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Biochemical Anomaly of Renal Parameters in Sickle Cell Anemia Patients

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ABSTRACT: Sickle cell disease is a chronic disease characterized by progressive multiorgan failure, particularly involving the liver and kidney. Chronic renal disease occurs in 25% of older adults and results in 50% of their deaths. Patients with sickle cell disease have increased mortality rates from renal failure compared with non sickle cell patients. Sickle cell disease (SCD) produces many structural and functional abnormalities in the kidney, including glomerular abnormalities.. Reduction of renal concentration capacity, urinary acidification, impaired potassium metabolism often observed in these patients. Glomerular filtration rate exceed the normal value in children and adults. Proteinuria is prevalent in 25% cases, microalbuminuria was seen among the Hb SS patients than in Hb AS which is important marker of glomerular injury with Hb SS patients which is associated with reduce creatinine clearance. In the present study we have examined prevalence of renal dysfunction in the individuals with Hb SS and Hb AS. In addition we have tried to establish the correlation between kidney dysfunction and duration of disease.

Key words: *Sickle cell anaemia, microalbuminuria, Glomerular filtration rate*

INTRODUCTION

Sickle cell disease (SCD) produces many structural and functional abnormalities in the kidney, including glomerular abnormalities. Albuminuria is the most common manifestation of glomerular damage, with a prevalence in adult patients. The pathophysiology of albuminuria in SCD is likely multifactorial, with contributions from hyperfiltration, glomerular hypertension, ischemia-reperfusion injury, oxidative stress, decreased nitric oxide (NO) bioavailability, and endothelial dysfunction. Although its natural history in SCD remains inadequately defined, albuminuria is associated with increased echocardiography-derived tricuspid regurgitant jet velocity, systemic blood pressure, and hypertension, as well as history of stroke, suggesting a shared vasculopathy pathophysiology. Patients with sickle cell disease have increased mortality rates from renal failure compared with non sickle cell patients (Vichinsky E et.al.). Given the high prevalence of albuminuria and its association with multiple SCD-related clinical complications, additional studies are needed to answer several clinically important questions (Ataga K.I. et. al.) . Renal disease is one of the most frequent and severe complications experienced by patients with sickle cell disease; its prevalence is likely to increase as the patient population ages. Proteinuria and hypertension should be managed aggressively and the patient referred to a specialist nephrology center when progressive decline in renal function is noted. For the few patients who develop advanced chronic kidney disease, timely planning for dialysis and transplantation can significantly improve outcome. It is important to remember that renal failure in conjunction with sickle cell disease does carry a significant burden of morbidity (Sharpe C.C. et. al). Sundaram *et al* reported that the renal complications affect nearly 30-50% of adults with sickle cell anemia (SCA), causing significant morbidity and mortality. Standard renal function tests like serum creatinine and glomerular filtration rate become abnormal in this disease only when renal damage has become extensive and largely irreversible. Garrett and his coworkers reported that Sickle cell disease (SCD) nephropathy and lower estimated glomerular filtration rate (eGFR) are risk factors

for early mortality(Xu J.Z. et. al.). Furthermore, rate of eGFR decline predicts progression to end-stage renal disease in many clinical settings. However, factors predicting renal function decline in SCD are poorly documented.

In the present study we have examined prevalence of renal dysfunction in the individuals with Hb SS. In addition we have tried to establish the correlation between kidney dysfunction and duration of disease.

MATERIAL AND METHOD

This study comprises of 25 SCD patients and 25 healthy of age in between 15 -50 yrs. age and sex matched controls. All the patients included were in the steady state of the disease. Some sickle cell blood samples were procured from Government medical College Nagpur and Indira Gandhi Medical College, Nagpur. The ethical guideline was followed during the sample collection in Kamptee region. Fasting intravenous blood samples were obtained for hematological test, creatinine, sodium, potassium, phosphate, uric acid, total protein and albumin and centrifuged at 3000 rpm for separation of serum to perform biochemical parameters. Blood samples was collected in sampling bottles and stored in ice box for protection from heat and light. Biochemical investigations and kidney function test were carried out in Biochemistry laboratory and pathology laboratory attached to the microbiology department of S. K. Porwal College Kamptee. Patients were free of pain crises during the study. HbSS diagnosis was based on family history. Total protein in urine was determined by biuret method, level of serum creatinine was determined by Jaffe's reaction . Creatinine clearance determination was based on collection of 24 hrs. urine and calculated as follows(urine creatinine 24 hrs urine volume)/ plasma creatinine. Instructions were given to patients for careful collection of urine at home. Microalbuminuria was determined by using commercially available kit. [5-12]

Statistical analysis

All results were expressed as mean ±SD. Statistical analysis was done using unpaired analysis in the sickle cell disease subjects and in healthy controls. Student's t-test was used to compare means of variables and Pearson's linear correlation analysis to test the significance of association. $P < 0.05$ was considered statistically significant.

RESULTS:

The laboratory data of the patients with sickle cell anemia is summarized in Table 1. None of the patients had a history of drug or alcohol abuse. The mean (± SD) value of hematocrit has shown in kidney dysfunction in sickle cell anemia patients are frequent.

Creatinine is formed from creatine and creatine phosphate in muscles and is excreted into the plasma at constant rate related to muscle mass. Plasma creatinine is inversely related to glomerular filtration rate (GFR) and it is commonly used to assess renal filtration function.

The mean concentration of serum creatinine mg/dl was found to be (0.544±0.2451) in sickle cell anemia patients. Increase in serum creatinine is seen in any renal impairment when its clearance is significantly reduced. Serum potassium and uric acid were significantly higher in patients than controls ($P<0.0001$). Sickle cell anaemia patients developed profound hyperuricemia and hyperuricosuria(Fig. 2 and Fig. 3) The main factors which influences serum urate concentration are metabolic production of urate and excreted by kidneys.

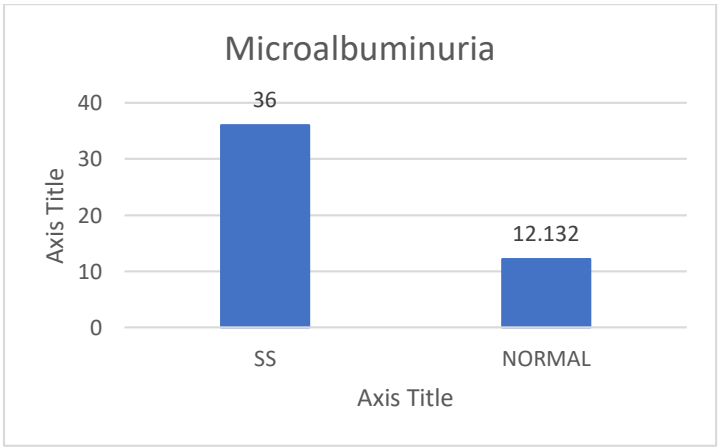

Fig 1: Microalbuminuria levels in the patients of Sickle cell as compared with normal individuals

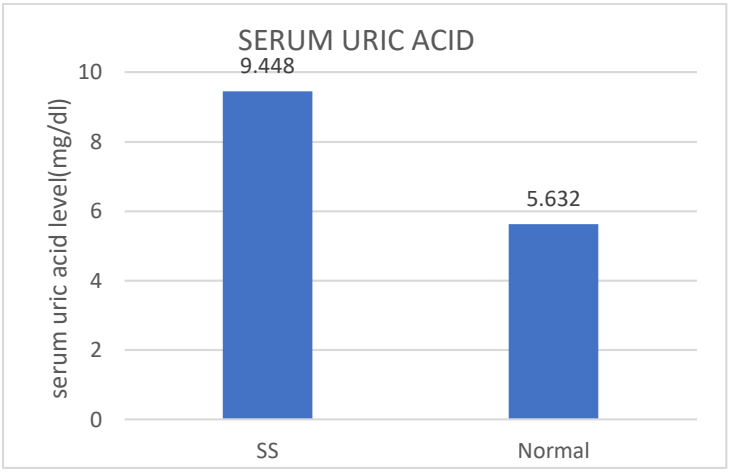

Fig 2: Serum Uric Acid levels in the patients of Sickle cell as compared with normal individuals.

The destruction of RBCs lead to increased nucleic acid degradation which lead to the formation of uric acid content in the cell. The mean concentration of serum uric acid was found to be (**9.44±1.75**) in SCA. Patients showing mild proteinuria(24 hrs urine protein >200) with a range between 65 to 382 mg (Fig. 4). They also had microalbuminuria with a range 21 to 45 µg/min(Fig 1). There were no significant difference in serum level of sodium . Haemoglobin level of sickle cell anaemia patients were normally between 6.0 to 8.0 gm% Intermittently there can be a severe drop in haemoglobin .

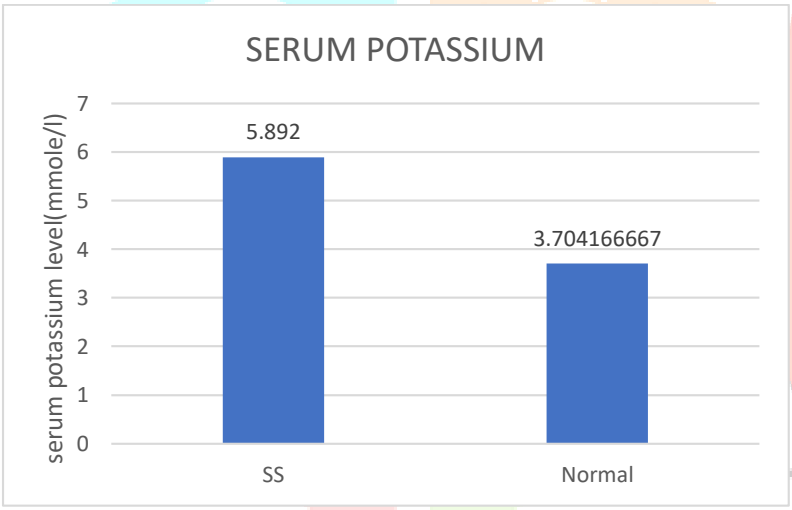

Fig 3: Serum Potassium levels in the patients of Sickle cell as compared with normal individuals

Table 1 : -Renal parameters in normal healthy control and SS patients sample

Analytes	Patients (n=25)	Control (n=25)	P value
Creatinine (mg/dl)	0.544±0.2451 ^{c}	0.72±0.0872	NS
Creatinine clearance(ml/min1.73m^2)	114.8±18.0785 ^{c}	120.08±7.6480	NS
Microalbuminuria(µg/min)	36±5.4467 ^{ccc}	12.132±1.3011	(P<0.0001)
Sodium (mmol/L)	140.584±2.211	139.012±2.804	NS
Potassium (mmol/L)	5.892±0.9213	3.704±0.528	(P< 0.0001)
Phosphate (mg/dl)	4.0125±0.5649 ^{c}	3.552±0.3015	NS
Uric acid(mg/dl)	9.44±1.75^{ccc}	5.632±2.038	(P< 0.0001)
Urine protein(mg/24hrs)	200.33±105.408^{ccc}	38.088±12.27	(P< 0.0001)
Hemoglobin (gm/dl)	7.508±1.1975^{ccc}	11.872±0.7785	(P<0.0001)

Note: significant value ^{c} P<0.05,
Highly significant value ^{cc} P<0.001,
Extremely significant value ^{ccc} P<0.00

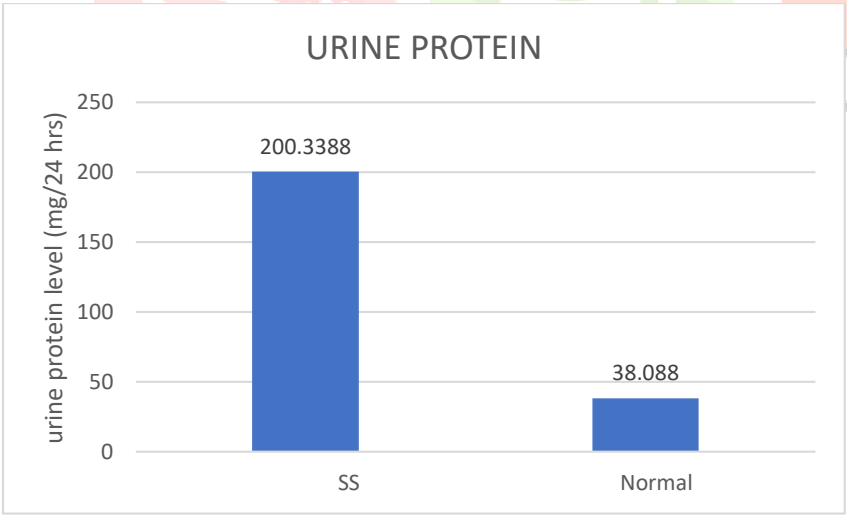

Fig 4: Urine Protein levels in the patients of Sickle cell as compared with normal individuals.

DISCUSSION

In this study, we evaluated renal function of SCA patients. It has been reported that patients with Hb SS showed several types of renal dysfunction (Strauss J. et. al.). The results clarified important aspects of tubular and glomerular dysfunction in these patients. In our study, there was no significant difference in both serum concentration of urea and creatinine between patients and controls. This is similar to the findings of Silva Junior *et al*. and Pandey *et al*.,but in contrast to that of al-Naama *et al*. who found a significant difference in the level of both analytes. But in some individuals serum creatinine levels were lower which is sensitive indicator of renal impairment. The level of serum creatinine is inversely related to GFR but it is independent of age, sex body size and diet (Shemesh O Golbetz et. al and Rahn K.H. et. al.). In this study serum creatinine level in patients with SS disease were lower than predicted from inverse relationship between GFR and serum creatinine.

There was comparatively lower concentration of serum sodium in SCA patients in our study. This is consistent with finding of other studies(Vichinsky E. et. al., Agoreyo F.O. et.al. and Ibe E.O. et. al) and it is attributable to increased and continued obligatory losses of body fluids and electrolytes which rapidly result in dehydration and subsequently salt (sodium) and other electrolyte imbalance(Ibe E.O. et. al., Vikas G. et. al. and Oladipo O.O. et. al.). It was suggested that dehydration and deoxygenation, caused excessive potassium losses from the cell into the extracellular fluid which caused a rise in plasma potassium concentration(Agoreyo F.O. et. al. Ibe E.O. et. al.). The above-stated suggestion could be a reason for the significantly higher serum potassium in SCA patients compared with controls in this study which is in agreement with findings of other studies (Vichinsky E. et. al. , Xu J.Z. et. al. Ibe E.O. et. al. Akah R.T. et. al and Vikas G. l. et. al.)

In agreement with findings of other studies(Pandey S. et. al. and Oladipo O.O. et. al.) the serum phosphate level was higher in SCA patients in our study. This finding is thought to be due to increase tubular reabsorption of phosphate (Pandey S. et. al.)and release of phosphate from the cells in the chronic haemolytic states occurring in these patients(Oladipo O.O. et. al.). In SCD patients significantly higher concentration of serum uric acid observed which agrees with the reports of other studies (al-Naama LM et. al. and Khalid EK et. al.) but is in contrast to the finding of Pandey *et al*. and Nduka *et. al*. The elevated level of uric acid in the patients could be due to a sustained high state of erythropoiesis in SCA patient which causes an increased turnover of purines and hence the generation of a greater than normal uric acid level(Nduka N. et. al.). Hyperuricemia could also be attributed to the failure of the kidney to keep pace with increased production, this often occurred as a result of impaired tubular function due to infarction and hypoxia resulting from sickling (al-Naama L.M. et. al.). We found a high prevalence of microalbuminuria in Hb SS patients, mainly those with longer duration of disease (older than 15 yrs). In some patients proteinuria was also increased. Although in this study patients had preserved renal function (creatinine clearance), microalbuminuria were detected in many of them. Microalbuminuria is an indicator of glomerular injury which may develop glomerulosclerosis or glomerulonephritis. Detection of microalbuminuria is an important marker of glomerular renal injury in patients with Hb SS (Guasch A. et. al.)

CONCLUSION: In our study we found moderate effect on renal function in SCD patients. Microalbuminuria, hyperkalemia and proteinuria are the common features of renal impairment in sickle cell anemia patients.. Renal function tests are not altered significantly, but this will help to understand future clinical manifestation of patients. The finding of our study suggests that the biochemical profile can play an important role in assessing the sickle cell patient's physiopathology and can be used for effective management of the disease.

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