Original Article

Proteinuria among adult sickle cell anemia patients in Nigeria

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Abstract

Background/Objective: The life expectancy of patients with sickle cell anemia (SCA) has improved with modern medical care, and this has led to frequent observation of various chronic complications of the disease including abnormalities in renal function. Proteinuria is not only a marker of renal disease but is also a predictor of disease progression. This screening study was aimed at evaluating the prevalence of proteinuria among adult SCA patients in Kano, Nigeria, which has not been reported previously.

Material and Methods: A total of 200 adult SCA patients were studied. They consisted of 100 men and 100 women. Blood was collected for the assay of serum urea, sodium, potassium, chloride, bicarbonate, and creatinine and estimated glomerular filtration rate (eGFR) was determined using the Cockcroft-Gault formula. Urine dipstick test for the presence of proteinuria and other abnormalities was done, and 24-hour urine protein was measured in those with significant proteinuria.

Results: Mean age of the male patients was 25.1 ± 1.0 years, whereas the mean age of the female patients was 22.8 ± 4.2 years. Twenty eight percent (32 males, 24 females) of the subjects were observed to have significant proteinuria. The mean estimated eGFR of the males was 88 ± 19.6 ml/min while that of the females was 92 ± 10.2 ml/min. The male SCA patients with proteinuria had a mean eGFR of 70 ± 6.9 ml/min, whereas the female SCA patients with proteinuria had mean eGFR of 101 ± 2.5 ml/min. Among the male patients with proteinuria, 50% had chronic kidney disease (CKD).

Conclusion: Proteinuria which is a marker of renal insufficiency is common among adult SCA patients, and routine screening for proteinuria may help detect those at increased risk of renal disease. CKD prevalence is high among SCA patients with significant proteinuria.

Keywords: Chronic kidney disease, proteinuria, sickle cell anemia

Résumé

Arrière-plan / Objectif: l'espérance de vie des patients souffrant d'anémie falciforme (SCA) a amélioré les soins médicaux modernes, et cela a conduit à l'observation fréquente de diverses complications chroniques de la maladie, y compris des anomalies de la fonction rénale. Protéinurie n'est pas seulement un marqueur de la maladie rénale, mais est également un indicateur de progression de la maladie. Cette étude visait à évaluer la prévalence de la protéinurie chez les patients adultes de SCA à Kano, au Nigeria, qui n'a pas été rapportée antérieurement.

Méthodes: Un total de 200 patients adultes de SCA ont été étudiés. Ils se compreaient d'une centaine d'hommes et de 100 femmes. Sang ont été recueillie pour le dosage de l'urée sérum, sodium, potassium, chlorure, bicarbonate et créatinine et taux de filtration glomérulaire estimée (FG) a été déterminé en utilisant la formule Cockcroft-Gault. Urine bandelettes de la présence de la protéinurie et autres anomalies a été fait, et protéines d'urine de 24 heures a été mesurée dans les importantes protéinurie.

Résultats: Moyenne âge des patients masculins était de 25,1 ± 1,0 années, alors que l'âge moyen des patients femelles était 22,8 ± 4,2 années. Pour cent vingt huit (32 mâles, 24 femelles) des sujets on a observé la protéinurie significative. La moyenne estimée FG des mâles était de 88 ± 19,6 ml/min alors que celle des femelles est 92 ± 10,2 ml/min. Les patients de sexe masculin SCA avec protéinurie avaient un FG moyenne de 70 ± 6,9 ml/min, tandis que les SCA patientes avec protéinurie FG moyenne de 101 ± 2,5 ml/min. Parmi les patients masculins avec protéinurie, 50% avaient insuffisance rénale chronique (IRC).

Conclusion: Protéinurie, qui est un marqueur de l'insuffisance rénale est fréquent chez les patients adultes de SCA et dépistage systématique de la protéinurie peut aider à déceler ceux à risque accru de maladie rénale. Prévalence de l'IRC est élevée chez les patients de la SCA avec protéinurie significative.

Mots clés: Insuffisance rénale chronique, protéinurie, anémie falciforme

Introduction

The prevalence of the hemoglobin S gene in Nigeria is observed to be between 20 and 25%;[1] the chronic hemolytic anemia experienced in sickle cell anemia (SCA) leads to adverse effects on oxygen transport by the blood as well as reduced oxygen availability to peripheral tissues. Limited tissue oxygen availability may lead to changes in events of the intracellular metabolism. Sickling of the red blood cells in various parts of the body causes acute and chronic ischemia, leading to progressive tissue damage.[2] The life expectancy of subjects with SCA has improved with better care, and this may lead to frequent observation of various chronic complications of SCA including kidney disease. With increase in the burden of chronic kidney disease (CKD), there is a call for prevention strategies including screening for early detection to prevent further injury and progressive loss of renal function. Whole population screening may be suitable in certain situations; however, targeted screening is also advocated as it may be more cost effective. Prevalence studies on CKD have been conducted in various population groups including healthy adult population; however, not much has been reported from this environment in this high-risk population group. Therefore, this study evaluates the prevalence of proteinuria among adult SCA patients in Kano, Nigeria.

Materials and Methods

This is a cross sectional study involving 200 adult SCA patients attending the sickle cell clinic of Aminu Kano teaching hospital, Kano, who had no history of CKD from other causes, not in any form of sickle cell crisis and consented to participate in the study. They consisted of 100 men and 100 women who were above 18 years of age. The study was approved by the ethical committee of the hospital and all patients gave informed consent. Socio-demographic data were obtained using a structured questionnaire, although complete physical examination was done on all the patients including the weight and height measurements.

5 ml of blood was collected from the antecubital vein placed in a plastic container and allowed to clot and centrifuged at 3000 rpm for 10 minutes. The sera were used to determine urea, sodium, potassium, chloride, bicarbonate, and creatinine. Urea was determined using urease colorimetric technique, creatinine was assayed using sodium hydroxide-picric acid, sodium and potassium were determined using flame photometric technique, and chloride and bicarbonate were assayed using titrimetric technique.[3] Cockcroft-Gault formula[4] was used to calculate the glomerular filtration rate (eGFR). Early morning urine specimens were collected and tested by dipstick for the presence of blood, protein, glucose, hemoglobin, and other abnormalities. Twenty-four hour urinary protein was determined in those subjects who had positive results (+1 and above) with dipstick proteinuria.

Results

The mean age of the male patients was 25.1 ± 5 years and that of the females was 22.8 ± 4.2 years. The mean systolic blood pressure s were 115 ± 5 and 105 ± 6 mmHg while the mean diastolic blood pressures were 68 ± 6 and 61 ± 5 mmHg for the male and female patients, respectively. Fifty-six subjects (28%) were observed to have significant proteinuria. Thirty-two were males while 24 were females. The mean 24-hour urinary protein in those with significant proteinuria was 0.26 g/day and none had a nephrotic range proteinuria. Of the 32 males with proteinuria, 16 (50%) had CKD defined as eGFR of less than 60 ml/minute. Table 1 shows urea, creatinine, electrolytes, and eGFR in SCA patients with proteinuria and those without proteinuria. Table 2 shows urea, creatinine, electrolytes, and eGFR in SCA patients with CKD and in those without CKD. Among the 32 male SCA patients with proteinuria, significant increases were observed for urea ($P<0.001$), creatinine ($P<0.001$), and sodium ($P<0.001$). In contrast, significant decreases were observed for potassium ($P<0.05$) and eGFR ($P<0.001$) compared with those with no proteinuria.

Table 1: Urea, electrolytes, creatinine, and estimated glomerular filtration rates in sickle cell anemia patients with proteinuria and those with no proteinuria

	Males with no proteinuria	Males with proteinuria	*P*-value	Females with no proteinuria	Females with proteinuria	*P*-value
No. of subjects	68	32	–	76	24	–
Age (years)	22.2 ± 3.8	26.4 ± 7.3	$P < 0.005$	21 ± 3.0	20.4 ± 7.6	NS
Weight Kg	45 ± 12.3	50 ± 7.2	$P < 0.001$	42 ± 7.6	47.4 ± 5.3	$P < 0.001$
Na+ mmol/l	134.7 ± 3.4	140 ± 3.8	$P < 0.001$	136 ± 5.4	141 ± 5.3	$P < 0.001$
K + mmol/l	4.2 ± 0.5	3.9 ± 0.5	$P < 0.05$	4.05 ± 0.35	3.9 ± 0.13	NS
Cl- mmo/l	97.4 ± 2.3	103 ± 4.1	$P < 0.001$	98.2 ± 5.3	101 ± 3.9	NS
Hco3- mmo/l	22.4 ± 2.0	21 ± 2.7	NS	22.3 ± 1.55	20.2 ± 3.0	$P < 0.05$
Urea mmol/l	2.46 ± 0.88	8.07 ± 2.2	$P < 0.001$	2.79 ± 1.77	2.46 ± 1.22	NS
CR μmol/l	59.2 ± 10.2	280 ± 22.3	$P < 0.001$	61.2 ± 12.4	67 ± 23.7	NS
eGFR ml/min	104 ± 22.8	70 ± 6.9	$P < 0.001$	97 ± 3.5	101 ± 2.5	NS

CR = creatinine, eGFR = estimated glomerular filtration rate, NS = not significant

Table 2: Urea, creatinine, electrolytes, and estimated glomerular filtration rates in sickle cell anemia patients with chronic kidney disease (Mean ± SD)

	Males with no CKD	Males with CKD	*P*-value
No. of subjects	68	16	–
Age (years)	22.2 ± 3.8	32.6 ± 3	$P < 0.001$
Weight (kg)	45 ± 12.3	54.4 ± 2.0	$P < 0.001$
Na+ (mmol/l)	134.7 ± 3.4	138 ± 2.8	$P < 0.001$
K+ (mmol/l)	4.2 ± 0.5	4.6 ± 0.4	$P < 0.001$
Cl- (mmol/l)	97.4 ± 2.3	105 ± 3.9	$P < 0.001$
Hco3- (mmol/l)	22.4 ± 2.0	21 ± 2.0	$P < 0.02$
Urea (mmol/l)	2.46 ± 0.88	14.0 ± 2.8	$P < 0.001$
CR (μmol/l)	59.2 ± 10.2	496 ± 78	$P < 0.001$
eGFR (ml/min)	104 ± 22.8	14.5 ± 2.0	$P < 0.001$

CR = creatinine, eGFR = estimated glomerular filtration rate, CKD = chronic kidney disease

In the 24 female SCA patients with proteinuria, significant increase was observed for sodium ($P < 0.005$) and significant decrease was observed for bicarbonate ($P < 0.05$). None of the female SCA patients with proteinuria had CKD.

The male SCA patients with proteinuria had a mean eGFR of 70 ± 6.9 ml/min, whereas the female SCA patients with proteinuria had a mean eGFR 101 ± 2.5 ml/min. The 16 male SCA patients with CKD had eGFR 14.5 ± 2.0 ml/min.

Discussions

This study showed that proteinuria was observed in 28% of adult SCA patients and this is consistent with findings by others,[5,6] although is higher than 16.8% reported by Arogundade *et al.* in a retrospective study[7] and lower than that reported by Aleem,[2] who reported a prevalence of 41% in adult SCA patients in Saudi Arabia. He attributed this high prevalence to older age of the study population. Age-dependent occurrence of dipstick proteinuria

in SCA patients has been reported. In a prospective study of children with SCA, it was reported that none of the patients under 6 years had proteinuria, but the prevalence rose to 7% in children aged 7 to 10 years and 10% in adolescents aged 13 to 17 years.[8] None of the patients in our study had nephrotic range proteinuria, even though nephrotic syndrome has been reported in SCA patients and is associated with higher frequency of renal failure.[9]

Proteinuria is a more sensitive marker than elevated serum creatinine values in detecting glomerular injury, and it has been reported to be an early manifestation of sickle cell nephropathy.[2,6] From this study, 50% of SCA male patients with proteinuria had CKD. This prevalence is higher than those reported by Murthy and Haywood[10] and Thomas *et al.*[11] They reported that approximately 18% of patients with SCA and proteinuria will have clinically manifested glomerular pathology and these patients developed renal failure with time. The high prevalence of CKD observed in this study may be due to the fact that the study was conducted in a tertiary health care referral centre, where there is the likelihood of having patient population with more severe disease. Proteinuria is a progression factor in CKD, heralding a further deterioration in renal function. Its detection is therefore very important in these patients as intervention at this stage has been shown to prevent or at least delay further renal damage.[12] This is particularly relevant because patients with SCA pose a management challenge on renal replacement therapy with dialysis or renal transplant compared with those with normal hemoglobin genotype, because of frequent vaso-occlusive crisis and other complications.[2] All the female SCA patients with proteinuria in this study had eGFR within the normal limit. However, this does not exclude an underlying kidney disease. Guasch *et al.*[6] observed that in SCA patients with

proteinuria but preserved GFR, the glomerular ultra-filtration coefficient was reduced compared with nonproteinuric SCA control subjects, which is an indication of underlying glomerular pathology.

The mean age of those with CKD from this study was 32.6 ± 3 years. This is higher than that reported by Powars *et al.*[13] They reported the mean age at which SCA patients developed renal failure to be 23.1 years. Studies have shown that renal structure and functions decrease with increasing age in SCA patients. Observed structural changes include decrease in size, weight, cortical scarring, and glomerular sclerosis as well as papillary necrosis.[6,12]

Hematuria was detected in 27% of the study population. This was also higher than 8.5% observed by Aleem.[2] Hematuria is usually a result of red cell sickling in the renal medulla and in some cases it may result from papillary necrosis.[12,14]

We would like to appreciate the limitation of this study being cross-sectional in nature and the use of Cockcroft-Gault formula in evaluating eGFR, because some have suggested that this formula is not accurate for lean people of sub-Sahara Africa.[15] Although others have reported that it correlates well with the creatinine clearance calculation.[16] This notwithstanding, this study highlights the presence of proteinuria and CKD in adult SCA patients from this environment, which has not been previously reported.

Conclusion

Proteinuria which is a marker of kidney disease is common among adult Nigerian SCA patients, and routine screening for proteinuria may help detect those at immediate risk of chronic renal disease.

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