IBOM MEDICAL JOURNAL
Vol.18 No.3 | July - September 2025 | Pages 539-544
www.ibommedicaljournal.org

Detection of Early Onset Nephropathy in Children with Sickle Cell Anaemia in Calabar, Nigeria Using Microalbuminuria

Chigozie I. Uzomba[1], Ekaette I. Nsa[1], Ekaete S. Brown[2], Callistus O. Enyuma[1], Lawson E. Ekpe[3], Egorp O. Ineji[1], Imaobong S. Etuk[1], Asindi A. Asindi[2]

[1]Department of Paediatrics, Faculty of clinical sciences, College of medical sciences, University of Calabar, Cross River State, Nigeria.
[2]Department of Paediatrics, University of Calabar Teaching Hospital, Calabar, Cross River State, Nigeria.
[3]Department of Chemical Pathology, Faculty of Basic Clinical, College of medical sciences, University of Calabar, Cross River State, Nigeria

Abstract

Background: Asymptomatic nephropathy in children with sickle cell anaemia starts in childhood and may progress to overt renal dysfunction in adult life. This study was carried out to detect early asymptomatic nephropathy in children with sickle cell anaemia (SCA) in steady state using microalbuminuria.
Methods: A cross-sectional study of 80 children aged 2 to 16 years, with sickle cell anaemia in steady state. Sociodemographic data, hydroxyurea use, packed cell volume (PCV) and number of blood transfusions given, were recorded. Two consecutive spot urine samples were collected for urinalysis and urinary albumin/creatinine estimations. Data were analysed using SPSS 22, with a p-value < 0.05 considered significant.
Results: Microalbuminuria was prevalent in 25% of the subjects. Urine albumin/creatinine ratio had significant negative correlation with steady state PCV. Body mass index, blood pressure, number of blood transfusions and use of Hydroxyurea, had no relationship with microalbuminuria.
Conclusions: Microalbuminuria was seen in children with sickle cell anaemia in our environment; hence, its early screening is recommended.

Keywords: Sickle cell, Nephropathy, Children, Nigeria.

Introduction

Sickle Cell Anaemia (SCA) is an autosomal recessive haemoglobinopathy with two abnormal haemoglobin being HbS. Out of the 200,000 SCA children born globally each year, 75% are in Sub-Saharan Africa, with Nigeria having the highest prevalence which ranges between 2.23 to 5 %.[1-3] Most SCA children die from infections, but there is an increasing morbidity and mortality from chronic kidney disease (CKD) usually in the second and third decade of life.[4] According to studies in Nigeria[5] and United States[6], the presence of CKD in SCA increases the risk of morbidity and other systemic problems and contributes to mortality by up to 14–18%. Sickle cell nephropathy (SCN)which develops early can start in infancy, without overt symptoms. It eventually advances to End Stage Renal Disease (ESRD) and is the main renal consequence of SCA causing CKD.[7] Hence, early detection in those at increased risk, such as SCA and HIV patients in resource-limited countries like Nigeria, is needed to

Corresponding Author:

Dr. UZOMBA CI
Department of Paediatrics, Faculty of clinical Sciences, College of Medical Sciences, University of Calabar, PMB 1115, Calabar, Nigeria.

chizomba2000@gmail.com | chizomba@unical.edu.ng

DOI: 10.61386/imj.v18i3.715

address the growing burden of morbidity from CKD.[7,8]

Microalbuminuria is the earliest manifestations of sickle nephropathy used as a marker of early onset nephropathy.[9] Hence, screening for microalbuminuria is important since renal complications may not be identified at early stages of SCN if the classic biomarkers (serum creatinine and proteinuria) of renal damage were used.[10]

Globally, there were varying reports of the prevalence of microalbuminuria; in the United State of America (USA) 23%,[11] in the United Kingdom 34%,[10] in India 18.8%[12], Kenya 39.1%,[13] Congo 18%[14] and Egypt 30.4%.[15] In Nigeria, the prevalence ranges between 11.3% to 42.7%.[16-18] Majority of these Nigerian studies were done using the semiquantitative method using micral strips which is subjective. However, this study used the quantitative method of assessing for microalbuminuria using the Urine Albumin/Creatinine Ratio (UACR).

The dual burden of morbidity from SCA and probable CKD from Sickle Cell Nephropathy (SCN) makes it important to screen and detect asymptomatic nephropathy early using microalbuminuria. This study aims to detect early onset nephropathy in SCA children while in their steady state in our environment.

Materials and methods:

Study Design, Location and Sample Size Determination

This was a descriptive cross-sectional study conducted at the Paediatric Sickle Cell Clinic, University of Calabar Teaching Hospital, Calabar, Nigeria from November, 2019 to March, 2020.

Sample size was calculated using Fisher's formular: $n = Z^2pq/d^2$ Where; n = sample size, Z = Confidence level at 95 % (1.96), p = reported highest prevalence of the target population (5%)[3], q = proportion of target population without the characteristic of the study population (1-p) and d = degree of accuracy desired usually set at 5 % (0.05). A minimum sample size of 73 was obtained . A total of 80 respondents were studied including a 10% non-response.

Study Population

Sickle Cell Anaemic (SCA) children aged 2-16 years in steady state who had protein negative urine samples on dipstick urinalysis were recruited consecutively until the calculated sample size was obtained. Steady state in SCA children in this study was defined as absence of painful crisis, inter-current illness, hospital admissions nor blood transfusions for at least four consecutive weeks.[19] Excluded were children with SCA who had a history of crisis, or febrile illness, or those on drugs apart from the routine medication within the preceding four weeks of the study, who have been involved in competitive sports/exercise within 24 hours of the study, females menstruating at the time of evaluation, those with known congenital renal disease or pre-existing renal impairment/CKD or overt symptoms of renal disease like facial puffiness, leg swelling and reduced urine output.

Ethical Consideration

Ethical approval was obtained from the Health Research Ethics Committee (HREC) of the University of Calabar Teaching Hospital (UCTH), Calabar, Cross River State, Nigeria. Written informed consent was obtained from the caregivers while assent was obtained from participants >7 years of age.

Study Procedure

Each participant had his/her genotype rechecked at first visit by haemoglobin electrophoresis using agarose gel at UCTH. Counselling about the disease and the clinical features was also done at first visit and continuous education at subsequent clinic visits. A questionnaire detailing socio-demographic data, medical history including age at diagnosis, Hydroxyurea use and number of blood transfusions and physical examination was completed for each participant. Blood Pressure, weight and height were taken and body mass index (BMI) calculated. The packed cell volume (PCV) was also determined for the subjects in steady state.

Two consecutive spot urine samples were collected from each recruited subject. Urinalysis was done on one of the samples, if negative for protein, the other sample was tested for urinary albumin and creatinine estimations using immunoturbidimetric assay and modified Jaffe Kinetic reaction method respectively.[20] The urine albumin and creatinine ratio (UACR) were calculated. Microalbuminuria was determined by using urine Albumin Creatinine

Ratio (UACR) and defined as UACR values 30-300mg/gm. Data was analysed using SPSS version 22. A p-value of < 0.05 was taken as significant.

Results:

Sociodemographic Characteristics of The Study Population: A total of 80 HbSS children between the ages of 2-16 years participated in the study, which comprised of 43 (53.8%) males and 37 (46.3%) females with a male to female ratio of 1.2:1. The mean age for the study population was 8.3±4.2 years with a median age of 8years (Table I)
Microalbuminuria was present in 20 subjects, thus giving a prevalence of 25% as shown in Table 2.

Table 1: Sociodemographic Characteristics of the study population

Variable	Frequency (N=80)	Percentage (%)
Age Group		
2-6	32	40.0
7-11	28	35.0
12-16	20	25.0
Sex		
Male	43	53.8
Female	37	46.2
Social Class		
Upper	38	47.5
Middle	29	36.3
Lower	13	16.2

Table 2: Prevalence of microalbuminuria in the study population

Microalbuminuria (mg/gm)	Frequency N (%)	Median	Mean (SD)	Range Q_1 Q_3
Present (30-300)	20(25.0)	17.1	30.2± 47.6	7.3, 30.3
Absent (0-29.9)	60(75.0)			

Table 3: Relationship between microalbuminuria and sociodemographic characteristics of subjects

Variables	Microalbuminuria			Statistical Test	p-Value
Age (Years)	Present (N=20)	Absent (N=60)	Total (N=80)		
2-6	6(18.8)	26(81.3)	32(100.0)	X^2=1.124, df=2	0.570
7-11	8(28.6)	20(71.4)	28(100.0)		
12-16	6(30.0)	14(70.0)	20(100.0)		
Sex					
Male	8(18.6)	35(81.4)	43(100.0)	X^2=2.028, df=1	0.154
Female	12(32.4)	25(67.6)	37(100.0)		
Social Class					
Upper	9(23.7)	29(76.3)	38(100.0)	FET=0.277, df=2	0.871
Middle	7(24.1)	22(75.9)	29(100.0)		
Lower	4(30.8)	9(69.2)	13(100.0)		

FET =Fischer's Exact Test

Table 4: Relationship between microalbuminuria and clinical characteristics of subjects

Variables n=80	Microalbuminuria Present n=20	Absent n=60	Total n=80	Test Statistics	p value
Blood Transfusions					
Transfused	11(28.9)	27(71.1)	38(100.0)	X^2=.602, df=1	0.438
Never Transfused	9(21.4)	33(78.6)	42(100.0)		
Hydroxyurea					
Takes	3(27.3)	8(72.7)	11(100.0)	FET=1.000, df=1	0.555
Doesn't take	17(24.6)	52(75.4)	69(100.0)		
Systolic BP Centile					
Normal	17(23.9)	54(76.1)	71(100.0)	FET=.531, df=1	0.844
Elevated	2(25.0)	6(75.0)	8(100.0)		
Stage 1	1(100.0)	0(0.0)	1(100.0)		
Diastolic BP Centile					
Normal	13(21.0)	49(79.0)	62(100.0)	FET=.338, df=2	0.767
Elevated	5(29.4)	12(70.6)	17(100.0)		
Stage 1	1(100.0)	0(0.0)	1(100.0)		
BMI Centile					
Thinness	2(18.2)	9(81.8)	11(100.0)	FET=1.429, df=3	0.544
Normal	17(27.9)	44(72.1)	61(100.0)		
Overweight	1(16.7)	5(83.3)	6(100.0)		
Obese	0(0.0)	2(100.0)	2(100.0)		
Steady State PCV (%)					
15-20	2(28.6)	5(71.4)	7(100.0)	FET=2.230, df=3	0.526
21-25	11(25.6)	32(74.4)	43(100.0)		
26-30	6(23.1)	20(76.9)	26(100.0)		
>30	1(25.0)	3(75.0)	4(100.0)		

FET =Fischer's Exact Test; BMI =Body Mass Index; PCV=Packed cell volume; BP =Blood Pressure.

Table 5: Correlation of clinical characteristics and comparison of their mean values with UACR

Variables	Mean ± SD		t-Test	p-value	R	p-Value
	Normoalbuminuria (UACR 0-29mg/gm)	Microalbuminuria (UACR 30-300mg/gm)				
Age	8.13 ±4.3	8.65 ±4.0	-0.471	0.639	0.018	0.872
BMI Centile	44.8 ±31.4	40.5 ±29.6	1.010	0.315	0.031	0.768
Steady State PCV	24.8 ±3.1	25.4 ±4.3	1.913	0.059	-0.251	**0.024****
No. of Blood Transfusion	1.0 ±1.4	1.3 ±2.3	-0.615	0.540	-0.014	0.899
Systolic BP Centile	54.8 ±13.2	54.0 ±12.3	-0.539	0.591	0.163	0.150
Diastolic BP Centile	58.8 ±16.8	60.0 ±17.8	-0.855	0.395	0.076	0.503

****Statistically Significant**

Discussion

The prevalence of early nephropathy using microalbuminuria in this study was 25%. This is in consonance with the prevalence of 20-26% documented in the studies by Ekpenyong *et al*[21] in Uyo, Imuetinyan *et al*[22] in Benin both in South-South Nigeria, Ocheke *et al*[17] in Jos, North-Central Nigeria, Olorukooba et al[23] in North-West Nigeria, and Yee et al[11] in Georgia, USA. It was higher than the prevalence of 11-18% in the studies by Eke et al[24] in Enugu, South-East Nigeria, Aloni et al[14] in Kinshasa, Congo. Al-Musawa & Al-Saqladi[25] in Yemen and Solarin *et al*[16] in Lagos, Nigeria had higher prevalence of microalbuminuria of 30.7% and 38.8% respectively than that of this current study. These differences in prevalence of microalbuminuria may be attributed to assay methods especially if the semi quantitative method of micral strip was used which is subjective. This study used an objective and fully quantitative

assessment of microalbuminuria. All the children in this study were homozygous HbSS in steady state for at least 4weeks. Two consecutive spot urine samples were used for microalbuminuria estimation. The wide age range of 2-16 years ensured a good spread for the study of early nephropathy which reflects the prevalence. It is also plausible that since SCA is a genetic disease with different haplotypes across and even within geographical regions, this may modify the presentation and onset of early renal dysfunction in children with SCA.

This study showed that the highest prevalence of microalbuminuria occurred in middle childhood. The mean age of the subjects with microalbuminuria, 8.6±4.0 years was higher than those without microalbuminuria. In this study, there was a positive correlation of age with UACR showing that its levels increase with increasing age. This finding has also been reported in other studies.[14,16,17] The repeated episodes of vaso-occlusion occurring in the kidneys of SCA individuals over the years eventually leads to glomerular damage and glomerulosclerosis with resultant leakage of proteins from the damaged nephrons.[3,17,26] The finding of high prevalence of microalbuminuria among the younger subjects in this study shows that renal vasculopathy from repeated sickling episodes occur early as postulated in literature.[17,23] This is also supported by the findings of late age of diagnosis more than three years in this study when repeated episodes of sickling may have already caused injury to the kidneys.

This study also had a higher prevalence of microalbuminuria among the female subjects compared to the males though not significant. In conducting this study, a careful clinical examination and probing history for the presence of urinary tract infections (UTIs) plus dipstick urinalysis was done to exclude the presence of nitrites or leucocytes esterase. Also, none of the female subjects were menstruating at the time of sample collection. The gold standard to detect presence of UTI by a urine culture was not done in this study and this could be a limitation. The study by Eke *et al*[24] reported similar higher prevalence among females even when urine culture was done and urine found to be sterile. Other studies[14,22] with either higher female or male prevalence have also reported no statistical relationship nor identified cause. It may be inferred that though there is the genetic predilection to onset of sickle cell nephropathy in SCA children, it may perhaps have no sex predilection.[17,27]

The BMI, blood pressure, number of blood transfusions and use of Hydroxyurea, did not statistically affect microalbuminuria in our series. The two obese and five overweight subjects did not have microalbuminuria in this study. This is similar to the findings by Olorukooba *et al*[23], in North-East Nigeria, where no significant association was found between microalbuminuria and overweight/obesed children. The relatively fewer numbers of overweight and obesed children in present study may be responsible. Though obesity is seen in children with SCA,[28] its overall prevalence is low, and therefore may lack a strong relationship to microalbuminuria in SCN. This is contrary to the observation that activation of the rennin-angiotensin-aldosterone system, plasminogen activator inhibitor-1, hyperlipidaemia and high serum level of adipocytes-specific metabolites such as leptin and adiponectin in children with obesity leads to leak of proteins in urine.[29]

The association between steady state packed cell volume with microalbuminuria was not significant in our study. This may be due to the relatively higher levels of steady state haematocrit levels at mean value 24.9±3.4 in this series. Interestingly, the mean haematocrit levels of the subjects with microalbuminuria at 25.4±4.3 was higher than the haematocrit levels of subjects without microalbuminuria at 24.7±3.1. The levels of haemoglobin F were not assessed in this study which may be a possible reason. However, the bivariate correlation of steady state haematocrit with Albumin Creatinine Ratio was negative and significant which is supported by other studies[30,31] that show a relationship between low haemoglobin values and microalbuminuria. Though the relationship between low haemoglobin levels, haemolysis and microalbuminuria is documented in literature[30], there is no consensus on what low steady state haemoglobin values is protective of microalbuminuria in SCA patients.

In conclusion, there was high prevalence of microalbuminuria in the study subjects at an earlier age. Hence, we recommend early screening for

microalbuminuria at about five years of age.

References

1. Federal Ministry of Health Nigeria. National Guideline for the control and management of Sickle cell disease. Abuja, 2014.
2. Nwogoh B, Adewoyin S, Ihenacho E, Bazuaye G. Prevalence of hemoglobin variants in Benin City, Nigeria. Ann Biomed Sci 2012; 11:60-64.
3. Diwe K, Iwu A, Uwakwe K, Duru C, Merenu I, Ogunniyan T, et al. Prevalence and Patterns of Sickle Cell Disease among Children Attending Tetiary and Non-Tertiary Health Care Institutions in a South Eastern State, Nigeria: A10 year Survey. J Res Med Dent Sci 2016; 4:183-189
4. Scheinman JI. Tools to detect and modify sickle cell nephropathy. Kidney Int 2006; 69:1927-1930
5. Fagbuele B, Joiner K. Pattern of Childhood mortality at the University of Ilorin Teaching Hospital. Niger J Paediatr 1987:14:1-5
6. Hamideh D, Alvarez O. Sickle cell disease related mortality in the United States (1999-2009). Pediatr Blood Cancer 2013; 60(9):1482-1486.
7. Alhwiesh A. An Update on Sickle Cell Nephropathy. Saudi J Kidney Dis Transpl 2014; 25(2):249-265.
8. Nsa EI, Uzomba CI, Etuk IS, Anah MU. Prevalence of Renal Disease in Human Immunodeficiency Virus-Infected Children in Calabar, Nigeria. Saudi J Kidney Dis Transpl, 33(Suppl 1):S30-S38.
9. Inusa BPD, Mariachiara L, Giovanni P, Ataga KI. Sickle Cell Nephropathy: Current Understanding of the Presentation, Diagnosis and Therapeutic Challenges. In: Hematology-Latest Research and ClinicalAdvances.InTech;2018:155-185
10. Sundaram N Bennet M. Wilheim J, Kim M, Atweh G, Devarajan P et al. Biomarkers for early detection of sickle nephropathy. Am J Hematol 2011;86(7):559-566
11. Yee MM, Jabbar SF, Osunkwo I, Clement L, Lane PA, Eckman JR et al. chronic kidney disease and albuminuria in children with sickle cell disease. Clin J Am Soc Nephrol 2011; 6(11):2628-33.
12. Datta V, Ayengar JR, Karpate S, Chaturvedi P. Microalbuminuria as a predictor of early glomerular injury in children with sickle cell disease. Indian J Pediatr 2003;70(4):307-309.
13. Mbiata M, Musoke R, Wamalwa D, Admani B. Prevalence and clinical factors associated with microalbuminuria in children aged 2-18 years with sickle cell anaemia at the national referral hospital in Kenya. Afr J Paediatr Nephrol 2017;4(1):10-17.
14. Aloni MN, Mabidi JL, Ngiyulu RM, Ekulu PM, Mbutiwi FI, Makulo JR et al. Prevalence and determinants of microalbuminuria in children suffering from sickle cell anemia in steady state. Clin Kidney J 2017; 10(4):479-86.
15. Mona HE, Marwa AE, Dalia E, Nouran M, Yasmeen MMS and Mai AES. The prevalence of Sickle Nephropathy among children with Sickle Cell Disease. Journal of Population Therapeutics and Clinical Pharmacology 2023;30(7):141-147.
16. Solarin AU, Njokamah FO, Kehinde O. Prevalence and clinical correlates of Microalbuminuria among Children with Sickle Cell Anemia attending Lagos state University Teaching Hospital. Afr J Paediatr Nephrol 2014; 1(1):37-45.
17. Ocheke IE, Mohamed S, Okpe ES, Bode-Thomas F, McCullouch MI. Microalbuminuria risks and glomerular filtration in children with sickle cell anemia in Nigeria. Ital J Pediatr 2019; 45(1):2-6
18. Yaguo-Ide LE, Akani NA, Nwauche CA. Prevalence of microalbuminuria in paediatric patients with sickle cell anaemia at the University of Port-Harcourt Teaching Hospital. Pediatr Nephrol 2010; 25: 1846. DOI10.1007/s00467-010-1577-z
19. Nlemadim AC, Okpara HC, Uzomba CI, Anah MU, Meremikwu MM. Hypocalcemia and vaso-occlusive painful crises in pediatric sickle cell anaemia. Niger J Med 2021;30(1):34-9.
20. Cheesbrough M (ed). (2006). District laboratory practice in tropical countries. 2nd ed. Cambridge: Cambridge University Press; Pg:333-358.
21. Ekpenyong EE, Ikpeme EE, Bassey EG, Dixon-Umo OT. Early Detection of Renal Injury in

Children with Sickle Cell Anemia using Microalbuminuria in a Tetiary Health Institution in Southern Nigeria. West Afr J Med 2020; 37(4):412-417.
22. Imuetinyan BA-I, Okoeguale MI, Egbuere GO. Microalbuminuria in children with sickle cell anemia. Saudi J Kidney Dis Transpl 2011;22(4);733-8.
23. Olorukooba A, Akuse R, Ogunride G, Mamman A, Yusuf R, Kajogbola G. Renal abnormalities among children with sickle cell anemia. Niger J Pediatr 2018; 45(2):112-117
24. Eke CB, Okafor HU, Ibe BC. Prevalence and correlates of microalbuminuria in children with sickle cell anemia: Experience in a tertiary health facility in Enugu, Nigeria. Int J Nephrol 2010; 2012:1-7
25. Al-Musawa FE, Al-Saqladi AM. Prevalence and correlates of microalbuminuria in Yemeni children with sickle cell disease. Saudi J Kidney Dis Transpl 2019; 30(4):832-842
26. Ataga KI, Derebail VK, Archer DR. The glomerulopathy of sickle cell disease. Am J Hematol 2014; 89(9):907-914.
27. Korman R, Jannot AS. Narjoz C, Ribeil JA, Manceau S, Delville M, et al. British Journal of Haematology 2017;179:323-335.
28. Ukoha OM, Emodi IJ. Ikefuna AN, Obidike EO, Izuka MO, Eke CB. Comparative study of nutritional status of children and adolescents with sickle cell anemia in Enugu, Southeast Nigeria. Niger J Clin Pract 2020;23(8):1079-1086.
29. Hunley TE, Ma LJ, Kon V. Scope and mechanisms of obesity-related renal disease. Curr Opin Nephrol Hyperten 2010;19(3):227-234.
30. Brewin J, Tewari S, Hannemann A, Al Balushi HS, Claire G, John S et al. Early Markers of Sickle Nephropathy in Children with Sickle Cell Anemia Are Associated with Red Cell Cation Transport Activity. HemaSphere 2017;1(1):1-7.
31. Mawanda M, Ssenkusu JM, Odiit A, Kiguli S,Muyingo A, Ndugwa C. Microalbuminuria in Ugandan children with sickle cell anemia: a cross-sectional study. Ann Trop Paediatr 2011; 31(2):115-21.