Evaluation of Glomerular functions in Patients with SCA in Maiduguri North-eastern Nigeria: a recommendation for early assessment and detection of dysfunction in a resource-poor setting

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ABSTRACT

Background: Sickle cell anaemia (SCA) is a disorder of Mendelian autosomal recessive inheritance, characterised by abnormal haemoglobin synthesis resulting in multi-systemic manifestations. The kidneys are largely affected by this disorder, but overt features of kidney disease mostly manifest after the second decade, even though insult and sub-clinical features may occur during childhood. Unfortunately, investigating these sub-clinical features is not routinely done in resource-scarce settings, partly due to the low socioeconomic status of most of our patients and the overwhelmed health care workers. **Objectives:** To investigate glomerular dysfunction in children with SCA in the context of the resource-poor setting. **Methodology:** This cross-sectional study was conducted at the University of Maiduguri Teaching Hospital (UMTH), over 6 months. One hundred and ten SCA (Hb SS) children aged 3 – 14 years in steady-state constituted the cases, while 110 non-SCA (Hb AA) age and sex-matched, apparently healthy children formed the control. Anthropometry, blood pressure, urinalysis and serum creatinine of the subjects was done. Glomerular filtration rate (GFR) was estimated using the Schwartz formula. **Results:** The mean systolic blood pressure (SBP) ± SD of the cases and controls were *96.8±9.34mmHg and 99.14±13.44mmHg respectively, (p = 0.13). The mean diastolic BP ± SD of the cases and controls were 60.18±6.85mmHg and 64.35±8.23mmHg respectively, (p = 0.0001). Glomerular filtration rate was significantly higher among the cases than the controls, 126±32ml/min/1.73m^2 and 93±16ml/min/1.73m^2 respectively (p <0.001). Proteinuria was higher among the cases (8.2%), with one (0.9%) having nephrotic range proteinuria.* **Conclusions:** The proteinuria and hyperfiltration found in some of the children with SCA in this study suggest that renal function abnormalities can be detected early in this group of children when appropriately and timely investigated.

Key words: *Glomerular function, Maiduguri, North-eastern Nigeria, Resource-poor, Sickle cell anaemia*

INTRODUCTION

Sickle cell anaemia (SCA) is the most common genetically inherited condition of the Mendelian autosomal recessive fashion of inheritance due to a mutation in the beta-globin gene which results in the replacement of the glutamic acid by valine at position 6 of the beta-globin chain, this results in the synthesis of an abnormal (sickle) haemoglobin molecule. Sickle cell anaemia is the most common genetic disorder worldwide. The highest frequencies of the disorder in the world occur in Sub-Saharan Africa, where 1 to 3% of the population is affected.[1] The gene for sickle cell commonly occurs in tropical regions with the intense transmission of malaria.

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Nigeria has the largest population of SCA patients worldwide. The prevalence of the carrier state is reported to be between 19% and 32.6% in different regions of the country.[2,3] Various population-based studies reported an estimated prevalence of homozygous sickle cell disease to be between 1.6% and 3% in Nigerian newborns with the incidence to be approximately 150,000 newborns per annum.[4-6] It has also been established that about 300,000 SCA children are born annually, and 75% of them are reported to be born in Sub-Saharan Africa.[7] A recent study in Maiduguri North-Eastern Nigeria showed a prevalence of 6.8% and this was attributed to the increased rate of intermarriages between ethnic groups that have the highest carrier rate of the disorder and consanguineous marriages in the north-eastern part of Nigeria.[8] The main haplotype of SCA in Nigeria is the Benin haplotype, the second most grievous form after the Central African Republic haplotype.[9]

The kidney is an excretory organ of substantial influence on the clinical course of homozygous sickle cell disease.[10] Even though Nigeria has the highest prevalence of SCA and the increased chance of chronic kidney disease (CKD), information about renal abnormalities in the paediatric population with SCA in our setting are largely under-reported, the paucity of paediatric nephrologists and haematologists in North-eastern Nigeria contribute to this reality.[11] Besides, SCA and renal diseases are not regarded as a major health problem particularly in the insurgency devastated North-eastern region of Nigeria compared to extreme poverty, malnutrition and infectious diseases.[11,12] Renal papillary necrosis (RPN) has been described in about 62% of asymptomatic individuals with SCA where they present with asymptomatic haematuria which could not have been detected except on routine urinalysis.[13] Routine urinalysis is not usually done in asymptomatic patients which posed a challenge in the early detection of renal dysfunction.

Molecular biology also plays a significant role in the pathogenesis of renal dysfunction among SCA children. Plasma Endothelin-1 (ET-1) levels are elevated in patients with SCD during steady-state periods as well as during acute vaso-occlusive crisis this ET-1 promotes sickling and tissue injury, induces vasoconstriction, inflammation, nociception as well as production of oxidant stress and the release of cytokines.[14] All these lead to glomerular dysfunction. Assessing this biological molecule is very difficult and expensive in our setting and posed a challenge in the early detection of glomerular dysfunction. Administration of ambrisentan, at the time of weaning and continued for 10 weeks, prevents glomerular dysfunction, tubulointerstitial inflammation and fibrosis.[14] It does that by significantly reducing the degree of iron deposit in renal tubules.

Conversely, plasma ET-1 levels are decreased in SCD patients treated with hydroxyurea.[14] Only hydroxyurea, which is very expensive, is readily available in our environment but ambrisentan is not readily available in a resource-poor setting like ours. The cost of hydroxyurea and the unavailability of ambrisentan posed a challenge in managing these patients.

The SCA patients have changes in plasma renin, endothelin and nitric oxide metabolites due to recurrent and long-standing vaso-occlusion with these changes affecting the balance between vasoconstriction and vasodilatation.[15] These plasma changes can affect the renal function and measurements of this plasma renin, endothelin and nitric oxide is important in the early detection of renal dysfunction. This is very challenging in a resource-poor region like ours as these metabolites are very expensive to assess in the plasma. Other arguments have been advanced for SCA patients having lower blood pressures, this not exclusively include the chronic hypoxic state secondary to the chronic anaemic state in these subjects.[16] Furthermore, SCA children are known to have higher serum concentrations of prostaglandin, which is a potent platelet aggregation inhibitor and thus lower peripheral vascular resistance.[17] Other factors attributable to low systemic blood pressure in children with SCA include salt-losing sickle cell nephropathy,[18] renal tubular damage with concentrating defects and increased renal tubular sodium and water excretion, thus promoting lower arterial pressure.[19] Patients with SCD have proximal tubule hyperfunction resulting in increased secretion of creatinine.[20,21] It is a well-known fact that some SCA children are on chronic use of analgesics due to repeated VOC and this can lead to analgesic nephropathy. This is challenging because there is no routine monitoring of serum

levels of these analgesics in our resource-poor facilities.

Studies have shown that lower Hb and VOC is associated with sub-clinical kidney injury as shown by elevated urine neutrophil gelatinase-associated lipocalin (NGAL) and Cystatin-C levels during VOC despite an unchanged serum creatinine.[22,23]

The renal pathologic findings in young patients with SCD include glomerular enlargement, congestion of capillary loops with sickled erythrocytes and hemosiderin as well as increased numbers of capillary lumens and epithelial, endothelial and mesangial cells.[24] Renal biopsy is required for these findings and this is very challenging for the fact that it is invasive and requires expertise that is not readily available in the resource-poor region.

The objective of this study is to assess renal dysfunction and give recommendations for early assessment and detection of glomerular dysfunction in children with SCA in resource-poor settings.

MATERIALS AND METHOD

This cross-sectional descriptive study was conducted at the Paediatric Haematology clinic and General Paediatric Outpatient clinic of the University of Maiduguri Teaching Hospital (UMTH) over six months. The study population were children with SCA in steady-state as defined by Akinola *et al,*[25] on folic acid and proguanil. The controls were age- and sex-matched healthy children with haemoglobin AA who recovered from minor ailments such as upper respiratory tract infection and acute diarrhoeal disease and were on follow-up at the General Outpatient Department (GOPD)/Paediatric Outpatient clinic.

Study design: This was a cross-sectional study

Study site: The study was conducted at the Paediatric Haematology clinic and General Paediatrics Outpatient clinics of UMTH

Study population: Children aged 3 – 14 years old. For each case, one control child matched for age, sex and social class were recruited into the study.

Participants were recruited systematically by choosing alternate patients as they presented at the Clinic after meeting the inclusion criteria.

Sample size: This was determined using Taylor's formula,[26] and P value was taken from a previous study by Tukur *et al* from north-eastern Nigeria who reported a prevalence of SCA to be 6.8%.[8] Thus, 110 SCA children (cases) and 110 HbAA children (controls) were enrolled in the study.

Inclusion criteria: Children aged 3 - 14 years with SCA constitute the cases, apparently healthy non-SCA children age and sex-matched constitute the control, both of whom were recruited after consenting/or assent.

Exclusion criteria: Children whose parents/caregivers did not give consent to participate in the study were exempted. Also excluded from the study were children below the age of 3 years because children at this age are known to have variation in GFR from their early childhood.[27] Children with established renal disease, as well as children with previously known proteinuria, hypertension, diabetes, HIV, HBV or HCV infection, renal and cardiovascular diseases, were excluded by appropriate clinical and laboratory investigations. Children on hydroxyurea therapy for whatever indication were also excluded.

Ethical considerations

Approval was sought after and obtained from the Hospital Research and Ethics Committee of the UMTH-(ADM/TH/75/Vol.III). Written informed consent was obtained from the caregivers after adequate education. Verbal assent was also obtained from children 7 years and older with unlimited liberty to deny consent/assent or opt-out of the study at any time or stage without any negative consequences. Participation was, therefore, completely voluntary and those who refused consent to participate were still having their children or wards being followed up appropriately at the clinics. The information and results obtained were kept confidential. Those detected with compromised renal function were linked to a Paediatric nephrology clinic for further evaluation and subsequent co-management.

Study protocol

The clinical and laboratory information collected and analyzed included (i) Demographic

characteristics (ii) blood pressure and (iii) serum creatinine.

All patients were free of pain for at least 15 days and had not been hospitalized and transfused for at least 90 days before the study.

Five mils of blood sample was collected and screened for haemoglobin phenotypes at the Haematology Laboratory of UMTH Maiduguri using standard methods, for the control while the cases were known SCA patients that were on follow-up in the Paediatric Haematology clinic, with their haemoglobin genotype result confirmed and documented in their case notes.

One hundred and ten children having sickle cell anaemia in steady-state were recruited. All children were homozygous for the β-globin S gene mutation (SS disease). One hundred and ten children with normal Hb (Hb-AA) matched for age and sex were selected as a control group.

The standing height (in cm) and weight (in kg) were measured using Wunder's stadiometer fitted with a weighing scale. The height was measured with the subject bare-footed, heels, back and occiput in contact with the stadiometer back support and measurement taken to the nearest 0.5 cm. Each subject was also weighed with as minimal clothing as possible with measurement to the nearest 0.5 kilograms with the pointer adjusted for zero error. The weighing scale pointer was readjusted to the zero marks before each measurement and a standard weight of 5kg was used to readjust the scale at the beginning of every day of the clinic. The axillary temperature was measured using a digital thermometer left in place until it stops blinking after about two minutes. Body surface area (BMI) was read off a standard nomogram using age (years), weight and height that were previously measured.

Blood pressure (BP) of each subject was measured in sitting position after five minutes of relaxing and was measured twice in the right arm at the heart level with Accoson's mercury sphygmomanometer using age-appropriate cuffs (one whose bladder covers two-third of the subject's right arm). Systolic blood pressure was taken as the point at which the first Korotkoff sound was heard and the diastolic blood pressure as the point at which the Korotkoff sound became muffled.[28] Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were defined as normal between the 5th and the 90th percentile for age, gender and height. *Hypertension* was defined as BP greater or equal to the 95th percentile for age, gender and height. *Hypotension* was defined as BP<5th percentile for age, gender and height. Blood pressure was classified using published normative data (US).[29]

Following these, 5mls of blood was drawn using an aseptic technique, from the most obvious peripheral vein on the dorsum of the hand or the forearm of each subject and collected into a lithium heparinised bottle. The plasma separated from the blood by centrifugation was used for the estimation of creatinine. No dietary restrictions were imposed. The test was performed in the Chemical Pathology laboratory of the University of Maiduguri Teaching Hospital.

Each batch of blood sample collected per clinic day was analysed for serum creatinine on the same day, by a laboratory scientist in the Chemical Pathology Laboratory of the UMTH, using the standard method of Heinegard and Tiderstrom.[30]

Glomerular filtration rate (GFR) was determined by use of the height/serum creatinine ratio, Schwartz formula, a method which despite its limitations is suitable for routine clinical work in a resource-poor setting; because of the advantages of rapid determination, reasonable accuracy and the avoidance of the cumbersome 24hours urine collection justify the use of this formula in the setting of paediatric practice in the resource-scarce setting.

The GFR (expressed as ml/min/1.73m^2) was calculated using the height/serum creatinine ratio, Schwartz formula.[31]

C represent a constant, which is taken as 0.55 for children and girls. While 0.7 for adolescent males' ≥ 13 years, S_{cr} represent serum creatinine, while 1.73m^2 is the standard adult BSA. A normal GFR range of 90 to 130ml/min/1.73m^2 (3-14yrs) was used.[32]

Hyperfiltration was defined as a GFR greater than 130 ml/min/1.73 m^2.[33]

Children were considered to have *renal insufficiency* if their total serum creatinine concentrations were greater than upper limits of normal for age and sex established by Schwartz *et al*.[31]

All children provided a urine sample and were analyzed using the Multistix; urinalysis reagent strip, Medi-Test Combi 9® (MACHEREY-NAGEL EURL, Hoerdt France) batch number B.P. 13567722. The urine testing was done three times on the same urine sample according to the manufacturer's instructions. Children were considered to have *Proteinuria* if three consecutive urinalyses of the same urine sample were at least 1+ for protein. When positive with dipstick and proteinuria of 3+, measurement of 24-hour urinary protein was obtained.

Data management and Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 16 of 2008 (SPSS, Chicago, Illinois, USA). Data are represented as means ±SD when the distribution was normal and median with range when the distribution was skewed. The student's t-test was used for comparisons of means. Categorical variables were compared using the Chi-square test. A p-value <0.05 was considered significant.

RESULTS

A total of 110 children with SCA in steady-state and 110 controls with Hb-AA were recruited during the study period. The age and sex distribution of the study population are shown in Table I. Of the 110 SCA children, 57 (51.8 %) were males while 53 (48.2%) were females giving a Male: Female ratio of approximately 1.08:1. There were 49 males and 61 females for the control subjects with an M: F ratio of 0.8:1. The age range was the same for both groups; with mean ages of Hb-SS subjects and controls of 9.0 ± 3.8yrs and 7.9 ± 3.0yrs respectively. There were no statistically significant differences between the mean ages of the Hb-SS and the Hb-AA controls (P>0.05).

Table 1: Age, Sex and Hb Genotype distribution of the study population

Age grp (yrs)	*Hb-SS*		*Hb-AA*	
	Male N (%)	*Female N (%)*	*Male N (%)*	*Female N (%)*
≤5	*18(31.6)*	*13(24.5)*	*15(30.6)*	*16(26.2)*
6 - 10	*10(17.5)*	*14(26.4)*	*18(36.7)*	*31(50.8)*
≥11	*29(50.9)*	*26(49.1)*	*16(32.7)*	*14(23.0)*
Total	*57(51.8)*	*53(48.2)*	*49(55.5)*	*61(55.5)*

Hb-SS= Haemoglobin SS, Hb-AA= Haemoglobin AA, N= Number

The mean weight, height and BMI were all higher in the SCA subjects than the normal children with Hb-AA, there was no significant difference between the two groups. Although, both the mean systolic and diastolic blood pressure of the control group were higher than those of the SCA group, only the mean diastolic blood pressure (DBP) was significant (Table-2). The systolic and diastolic blood pressure level was lower in the Hb-SS group than in the Hb-AA groups in both sexes. However, only the mean DBP was statistically significant between the two groups (P=0.0001).

Table 2: Anthropometric parameters and mean blood pressure of the study population

Parameters	*Hb-SS*	*Hb-AA*	
	Mean(SD)	*Mean(SD)*	*P-value*
Weight(kg)	*26.3(11.4)*	*23.5(10.6)*	*0.057*
Height(cm)	*128(22.2)*	*123(17.96)*	*0.079*
BMI(kg/m^2)	*15.1(7.2)*	*14.8(2.07)*	*0.074*
SBP(mmHg)	*96.8(9.34)*	*99.1(13.4)*	*0.135*
DBP(mmHg)	*60.2(6.85)*	*64.4(8.23)*	*0.0001**

Kg= kilogram, cm= centimeter, BMI= Body mass index, SBP= Systolic blood pressure, DBP= Diastolic blood pressure, mmHg= millimeter of mercury. *p=<0.05

A significantly higher percentage (9.1%) of subjects with systolic hypotension were children with Hb-SS, compared to (0.9%) in children with Hb-AA. Diastolic hypotension was found in only (1.8%) of subjects with Hb-SS and none in children with Hb-AA. Hypertension was found to be lower (5.5%) in subjects with Hb-SS, compared to (9.6%) in children with Hb-AA.

Creatinine was significantly lower in subjects with Hb-SS than in children with Hb-AA. The difference in creatinine level between the two groups was statistically significant (Table-3).

Table 3: Biochemistry profile of renal function of the study population

Variables	*Hb-SS N=110 Mean (SD)*	*Hb-AA N=110 Mean (SD)*	*P*
Creatinine (mg/L)	*0.63±0.19*	*0.79±0.24*	*0.0001*
GFR (ml/min/1.73m^2)	*126±32*	*93±16*	*<0.001*

GFR: Glomerular filtration rate.

Mean GFR was markedly increased in the Hb-SS group compared to the Hb-AA group. The absolute values for GFR corrected for body surface area (BSA) were significantly higher in the Hb-SS group compared to the Hb-AA group (Table-3).

A significantly higher proportion (33.6%) of subjects with hyperfiltration were children with SCA. Only one (0.9%) of the studied children with Hb-AA had hyperfiltration.

Moderate reduction of GFR (<60 ml/min/m^2) was present in only 1(0.9%) of children suffering from SCA while 6(5.5%) of the studied children with Hb-AA had moderate renal insufficiency.

Proteinuria was found in 9(8.2%) of children with SCA and only one of the SCA children had nephrotic-range proteinuria. No case of Nephrotic-range proteinuria was detected in the Hb-AA control group.

DISCUSSION

The finding of significantly high mean GFR in subjects with Hb-SS compared to Hb-AA control children in this research is consistent with the findings of Oyinade.[34] Similar findings were also reported by the much-cited earlier works on GFR in SCA that demonstrated elevated GFR in children with SCA from West Indies and North America.[35,36] However, the findings of significantly high mean GFR in steady-state SCA children as compared to Hb-AA controls in this study is at variance with works of Olowu *et al*,[37] Okoro and Onwuameze.[33] Similarly our finding is at variance with the early work on GFR in children with SCA by Calcagno *et al*;[38] where they used the Thiosulphate clearance method to study GFR in 5 children with SCA and a reduced GFR value was found. The thiosulphate clearance method used by Calcagno *et al* might have contributed to this difference, the small sample size used may probably be due to the cumbersome nature of the analytic technique. Notwithstanding the small number of subjects, they studied may have contributed to the finding of reduced GFR if an appropriate sample size was used their findings would probably be different.

Hypotension was more commonly present in children of the homozygous sickle cell group and was diagnosed respectively in 33.6% of children with Hb-SS and 0.9% in those with Hb-AA for SBP. This reported hypotension is similar to what was earlier reported in the literature.[32,35] In this series, children were comparable for weight and height components of the anthropometric parameters and the lower BP in SCA cannot be attributable to low weight. This situation was previously described by Horni *et al*,[35] these results suggest that specific pathophysiological models should be defined in SCA. A possible explanation for these findings is the fact that SCA patients have changes in plasma renin, endothelin and nitric oxide metabolites due to chronic vaso-occlusion with those changes affecting the balance between vasoconstriction and vasodilatation.[17] Other reason advanced for why the SCA children have lower blood pressures include the chronic hypoxia secondary to the chronic anaemic state in subjects with SCA, this cause vasodilatation leading to lower peripheral vascular resistance and hence lower systemic blood pressure.[16] Furthermore, SCA children are known to have a higher serum concentration of prostaglandin which is a potent platelets aggregation inhibitor and thus lowers peripheral vascular resistance.[17] Other factors attributable to low systemic blood pressure in children with SCA include salt-losing sickle cell nephropathy,[18] renal tubular damage with concentrating defects and increased renal tubular sodium and water excretion thus; promoting lower arterial pressure.[19]

Anthropometric parameters in this study are similar to those described in most literature that children with SCA have delayed growth which starts as early as two years of age, and this delay affects weight more than the height with progression through the adolescent years.[39]

The major factors influencing serum creatinine is muscle mass. In our study, children with Hb-SS were comparable for the anthropometric

parameters with the Hb-AA groups. The creatinine was lower in children with Hb-SS than in Hb-AA subjects. Similar findings were previously reported.[32,40] The serum creatinine is lower in the Hb-SS subjects is expected because it is compromised by the renal hypersecretion of creatinine. Thus, the interpretation of serum creatinine must be in the context of this factor. Values at the upper limit of the normal range should raise the suspicion for possible compromised renal function. GFR was significantly increased in the Hb-SS group compared to the Hb-AA group. This observation appears to be consistent with such evidence that an increase in GFR is predominantly seen in sickle cell paediatric series.[11,40] In contrast, this finding is, however, at variance with the research findings of Olowu *et al,*[37] Okoro and Onwuameze[33] from Nigeria. Olowu *et al* used 24-hours urine protein estimation while used serum creatine and Schwartz formula for GFR calculation this possibly explain the differences with our findings, the difference in our findings with Okoro and Onwuameze is not clear as the same method were used.

In our study, glomerular dysfunction in this population of children with SCA is found to be significant in the sense that hyperfiltration was present in 33.6% of children with Hb-SS. This is, however, low when compared with the prevalence of 76% reported by Aygun *et al* in the USA.[41] The high prevalence of Aygun research was probably because the method used for GFR estimation was Tc 99 clearance. Hyperfiltration is, however, a common finding in young patients suffering from SCA due to glomerular hypertrophy.[42] More recently, this theory has been challenged and suggests that increased nitric oxide synthetase activity leads to glomerular hyperfiltration in sickle cell disease.[43] In SCA, creatinine clearance overestimates the rate of glomerular filtration due to several abnormalities in proximal tubular function with an increased rate of creatinine secretion yet our findings was lower than Aygun et al findings, the reason for this is, however, not clear.

In this study, a moderate reduction of GFR suggesting moderate chronic renal insufficiency with GFR (<60 ml/min/m^2) using the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI),[44] was present in 0.9% of children with SCA. The prevalence of renal complications in our cohort was found to be very low compared to 12.3% in the series of Aloni *et al*[32] among Congolese children with SCA who developed an increase in serum creatinine.

Persistent proteinuria is believed to be a precursor of developing chronic renal failure in SCA patient.[32] In our series, the prevalence of proteinuria detected by dipstick was similar to the findings reported in DRC and Ghana.[32,44] One child with SCA was found to have asymptomatic Nephrotic-range proteinuria. Nephrotic syndrome in children with SCA has been reported in Nigeria.[45]

The non-availability of appropriate diagnostic tools remains a formidable hindrance to be surmounted in the establishment of the prevalence of proteinuria in the paediatric population with SCA in resource-constrained settings. The determination of the prevalence of proteinuria with precision was most likely more than indicated because of the inherent inability to concentrate urine that is normally a frequent occurrence in SCA patient. In this condition, reagent strip analysis probably underestimates the presence of proteinuria in our study. Unfortunately, microalbuminuria was not done to confirm that proteinuria was present in those children that tested negative for proteinuria with the dipstick method. In previous studies, the prevalence of proteinuria in SCA patient significantly increases when microalbuminuria was assessed.[46] The care of children with SCA in Nigeria and especially in the insurgency devastated North-Eastern region is compromised by resource scarcities that range from inadequate healthcare budgets, poor socio-economic status of our population, paucity of appropriately trained personnel to scarce laboratory facilities. The expensive nature of some investigative procedures also hinders some investigations to be done in this part of the country.

CONCLUSIONS

Glomerular dysfunction is common and may be under-reported without appropriate diagnostic tools most especially in children with SCA. In a

resource-constrained setting like ours, hyperfiltration is an appropriate indicator of deterioration in renal function in children with SCA, which occurs earlier than proteinuria and/or decreased creatinine clearance.

Recommendations

1. All patients with SCA on routine clinic visits should have their urinalysis and their GFR determined as an early screening test for renal dysfunction as urinalysis is cheap and GFR can detect glomerular hyperfiltration.
2. Paediatric Haematologist and Paediatric Nephrologist should engage in co-managing children with SCA. This is because the Haematologist would not have thought of assessing for renal function during the routing clinic visits of SCA children and the Nephrologist have no access to SCA children unless they come with frank features of renal dysfunction.
3. The patients with SCA must be considered at-risk for CKD and should have regular (at least once per year) measurements of the urinary albumin to creatinine ratio (UACR) for early detection in children after 7 years of age, particularly in the severe cases of SCA.
4. Novel screening methods like urine neutrophil gelatinase-associated lipocalin (NGAL), Cystatin-C and other serum bio-molecular metabolites like plasma Endothelin-1 (ET-1) levels should be made available as a routine screening tool for early detection of glomerular dysfunction in children with SCA.
5. Renal biopsy should be part of the investigative protocols because this can detect early pathologic features of renal dysfunction.

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