

Original Research Article

**CORRELATION OF MICROALBUMIN WITH
BIOCHEMICAL AND ANTHROPOMETRIC
PARAMETERS IN SICKLE CELL ANAEMIA PATIENTS
IN SOUTHERN NIGERIA.**

ABSTRACT

The renal manifestations of sickle cell anaemia can range from haematuria and abnormal tubular function to massive proteinuria and end stage renal disease. This study was designed to determine the frequency of occurrence of renal complications in sickle cell anaemia patients. This was achieved by determining the presence of microalbuminuria in these patients using Albumin Creatinine Ratio (ACR) in a spot urine. A total of 98 asymptomatic sickle cell anaemia patients and 30 non sickle cell anaemia controls were used for the study. These patients were grouped into two: those with analbuminuria and others with microalbuminuria using the $ACR \geq 3.5\text{mg}/\text{mmol}$ which approximates 24hr urinary albumin excretion in mg. Results obtained showed a mean significant increase ($P < 0.05$) in plasma urea and a non-significant increase ($P > 0.05$) in plasma creatinine in the SCA patients ($6.34 \pm 0.54\text{mmol}/\text{L}$ and $86.70 \pm 6.08 \mu\text{mol}/\text{L}$) than in the control ($3.33 \pm 0.16\text{mmo}/\text{L}$) and $73.98 \pm 2.95\mu\text{mol}/\text{L}$). There was also a significant increase ($P < 0.05$) in ACR in the SCA patients ($5.34 \pm 0.26\text{mg}/\text{mmol}$) than in the control subjects ($2.19 \pm 0.10\text{mg}/\text{mmol}$). PCV was significantly higher ($P < 0.05$) in the control subjects (40.65 ± 0.62) than in the SCA patients (23.48 ± 0.94). There was a significant positive correlation between ACR and plasma urea in SCA patients with nephropathy ($n = 47$; $r = 0.56$, $P < 0.05$) and a non-significant positive correlation in those without nephropathy ($n = 21$; $r = 0.42$, $P > 0.05$). There was also a positive non-significant correlation between ACR and plasma creatinine in SCA

patients with nephropathy ($n = 47$; $r = 0.34$, $P > 0.05$) and in those without nephropathy ($n = 21$; $r = 0.23$, $P > 0.05$). The relationship between ACR and PCV was a significant negative correlation in SCA patients with nephropathy ($n = 47$; $r = -0.36$, $P < 0.05$) and a negative non-significant correlation in those without nephropathy ($n = 21$; $r = -0.03$, $P > 0.05$). Our analysis also indicated that there was a significantly higher waist hip ratio (WHR) and systolic blood pressure in sickle cell anaemia patients (0.89 ± 0.01 , 120.39 ± 1.56 mmHg; $P < 0.05$) than in the control (0.86 ± 0.01 , 111.62 ± 1.97). The study also showed that the incidence of nephropathy amongst sickle cell anaemia patients in Southern Nigeria is 69.1%.

KEY WORDS: Sickle cell anaemia, Sickle cell nephropathy, Albumin creatinine ratio, Plasma creatinine, Waist- hip ratio, Body mass index.

INTRODUCTION

Sickle cell anemia is a genetic disorder characterized by red blood cells that assume an abnormal rigid sickle shape [1]. The major consequences of sickle cell anemia are vascular occlusion by sickled cells and anemia because of red blood cell destruction. Sickle cell anemia (SCA) is a heterogenous disorder with clinical manifestations including chronic haemolysis, an increased susceptibility to infections and vaso-occlusive complications often requiring medical care. Patients with SCA can develop specific and sometimes life-threatening complications, as well as extensive organ damage reducing both their quality of life and their life expectancy [2].

The survival of children with SCA into adulthood has increased the probability of developing some degree of renal insufficiency [3] . Every year 150,000 babies are born homozygous for SCA in Nigeria which is by far the most populous country in the West African sub-region. The frequency of the sickle cell trait (healthy carriers) is 5% of the world population and 15% - 30%

47 in West African countries such as Ghana and Nigeria [4]. The prevalence of chronic renal
48 insufficiency in SCA from a previous study was 4.6% [5].

49 The sickling process may cause haematuria, renal papillary necrosis and urinary concentrating
50 defect which may progress to sickle cell nephropathy [6]

51 Sickle cell nephropathy is now a well characterized entity with specific manifestations risk
52 factors and prognosis [7]. Progressive severe anaemia occurring in these patients secondary to
53 ineffective erythropoiesis is a major risk factor in renal disease [8]. This study intends to screen
54 for microalbuminuria in SCA patients and also assess the coexistence of frequently documented
55 biochemical changes in sickle cell nephropathy.

56 **PATIENTS AND METHOD**

57 This study was carried out in the Department of Biochemistry University of Benin and the sickle
58 cell Centre of the Ministry of Health Benin City, Edo State, Nigeria. A written informed consent
59 was obtained from each volunteer. Ethical clearance was obtained from the research and
60 ethical committee of the Ministry of Health Benin City, Edo State. Data was obtained from all
61 consenting volunteers (68 SCA patients and 30 non SCA control subjects), using a structured
62 questionnaire to obtain information such as age, sex, religion, occupation, family history of SCA,
63 and educational status.

64 **SAMPLE COLLECTION**

65 In the morning (at about 9.00AM) of their appointment at the Sickle Cell Centre, 3.0ml of blood
66 was obtained from cubital fossa using a 5.0ml syringe and dispensed into lithium heparin

specimen bottle for plasma urea and creatinine estimation. Spot urine specimen was also collected into a sterile universal bottle for urine albumin and creatinine estimation. Since this was more convenient for the patients than a timed (24hrs or overnight) urine collection. The blood specimens were immediately centrifuged at 3000g for 5 minutes to separate plasma from the cellular components. The plasma was stored at 20⁰C until analysis was carried out for the different assays while urine was assayed immediately for albumin and creatinine.

BIOCHEMICAL ANALYSIS

Plasma urea was estimated by the urease – Berthelot method as outlined by Weatherburn [9], plasma creatinine by the modified Jaffe’s method as outlined by Spierto et al [10] and urinary albumin by the Lowry method [11].

DATA ANALYSIS

Data analysis was done using the statistical package for social science (SPSS) version 16.0. Different results were presented as mean ± standard error of mean (SEM). Comparison of two independent variables was done using regression coefficient correlation and analysis of variance (ANOVA) was applied for comparison between different groups. The confidence limit was 95% and P-value was considered significant as a value less than 0.05. Also bar chart was used to express occurrence of distribution.

RESULT

Table 1 showed the anthropometric parameters of the control (non-sickle cell anaemia) subjects. The SCA patients had significantly higher body mass index (BMI), waist hip ratio (WHR)

and systolic blood pressure (SBP) ($P < 0.05$), while the diastolic blood pressure was non-significantly ($P > 0.05$) elevated. There was also a significantly lower packed cell volume (PCV) in the SCA patients ($P < 0.05$). The biochemical parameters in table 2 showed a significantly elevated plasma urea and albumin creatinine ratio (ACR) ($P < 0.05$) and a non-significantly elevated plasma creatinine in SCA patients than in the control subjects ($P > 0.05$). This study showed a significant positive correlation between ACR and plasma urea and a significant negative correlation between ACR and PCV ($P < 0.05$) while there was a non-significant positive correlation between ACR and plasma creatinine ($P > 0.05$) (table 3).

Table 4 showed a non-significant positive correlation between ACR and urea and creatinine ($P > 0.05$) and a negative correlation between ACR and PCV which was also not significant ($P > 0.05$). Fig 1 showed the frequency of age distribution among the SCA patients with majority of the patients being in the age range of 18 – 27 years. Figure 2 displays the relationship between ACR and PCV in the SCA patients.

TABLE I

Anthropometric parameters control subjects ($n = 30$) and SCA patients ($n = 68$).

Anthropometric parameter	Control subjects $n = 30$	SCA patients $n = 68$	P-value
Gender (male/female)	15/15	26/42	0.49
Age (years)	28.35 ± 0.42	30.12 ± 1.4	0.08
BMI (kg/m^2)	24.63 ± 0.68	20.85 ± 0.38	< 0.001
WHR	0.86 ± 0.01	0.89 ± 0.01	0.04
SBP (mmHg)	111.62 ± 1.97	120.39 ± 1.56	0.04
PCV	40.65 ± 0.62	23.48 ± 0.94	< 0.001
DBP	75.00 ± 1.64	82.36 ± 1.62	0.14

103 BMI = Body Mass Index

104 WHR = Waist Hip Ratio

105 SBP = Systolic Blood Pressure

106 PCV = Packed Cell Volume

107 DBP = Diastolic Blood Pressure

108 **TABLE 2**

109 Biochemical parameters of SCA patients

Biochemical parameter	Control subjects n = 30	SCA patients (n = 68)			P-value
		With nephropathy (n = 47; ACR ≥ 3.5mg/mmol)	Without nephropathy (n = 21; ACR < 3.5 mg/mmol)	Total n = 68	
Plasma urea (mmol/L)	3.33 ± 0.16	6.70 ± 0.69	5.82 ± 0.69	6.43 ± 0.54	< 0.001
Plasma creatinine (μmol/L)	73.98 ± 2.95	85.15 ± 6.19	90.16 ± 8.99	86.70 ± 6.08	0.06
ACR (mg/mmol)	2.19 ± 0.10	5.34 ± 0.26	2.63 ± 0.10	4.50 ± 0.24	< 0.001

110

111 ACR = Albumin Creatinine Ratio

112 SCA = Sick Cell Anaemia

113 **TABLE 3**

114 Correlation between ACR and plasma urea and creatinine in SCA patients with nephropathy (n = 47).

Biochemical parameters	r-value	P – value
Plasma urea	0.56	0.04
Plasma creatinine	0.34	0.27
PCV	-0.36	0.01

115

116 ACR = Albumin Creatinine Ratio

117 PCV = Packed Cell Volume

118 SCA = Sick Cell Anaemia

119

120 **TABLE 4**

121 Correlation between ACR and plasma urea and creatinine in SCA patients without nephropathy (n = 21).

Biochemical parameter	r – value	P –value
Plasma urea	0.42	0.06
Plasma creatinine	0.23	0.32
PCV	-0.03	0.42

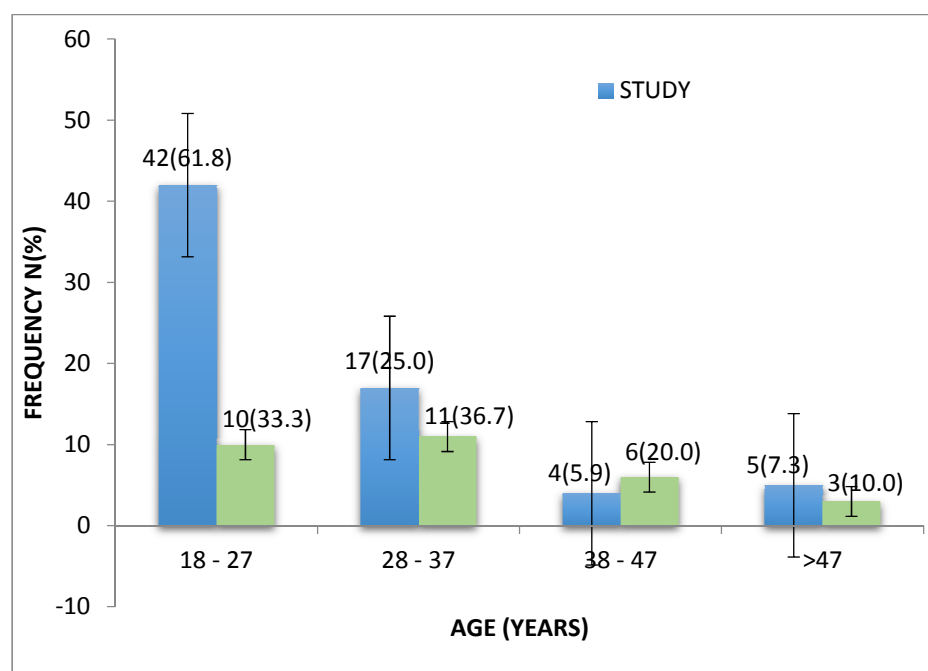
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123 ACR = Albumin Creatinine Ratio

124 PCV = Packed Cell Volume

125 SCA = Sickie Cell Anaemia

126



127

128 Figure 1: Age distribution of Sickie cell anaemia (n = 68) and non-sickie cell anaemia (control)

129 respondents (n = 30). Values in parenthesis represent percentage distribution.

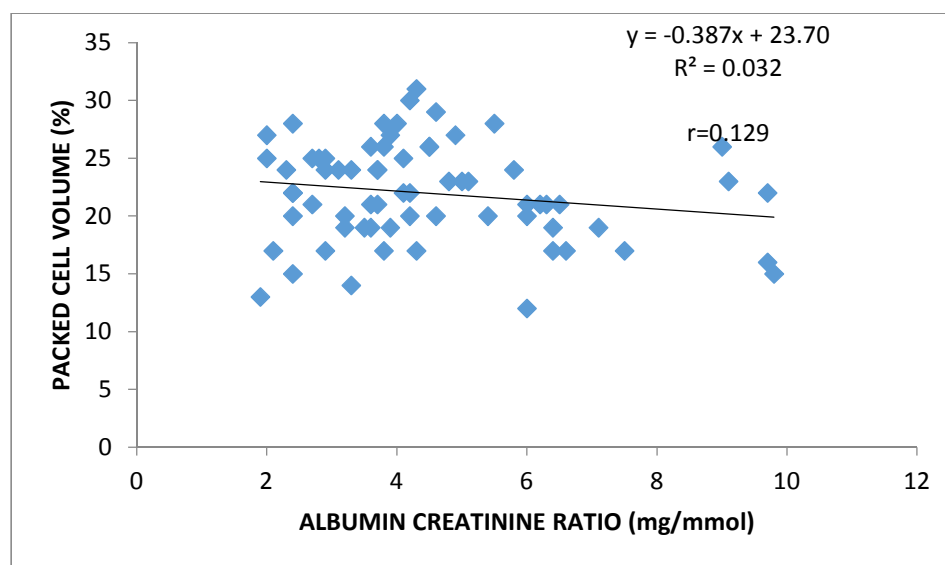


Figure 2: Relationship between Albumin Creatinine Ratio and Packed Cell

Volume of sickle cell anaemia respondents (n=68)

Discussion

In Nigeria which is by far the most populous country in sub Saharan Africa, the prevalence of sickle cell anaemia (SCA) is about 2% [4]. Patients with SCA can develop life threatening complication as well as extensive organ damage reducing their quality of life and life expectancy [2]. Sickle cell nephropathy (SCN) is a major mortality risk factor in sickle cell anaemia patients and it is associated with proteinuria that promotes progressive decline in renal function [12].

Microalbuminuria also called incipient nephropathy refers to albumin excretion rate of $>300\text{mg/day}$ ($20 - 200\mu\text{g/min}$) or $\text{ACR} \geq 3.5\text{mg/mmol}$ in a spot urine [13]. Among the SCA patients in this study, 69.1% had microalbuminuria ($\text{ACR} \geq 3.5\text{mg/mmol}$). This is much higher than what Van Eps and de Jong obtained in their study where they found proteinuria in 30% of their patients during long term

145 follow up [14]. Also, Bolarinwa et. al., in their study had 50% of their patients with
146 albuminuria [15].

147 The mean ACR in SCA patients with microalbuminuria was 5.34 ± 0.26 mg/mmol
148 which was much higher than in those without microalbuminuria ($2.63 \pm$
149 0.10 mg/mmol). This corroborates earlier reports by Bolarinwa et. al., in their
150 study in which they found a mean ACR of 97 ± 13.2 µg/mg (10.97 mg/mmol) in
151 patients with microalbuminuria and 10.3 ± 6.8 µg/mg (1.17 mg/mmol) in those
152 without microalbuminuria [15].

153 The SCA patients had normal plasma urea (6.43 ± 0.5 mmol/l) and creatinine
154 (86.70 ± 6.03 µmol/l) though higher than in the control subjects. This finding is
155 similar to that obtained by Bolarinwa et. al.[15].

156 The finding that PCV or haematocrit level correlated negatively with ACR
157 corroborated the finding of Faulkner et. al., where they indicated that the lower
158 the hematocrit level, the higher the urinary albumin excretion rate [16]. Powars
159 et. al. also reported progressive severe anaemia as a risk factor for renal disease
160 in SCA patients [17].Faulkner et. al. also postulated that renal injury could result
161 from progressive medullary ischemia due to severe progressive aneamia which
162 may lead to continuous activation of the prostaglandin pathway to produce
163 vasodilator prostaglandins as a compensatory mechanism to help maintain renal
164 blood flow and glomerular filtration rate (GFR) [16].

165 **Conclusion:** This study revealed that albuminuria is a common finding amongst
166 SCA patients. Albuminuria indicates the presence and progression of renal

insufficiency. Therefore regular monitoring of urine albumin is advocated in SCA patients to delay progression of renal dysfunction to end stage renal disease.

Consent: All the participants were properly briefed about the study and an informed consent was obtained from them before venous blood and urine was collected.

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