HBV infection among various populations and locations in Nigeria and reported a median prevalence of 6.9%, similar to the overall HBV prevalence of 6.1% found in our study.

According to the WHO an estimated 71 million people are chronically infected with HCV, with about 20% of these infections occurring in Africa [16] [44]. The global incidence of HCV was 23.7 cases per 100,000 population (95% uncertainty interval; range 21.3 - 28.7) with an estimated 1.75 million new HCV infections diagnosed in 2015. The overall prevalence of HCV found in this study was 1.6%. This is similar to the prevalence of HCV found among the general population in Nigeria, ranging from 1.5% to 2.5% [45]. This is also within the range of the estimated prevalence of HCV infection in West Africa [46]. We found that the prevalence of HCV was lower among those with SCD than those without SCD. However, it is lower than the prevalence of HCV reported among SCD

patients in different parts of the country. For example, Lesi and Kehinde [47] found a prevalence of 5% among SCD patients in Lagos, Omote *et al.* [48] reported a prevalence of 5% in SCDs in Jalingo, Taraba state, and Ejiofor found a prevalence of 5% among SCD in Benin City [49]. In a previous study among 180 SCD samples collected from patients in 1998 in Ibadan, by Fasola *et al.* [5] reported an HCV prevalence of 7.2%. The difference in the prevalence found in this current study and our previous study of about 20 years ago may be an indication of the improvement in blood safety over the years. Prior to the Fasola study [5], HCV screening was not routinely incorporated into blood donation services in the country. In addition, the relatively small sample size may have contributed to the higher rate reported in the previous studies. The overall (1.6%) prevalence of HCV among those with SCD (1.0%) and those without SCD (2.2%) found in this study are higher than the prevalence of 0.4% found among 1572 undergraduate students of a University in Oyo State, Nigeria [50]. It is also higher than the 0.8% reported among HIV negative individuals in a tertiary hospital in Lagos. [40]

Although the difference was not significant, a higher prevalence of HCV infection was found among the never transfused than those with history of blood transfusion. This is similar to the findings of Lesi and Kehinde [47], who reported a higher prevalence of HCV infection among the never transfused (7%) than the transfused (5%) among SCD patients in Lagos, Nigeria. Some researchers suggested that blood transfusion may not be the major mode of transmission of HCV [41] [47]. The finding of this study seems to support this suggestion which is further corroborated by our yet to be published data that showed that certain lifestyles predispose to TTIs more than history of blood transfusion. This may also explain why the prevalence of HCV is lower among SCD patients than the controls, even though the history of blood transfusion was significantly higher among those with SCD than the control group. However, in a study on the prevalence of antibodies to HCV among Nigerian patients with HIV infection, Inyama *et al.* [51] reported a higher prevalence of HCV infection among those with history of blood transfusion.

All three infections were lower in the pediatric (<18 years) than the adult (>18 years) population. It is well known that for viruses that cause chronic or latent infection, the prevalence of infection increases with age due to cumulative infection [52]. This, together with increased availability of vaccine for HBV, prevention of mother-to-child transmission (PMTCT) programmes for HIV, and improvement in screening of blood for transfusion may explain the lower prevalence of all three infections in the pediatric population. However, it must be noted that the prevalence of the three infections in this study were higher than what has been reported in some other countries. In a study conducted among SCD patients in Oman by Alkindi *et al.* [11], a prevalence of 0%, 2.3% and 12.6% were reported for HIV, HBV and HCV infections, respectively. A lower prevalence of HBV (1%) and HCV (0.5%) was also reported among apparently healthy preg-

nant women in Ayingba [53], although the prevalence of HIV infection in their study was higher. Al-kadassy *et al.* (2018) also reported a lower prevalence of HIV (0%), HBV (3.3%) and HCV (0.8%) among SCD patients in Hodeidah City, Yemen [54].

Co-infection of HIV, HBV and HCV infections are severe global public health problems, particularly in resource limited countries in sub-Saharan Africa where all three viruses are prevalent [38]. The three viruses share common route of transmission including sexual, mother-to-child, blood product, and co-infection is known to be associated with increased morbidity and mortality [25] [38] [43]. This makes detection of the infections in an individual a priority. Different rates of co-infection with these viruses have been reported in various populations in different parts of the country. The rate of 0.15% and 0.05% obtained respectively for HBV/HCV and HCV/HIV coinfection is low compared to previous reports in the country. Fasola *et al.* [5] reported an HBV/HCV coinfection rate of 7.2% among SCD patients in Ibadan, while Omote *et al.* [48] found an HBV/HCV prevalence of 1% among patients attending a tertiary hospital in Taraba state. However, the results of our study are similar to those of a study on HIV, HBV and HCV among pregnant women in Anyigba, Nigeria, in which an HIV/HCV coinfection rate of 0.5% was found [53]. Also similar to our study, the Anyigba study did not find anyone co-infected with all three viruses. In summary, the rate of HIV in this study is similar to the prevalence of 0.9% for Oyo State reported in the recent NAIIS [28]. The lower prevalence of HIV, HBV and HCV infection among SCD patients compared to earlier reports of about 2 decades ago suggests an improvement in the transfusion safety measures in the region. Furthermore, the prevalence of HBV and HCV found in this study are higher than observed in other reports among different populations and regions of Nigeria as well as other countries.

5. Limitation

The markers used for detection of HBV infection in this study measured current or ongoing infection, hence we are unable to identify individuals who were exposed to HBV but cleared the infection. Anti-HBs is a marker of previous infection, however it is challenging to differentiate anti-HBs produced in response to natural infection and that produced in response to vaccination.

6. Conclusion

The prevalence of HIV, HBV and HCV infection among SCD patients when compared with prevalence reported about a decade ago in the same population indicates an improvement in the transfusion safety measures in the region. However, the prevalence of HBV and HCV found in this study is still relatively high when compared with reports from some other regions of the world. There is therefore a need for continued surveillance and subsidized cost of drugs for treatment of these infections, especially for SCD patients who already have a compromised

immunity. In addition, it is important to strengthen the preventive measures *i.e.* availability of vaccine for HBV, prevention of mother-to-child transmission (PMTCT) programmes for HIV, and improvement in screening of blood for transfusion in order to further reduce the rate of these infections in the study population. We also recommend that SCD patients be tested regularly for the presence of these viruses especially in communities with less rigorous blood screening so that infection can be detected early, and appropriate interventions administered to positive individuals. In addition, other regions or countries with higher frequencies of HBV should pay more attention to the efficiency of their immunization program and their lifestyles to further reduce the level of these infections in the SCD and other at-risk populations.

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Authors' Contributions

Conceptualization AGF, Study Design AGF, GNO, OMA; Methodology AGF, GNO, FF, AO, OAB; Data analyses & data cleaning OMA; all authors provided critical revisions to the manuscript and do accept responsibility for the content of the article.

Consent to Participate

All participants provided written informed consent to participate in the study.

Ethical Approval

The study proposal was submitted by Sickle Cell Hope Alive Foundation (SCHAF) to the Joint Ethics Committee of the University of Ibadan/University College Hospital, Ibadan with an IRB **Approval # UI/EC/17/0400.**

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Data Sharing

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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