Arch Nephrol Urol 2018; 1 (1): 001-008 DOI: 10.26502/anu.2644-2833001

Research Article

Renal Function of Sickle Cell Subjects in Edo State-Nigeria

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Received: 28 November 2018; **Accepted:** 10 December 2018; **Published:** 18 December 2018

Abstract

This study compares renal function of Sickle cell disease (SCD) patients and healthy subjects and investigates the influence of age and sex. The study involves 30 each of SCD patients and healthy subjects recruited within Edo State. Blood samples from patients and subjects who met the criteria for inclusion and gave consent were evaluated for kidney function as well as electrolytes profile. The results were compared using "t test" and ANOVA where appropriate with $p<0.05$ considered significance. The results showed significant higher ($p<0.05$) bicarbonate and creatinine levels in SCD patients compared to healthy subjects. However, there were non-significant difference ($p>0.05$) in Na^+, Cl^-, K^+ and urea levels between the groups. On the impact of sex, K^+ and Creatinine levels were significantly different ($p<0.05$) between the groups. On age impact, there was significant difference ($p<0.05$) in K^+, bicarbonate and creatinine in the different age groups between SCD and healthy subjects. The findings of this study suggest the need for routine evaluation of kidney function to help SCD patients to avert the inherent danger of kidney diseases and destruction.

Keywords: Renal function; Sickle cell disease; Creatinine; Electrolytes

1. Introduction

Sickle cell disease (SCD) is a group of inherited disorders of hemoglobin (Hb) in which the sickle Hb is present in association with abnormal Hb [1]. The sickle cell disease (SCD) is an inherited genetic disorder caused by a middens mutation in the amino acid sequence coding for hemoglobin gene in the red blood cells [2]. It was reported

that SCD is endemic in malaria-prevalent regions due to the protective nature of the carrier state [3]. It is the most common single gene disorder in the world and up to 312,000 people are born yearly with HbSS globally; majority of these births (236,000) occur in Sub-Saharan Africa [4, 5] with highest frequencies occurring in sub-Saharan African where 3 to 4% of populations are affected [6]. SCD is a very devastating condition caused by an autosomal recessive inherited haemoglobinopathy. According to Hart and Ruvolo [7], SCD is due to substitution of amino acid valine for the glutamic acid at the 6^{th} position of β chain of haemoglobin resulting to biochemical abnormalities of sickle cell patient. The haemoglobin molecule is a tetramer which comprises of two alpha subunits and two beta subunits. In SCD, the sickle cells do not deliver oxygen to tissues with the same capacity and efficiency as the normal blood cell does, and they often submerged and get caught up in small blood vessels leading to blockages. This causes pains that are often extreme and leads to organ damages such as the brain, heart, kidneys and muscles [8]. The disease is characterized by multisystem involvement, with episodes of acute illness and progressive organ damage [9].

Chronic renal failure has been reported as a known cause of death in adults with SCD [10]. Young patients with sickle cell disease (SCD) have supra normal renal hemodynamics with increase in both effective renal plasma flow (ERPF) and glomerular filtration rate (GFR) [10]. Among the challenges in the management of renal complications of SCD are identifying early indicators, reducing glomerular damage and progression to end stage renal failure [11]. These showed that there might be several structural and functional abnormalities of the kidney in patients with SCD related hemoglobinopathies. Because the rate of oxygen consumption by the kidney is very high, a rate exceeded only by that of the heart [12] and glomerulosclerosis has been identified as the commonest renal pathology in SCD patients. Patients with SCD have been reported to have abnormalities in renal hemodynamics, and young patients present increased glomerular filtration rate (GFR), which seems to be associated with increased sensitivity to prostaglandins, since treatment with indomethacin significantly reduces GFR among these patients [13]. According to Powars et al. [14], early diagnosis and inclusive care can help to reduce mortality and morbidity rate significantly in children with sickle cell disease; hence the need for early renal assessment cannot be over emphasized. In-depth and thorough researches to provide awareness and possible early preventive measures to health care providers are lacking especially in Nigeria. The aim of this study is to assess and compare plasma Na^+, K^+, Cl^-, HCO_3^-, urea and creatinine of sickle cell and apparently healthy subjects in Edo State with a view to investigate the influence of age and sex.

2. Materials and Methods

2.1 Area of study

This study was carried out in Edo State, Nigeria. Edo state is in southern Nigeria and located at latitude 6.30°N and longitude 6.00°E with an estimate of 3,497,502 people [15]. Benin City is the capital; a city approximately 40 kilometers north of the Benin River. It is situated 320 kilometers (200 miles) by road East of Lagos. Edo state comprises of 18 local governments, with Oredo the most populous local governments. Edo state is a multicultural state inhabited by Traditional rulers, politicians, Civil servants, students, business men and women, market women, taxi drivers and okada riders, etc.

2.2 Study population

The subjects in this study comprise of sickle cell patients attending the Sickle Cell Centre in Benin City. A total of 60 samples were collected for this study which consist 30 sickle cell subjects and 30 subjects with haemoglobin genotype AA which serve as control.

2.3 Inclusion/exclusion criteria

Sickle cell disease subjects that are not in crisis were recruited for this study and non-sickle cell subjects without chronic or acute renal failure disease were recruited for this study. However, Sickle cell disease subjects that are in crisis, pregnant and chronic or acute renal failure were excluded. Also, non-sickle cell disease subjects that are pregnant were excluded from the study.

2.4 Sample collection and analysis

With the aid of a questionnaire, this study was carried out within three months. Subject data such as age and sex and name were obtained. Blood samples were collected from each subject having obtained their informed consent to participate in the study. Using a 5 ml syringe and by venipuncture, 5 ml of blood were collected from the middle cubital vein in the antecubital fossa into tubes containing lithium heparin and in EDTA sample containers. The sample in the lithium heparin tubes were centrifuged at 4000 rpm for 10min at room temperature within two hours of sample collection, the plasma were collected in plane containers and store frozen at -80°C until electrolytes, urea and creatinine value were quantified. The samples collected into EDTA tubes were used for hemoglobin electrophoresis to confirm the hemoglobin genotype of the each subject.

The examinations of samples collected were carried out in the Research and Diagnostic Laboratory of the Department of Medical laboratory Science, College of Medical Sciences, Ambrose Alli University Ekpoma. Creatinine was determined using the Jaffe-Slot modified alkaline picrate colorimetric method of measuring serum or plasma creatinine [16]. Urea was determined using enzymatic method [17]. Sodium and potassium were determined using Flame emission spectrophotometry [18]. Chloride assay was carried out using Mecuric Nitrate [19]. Bicarbonate assay was carried out by the Mohair titration method as described by Varley, et al. [20].

2.5 Statistical analysis

The data generated from this study were analysed using Statistical Package for the Social Sciences (SPSS) version 20 to determine the mean and standard deviation. The level of significance was set at $\alpha=0.05$, and a p-value less than 0.05 ($P<0.05$) was considered statistically significant. The significance of difference among the groups was assessed using student “t” test and where applicable ANOVA.

3. Result

Table 1 compares the Electrolyte (Na, K, Cl and CO_3), Urea and Creatinine levels of sickle cell disease patients and apparently healthy control subjects. The results showed that SCD patient has a significantly higher ($p<0.05$) mean K

(4.16 mg/dl vs. 3.64 mg/dl), urea (39.27 mg/dl vs. 31.01 mg/dl) and creatinine (1.25 mg/dl vs. 0.499 mg/dl) levels compared to healthy subjects. On the other hand, the healthy control subject has a significantly higher ($p<0.05$) mean HCO_3 (25.67 mg/dl vs. 19.77 mg/dl) compared to SCD patient. The healthy control subject has a non-significantly higher ($p>0.05$) mean Na level (137.63 mg/dl vs. 136.297 mg/dl) while the SCD patient has a non-significant higher ($p>0.05$) mean Cl level (101.27 mg/dl vs. 100.43 mg/dl).

Parameters (mg/dl)	Control (n=30)		SCD Subjects (n=30)		T value	P value	Significance
	MEAN	SD	MEAN	SD			
Na	137.63	1.54	136.297	4.26	-1.617	0.55	NS
K	3.64	0.15	4.16	0.57	4.811	0.00001	S
Cl	100.43	2.42	101.27	1.86	1.498	0.698	NS
HCO_3	25.67	1.67	19.77	3.18	-8.998	0.00001	S
Urea	31.01	6.26	39.27	24.61	1.782	0.04	S
Creatinine	0.499	0.19	1.25	1.05	3.872	0.0001	S

Values are mean and standard deviation, Na-Sodium; K-Potassium; Cl-Chlorine; HCO_3-Bicarbonate; SCD-Sickle Cell Disease; n-Sample size; NS-Not Significant and S-Significant

Table 1: Electrolytes and kidney function enzymes levels of sickle cell disease patients compared with the healthy subjects.

Table 2 compares of the electrolyte (Na, K, Cl and HCO_3) and urea and creatinine levels of sickle cell disease male patients and healthy male control subjects. There was a significant higher K (4.21 vs. 3.63) and creatinine (1.19 vs. 0.50) levels in male SCD patients compared to the healthy male control subjects. However, the healthy male control subject had significantly higher HCO_3 (25.33 vs. 20.06) compared to the male SCD patients.

Parameters (mg/dl)	Male Control N= 18		Male SCD Subjects N=18		T-value	P-value	Significance
	Mean	SD	Mean	SD			
Na	137.33	1.28	136.74	4.69	-0.69907	0.244631	NS
K	3.63	0.17	4.21	0.58	3.99135	0.000166	S
Cl	100.5	1.82	101.22	1.83	0.89463	0.188549	NS
HCO_3	25.33	1.33	20.06	3.30	-6.29722	0.00001	S
Urea	30.23	4.90	40.29	28.24	1.48915	0.072833	NS
Creatinine	0.50	0.21	1.19	0.99	22.86948	0.00351	S

Values are mean and standard deviation; Na-Sodium; K-Potassium; Cl-Chlorine; HCO_3-Bicarbonate; SCD-Sickle Cell Disease; n-Sample size; NS-Not Significant and S-Significant

Table 2: Electrolytes and kidney function enzymes levels SCD male patients and healthy male control subjects.

Table 3 compares of the electrolyte (Na, K, Cl and HCO_3) and urea and creatinine levels of sickle cell disease female patients and healthy female control subjects. There was a significant higher K (4.09 vs. 3.65) and creatinine (1.35 vs. 0.50) levels in female SCD patients compared to the healthy female control subjects. However, the healthy female control subject had significantly higher Na (138.08 vs. 135.63) and HCO_3 (26.17 vs. 19.33) levels compared to the male SCD patients.

Parameters (mg/dl)	**Female Control N=12**		**Female SCD Subjects N=12**		**T-value**	**P-value**	**Significance**
	Mean	**SD**	**Mean**	**SD**			
Na	138.08	1.83	135.63	3.78	-2.01831	0.027957	S
K	3.65	0.12	4.09	0.57	2.61026	0.007989	S
Cl	100.33	3.20	101.33	1.97	0.92184	0.183306	NS
HCO_3	26.17	2.04	19.33	3.08	-6.40312	0.000001	S
Urea	32.18	7.99	37.74	18.97	1.13832	0.133353	NS
Creatinine	0.50	0.18	1.35	1.16	2.51197	0.009921	S

Values are mean and standard deviation, Na-Sodium; K-Potassium; Cl-Chlorine; HCO_3-Bicarbonate; SCD-Sickle Cell Disease; n-Sample size; NS-Not Significant and S-Significant

Table 3: Electrolytes and kidney function enzymes levels SCD female patients and healthy female control subjects.

Table 4 compares of the electrolyte (Na, K, Cl and HCO_3) and urea and creatinine levels of sickle cell disease patients in different age groups. There was age dependent significant increase ($p<0.05$) in K (F=6.332), urea (F=0.002) and creatinine (F=2.520) levels. SCD patient in 21 to 30 years age group had significantly lower ($p<0.05$) HCO_3 level compared to SCD patients within 1-10 or 11 to 20 years.

Parameters (mg/dl)	**1-10 (n=8)**		**11-20 (n=18)**		**21-30 (n=4)**		**F value**	**P value**	**Significance**
	Mean	SD	Mean	SD	Mean	SD			
Na	136.95	1.96	137.23	4.45	130.78	2.64	1.709	0.200	NS
K	3.84	0.22	4.14	0.57	4.90	0.45	6.332	0. 006	S
Cl	101.5	1.77	101.11	1.97	101.50	1.91	0.149	0.862	NS
HCO_3	20.50	0.93	20.56	2.99	14.75	2.50	8.851	0.001	S
Urea	31.61	12.98	34.49	14.19	76.09	47.09	0.002	0.002	S
Creatinine	0.56	0.25	1.17	0.91	2.995	0.60	2.520	0.009	S

Values are mean and standard deviation, Na-Sodium; K-Potassium; Cl-Chlorine; HCO3-Bicarbonate; SCD-Sickle Cell Disease; n-Sample size; NS-Not Significant and S-Significant

Table 4: Comparison of the electrolyte (Na, K, Cl and HCO_3) and urea and creatinine levels of sickle cell disease patients in different age groups.

4. Discussion

Sickle cell disease is a chronic, debilitating disorder with a myriad of symptoms that make disease treatment challenging. In this study, the renal function profile of sickle cell subjects in Edo state was evaluated and compared with those apparently healthy subjects. The findings showed that SCD patients present with significantly higher K, urea and creatinine levels and a significantly lower HCO_3 level compared to apparently healthy counterpart. These results suggest impaired renal function and electrolytes balance in SCD patients. In line with this assertion, patients with Hb-SS had been reported to present several types of renal dysfunction including hyposthenuria, hematuria, nephrotic syndrome, acidosis, renal failure, and changes in arterial blood pressure [21]. In fact, a study by Sesso et al. [22] has reported patients with sickle cell anemia or sickle cell trait to present several types of renal dysfunction. In support of the finding of this study with respect to higher K level in SCD patients, Clark, et al. [23] has reported a higher concentration than the control group. Harvey [24] reported that dehydration and hypoxia are characteristic features of crisis state in SCD. This may account for the potassium losses experienced from the cell into the extracellular fluid which caused a rise in plasma potassium concentration.

In this study, we also showed that sex to have impact on the renal function and electrolytes balance of SCD patients in comparison with apparently healthy subjects. Specifically, this study revealed significantly higher K and creatinine levels in male and female SCD patients and significantly lower HCO_3 in SCD male and Na and HCO_3 levels in SCD female compared to their corresponding healthy control. This finding suggest that the difference in renal function and electrolytes balance in SCD patients may not be related to sex hormones differences except for the plasma bicarbonate differences that was observed in the female. The difference in electrolytes between the SCD patients and healthy control suggest differences in fluid balance. In fact compared to the healthy control we observed a lower Na concentration in the SCD patient which attests to the fact of altered fluid balance in SCD. Brugnara [25] reported that the hyponatremia observed was due to dehydration and Clark et al. [23] reported that dehydration was one of the causes of sodium movement into the sickle cell. It may therefore indicate that the SCD patients experienced dehydration, which could be a possible cause of sodium loss from the extracellular fluid into the intracellular fluid. Females were reported to present a high level of bicarbonate in the blood which can be from metabolic alkalosis. Metabolic alkalosis can happen from a loss of acid from the body, such as through vomiting and dehydration and Clark et al. [23] has previously reported increased level of bicarbonate in the sickle cell. It was also revealed in this study that age has a significant impact on the renal function and electrolytes balance of SCD patients. Specifically, this study showed that the alterations in renal functions and electrolytes balance in SCD patients aggravates with advancing age. This assertion was made owned to the manifested age dependent elevation in K, urea and creatinine levels in the SCD patients. The elevation of creatinine with advancing age, suggest that loss of renal function occurs with the progression of SCD and can be associated with uncontrolled disease, since these patients had more frequent anemia as supported by findings by Silver et al. [26].

In conclusion, the findings of the study showed that there are alterations in renal function and electrolytes balance in SCD patients. However, it is recommended that further investigations to assess the GFR of SCD patients to identify

those at risk of glomerular dysfunction. Studies are also warranted to elucidate the cause and to allow for earlier therapeutic intervention to decrease incidence and prevalence of sickle cell nephropathy in Edo state environment.

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Citation: Airhomwanbor KO, Idehen IC, Okparaku SO, Dic-Ijewere EO, Ehimare RI, Osarobo E, Omolumen LE, Edetanlen GE. Renal Function of Sickle Cell Subjects in Edo State-Nigeria. Archives of Nephrology and Urology 1 (2018): 001-008.