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Sickle Cell Anaemia (SCA) related priapism in Kano, North-Western, Nigeria; re-emphasizing the important role of haemolysis

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Abstract

Background: Priapism is a common albeit under reported complication of Sickle Cell Anaemia (SCA) despite the pain, psychological stress and attendant risk of erectile dysfunction. Some changes in both clinical and laboratory parameters have been associated with priapism in SCA. **Aim:**This study seeks to determine the clinical and laboratory characteristics of patients with SCA related priapism. **Method:** A total of 102 adult male patients with SCA were recruited at steady state into this cross-sectional study. Clinical data was extracted using interviewer administered questionnaire and clients' folders while FBC, haemolytic and biochemical markers were determined for each participant. Data was analysed using SPSS version 21.0 and $p < 0.05$ was considered significant. **Results:** The prevalence of priapism was 36.3%. There was no significance difference between SCA patients with and without priapism in terms of age ($p = 0.11$), age at diagnosis ($p = 0.81$), marital status ($\chi^2 = 2.06$, $df = 4$, $p = 0.09$), painful crisis ($\chi^2 = 0.95$, $df = 4$, $p = 0.41$) and history of hospital admission ($\chi^2 = 0.28$, $df = 4$, $p = 0.59$). However, SCA patients with priapism had more blood transfusions ($\chi^2 = 46.70$, $df = 4$, $p = 0.01$), lower haemoglobin ($p = 0.01$), higher reticulocyte count ($p = <0.001$) and serum LDH ($p = <0.001$) compared to SCA patients without priapism. History of blood transfusion (OR = 3.4, 95% CI = 1.6 – 6.5, $p = 0.03$), higher reticulocyte count (OR = 8.9, 95% CI = 2.4 - 14.8, $p = 0.01$) and serum LDH (OR = 13.6, 95% CI = 7.6 – 24.3, $p = 0.01$) were positive predictors of priapism among adults with SCA. **Conclusion:** Priapism is a high among patients with SCA and haemolytic markers can serve as important determinants of SCA related priapism. There is need for increase awareness of this complication and researches to exploit mechanistic pathways of priapism in SCA.

Keywords: Sickle cell anaemia, Priapism, Haemolytic markers, Steady state, Kano, Nigeria.

INTRODUCTION

Sickle Cell Anaemia (SCA) is an inherited genetic disorder with diverse clinical manifestations in which multitude of complications set in to further compound its course.[1-4] Some complications of SCA can easily be placed mechanistically on either haemolytic or vaso-occlusive pathway while others cannot be so.[3,4] Priapism; a persistent painful penile erection with or without sexual stimulation, is one of the less mechanistically characterized complication of SCA owing to conflicting reports from the literature.[3-6] Priapism is common among patients with SCA where it ranges between 5 to 89% but then frequently under reported, resulting in delays to initiate appropriate treatment; a situation that could lead to erectile dysfunction with attendant psychosocial problems to individual, family and society.[2,3,6-9] Detail understanding of clinical and laboratory characteristics of individual with SCA related priapism in our environment will help clinicians who provides care to SCA patients, to prioritized those at risk and most importantly devise pre-emptive strategies or institute early intervention as the situation demand. Hence, this study seeks to determine the clinical and laboratory characteristics of patients with SCA related priapism.

MATERIAL AND METHODS

A descriptive cross-sectional study was conducted among 102 adult male patients with SCA who presented for follow-up in a steady state at Haematology clinic of Aminu Kano Teaching Hospital (AKTH), Kano, Nigeria from March to July, 2019.

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Exclusion criteria in the study were non-SS haemoglobin phenotype, sickle cell related complications other than priapism, self-reported history of major priapism without verifiable documented evidence in the patient folder, chronic viral infections (HIV, Hepatitis B and C) and usage of hydroxyurea. Informed written consent was obtained from all participants of the study and ethical approval to conduct the study was obtained from AKTH Ethical Review Board.

Socio-demographic and clinical data were extracted from hospital case note of the participants and any missing information was supplemented with interviewer administered questionnaire. Three (3) millilitre each of venous blood was collected into Gel agitator and K_2-EDTA sample bottles through a Vacutainer and all samples were analysed within 4 hours of collection except sample for LDH assay which was stored at 4^0C until analysis. Full blood count was performed with Swelab Alfa 3-part differentials Coulter (Boule Medical Diagnostics, Sweden) whereas reticulocyte count, LFT and E/U/Cr were performed with manual methods. Lactate Dehydrogenase (LDH) was determine using calorimetric assay at 450nm (Sigma-Aldrich(R) MAK066 reagent). Human immunodeficiency virus, Hepatitis B and C virus infections were screened with Determine, Ascon and Healgen respectively.

Data was analyzed with Statistical Package for Social Sciences (SPSS) version 21.0 (IBM Corp. Armonk, NY) and result presented as mean with standard deviation and proportion with percentage as appropriate. Chi-square (χ^2) and logistic regression analysis at 95% confidence interval were employed to test for association and estimate risk respectively. *P* – value of less than 0.05 was accepted as significant statistical relationship.

Definition of Terms

Steady state is the absence of febrile illness, sickle cell related crisis in the preceding 6 weeks and blood transfusion in the last 3 months. [10] Priapism is self-reported history of priapism lasting for at least 4 hours supported with verifiable documented evidence in the patient hospital case note.[3] Stuttering priapism is self-reported history priapism which resolved before 4 hours either spontaneously or following any form of intervention.[1]

RESULTS

Out 102 SCA patients 37 had priapism giving a prevalence of 35.6% and no significant difference between SCA patients with and without priapism with respect to age in year [20.05±3.93 and 21.48±4.87, *p*=0.11] and age of diagnosis of SCA in month [14.59±7.62 and 14.96±6.89, *p*=0.81].

Socio-demographic and clinical characteristic of the participants are presented in Table 1. No significant difference between SCA with and without priapism with respect to bone pain crisis [χ^2=0.95, *d*f=4, *p*=0.41], hospital admission [χ^2=0.28, *d*f=4, *p*=0.59] and stuttering priapism [χ^2=1.23, *d*f=4, *p*=0.81] but SCA patients with priapism in comparison to their counterparts without priapism, had more blood transfusion [χ^2=46.70, *d*f=4, *p*=0.01].

Haematological, biochemical and haemolytic parameters of the participants are shown in Table 2. SCA patients with priapism in relation to their counterparts without priapism, had lower Haemoglobin [6.96±1.23g/dL and 8.74±1.33g/dL, *p*=0.01], higher WBC count [15.28±4.73x10^9/L and 12.58±3.31x10^9/L, *p*=0.03], serum total bilirubin [26.00±12.99µmol/L and 13.23±5.52 µmol/L, *p*<0.001] and serum lactate dehydrogenase [272.62±95.31U/L and 161.28±48.39U/L, *p*<0.001], however, no significant difference between the two groups of SCA patients with respect to platelet count [367.89±176x10^9/L and 341.58±112.87x10^9/L, *p*=0.36] and serum urea [5.09±3.55µmol/L and 5.03±3.52µmol/L, *p*=0.32].

Clinical and laboratory predictors of priapism in SCA patients are depicted in Table 3. Out of both clinical, haematological, biochemical and haemolytic parameters of the SCA patients with priapism tested, only history of blood transfusion [OR(95% CI) 3.41(1.60 - 6.50), *p*=0.03], reticulocyte count >3.99% [OR(95% CI) 8.90(2.43 - 14.82), *p*=0.01] and serum LDH >161.28U/L [OR(95% CI) 13.63(7.62 - 42.45), *p*=0.01] turns out as independent predictors of priapism in adult SCA patients.

DISCUSSION

The prevalence of priapism in this study is in line with the reported prevalence of priapism of 21.4% to 39.1% among similar patients from across the country [11-14]. This highlighted priapism as very common complication in males with SCD especially in Nigeria and most importantly call for increase awareness from the patients as well as directed questions on priapism at every contact with SCA patient by the health care worker in order to averts erectile dysfunction which complicates up to 26.3% of all cases of SCD related priapism in Nigeria. [11,14]

The finding of the study with respect to age of the participants is at variance with reports from Enugu and Cooperative Study of Sickle Cell Disease (CSSCD) where patients with priapism were said to be older than those without. [11,15] The CSSD included both adults and children as well as stuttering and major priapism while the study from Enugu was not categorical on the type of cases (major, stuttering or both) included as against this study which enrolled adult patients with major priapism only. These differences in the enrolment criteria could be responsible for the observed variation with respect to the age, as older patients will more likely remember any priapic episode than the younger ones and as such priapism may appear to be more common in older patients. Whereas stuttering priapism which many patients inclined to tolerates, was earlier highlighted to proceed acute episode, and the occurrence of major episode following stuttering event could make priapism to appear more common in older patients when the two forms of priapism (major and stuttering) were not distinguished during enrollment process.[13]

The history blood transfusion and lower haemoglobin and haematocrit at steady state among participants with priapism in the study suggests more haemolysis in these patients than their counterparts without priapism. These findings together with higher level of haemolytic markers (bilirubin, LDH and reticulocyte counts) in SCA patients with priapism have further reemphasized the important role of haemolysis in the pathogenesis of SCD related priapism as earlier proposed by Kato GJ and colleagues.[16] The role of haemolysis in the pathogenesis of priapism among our participants can be better appreciated by the predictive significance of history blood transfusion, reticulocyte count and serum LDH in logistic regression analysis using various clinical and laboratory parameters of SCA patients with priapism.

The frequency of crisis and hospital admission per annum even though traditionally been used as indicators of disease severity did not show a positive association with the occurrence of priapism in our study participants. This could be due to under reporting in an attempt by the patient to avoid embarrassment in poorly enlighten society; a scenario with detrimental consequence to the outcome and call for strategies to bolster awareness in the society or probably patient with priapism rarely have frequent Vaso-Occlusive Crisis (VOC) warranting regular emergency hospital visit; which will put priapism to some extent different from other forms crises in sickle cell disease that requires recurrent hospitalization highlighting distinct pathophysiologic mechanism from VOC. This finding is similar to a work done by Madu AJ et al where there was no correlation between occurrence of priapism and frequency of crises.[11] The findings of this study with respect to other haematological and biochemical parameters are line with findings of other studies in which no difference was observed between the SCD patients with and without priapism in term of

platelet count, urea, creatinine and aspartate amino transferase. [11.15,17]

Table 1: Socio-demographic and clinical characteristics of the participants

Parameter	**Priapism (N = 37)**	**No priapism (N = 65)**	***P* – value**		
	Mean ± SD	Mean ± SD			
Age (year)	20.05 ± 3.93	21.48 ± 4.87	0.11		
Age at diagnosis (month)	14.59 ± 7.62	14.96 ± 6.89	0.81		
	Frequency (%)	Frequency (%)	χ^2	*d*f	*P* – value
Marital status					
Married	8 (21.6)	9 (13.8)			
Unmarried	29 (78.4)	56 (86.2)	2.06	4	0.09
Occupation					
Student	27 (72.9)	48 (73.8)			
Civil servant	2 (5.4)	4 (6.2)			
Business	0 (0.0)	2 (3.1)			
Artisan	8 (21.6)	11 (16.9)	6.23	8	0.07
Blood transfusion					
Yes	22 (62.9)	20 (30.8)			
No	15 (37.1)	45 (69.2)	46.70	4	0.01
Bone pain crisis					
< 3/year	19 (51.4)	41 (63.1)			
≥ 3/year	18 (48.6)	24 (36.9)	0.95	4	0.41
Hospital admission					
< 3/year	19 (51.4)	38 (58.5)			
≥ 3/year	18 (48.6)	27 (41.5)	0.28	4	0.59
Stuttering priapism					
Yes	35 (94.6)	61 (93.8)			
No	2 (5.4)	4 (6.2)	1.23	4	0.81

Table 2: Haematological, biochemical and haemolytic parameters of the participants

Parameter	**Priapism (N = 37) Mean ± SD**	**No priapism (N = 65) Mean ± SD**	***P* – value**
Haemoglobin (g/dL)	6.96 ± 1.23	8.74 ± 1.33	0.01
Hct (%)	20.26 ± 4.22	25.84 ± 4.83	0.02
MCV (fL)	89.82 ± 8.36	90.33 ± 6.26	0.73
WBC x 10^9/L	15.28 ± 4.73	12.58 ± 3.31	0.03
ANC x 10^9/L	7.17 ± 2.80	5.47 ± 2.00	0.02
Platelet count x 10^9/L	367.89 ± 176.65	341.58 ± 112.87	0.36
Reticulocyte count (%)	10.58 ± 6.53	3.94 ± 1.79	<0.001
AST (U/L)	49.54 ± 20.13	47.49 ± 18.66	0.60
Tbil (µmol/L)	26.00 ± 12.99	13.23 ± 5.52	<0.001
Dbil (µmol/L)	12.08 ± 5.43	7.40 ± 3.76	<0.001
LDH (U/L)	272.62 ± 95.31	161.28 ± 48.39	<0.001
Potassium (µmol/L)	4.38 ± 1.59	4.48 ± 1.47	0.86
Urea (µmol/L)	5.09 ± 3.55	5.03 ± 3.52	0.32
Creatinine (µmol/L)	163.11 ± 110.54	166.03 ± 108.74	0.95

Hct = Haematocrit, MCV = Mean Cell Volume, WBC = White Blood Cell Count, ANC = Absolute Neutrophil count, AST = Aspartate aminotransferase, Tbil = Total Bilirubin, DBil = Direct Bilirubin, LDH = Lactate Dehydrogenase

Table 3: clinical and laboratory predictors of priapism in SCA patients

Parameter	Odd Ratio (OR)	95% Confidence Interval (CI)		*P* - value
		Lower	Upper	
History of blood transfusion	3.41	1.60	6.50	0.03
Low Haemoglobin	0.03	0.01	0.72	0.30
Low PCV	0.03	0.01	1.42	0.08
High WBC	9.81	0.84	114.51	0 .07
High ANC	0.04	0.02	0.83	0.05
High Reticulocyte count	8.90	2.43	14.82	0.01
High Tbil	2.18	0.18	26.42	0.54
High Dbil	3.41	0.30	39.48	0.33
High LDH	13.63	7.62	24.25	0.01

Low PCV = Packed cell volume <6.96g/dL, High WBC = White blood cell count >12.58x10^9/L, High ANC = Absolute neutrophil count >5.47x10^9/L, High reticulocyte count = Reticulocyte count >3.94%, High TBil = Total serum bilirubin >13.23µmol/L, High DBil = Direct Serum bilirubin >7.40µmol/L, High LDH = Serum lactate dehydrogenase >161.28U/L

CONCLUSION

Major priapism is quite common in male patients with SCA in our environment especially those with low haemoglobin and high serum bilirubin and LDH. Haemolytic markers (mainly high reticulocyte count and LDH) and history of blood transfusion are important risk factors for SCA related priapism in adults. There is need for increase awareness of priapism among SCA patients and healthcare providers and importantly for physicians managing this patient to make specific inquiry on priapism at every contact. This is necessary to prevent erectile dysfunction with attendant psychosocial problems to individual, family and society.

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No conflict of interest to disclose in respect of this work.

REFERENCES

1. Chinegwundoh FI, Smith S, Anie KA. Treatments for priapism in boys and men with sickle cell disease. Cochrane Database of Systematic Reviews 2017, Issue 9. Art. No.: CD004198. DOI: 10.1002/14651858.CD004198.pub3.
2. Okpala I, Westerdale N, Jegede T, Cheung B. Etilefrine for the prevention of Priapism in adult Sickle Cell Disease. British journal of Haematology, 2002,118.918-921.
3. Olujohungbe A., Burnett A.L. How I manage priapism due to Sickle Cell Disease. British journal of Haematology, 2013, 160, 754-765.
4. Kato GJ, Steiberg MH, Gladwin MT. Intravasclar haemolysis and pathophysiology of Sickle Cell Disease. Journal of Clinical Investigations, 2017, 127.750-760.
5. Ahmed SG, Ibrahim UA, Hassan AW. Haematological parameters in Sickle Cell Anaemia patients with and without Priapism. Ann Saudi Med 2006;(26):439-443.
6. Saad ST, Lajolo C, Gilli S, Marques JF, Lima CS, Costa FF et al. Follow-up of Sickle Cell Disease patients with Priapism treated by Hydroxyurea. Am. J. Hematol. 2004;(77):45-49.
7. Al Jam AH, Al Dabbous IA. Hydroxyurea in the treatment of Sickle Cell associated Priapism. The Journal of Urology. 1998;(159):1642.
8. Akinbami A, Uche E, Dosunmi A. Priapism in Sickle Cell Disease: Emergency Room Intervention. Ann Trop Pathol.2017;8:5-10.
9. Arduini GA, Trovó de Marqui AB. Prevalence and characteristics of priapism in sickle cell disease. Hemoglobin. 2018;42(2):73-7.
10. Bookchin RM, Lew VL. Pathophysiology of Sickle Cell Anaemia. Hematology/Oncology Clinics of North America,1996;(10):6.1241-1253.
11. Madu JA, Ubesie A, Ocheni S, Chinawa J, Mad KA, Ibegbulum OG et al. Priapism in Homozygous Sickle Cell Patients: Important Clinical and Laboratory Associations. Med Princ Pract 2014;(23):259-263.
12. Adediran A, Wright K, Akinbami A, Dosnmu A, Oshinaike O, Osikomaiya B. et al. Prevalence of Priapism and its Awareness among Male Homozygous Sickle Cell Patients in Lagos, Nigeria. Advances in Urology. 2013;1-5
13. Adeyoju AB, Olujohungbe AB, Morris J, Yardumian A, Bareford D, Akenova A et al. Priapism in sickle-cell disease; incidence, risk factors and complications–an international multicentre study. BJU international. 2002;90(9):898-902.
14. Idris IM, Abba A, Galadanchi JA et al. Men with Sickle Cell Disease experience greater sexual dysfunction when compared with men without sickle cell disease. Blood Adv 2020;4(14): 3277-3283.
15. Nolan VG, Wyszinsky DF, Farrer LA et al. Haemolysis-associated Priapism in Sickle Cell Disease. Blood, 2005;106:3264-3267.
16. Kato GJ, Gladwin MT, Steinberg MH. Deconstructing sickle cell disease: reappraisal of the role of hemolysis in the development of clinical subphenotypes. Blood reviews. 2007;21(1):37-47.
17. Cita KC, Brureau L, Lemonne N, Billaud M, Connes P, Ferdinand S et al. Men with sickle cell anemia and priapism exhibit increased hemolytic rate, decreased red blood cell deformability and increased red blood cell aggregate strength. PLoS One. 2016;11(5):e0154866.