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Renal Physiological Status of Sickle Cell Anemic Patients, District Amravati, MS India

Andhale RB[1], Sangita Lodha[2] and Varsha Wankhade[1]*

[1]*Department of Zoology's University of Pune, Pune, Maharashtra, India*
[2]*Thalassemia Center, Jankalyan Blood Bank, Nashik, Maharashtra, India*

Abstract

Sickle cell anemia is a genetic disorder caused by mutation in globin gene in which serious morbidity and mortality can be resulted. Patients with Sickle cell anemia need regular blood transfusion. Anemia may cause physiological failure of various organ systems. Accumulation of iron due to hemolysis can cause damage to various organs. In the present study, few biochemical indices for renal tubular functions were investigated. In total 67 urine samples from sickle cell anemia patients were studied. Samples were estimated for markers such as Creatinine, Protein, Urea, Sodium (Na^+), Potassium (K^+); Uric acid and Specific gravity and Urea. It was observed that many parameters were in abnormal range indicating impaired renal function.

Keywords: Sickle cell anemia; Renal function; Urinalysis

Introduction

Sickle Cell Anemia (SCA) affects most of the tissue of the body. In later stages of this disorder renal dysfunction causes sickle nephropathy. Sickle cell anemia is characterized by sickled erythrocytes, which causes microinfarct, ischemia, decreased medullary blood flow and papillary necrosis [1]. SCA results in both anatomical alterations and disturbances in renal function. Most of the sickle cell anemic patients have large kidneys, which may be due to increased renal blood volume [2].

Every year over 300,000 babies who are homozygous for SCA are born worldwide. The majority of which are in middle and low income countries. About 5% of the world population is the carriers of gene for sickle cell anemia. Percentage of the disease is high in Asia, the Mediterranean basis, the Middle East and Africa [3]. Few studies reported high mortality rate in children with sickle cell disease during the first five years of life due to infection and splenic sequestration [4-6]. Early diagnosis and inclusive care can reduce mortality and morbidity rate significantly in children with sickle cell disease [7-10]. Prophylaxis with penicillin in preventing *Streptococcus pneumonia* septicemia were confirmed to be beneficial in a blinded, randomized, control study and offered a solid scientific rationale for new born screening [11].

The defect in urine concentrating ability in sickle cell trait is believed to be the result of intracellular polymerization of HbS in erythrocytes that causes occlusion of smaller capillaries in the vasa recta of the renal medulla. The severity of the defect in concentration of urine might be linked to the percentage of sickling phenomenon of erythrocytes. Gupta et al. reported correlation between urine concentrating ability and the percentage of sickled hemoglobin, which was maximum in the individuals with normal alpha-globin genotype and minimum in those homozygous for the deletion [12].

Methodology

Study area and population

The study population consisted of 67 randomized sub¬jects with Sickle cell anemia from the district Amravati, MS, India. This study was approved by Institutional Human Ethics Committee. The study protocol and laboratory examinations were discussed with patients and their parents' and written consents were taken. The mean age of the participants was 20.45 years. All selected participants were earlier diagnosed for sickle cell anemia.

Urine collection and study of urine parameters

Collection of sample: Clean catch urine samples were collected. A standard spontaneous voiding procedure was followed to collect urine samples from the participants [13]. Urine collection was done at noon to avoid contamination of urine by contents of urethra or vagina and therefore its constituents are more likely to reflect kidney origin. First void samples were also collected as they are informative and concentrated samples. Urine samples were collected in a sterile, labeled bottle containing 4% formaldehyde. Once urine was collected, it was transported to the laboratory immediately in an ice bag. All the analysis was performed within a week [14,15].

Physical observations of urine: Urine sample was observed for colour pattern, turbidity etc. pH was measured by pH Tutor (Make:Oakton) and Specific gravity by Urinometer (Make:Davinder Glass works, Delhi, India).

Biochemical examination of urine of SCA: Biochemical estimations such as estimation of Potassium ion, Sodium ion, Urea, Creatinine, Uric Acid and bilirubin were performed using commercially available kits.

Statistical analysis: Comparative student t-test was calculated. P-value of <0.05 was considered as statistically significant value. Data was presented in arithmetic mean; standard deviation and standard error were calculated by SPSS and Mega stat software.

Results

It was observed that many urine parameters in sickle cell anemia patients are not in the normal range. Urine pH was 6.57+0.523 and value

*Corresponding author: Varsha Wankhade, Department of Zoology's University of Pune, Pune, Maharashtra, India, Tel: 9763968646; E-mail: varsha3w@unipune.ac.in

of specific gravity was 1.00+0.220 which were not significantly altered in patients. Urine creatinine level was 0.36+2.41 mg/dl, urine urea was 182.72+10.4 mg/dl which was significantly high in the patients; urine sodium value was 217.85 ± 9.864 mmol/l; urine potassium level was 34.86+4.472 mmol/l; urine uric acid was 1.44+0.317 mg/dl. Protein level is found to be significantly high in sickle cell anemic patients than normal participants. Urine mean protein value in normal was 0.03 ± 0.556 while in SCA was 1.832 ± 0.203 mg/ml of urine. The values of various biochemical parameters of urine in sickle cell anemia are shown in Table 1.

In majority of the sickle cell urine, biochemical and physical parameters are found to be altered. This may be due to the side effects of chelating drug, deposition of iron in renal tissue, renal infarction due to increased platelet aggregation, decreased serum level of protein and anti-thrombin III [16]. Urine creatinine level (0.36+2.41 mg/dl) and urine urea (182.72+10.41 mg/dl) were significantly higher in the patients compared to the normal participants.

 It indicates kidney damage and affected glomerular filtration [17]. Urea level was significantly greater indicating nephron damage and impairment of tubular re absorption and secretion processes. Uric acid in urine of Sickle cell disease and sickle cell trait was significantly less than normal. Level of uric acid in sickle cell patients was 1.44 ± 0.317 mg/dl of urine.

Potassium ion concentration in sickle cell patients was 34.86+4.472 mmol/dl and in normal participants it was 73.35+4.129 mmol/dl of urine. Abnormal values of potassium in the urine of sickle cell anemic indicate the derangement of production of adrenocortical or pituitary hormones [17]. Pituitary gland and adrenal cortex function may be affected due to hypoxic condition in SCA.

Sodium ion concentration in the urine of Sickle cell disease was less than in the urine of normal persons. Sodium ion concentration in sickle cell patients was 217.85+9.864 and in normal participants it was 236.16+17.685 mmol/dl of urine. The level of Urea is significantly greater in sickle cell anemic patients as compared to normal. Mean value of Urea in urine of SCA was 182.72+10.41 mg/100 ml of urine while in normal participants the value was found to be 42.15+15.73 mg/100 ml of urine. Thus value of urea in SCA indicates nephron damage and thus tubular reabsorption and secretion processes at nephron are affected in such persons. The level of creatinine is significantly less as compared to normal. Mean value of creatinine concentration in urine of SCA was 0.36 mg/dl of urine while in normal participants the value was found to be 1.143 mg in 100 ml of urine. From above data it may be suspected that kidney is damaged in SCA and glomerular filtration is highly affected [17].

Sr No	Urine Parameter	SCA +SE	Control+SE
1	pH	6.57 + 0.523	5.86 + 0.435
2	Specific gravity	1.00 + 0.220	1.01 + 0.346
3	Uric acid in mg/dl	1.44 + 0.317	1.67 + 1.054
4	Potassium in mmol/l	34.86 + 4.472 **	73.35 ± 4.129
5	Urea mg/dl	182.72 + 10.41**	42.15 + 15.73
7	Creatinine in mg/dl	0.36 + 2.41**	1.14 + 2.56
8	Sodium ion mmol/100 ml	217.85 ± 9.864 **	236.16 ± 17.685
9	Protein mg/ml	1.832 ± 0.203**	0.03 ± 0.556

**=significant value. P value is 0.05

Table 1: Comparative analysis of few biochemical parameters of urine of sickle cell anemia.

Discussion

SCA patients at district Amravati are under the threat of urinary tract infection, urinary tract inflammation, Glomerulonephritis, Interstitial nephritis, tubular necrosis, Pyelonephritis etc. [18]. On the basis of qualitative and quantitative microscopic analysis of urine of SCA it could be concluded that the kidney of such patients are under risk and suffering from various complications like nephrites, glomerular damage, hematouria etc. [18,19].

The defect in urine concentrating ability in persons with sickle cell trait is thought to result from intracellular polymerization of Hb S in erythrocytes. In the vasa recta of the renal medulla, this causes micro vascular occlusion. Percentage of sickle hemoglobin present in erythrocytes influences the severity of the pathophysiology. There is association between percentage of sickle hemoglobin and urine concentrating ability [20]. Microalbuminia is a marker of SCA glomerulopathy [21]. Sickle cell anemia is characterized by chronic organ failure; renal dysfunction in adults (7,22). In 80% of aging SCA patient's renal failure and nephropathy is observed [22,23]. Oxidative peroxidation of lipids due to overload of iron leads to proximal tubular damage [24]. Kidney in sickle cell anemia (HbSS) is affected by hemodynamic changes of chronic anemia vaso-occlusion in the renal medulla [25,26]. There could be defects in potassium metabolism urinary acidification and urine concentrating capacity in SCA due to disruption of distal nephron and medullary function [27,28]. In all sickle cell disorders, kidney is unable to concentrate urine [29,30]. Chronic renal failure is the most common cause of death among HbSS above 40 years of age in some countries [26,31]. A 5 to 18% of SCD population patient is suffered from renal disorders [32]. Sickle cell hemoglobin C is affected by affected by renal failure [33]. There is mortality due to renal failure in SCD [34]. Renal failure is one of the main factors behind the mortality in SCD [35].

Nissenson and Port reported nephropathy in sickle cell patients in the U.S. [31]. Increased Glomerular Filtration Rate (GFR) and Renal Plasma Flow (RPF) have been well described in patients with sickle cell disease [36,37]. Progressive renal insufficiency in these patients has been ascribed to hyperfiltration-mediated sclerosis of the glomerular capillaries [38,39]. In the review article Pham et al. explained the association of the glomerular and tubular disorders with sickle cell nephropathy [40]. Proteinuria has been reported in 20 to 25% patients of SCA and drop off in the kidney function was observed in 5 to 30% of SCA patients [35,41]. Falk et al. reported the pathological features of sickle cell nephropathy in SCA [42].

Conclusions

From above data and findings it could be concluded that renal tubular functions of sickle cell anemia is impaired. The most of the urine biochemical parameters vary significantly from the normal indicating glomerular dysfunction may be due to glomerular damage, tubular damage and nephritis.

Limitations of our study: Various factors affecting on random urine sample collections such as hydration status, environmental factors (seasonal variations), and physical exercise like travelling, exact time of random urine collection and gender difference were not considered.

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