Human Immunodeficiency and Hepatitis B Viral Infections Among Patients With Sickle Cell Disease in Dar Es Salaam City, Tanzania: A Descriptive Study

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Research Article

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Abstract

Background: Tanzania is not only the fourth in the world with the highest number of sickle cell disease (SCD) births but also endemic to Human immunodeficiency virus (HIV) and Hepatitis B virus (HBV) infections. This study was done to determine the prevalence of HIV and HBV infections and their associated factors among SCD patients in Dar es Salaam, Tanzania.

Methods: A multicenter hospital-based descriptive cross sectional study was done among participants aged ≥ 16 years. Participants' socio-demographic and clinical data were recorded. Blood samples were drawn for HIV and HBV diagnosis. Categorical variables were summarized into frequencies and compared using Fisher's exact test while continuous variables were summarized into mean and standard deviation. Logistic regression was done to ascertain predictors of HIV infection. P values < 0.05 was considered statistically significant.

Results: There were 185/325 (56.7%) females. Mean (SD) age and hemoglobin were 23.04 ± 7.45 years and $7.4 (\pm 1.58)$ g/dl respectively. The prevalence of HIV and HBV were 1.8% and 1.2% respectively. None of the risk factors was associated with HIV. No associations were calculated for HBV owing to small numbers.

Conclusions: Prevalence of HIV and that of HBV infection are much lower in SCD patients in Dar es Salaam than the national prevalence of the two infections in the general population. The findings could not associate any risk factor with HIV infection. A nationwide similar study should be conducted to obtain enough numbers for characterization of the two infections in these patients.

Background

It is estimated that 300,000 children are born annually in the world with sickle cell disease (SCD). An estimated 75% of SCD affected children live in sub-Saharan Africa[1,2]. Tanzania is ranked the fourth country in the world with the highest number of SCD births after Nigeria, Democratic Republic of Congo (DRC) and India[2,3].

Improvements in the care for SCD has resulted into longer life spans thus in the due course SCD children grow into adulthood and face other health risks, including infections. Human immunodeficiency virus (HIV) and Hepatitis B virus (HBV) infections are transfusion transmissible diseases that may add a burden to SCD patients. Sub-Saharan Africa has nearly one adult living with HIV in every 25 people thus accounting for nearly two-thirds of the people living with HIV worldwide [4]. In Tanzania, adult HIV prevalence was estimated to be five percent in the year 2017[5]. Globally, HBV prevalence was estimated to be 3.5% in 2015 resulting in an estimated 887 000 Hepatitis B-related deaths, mostly from complications such as liver cirrhosis and hepatocellular carcinoma. Africa and Western Pacific regions accounted for 68% of those infected with HBV [6]. Tanzania is among the countries with highest HBV infection rates. A prevalence of six percent was reported in 1998 among the general population of the largest city in the country, Dar es Salaam [7]. Another study done between 2004 and 2005 among blood donors in the same city revealed a prevalence of 8.8% and 3.8% for HBV and HIV respectively[8].

The trio (HIV, HBV and SCD) in co-existence cause immeasurable morbidity and mortality. Both HIV and HBV have the same modes of transmission, therefore, co-infection with both viruses is common [9,10]. More HIV/HBV co-infected patients have been reported to develop chronic HBV than monoinfected HBV patients[11]. HIV and SCD co-existence may pose treatment challenges on choosing antiretroviral therapy (ART) especially so if one drug causes hypersensitivity and other drugs are contraindicated in anemia or not available in the guidelines as it was the case for a single case report in Kenya [12].

On the other hand, SCD has been thought to be protective against acquisition of HIV[13,14] and reported to slow down HIV disease progression [15] through host factors such as asplenia or the use of Hydroxyurea drug that has synergistic antiviral activities with some reverse transcriptase inhibitors [16,17]. Despite these findings, patients with SCD and HIV infection tend to have more complicated hospitalization than those without HIV infection[18]. Infections with encapsulated organisms is more common in SCD patients with functional asplenia, the susceptibility for these infections appear to increase in the presence of HIV infection [19,20].

Blood transfusion has been reported to be a risk factor for HIV acquisition in SCD patients in studies conducted in some African countries such as Congo [21], Enugu in Nigeria [22] and in Yaoundé Cameroun [23]. Unsafe blood is as well a risk factor for HBV infection. Contrary to findings in some countries in Africa, in the U.S.A it was found that among adult African –Americans the frequency of HIV in SCD patients was 1.5% as compared to 3.3% in patients without SCD, suggesting blood transfusion was not a risk factor.

This study was conducted to investigate the burden of HIV and HBV and associated factors among SCD patients receiving SCD care in Dar es Salaam, Tanzania. This article was previously presented as a meeting abstract at the 7th MUHAS Scientific Conference on June 27-28, 2019.

Methods

Design and setting of the study

A cross sectional multisite hospital-based study was conducted from August 2018 to January 2019 among sickle cell patients attending clinics in Dar es Salaam. Dar es Salaam is the largest city in Tanzania and has five municipal districts and estimated population of 4,364,541 as per 2012 National census[24]. The study participants were obtained from 4 study sites, one being a tertiary hospital (Muhimbili National Hospital) and three regional referral hospitals (Amana, Temeke and Mwananyamala). Sickle cell patients at Muhimbili National hospital (MNH) received care in the department of Haematology and blood transfusion while those in the three regional hospitals received care in departments of internal medicine. All clinics ran once a week and received an average of 15 adult patients per week.

Study population

All consenting SCD patients aged 16 years or older who attended sickle cell clinics in Dar es Salaam were consecutively enrolled into the study. None of the patients was excluded.

Data collection procedure

A structured interview was done to all patients who consented to participate in the study. Independent variables collected were socio-demographic characteristics including age, sex, marital status, level of education, residency and occupation. Others were behavioural characteristics and risky interventions like condom use, multiple sexual partners, tattooing, piercing, intravenous drug abuse, history of blood transfusion, hospital admission, surgery, tooth extraction and alcohol use, sexual vulnerability behaviours such as alcohol use and forced sexual intercourse. Result of last measured hemoglobin (HB) level was obtained from the SCD card. The HB was considered valid if it was done within 1 month of data collection. All methods were performed in accordance with the relevant guidelines and regulations.

Four milliliters of blood was drawn aseptically from a vein on the cubital fossa and put into an empty sterile red stoppered vacutainer for HIV and HBV screening. Samples were stored in a cool box and transferred to MUHAS Hematology Clinical and Research Laboratory at the end of each clinic day. Upon reaching the laboratory, samples were centrifuged, sera taken and tested for HBV surface antigen and HIV serology. HIV diagnosis was in accordance to Tanzanian algorithm[25] whereby SD Bioline HIV-1/2 3.0 (Standard Diagnostics, Inc, Republic of Korea) was done first. Negative results underwent no additional testing. Positive samples were retested using Uni-Gold™ HIV (Manufacturer: Trinity Biotech Plc, Bray, Co. Wicklow, Ireland). Samples reactive to both tests were considered positive for IgG anti HIV antibodies.

Hepatitis B surface Antigen was detected by the Onsite HBsAg rapid test by CTK Biotech, Inc, San Diego, USA. The test is a lateral flow chromatographic immunoassay for the qualitative detection of HBsAg in human serum or plasma. The test has sensitivity and specificity of approximately 100% and 100% respectively when performed according to the instructions of the manufacturer. Negative results underwent no additional testing. Positive results were confirmed by ELISA using Murex HBsAg version 3 test kits manufactured by DiaSorin S.p.A, United Kingdom.

Statistical analysis

Data analysis was done using SPSS software version 20.0. Categorical variables were summarized into frequencies and percentage and their associations assessed by Fisher's exact test. Continuous variables were summarized into mean and standard deviation and their association was assessed using student's T-test. Odds ratio and 95% CI were estimated using logistic regression analysis to identify the association between variables and occurrence of HIV. P values <0.05 was considered statistically significant.

Results

A total of 325 patients were enrolled into the study, 185(56.9%) were female. Mean age ($\pm$ SD) was 23.0 ± 7.5 years ranging from 16 – 52 years. Majority of the study participants, 231 (71.1%) were in the age group 16-25 years. Majority of the subjects were single 278 (85.5%), had secondary level or higher education 236(72.3%), and had previous hospital admission 296 (91.1%). The most reported reason for admission was vaso-occlusive crisis which was reported by 166/296 (56.1%) of the study participants who had ever been admitted. A total of 61/325 (18.8%) subjects were using hydroxyurea. Mean Hemoglobin level ($\pm$ SD) for the 325 study subjects was $7.4 (\pm 1.58)$ g/dl. (Table 1)

Of 325 study participants, 6 (1.8%) (95% CI: 1.97 – 1.99) were HIV-infected while 4 (1.2%), (95% CI: 1.98 – 2) were infected with HBV. None of the study participants was HIV and HBV co-infected (not shown in Table 1)

A total of 243/325 (74.7 %) SCD patients had received at least 1 unit of blood transfusion in their life time, majority of them 185/243 (76.1%) were female. More than a quarter of the participants 82 (26%) had never been transfused.

HIV rate was similar between males 2/140 (1.4%) and females 4/185 (2.2%), $p = 0.703$. All 6 HIV infected participants had a previous history of hospital admission. Stroke, surgery and obstetric reasons, altogether were strongly associated with HIV, so was anemia as a reason for admission, $p = 0.009$. There was no association between HIV infection and other socio-demographic and clinical characteristics, $p > 0.05$. (Table 2)

Reasons for last hospital admission among HIV infected patients were anemia (3/6), stroke (1/6), malaria (1/6) and obstetric reasons (1/3). (Not shown in Table 2)

Four patients tested positive for hepatitis B surface antigen, 2 males and 2 females. All 4 had a previous history of hospital admission. Other reasons for hospital admission (stroke, malaria, surgery, obstetric reasons) were associated with HBV infection ($p = 0.012$). A primary level education or no formal education was associated with HBV infection ($p = 0.005$), Table 3.

Table 4 shows Distribution of factors for Hepatitis B viral infection among SCD patients attending clinic in Dar es Salaam, All 4 HBV infected patients had a history of blood transfusion. Three of them were sexually active out of which only one reported to use condom during the last sexual act. Three HBV infected participants (3/4) reported to have a history of multiple sexual partners. All four did not have a history of tattooing or surgery. However, there was no statistically significant association between Hepatitis B viral infection and the risk factors.

Discussion

The mean age ($\pm$ SD) of the study population was 23.0 ± 7.5 years. There was no difference in sex distribution. Contrary to past research findings where majority of the study populations had primary level education, the present study witnessed majority of the participants having secondary or higher level education owing to the building of secondary schools in each ward in Tanzania in 2010 as well as the introduction of free Education Policy for Secondary education in Tanzania in 2015. Therefore, since the majority of the studied population fell under the mean age of 23 years, these are obviously the beneficiaries of these two policies.

In this study HIV prevalence of 1.8% was lower than the reported HIV prevalence in the general population of Dar es Salaam which was 4.7% in the year 2016-2017[26]. Furthermore, the HIV prevalence was lower than a similar study in Tanzania among SCD children which reported a HIV prevalence of 4.4% (unpublished data by Kamaria Kassim *et al*). Also, lower than prevalence in studies in Cameroon (5.6%), Democratic Republic of Congo (11.3%) and Togo (5.04%), countries endemic for HIV [21,23]. The observed low prevalence could partly be due to different age groups studied in Cameroon, Democratic Republic of Congo and Togo in which study participants included children and adults while in the present study only adults were studied. The adult population in the present study might have represented survivors if perinatally infected SCD children are assumed to have died during childhood. Moreover the findings could be reflecting the ongoing decline of HIV prevalence which has been observed in Tanzania over the recent years.

In the present study, the prevalence of HIV was higher among females than among males, 2.2% and 1.4% respectively. This is in agreement with epidemiological data in Tanzania which informs that women are more infected by HIV than men[26]. In the present study all 6 HIV infected SCD had a history of blood transfusion although this was not statistically significant. A study in Yaoundé Cameroon had found that the number of blood transfusions increased the risk of HIV infection [23], this wasn't the case for the present study.

In this study, there were 4 study participants who tested positive to HBV infection, representing 1.2% of the study population. The prevalence of the present study was however higher than the prevalence of HBV among children with SCD in Dar es Salaam, Tanzania in the year 2010 which was found to be 0.6% by Kamaria Kassim *et al* (unpublished data). This finding could be due to the fact that there is more risk of exposure to Hepatitis B virus infection during life time, therefore, prevalence increases with age. Also decreased HBV positivity in those children could be because of the vaccination against Hepatitis B particularly in those who were born from 2002 when the vaccine against HBV was introduced in the Extended Programme for Immunization (EPI) in Tanzania. In the present study all HBV infected participants were born before the introduction of HBV vaccine in the country.

On the other hand, the findings from the present study regarding HBV prevalence are consistent with a study among SCD patients in Brazil (3.1%) [27]. Other countries had reported a higher prevalence for HBV infection among SCD patients than the findings in the present study. The prevalence of HBV infection was 10% among SCD patients in Democratic republic of Congo published in the year 2007 (28).

In this study none of the study participant was found to be co-infected with both HIV and HBV. This is similar to a study which was done in Nigeria among SCD patients which could not find any co-infection [29]. However co-infection prevalence rate of 8.6% and 2.8% were obtained from previous studies among blood donors and adult HIV patients in Tanzania, respectively [8,30]. Absence of co-infection in the present study might represent a notion that if there were any HIV/HBV co-infected Sickle cell patients then these had severe presentation of both infections and possibly died before reaching adulthood. Most likely the studied population is the survivor group.

Study Limitation

Prevalence of HBV infection was very small that no associations with risk factors were calculated.

Conclusion

The findings of this study suggest that the prevalence of HIV and HBV infection among SCD patients aged 16 years or older is no higher than the prevalence in the general population of Dar es Salaam. For the few SCD patients who are either HIV or HBV infected we do not know the source of infection. Since about 75% of SCD patients had received blood transfusion (BT), and just a few were HIV or HBV positive; there is no reason to suspect that they had been infected via blood transfusion. HIV and HBV screening should be emphasized in caring adult SCD patients in order to provide early management measures.

Declarations

Ethics approval and consent to participate

Ethical approval for the study was obtained from the Muhimbili University of Health and Allied Sciences (MUHAS), Research and Publication Ethical Committee. Permission to conduct the study was obtained from the administration of MNH, Temeke, Mwananyamala and Amana hospitals. All patients provided a written informed consent. Patients diagnosed with HIV and/or HBV were referred to respective clinics for treatment.

Consent for publication

Not applicable

Availability of data and materials

The data set for this study can be found from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

This study was conceived by IM, GS and LL. Data collection, data entry and cleaning was done by IM and supervised by GS and LL. Analysis was done by IM and GS. Manuscript draft was written by GS. All co-authors read and approved the manuscript for publication.

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Tables

Table1: Socio-demographic and clinical characteristics of the study participants N =325

Characteristic	Number (percentage)
Age groups	
16-25 (%)	231 (71.1)
26-35	69 (21.2)
36+	25 (7.7)
Gender	
Male	140 (43.1)
Female	185 (56.9)
Marital Status	
Single	278 (85.5)
Married	30 (9.2)
*Others	17(5.2)
Education level	
Primary or no formal education	89(27.4)
Secondary education or higher	236(72.6)
Occupation	
Unemployed	88(27.1)
Employed	104(32)
Student	133(40.9)
Past hospital admission	
Yes	296(91.1)
No	29(8.9)
Reason for last admission	
Painful crisis	166(56.1)
Anemia	85(28.7)
Acute Chest Syndrome	5(1.7)
Others	40(13.5)
Residence	
Ilala	108(33.2)
Ubungu	46(14.2)
Temeke	77(23.7)
Kinondoni	94(28.9)
Hydroxyurea use	
Yes	61(18.8)
No	264(81.2)

*Others include divorced, widowed or separated

Table 2: Socio-demographic and clinical characteristics of SCD patients by HIV status N=325

		HIV Status			
		Negative	Positive		
Characteristic		n (%)	n (%)	Total number	P value
Sex	Male	138(98.6)	2(1.4)	140	0.703
	Female	181(97.8)	4(2.2)	185	
Age	<26	228(98.7)	3(1.3)	231	0.361
	26+	91(96.8)	3(3.2)	94	
Marital status	Single	274(98.6)	4(1.4)	278	0.210
	Ever Married	45(95.7)	2(4.3)	47	
Education	Primary/no formal education	86(96.6)	3(3.4)	89	0.352
	Secondary or higher education	233(98.7)	3(1.3)	236	
Occupation	Unemployed/student	217(98.2)	4(1.8)	221	1
	Employed	102(98.1)	2(1.9)	104	
Past hospital admission	Yes	290(98.0)	6(2)	296	1
	No	29(100)	0(0)	29	
Reason for last admission		166(100)	0(0.0)	166	0.009
	Painful crisis				
	Anemia	82(96.4)	3(3.6)	85	
	ACS	5(100)	0(0.0)	5	
	Others*	37(92.5)	3(7.5)	40	
History of BT	Yes	237(97.5)	6(2.5)	243	0.345
	No	82(100)	0(0.0)	82	
Number of BT N=243					
	1 unit	82(97.6)	2 (2.4)	84	0.291
	2-5units	124(99.2)	1(0.8)	125	
	> 5 units	31(91.2)	3(8.8)	34	
Hydroxyurea use	Yes	61(100)	0(0)	61	0.598
	No	258(97.7)	6(2.3)	264	

*Others = Stroke, surgeries and obstetric reasons, ACS=Acute chest syndrome, BT= Blood transfusion

Table 3: Socio-demographic and clinical characteristics of SCD patients by HBV infection status N=325

		Hepatitis B Infection			
		Negative	Positive		
Characteristic		n (%)	n (%)	Total	P-Value
Sex	Male	138(98.6)	2(1.4)	140	1
	Female	183(98.9)	2(1.1)	185	
Age	<26	230(98.6)	1(0.4)	231	0.075
	26+	91(96.8)	3(3.2)	94	
Marital Status	Single	275(98.9)	3(1.1)	278	0.466
	Ever married	46(97.9)	1(2.1)	47	
Education	Primary/no formal education	85(95.5)	4(4.5)	89	0.005
	Secondary Education +	236 (100)	0(0)	236	
Occupation	Unemployed/students	220(99.5)	1(0.5)	221	0.098
	Employed	101(97.1)	3(2.9)	104	
Previous admission	Yes	292(98.6)	4(1.4)	296	1
	No	29(100)	0(0)	29	
Reasons for last admission (N=296)	Painful crisis	166(100)	0(0)	166	0.012
	Anemia	84(98.8)	1(1.2)	85	
	ACS	5 (100)	0(0)	5	
	Others	37(92.5)	3(7.5)	40	
History of	Yes	59(96.7)	2(3.3)	61	0.161
Hydroxyurea use	No	262(98.2)	2(0.8)	264	

Table 4: Distribution of risk factors for Hepatitis B viral infection among adult SCD patients attending clinics in Dar es Salaam. N=325

		Hepatitis B Infection			
		Negative	Positive	Total	P-Value
Risk factors for HBV infection		n (%)	n (%)	N	
History of BT	Yes	239(98.3)	4 (1.7)	243	0.576
	No	82(100)	0 (0)	82	
Number of BT	One unit	83(98.8)	1 (1.2)	84	0.621
	2-5 units	123(98.4)	2 (1.6)	125	
	More than 5 units	33(97.1)	1 (2.9)	34	
Sexually active	Yes	185(98.4)	3 (1.6)	188	0.641
	No	136(99.3)	1 (0.7)	137	
Condom use (N=188)	Yes	67(98.5)	1 (1.5)	68	1
	No	118(98.3)	2(1.7)	120	
Multiple sexual partners (N=188)	Yes	86(97.7)	2(2.3)	88	0.6
	No	99(99)	1(1)	100	
Tattooing	Yes	2(100)	0(0)	2	1
	No	319(98.8)	4(1.2)	323	
Ear piercing	Yes	175(98.8)	2(1.2)	177	1
	No	146(98.6)	2(1.4)	148	
Tooth extraction	Yes	187(98.9)	2(1.1)	136	0.739
	No	134(98.5)	2(1.5)	189	
Surgery	Yes	68(100)	0(0)	68	0.583
	No	253((98.4)	4(1.6)	257	