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Observational Study of Renal Function in children with Sickle Cell Disease: in a Tertiary Care Hospital of Jharkhand

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Abstract
Background: *Sickle cell disease has been reported from all over the world including India. The early detection of sickle cell nephropathy & its treatment is essential for improving quality of life in these children.*
Objective: *Current study aims at to study the features of renal involvement in sickle cell disease patients.*
Materials & Method: *81 consecutive cases admitted to hospital with sickle cell disease were studied by history, thorough examination & stepwise investigations including urine routine examination, culture-sensitivity & concentration test; Blood urea and serum creatinine.*
Results: *The mild proteinuria, microscopic hematuria, pyuria and casts had been noted in 19.5% (16 cases), 14.8% (12 cases), 19.5% (16 cases) and 4.9% (4 cases) of sickle cell disease patients respectively. The concentrating capacity of the tubules was significantly affected in children with sickle cell disease in elderly age groups. But no significant changes were observed in the younger children, in the age group of 2 to 5 years.*
Conclusion: *There is a significant impairment in concentrating capacity of kidney with increasing age among sickle cell disease patients but no difference in earlier age group.*
Keywords: *Sickle cell nephropathy, hyposthenuria.*

Introduction

Sickle cell disease has been reported from all over the world including India. According to a study conducted by the Jharkhand health department, > 9 lakhs tribals are suffering from the fatal sickle cell disease. This accounts for 10% of the state's total tribal population as per the 2011 census, right next to Chhattisgarh (10 lakhs) as the worst- hit state, and ahead of Odisha (6 lakhs).[1] The presence of renal failure in sickle cell disease

(SCD) ranges from 5 to 18% of the total population of SCD patients. Therefore, early detection of Sickle cell nephropathy and its treatment is essential for improving quality of life in these children.

Methods

This study was a hospital based prospective cross sectional study conducted from June 2016 to May 2017 in Department of Paediatrics and Neonatology, Rajendra Institute of Medical Sciences, Ranchi. In this study, 81 confirmed cases of Sickle cell disease diagnosed on the basis of Sickling test or HPLC {High Performance Liquid Chromatography) .Children in age group between 2 to 14 years were included for assessment of their renal profile and its clinical correlation. The same functions have also been carried out in 20 control children.

Laboratory tests included –

i. Routine and microscopic examination of urine,
ii. Urine culture and sensitivity,
iii. Urine concentration tests,
iv. Serum electrolytes,
v. Blood urea and Serum creatinine.

On the basis of age, the patients were divided into 3 groups –

i. 2 - 5 yrs ,
ii. 6 - 10 yrs
iii. 11 - 14 yrs.

Detailed history and thorough examination was done in each case and a tentative diagnosis was made. Depending upon the Urine and RFT analysis; patients were divided into cases and controls. Cases are children with sickling test / HPLC positive but Controls are children with sickling test / HPLC negative.

Results

Renal function tests were carried out in 81 children suffering from sickle cell disease, admitted to Rajendra Institute of Medical Sciences during the period 2016-2017. The following are the findings of renal function tests -

1. Out of 81 patients, 47 were male and 34 were female. In the age group of 2-5 years, 26 cases were studied (18 male, 8 female). In the age group of 6-10 years, 26 cases were studied (18 male, 8 female). In the age group of 11-14 years 29 cases were studied (11 male, 18 female).
2. It was observed that there had been no significant difference in the blood urea levels, serum creatinine levels and glomerular filtration rate in sickle cell disease children and control children as shown in fig 1, 2, 3.
3. Proteinuria has been found in 19.5% of cases (16 cases). 12.2% of these cases (10 cases) were in 11-14 years of age group, indicating that renal changes in sickle cell disease are markedly influenced by age as shown in table 1.
4. Haematuria has been found in 14.8% of the cases (12 cases). 9.9% of the cases (8 cases) were in 11-14 years of age group. These findings warrant prolonged follow up of such patients for understanding the progression of renal pathology as shown in table 1.
5. Evidence of urinary trait infection is present in 17.3% of children in this study (14 cases) which needs further corroboration. 9 cases showed klebsiella and 5 cases showed E.Coli on urine culture and sensitivity as shown in table no 1.
6. From the analysis of specific gravity of urine it is apparent that in the whole series, about 66.67% of the cases (54 cases) had hyposthenuria. In the age group of 2-5 years, 5 patients had hyposthenuria out of 26 cases (19.2% cases). In the age group of 6-10 years, hyposthenuria has been observed in 20 patients out of 26 cases (76.9% cases). In the age group of 11-14 years all patients had demonstrated hyposthenuria (100% cases). The table also shows that there is progressive decrease in the mean of specific gravity of urine in the successive age groups in sickle cell disease children where as there is no such

decline in the specific gravity of urine in the control groups as shown in fig 4.

7. The overall prevalence of Sickle cell nephropathy was 74%.

Table 1: urinary finding in relation to different age groups

Urinary finding	No of cases having the abnormality				
	2-5 yrs	6-10 yrs	11-14 yrs	Total	%
Protein	2	4	10	16	19.5%
RBC	2	2	8	12	14.8%
Pus cells	2	8	6	16	19.5%
Casts.	0	0	4	4	4.9%
Culture & Sensit.	6	4	4	14	17.3%

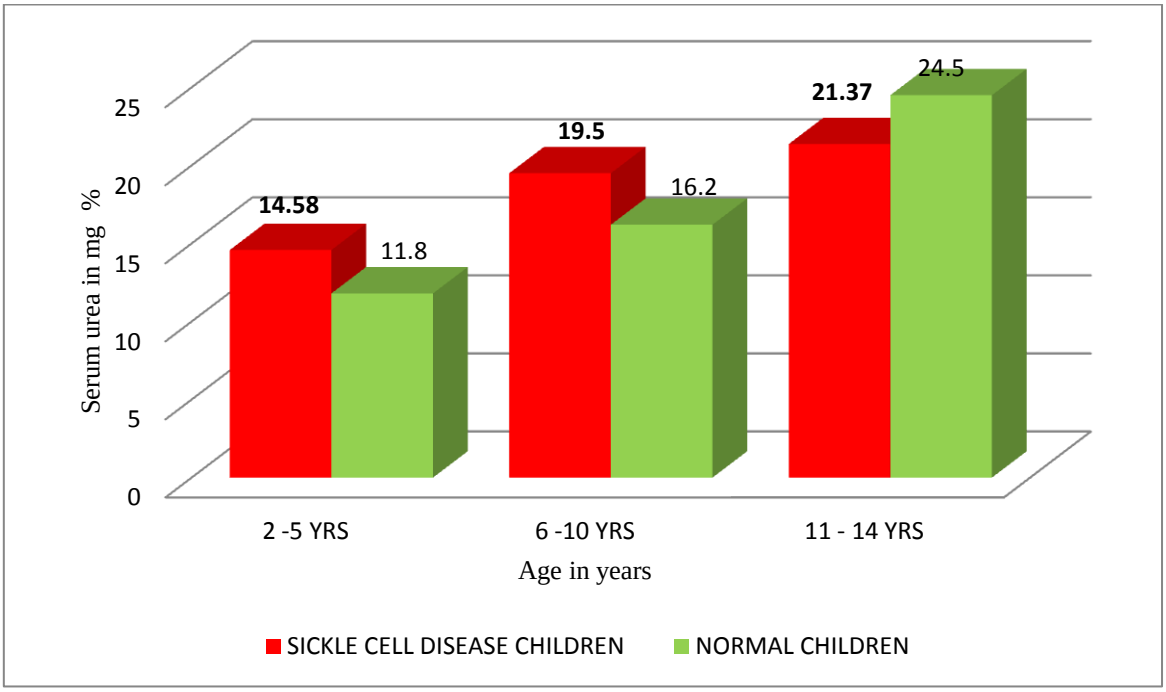

Fig .1: Changes in Serum urea level with age

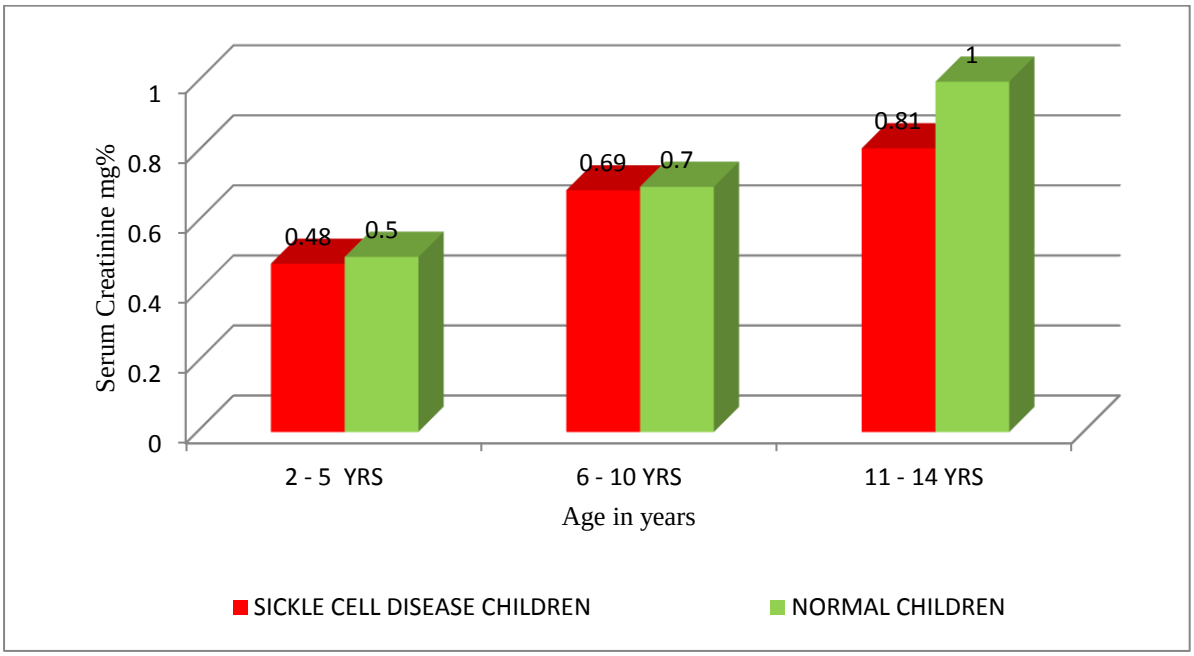

Fig.2: Changes in Serum creatinine level with age

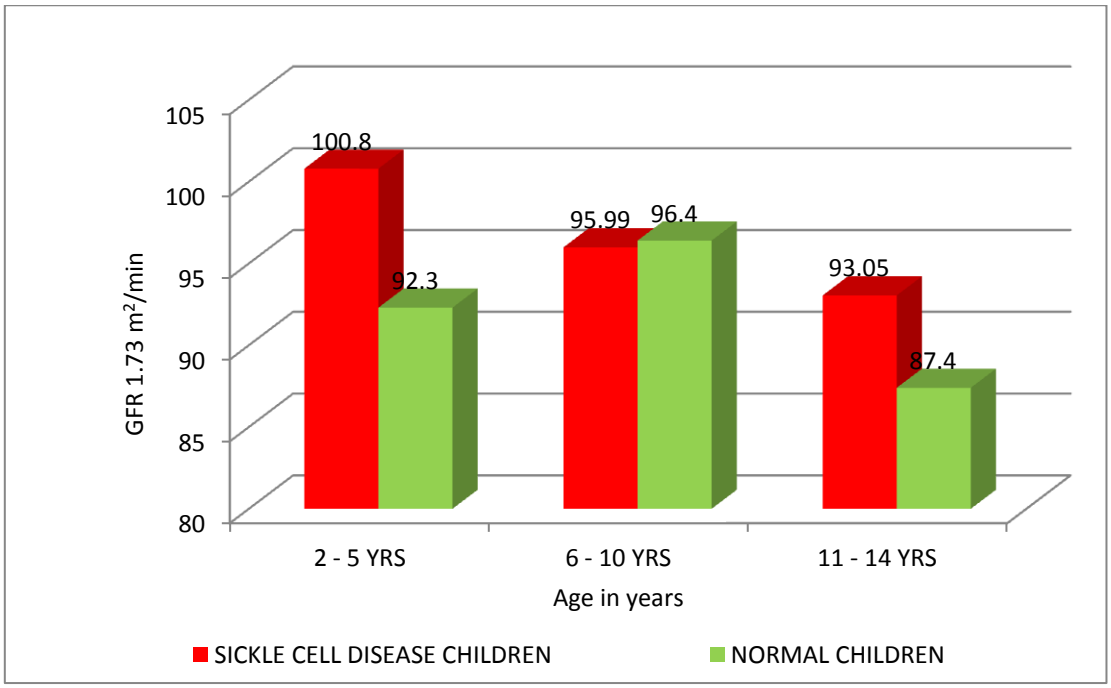

Fig.3: Distribution of Glomerular Filteration Rate (1.73m^2/ min) with age.

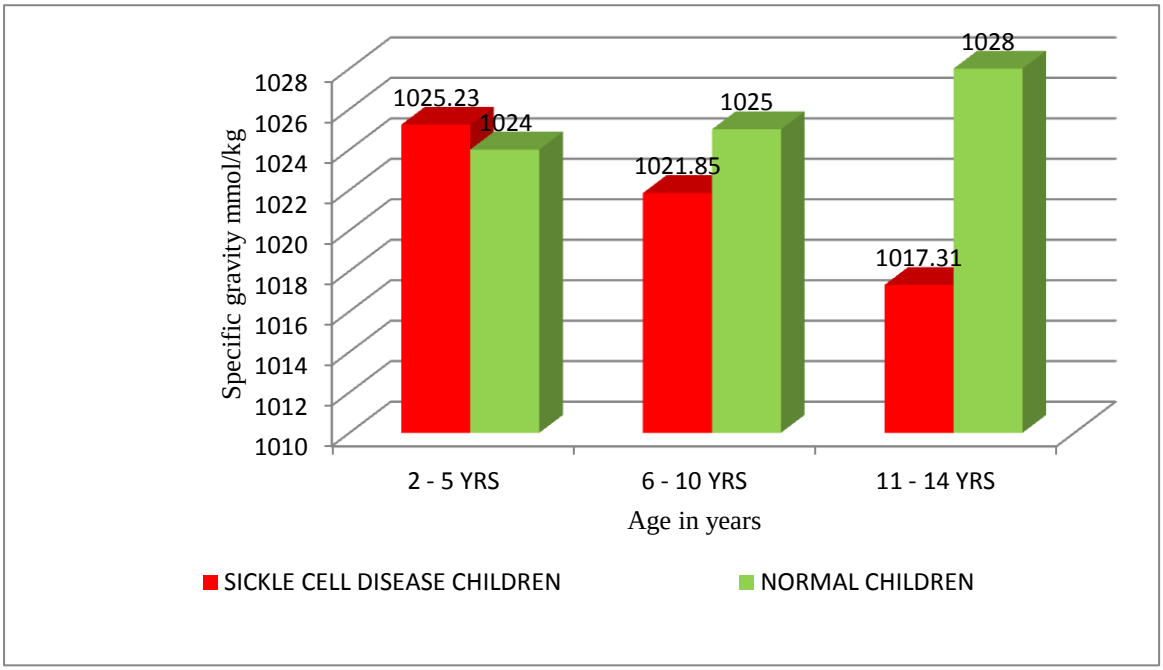

Fig.4: Distribution of specific gravity (mmol / kg) with age

Discussion

In the present study renal functions had been carried out in a group of children of varying ages, who were suffering from sickle cell disease (with haemoglobin `SS').

Mild proteinuria, microscopic hematuria, pyuria and casts had been noted in 19.5% (16 cases), 14.8% (12 cases), 19.5% (16 cases) and 4.9% (4 cases) of sickle cell disease patients respectively in the present study. These urinary abnormalities had also been noted by others in their study of sickle cell disease cases Alleyne et al.[2] Bacterial growth was noted in 17.3% of the cases (14 cases). The abnormal findings in the urine might be due to associated urinary tract infection, probably due to increased susceptibility to infection resulting from chronic anoxia, secondary to intravascular sickling (Lucas et al, 1960)[3]. But

however hematuria could occur due to other mechanism such as congestion and rupture of peri tubular and pelvic mucosal capillaries as a result of sickling of erythrocytes in the capillaries of hypertonic renal medulla (Perillie et al[4], 1963, Statius Van Eps et al[5], 1970 and Chaubey et al[6], 1975). But due to general lowering of immunity, urinary tract infection might occur which could be responsible for recurrent crises in sickle cell disease (Konotey-Ahulu[7], 1974).

The concentrating capacity of the tubules was significantly affected in children with sickle cell disease in elderly age groups. But no significant changes were observed in the younger children, in the age group of 2 to 5 years. As age advanced there was definite change in the concentrating capacity of the kidneys. The concentrating capacity of the kidney mostly depends on the functions of the tubules. Hence it could be concluded that tubular functions were deranged in sickle cell disease, especially in long standing cases.

The mechanism of concentrating defects in not yet clear. There had been several postulations on the subject given by Bauer[8], 1940; Hatch et al[9], 1967; Buckalew et al[10], 1974 and Chaubey et al[6], 1975. Normally water is reabsorbed from the distal tubules due to increased osmolarity in the interstitial space of the medulla of the kidney which is further influenced by the concentration of solutes over there. The concentration of the solutes in medulla depends on two ingredients such as sodium chloride and urea. Sodium chloride is absorbed from the ascending loops of Henle by an active process. But there is no simultaneous water absorption in this region (ascending loops of Henle is water impermeable). Urea is absorbed from the distal tubules and collecting ducts (Kokko et al[11], 1972). The high solutes in the medulla help in drawing water from urine while it passes the descending loops of Henle and the distal tubules. This results in concentration of urine. The concentration of urine is further increased while water is deprived.

In sickle cell disease the concentration of solutes in the interstitium is low. Therefore the water not absorbed properly from the tubules. This leads on to diluted urine in sickle cell disease patients even when they are deprived of water. There are some theories as to why the concentration of solutes in the interstitial is lowered in sickle cell disease. According to Jamison[12] (1973) there were certain nephrons which were very long enough to reach the papillary tip of the inner medulla of the kidney. These nephrons were necessary for maintaining the maximum osmolarity of urine. Basing on this, he suggested that since there occur papillary necrosis in sickle cell disease cases, these long loops of Henle get destroyed. Due to destruction of these nephrons the absorption of sodium chloride and urea into the interstitium was reduced, leading on to a lower concentration of the solutes over there. Papillary necrosis was caused by the rheology of R.B.C. which took up a different shape in sickle cell crisis resulting in capillary blockage and avascularisation of the part.

There had been no significant changes in the blood urea and serum creatinine concentration. Ettledorf et al[13] (1955), Morgan et al[14] (1981) had also not found any change in their studies.

The glomerular filtration rate was based on a calculation derived by schwartz et al[15] (1976). This calculation was done after determining the serum creatinine and body length of the patients in centimeters. It was observed in the present study that there had been no change in the glomerular filtration rate indicating that glomeruli had not been functionally damaged. Thus advanced age might be the reason for this altered glomerular filtration rate. However no such changes were observed in the present study, which might be due to the younger age of the patients.

Conclusion

Sickle cell disease has been reported from all over the world including India. The early detection of sickle cell nephropathy & its treatment is essential

for improving quality of life in these children. From our study it is concluded that –

1) In earlier age group, there was no difference among sickle cell patients regarding the renal concentrating capacity but with increasing age there had been significant impairment in concentrating capacity of kidney.
2) It has been observed that there had been no difference in the urea and creatinine levels and GFR, in both the groups.
3) Analyzing all these, it could be inferred that the renal concentrating capacity was impaired in sickle cell disease patients.

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