

Hepatitis B, C and Human Immunodeficiency Virus (HIV) Co-infection in Nigerian Children with Sickle Cell Anaemia.

Type of Article: **Original**

¹Lucy Eberechukwu Yaguo Ide, ²Seye Babatunde

Departments of ¹Paediatrics And Child Health and ²Community Medicine² University Of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria.

ABSTRACT

BACKGROUND

Nigeria which has one of the world's highest burden of children living with Sickle cell anaemia is also endemic for hepatitis B, C and the Human immunodeficiency virus (HIV). This study set out to determine the prevalence of Hepatitis B surface antigen (HBsAg), antibodies to Hepatitis C Virus (HCV) and Human Immunodeficiency Virus (HIV) among children with Sickle cell anaemia (SCA) at the University of Port Harcourt Teaching Hospital (UPTH).

METHODS

This was a prospective hospital based study of children with sickle cell anaemia aged 0.5 years to 18years presenting at the haematology clinic of UPTH. A serological screening was carried out over a period of five months to determine the presence of hepatitis B virus (HBV), HCV and HIV 1 and 2 infection. Other data obtained included sex, age and other demographic data.

RESULTS

There were 132 SCA patients with 72 (54.5%) males and 60 (45.5%) females. Results of HCV anti-body, HBSAg, and HIV were available for 84 patients. Mean age was 7.45 ± 1.6 years, age range was 0.5-18years Seventy-eight (59.1%) had no previous blood transfusion, forty (30.3%) had one previous transfusion while eight (6.1%) had more than one previous

transfusions. HBsAg was positive in three patients giving a prevalence of 3.6%; Anti-HCV antibody was not found in any patient while two (2.4%) were positive for HIV 1. There was no patient with Hepatitis, HIV and SCA.

CONCLUSION

This study showed no co-infection with Hepatitis B, C and HIV viral infection among children with SCA at UPTH, Nigeria.

KEYWORDS: HBsAg; Anti- HCV antibody; HIV; SCA, Co-infection.

Correspondence: Dr L.E. Yaguo Ide
E-mail: lucyaguolucy@gmail.com

INTRODUCTION

Sickle cell anaemia (SCA) is an inherited form of haemolytic anemia and one of the most common in our society.¹ It is a major cause of morbidity and mortality in Nigeria with a prevalence rate of 3%.¹ It is an autosomal recessively inherited disorder resulting in a chronic and frequently life-threatening anaemia that often requires red cell transfusion in its management.²

Individuals living with SCA are known to experience complications such as iron overload, red cell alloimmunization and transmission of infections such as malaria, hepatitis B (HBsag), hepatitis C (HCV) and Human Immunodeficiency Virus (HIV).³

Co-infection with HIV and Hepatitis viruses are severe and frequent in sub-Saharan Africa especially in adults.⁴⁻⁷ However, in a systematic review, the co-infection with all three viruses was only been reported in one Nigerian child.⁸ The prevalences of HIV/HBV in children from Tanzania and Cote d'Ivoire have been reported as 1.2%⁹ and 12.1%¹⁰ respectively, while the prevalence of HIV/HBV co-infection among Nigerian children was 8.3%⁸. The rate of HIV/HCV co-infection in Tanzanian children was 13.8%⁹. No child was found to be co-infected with HCV in an Ivorian study¹⁰. A HIV/HCV co-infection rate of 2.7% was reported among some Nigerian children in a study⁸.

Common medical interventions for SCA patients in Nigeria include blood transfusion and injections, scarifications, tattooing and ritual marks by herbalists. These interventions predisposes them to risk of infection with transfusion transmissible viruses as suggested by the report of some studies^{2,11} which document an increased risk of transfusion transmissible viral infection in patients with SCA^{2,11}.

The transmission of Hepatitis B has been documented to be more common than that of Hepatitis C as shown by the result of some studies¹²⁻¹⁴, which documented a risk of HCV transmission through needle stick injury is in the order of 1-3%, compared with 30% for hepatitis B virus and 0.3% for HIV¹²⁻¹⁴.

Though Hepatitis B, C and HIV share similar mode of transmission through sexual intercourse, mother-to-child, and blood transfusion¹⁵⁻¹⁷, the risk of transmission and virulence of these viruses is known to be different.

Patients with SCA are subjected to recurrent blood transfusion as part of their management. In spite of the progress made in the prevention of transfusion-transmitted infections over the last years, the risk of transfusion transmitted infection is still likely to occur especially in multi-transfused

patients such as sickle cell anemia (SCA) patients^{18,19}.

Though HIV co-infections with HBV and HCV have been documented in children⁸, there is a paucity of data on this subject among children with SCA especially in Nigeria despite their substantial risks for infection. This descriptive study was therefore designed to estimate the prevalence of co-infections with HIV, hepatitis B and C viruses in Nigerian children with SCA presenting to the Paediatric haematology clinic of UPTH.

MATERIALS AND METHOD

A case control study of 132 children with sickle cell anaemia aged 0.5 to 18 years presenting at the Haematology Clinic of the University of Port Harcourt Teaching Hospital over a five month period was done. The following information: age, gender, haemoglobin genotype and anti-HCV anti-body titre, serum HBsAg level, HIV 1 and 2 status were obtained from the subjects. The control group were 101 paediatric patients in the same age bracket who were transfused in the paediatric wards of UPTH for various reasons other than SCA. All the patients were screened prior to blood transfusion. Serum samples were collected from 132 consecutive known SCA patients, presenting to Haematology Clinic of the department of Paediatrics, UPTH. Some of the mothers of those who were positive were also screened. A second-generation rapid screening test, the HEP C SPOT HCV assay was used for HCV. Initial reactive results were confirmed by repeat testing with UBI HCV EIA 4.0 enzyme immunoassay. The samples were screened for HBsAg by latex agglutination technique. All positive samples were tested using Enzyme linked Immunosorbent Assay (ELISA) technique (pathogyme Omega Diagnostics, UK) for confirmation, while HIV status was screened for by ELISA. Analysis was done using the statistical package for social sciences version 20, p-value ≤ 0.05 was considered statistically significant. Ethical clearance was obtained from the University of Port Harcourt Teaching Hospital, (UPTH), research and ethics

committee. Patient confidentiality was given the utmost priority in the course of the study.

RESULTS

The subjects comprised 132 sickle cell anaemia patients 72(54.5%) males and 60(45.5%) females. The mean age of the patients was 7.45 ± 4.6 years (range 0.5-18 years) Seventy-eight(59.1%) had no previous transfusion, forty (30.3%) had one previous transfusion while eight (6.1%) had more than one previous transfusions Results of HCV anti-body, HBsAg, and HIV was available for 84 patients 44(52.4%) males and 40(47.6%) females Hepatitis B surface antigen markers was found in the sera of three patients (1 male and two females) giving a prevalence of 3.6%, Anti-HCV antibody was not found in any patient giving a prevalence of 0% , while two (2.4%) were positive for HIV 1. There was no SCA patients with HIV, HBV and anti HCV, neither was there any Coinfection of HIV and HBV or HIV and HCV in any of the subjects with sickle cell anaemia.

Of the two SCA patients who were HIV positive, one(1.2%) was via blood transfusion while the second one (1.2%) was via vertical transmission. The three subjects who were HBSag positive all had previous history of blood transfusion.

In the control samples of 101 subjects. Serologic reactivity for antibody to HCV was found in four (4%), HBsAg one (1%) and HIV 1 forty-three (42.5%). There was also no Coinfection of all three viruses (HIV, HBsAg and anti HCV antibody) nor was there any coinfection of HIV/HCV or HIV/HBSag in the control samples.

The sex distribution of the subjects and HIV, HCV anti-body and HBSag status is as shown in Tables 1, 2 and 3.

Table 1: Sex Distribution and Anti-HCV Status of 84 children with Sickle Cell

Anaemia Age (years)	Anti-HCV status		
	Positive	Negative	Total %
Male	0	44	52.4
Female	0	40	47.6
Total	0	84	100

Table 2: Sex Distribution and HIV Status of 84 children with Sickle Cell Anaemia

Age (years)	Anti-HCV status		
	Positive	Negative	Total %
Male	2	42	52.4
Female	0	40	47.6
Total	2	82	100

Table 3: Sex Distribution and HBSag Status of 84 children with Sickle Cell

Anaemia Age (years)	Anti-HCV status		
	Positive	Negative	Total %
Male	1	43	52.4
Female	2	38	47.6
Total	3	81	100

DISCUSSION

The prevalence of HBsAg in children with SCA in our study which has been reported earlier is 3.6%²². This is slightly lower when compared with a previous study²³ from our Centre which showed a prevalence of 4.9%. The observed difference may result from the fact that uneven risk groups were used in the two studies. While this study was done on subjects with sickle cell disease the other done was among all blood donors. The prevalence of HbSag, HCV and HIV co-infection reported in this study is however; lower than that of previous Nigerian studies^{24, 25} which showed HBV carrier rates of 8-22%.

The prevalence of HCV anti-body in children with SCA in Port Harcourt is 0% This is within the range of 0-1.5% reported in South Africa²⁸, but lower than the prevalence rate of 5.3% and 6.6% reported among non-transfused and transfused SCA patients in Enugu, Nigeria¹¹. The difference in the rates noted between the study in Enugu and this study may be influenced by the overall prevalence of HCV in both areas, the quality of blood screening, the number of transfusions which increased the risk and the impact of scarification which was a significant predictor in the Enugu study¹¹. The serological screening for anti-HCV at blood banks after 1992 has contributed to a better control of the dissemination of HCV infection. This might also account for the 0% prevalence rate for antibody to HCV observed in this study as blood is routinely screened for antibody to HCV in University of Port Harcourt teaching Hospital.

The prevalence of HIV was 2.4% among SCA patients in this study. It is low when compared to the national AIDS prevalence of 3.1% in the population²¹. One of the mothers of the two SCA patients who were sero-positive for HIV in this study was negative while the second mother was positive. This implies that one of the children was probably infected through vertical transmission from his mother while the second may have been infected via blood transfusion as an infant.

In Zaria a prevalence of HIV of 1.8%²⁷ was observed among SCA patients, however the population studied was younger than those in this study and the sample size was also smaller, these factors may have accounted for the variation. A 0% prevalence was found in Senegal among patients with sickle cell anaemia²⁸ which is lower than that gotten in this study though the blood transfusion rate in the Senegal study was 41%²⁸ while the blood transfusion rate in this study was 30%. In the developed nations of the world the risk of transfusion-transmissible viral infection is primarily due to failure of serologic screening tests to detect recently infected blood donors in the pre-seroconversion "window" phase of infection.²⁹ In order to reduce this "window" period nucleic acid testing (NAT) techniques are beginning to find applications in developed countries.²⁹ The NAT techniques are complex, labourious, and presently time-consuming tests, and may take a while before getting to third world countries where HIV infection is prevalent. As a result serologic testing will remain the mainstay of screening blood donors.

There was a 0% prevalence of Coinfection of HCV antibody, HBSag and HIV among patients with sickle cell anaemia in Port Harcourt Nigeria. The control group also showed a prevalence of 0% Coinfection of all three viruses.

This is similar to other studies on co-infection in Nigeria^{8,30, 31} and Cote d'Ivoire¹⁰. It is however lower than the prevalence rate of coinfection of 0.04% to 7.2% found in

Cameroon, keffi and Ibadan among adults.. The fact that the study population were adult non SCA may have accounted for this difference.

This study also recorded a 0% prevalence of HIV/HBSag coinfection rate in SCA patients and their control in Port Harcourt. This is lower than the prevalence rates of 0.78% and 31.4%, obtained from previous studies on co-infection within and outside Nigeria^{5,8-10,30,31} This shows that rate of co-infection varies from one locale to another across Africa.

The rate of HIV/HCV co-infection of 0% in this study is similar to an Ivorian and a Nigerian study^{10,30} but lower than varied HIV/HCV co-infection of rates 0.06% to 13.8% reported by other workers.^{5,7-9,31} These other studies were mostly among adult HIV patients and blood donors, which may have accounted for this difference.

CONCLUSION

No co-infection of HbSag, HCV and HIV was reported among patients with SCA in Port Harcourt. The prevalence of solitary Hepatitis B and HIV infection reported in this study was also lower than the general prevalence in Port Harcourt and other areas of Nigeria. These findings indicate the need to promote optimal blood screening before transfusion as well as routing implementation of safe blood transfusion practice. Other management strategies which will reduce the risk and need of transfusion in SCA patients should be encouraged in order to reduce the co-morbidity associated with SCA in Nigeria.

REFERENCES:

1. Akinyanju O A. A profile of Sickle cell disease in Nigeria. *Ann NyAcadSci* 1989; 565: 126-136.
2. Blood safety: proposal to establish World Blood Donor Day. Report by the Secretariat. Executive Board 115th Session. World Health Organization, 2004

3. Ware RE, Zimmerman SA, Schultz WH. Hydroxyurea as an alternative to blood transfusion for the prevention of recurrent stroke in children with sickle cell disease. *Blood* 1999;94:3022-3026
4. Barth R.E, Huijgen Q, Taljaard J, Hoepelman A.I.M, "Hepatitis B/C and HIV in sub-Saharan Africa: an association between highly prevalent infectious diseases. A systematic review and meta-analysis," *IJID*,2010; 14: 1024-1031.
5. Ymele F.F, Keugoung B, fouedjio J.H, Kouam N, Mendi S, Maboubi J.D. High rates of hepatitis B,C and HIV infections among blood donors in Cameroon: A proposed blood screening alogarithm for blood donors in Resource-limited settings *Journal of blood transfusion*. 2012; 1155-1162.
6. Forbi FC, Gabadi S, Alabi R, et al. The role of triple infection with hepatitis B virus, hepatitis C virus and human immunodeficiency virus (HIV) type 1 on CD4+ lymphocyte levels in the highly infected population of north central Nigeria. *Mem Inst Oswalso Cruz* 2007;102:535-537.
7. Otegbayo JA, Babafemi TO, Akingbola TS, et al. Prevalence of hepatitis B and C seropositivity in a Nigerian cohort of HIV infected patients. *Ann Hepatol* 2008;7:152- 156.
8. Rawizza H, Ochigbo S, Chang C, et al. Prevalence of hepatitis coinfection among HIV infected Nigerian children in the Harvard PEPFAR ART program. Presented at the 17th Conference on Retroviruses and Opportunistic Infections, San Francisco, 16-19 February 2010. Poster abstract S-181. retroconference.org/2010/abstracts/39148.htm (accessed 13 May 2010).
9. Telatela SP, Matee MI, Munubhi EK. Seroprevalence of hepatitis B and C viral coinfections among children infected with human immunodeficiency virus attending the paediatric HIV care and treatment center at Muhimbili National Hospital in Dar-es- Salaam, Tanzania. *BMC Public Health* 2007;7:338-343.
10. Rouet F, Chaix M, Inwoley A, et al. Frequent occurrence of chronic hepatitis B virus infection among West African HIV type 1 infected children. *Clin Infect Dis* 2008;46:361-366.
11. Ejiofor O.S, Ibe B.C, Emodi I.J, Ikefuna A.N, Ilechukwu G.C, Emechebe G, et al The role of blood transfusion on the prevalence of Hepatitis C virus antibodies in Nigerian children with Sickle cell anaemia in Enugu, South East Nigeria. *Nig. J clin.pract.* 2009;12 :355-358
12. Fallahian F, Najafi A. Epidemiology of hepatitis C in the Middle East. *Saudi J Kidney Dis Transpl* 2011;22:1-9.
13. Irshad M, Ansari MA, Singh A, et al. HCVgenotypes: a review on their origin, global status, assay system, pathogenecity and response to treatment. *Hepatogastroenterology* 2010; 57:1529-38.
14. Chayama K, Hayes CN. Hepatitis C virus: How genetic variability affects pathobiology of disease. *J Gastroenterol Hepatol* 2011;26:83-95.
15. Rossi S.J, Pharm D, Paul A, Volberding M.D, Teresa L, and Wright M.D, "Does hepatitis C virus infection increase the risk of HIV disease progression?" *Journal of the American Medical Association*, 2002;288:241-243.
16. Sulkowski M.S, .Moore R.D, Mehta S.H, Chaisson R.E, and Thomas D.L, "Hepatitis C and progression of HIV disease," *Journal of the American Medical Association*, 2002;288:199-206.
17. Cooper C.L, Mills E, Wabwire B.O, Ford N, and Olupot-Olupot P, "Chronic viral hepatitis may diminish the gains of HIV antiretroviral therapy in sub-Saharan Africa," *International Journal of Infectious Diseases*,2009;13: 302-306.
18. Burnett R.J, Francois G, Kew M.C et al., "Hepatitis B virus and human immunodeficiency virus co-infection in sub-Saharan Africa: a call for further investigation," *LiverInternational*, 2005; 25:201-213.
19. Alswaidi FM, O'Brien SJ. Premarital

- screening programmes for haemoglobinopathies, HIV and hepatitis viruses: review and factors affecting their success. *J Med Screen* 2009;16:22-28.
20. Ocak S, Kaya H, Cetin M, et al. Seroprevalence of hepatitis B and hepatitis C in patients with thalassemia and sickle cell anemia in a long-term follow-up. *Arch Med Res* 2006;37:895-898.
 21. HIV AIDS in Nigeria available at WWW.avert.org/hiv-aids-nigeria.html.
 22. George I.O , Yaguo Ide L.E. Hepatitis B virus infection Nigerian children with sickle cell anaemia. *Journal of Medicine and Medical Sciences*2011; 2:1213-1215.
 23. Ejele QA, Ojule AC . The prevalence of Hepatitis B surface antigen among prospective blood donors and patients in Port Harcourt, Nigeria. *Niger. J. Med.* 2004;13: 336-338.
 24. Harry TO, Bajani MD, Moses AE . Hepatitis B virus infection among blood donors and pregnant women in Maiduguri, Nigeria. *East Afr. Med. J.*1994; 71: 594-599.
 25. Bojuwoye OJ. The burden of Viral Hepatitis in Africa. *West Afr. J. Med.*, 1997;16(4); 198-203.
 26. Ellis L.A Brown J D, Conradie J D, Paterson A, Sher R, Millo J , et al Prevalence of hepatitis C in South Africa. Detection of anti HCV in recent and stored serum. *J Med. Virol.* 1990 ; 32 : 249-251.
 27. G. O. Ogunrinde, M. I. Keshinro and S. O. Ige HIV seropositivity in children with sickle cell disease *Annals of African Medicine.*2005; 4: 104 - 106
 28. Diagne I, Soares GM, Gueye A et al. Infections in Senegalese children and adolescents with sickle cell anemia: epidemiological aspects. *Dakar Med* 2000;45:55-58
 29. Kuliya-Gwarzo A. Screening For Blood Transfusion Transmissible Viruses In Resource Limited Settings. *The Internet Journal of Infectious Diseases.* 2011; 9:
 30. Olatunji P.O , Iseniyi J.O. Hepatitis B and C viruses coinfection with Human immunodeficiency virus in infected patients at UITH, Ilorin. *Nig. Med.Practical* ,2008; 54: 8-10
 31. Sadoh A.E, Sador W.E, Iduoriyekemwen N.J. HIV co-infection with hepatitis B and C viruses among Nigerian children in an antiretroviral treatment programme *SAJCH* 2011; 5 : 10-17