Chronic Kidney Disease and Albuminuria in Children with Sickle Cell Disease

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Summary

Background and objectives Sickle cell nephropathy begins in childhood and may progress to renal failure. Albuminuria is a sensitive marker of glomerular damage that may indicate early chronic kidney disease (CKD).

Design, setting, participants, & measurements The aims of this study were to determine the cross-sectional prevalence and clinical correlates of albuminuria and CKD among children with sickle cell disease (SCD). Over a 10-year period (1995 to 2005) 410 pediatric SCD patients ages 2 to 21 years were enrolled: 261 with hemoglobin SS (HbSS) or HbSβ0 thalassemia (HbSβ0) and 149 with HbSC or HbSβ+ thalassemia (HbSβ+). The albumin/creatinine ratio (ACR) of spot-urine specimens and serum creatinine were measured; abnormal albuminuria was defined as urinary ACR ≥ 30 mg/g.

Results The prevalence of abnormal albuminuria was 20.7% (23.0% in HbSS/HbSβ0, 16.8% in HbSC/HbSβ+). Among HbSS/HbSβ0, abnormal albuminuria was associated with increasing age and lower baseline hemoglobin. GFR, estimated in 189 patients using the updated Schwartz formula, correlated negatively with age (r = −0.27, P = 0.0002). CKD defined according to the Kidney Disease: Improving Global Outcomes study was present in 26.5% (50 of 189) of patients: stage 1 in 27 (14.8%) and stage 2 in 22 (11.6%). In multivariate analysis, age and HbSC/HbSβ+ genotype were associated with CKD.

Conclusions This is the first study to stage CKD in children with SCD and highlights a high prevalence of albuminuria and glomerular injury early in life. Detecting CKD in childhood could allow for earlier intervention and prevention of renal failure in adulthood.


Introduction

Sickle cell disease (SCD) is an autosomal recessive disorder due to a mutation in the β-globin gene of hemoglobin that causes red blood cell sickling, vaso-occlusion, and hemolysis. SCD may occur as homozygous inheritance of hemoglobin S (HbS), compound heterozygous inheritance of HbS with other β-globin mutations such as hemoglobin C, or quantitative mutations that result in decreased or absent β-globin synthesis (hemoglobin β+ and β0 thalassemia, respectively). Hemoglobin SS (HbSS) and HbSβ0 are clinically identical disorders that are associated with severe anemia and disease complications, whereas HbSC and HbSβ+ thalassemia tend to have fewer and less severe acute complications. Chronic organ damage, including renal damage, is a feature of all forms of SCD.

Nephropathy is a serious complication of SCD that begins in childhood and may progress to overt renal failure (1). Sickle cell nephropathy involves damage to multiple structures within the kidney, including the glomeruli within the renal cortex and the renal tubules and vasa recta within the hypoxic, hyperosmolar renal medulla. ESRD develops in 4.2 to 11.6% of adults with HbSS and is an independent predictor of premature mortality in young adults (1,2). Common clinical markers of renal function such as serum creatinine are not reliable indicators of early stage glomerulopathy in SCD because of the increased GFR, lower muscle mass, and increased tubular secretion of creatinine in individuals with SCD (3–5).

Glomerular changes begin as early as the first decade of life in otherwise asymptomatic SCD patients (6). Early glomerular changes in SCD are characterized by high renal blood flow, glomerular hyperfiltration and hypertrophy (6–9), and a gradual loss of glomerular filtration permselectivity such that larger molecules such as albumin abnormally permeate the restrictive pores of the glomerular capillary wall. Thus, albuminuria is a sensitive and early clinical marker of glomerulopathy (10,11). We previously demonstrated a significant loss of glomerular permselectivity and ultrafiltration coefficient in albuminuric adults with SCD and normal GFR, with the great-
est reductions in permselectivity observed in patients with renal insufficiency, suggesting that progressive glomerular injury is a major determinant in the development of renal failure in SCD (11,12). Additionally we demonstrated that the ultrafiltration coefficient correlates inversely with the fractional clearance of albumin, providing evidence that albuminuria is a reliable indicator of sickle glomerulopathy (12). Moreover, abnormal albuminuria becomes increasingly prevalent with age and occurs in most adults with SCD (13). In our study of SCD patients at the Georgia Comprehensive Sickle Cell Center, we found that 68% of adults with HbSS and 42% of adults with non-HbSS SCD had abnormal albuminuria. In adults 40 years of age and older, these frequencies increased to 79% for HbSS and 59% for non-HbSS SCD (13). Other cohort studies of younger populations have shown abnormal albuminuria in 16% to 28% of children and young adults with HbSS and HbSβ0 (14–18).

The aims of this study were to define the cross-sectional prevalence of chronic kidney disease (CKD) and albuminuria among a large population of children and adolescents with SCD of all hemoglobin genotypes and to determine if clinical variables including baseline hematologic parameters are associated with increased prevalence of albuminuria and CKD in a subset of this cohort.

Materials and Methods

Patient Population

A cross-sectional observational study of albuminuria in pediatric SCD patients was undertaken at the Georgia Comprehensive Sickle Cell Clinic of Grady Memorial Hospital from 1995 to 2005. The institutional review board of Emory University granted approval of this study, in accordance with the Declaration of Helsinki, and written informed consent was obtained from the patients or guardians. During the study period, approximately 450 active pediatric patients (at least one visit per year) were followed at this center. Patients aged 2 to 21 years with HbSS or a compound heterozygous SCD genotype were eligible for enrollment. Patients were enrolled at the time of a routine outpatient clinic visit. Samples were not collected when patients had pain crisis, acute illness, symptoms suggestive of urinary tract infection, or gross hematuria. All testing was performed on single random-spot, clean-catch specimens. Baseline hematologic parameters (white blood cell, hemoglobin, platelet count, reticulocyte counts), serum creatinine, and other clinical parameters were collected by retrospective review of medical records and reflect measurements done either on the same date or on the most recent well-visit encounter.

Laboratory Studies

Urinary albumin was measured by RIA (DPC Laboratories, Los Angeles, CA). Urinary creatinine was measured by kinetic modification of the Jaffe reaction using a Beckman II creatinine analyzer (Beckman Instruments, Fullerton, CA). Albumin/creatinine ratio (ACR) was expressed as milligrams of albumin per gram of urinary creatinine. Albuminuria was categorized as follows: normoalbuminuria was defined as ACR < 30 mg/g, microalbuminuria as ACR 30 to 299 mg/g, and macroalbuminuria as ACR ≥ 300 mg/g. The estimated GFR (eGFR) was calculated using the updated pediatric Schwartz formula: 

$$eGFR = 0.413 \times \frac{\text{height in cm}}{\text{serum creatinine in mg/dl}}$$

(19). One calculated eGFR value >400 ml/min per 1.73 m² corresponded to a serum creatinine of 0.1 mg/dl and was excluded from analysis because of presumed inaccuracy. CKD was classified according to international consensus guidelines as follows: stage 1, kidney damage (including albuminuria) and GFR ≥ 90 ml/min per 1.73 m²; stage 2, kidney damage with GFR 60 to 89 ml/min per 1.73 m²; stage 3, GFR 30 to 59 ml/min per 1.73 m²; stage 4, GFR 15 to 29 ml/min per 1.73 m²; stage 5, kidney failure with GFR <15 ml/min per 1.73 m² (20).

Statistical Analyses

The primary outcome variable was detection of abnormal albuminuria, defined as ACR ≥ 30 mg/g. Patients were stratified by hemoglobin genotype into two groups: HbSS/HbSβ0 and HbSC/HbSβ+. For statistical comparisons, one patient with HbSD was categorized in the HbSS/HbSβ0 group, and one patient with HbS-Lepore was categorized in the HbSC/HbSβ+ group. The chi-squared test comparison was used to compare the prevalence of albuminuria by hemoglobin genotype, age group, and chronic transfusion status. Associations of albuminuria with age and hematologic parameters (white blood cell, hemoglobin, platelet, and reticulocyte counts) were assessed by the t test or Wilcoxon rank sum test, as appropriate. ANOVA was used to compare eGFR values in patients with HbSS/HbSβ0 versus HbSC/HbSβ+. The Breslow–Day test was used to examine the interactions of gender and age. Pearson correlation coefficient (r) was calculated to assess the linear relationships of eGFR with ACR and age. A multivariable logistic regression analysis model of CKD was constructed using a stepwise selection process; introducing the variables hemoglobin genotype, age, gender, baseline hemoglobin, and chronic transfusion therapy; and eliminating variables NS at α = 0.15. Odds ratios for categorical variables were calculated by maximal likelihood estimates analysis. Statistical analysis was performed using the SAS version 9.2 (SAS Institute, Cary, NC) statistical software package.

Results

Patient Characteristics

The study cohort consisted of 410 patients (214 male, 196 female) ranging in age from 2 to 21 years (mean 11.3 years). Patient clinical characteristics are shown in Table 1. Enrollment consisted of 101 patients from 1995 to 2000 and 309 patients from 2001 to 2005. There were 256 (62.4%) with HbSS, 117 (28.5%) with HbSC, 31 (7.6%) with HbSβ+, 4 (1.0%) with HbSβ0, 1 with (0.2%) HbSD, and 1 with (0.2%) HbS-Lepore. Forty patients (39 HbSS and 1 HbSβ+) were receiving chronic transfusion therapy at the time of study enrollment. Only 17 patients (6.5% of the HbSS/HbSβ0 group) were receiving hydroxyurea therapy. Three patients with macroalbuminuria previously had kidney biopsies for evaluation of proteinuria revealing glomerulosclerosis and mesangial hypercellularity, consistent with sickle nephropathy. No patients were receiving angiotensin-con-
verting enzyme inhibitor or angiotensin receptor blockade medications during the study.

**Albuminuria**

In the entire SCD cohort (HbSS/HbSβ and HbSC/HbSβ+ groups), the prevalence of abnormal albuminuria (≥30 mg/g) was 20.7% (85 of 410 patients). Mean ACR was 25.3 mg/g, and median ACR was 10.1 mg/g (range 0.2 to 429.6 mg/g). Three patients had macroalbuminuria (≥300 mg/g), all with the HbSS genotype. The mean age of patients with normal-range albuminuria (13.0 years, and 35 of 98 (35.7%) patients ages 13 to 19 years

Patients were classified by age and gender into four groups: age 2 to 6 years, age 7 to 12 years, and ages 13 to 19 years. Abnormal albuminuria occurred in 4 of 58 (6.9%) patients ages 2 to 6 years, 21 of 105 (20.0%) patients ages 7 to 12 years, and 35 of 98 (35.7%) patients ages 13 to 19 years (P = 0.0001).

Characteristics of patients with and without abnormal albuminuria, stratified by SCD genotype, are given in Table 2. In the HbSS/HbSβ group, 60 of 261 (23.0%) had abnormal albuminuria ≥30 mg/g, and in the HbSC/HbSβ+ group, 25 of 149 (16.8%) had abnormal albuminuria (P = 0.14). Abnormal albuminuria was associated with age in the HbSS/HbSβ group (P < 0.0001) but not in the HbSC/HbSβ+ group (P = 0.53). In the HbSS/HbSβ group, abnormal albuminuria occurred in 4 of 58 (6.9%) patients ages 2 to 6 years, 21 of 105 (20.0%) patients ages 7 to 12 years, and 35 of 98 (35.7%) patients ages 13 to 19 years (P = 0.0001).

The median ACR was higher in females than in males (median 12.0 mg/g versus 9.4 mg/g, P = 0.03). Abnormal albuminuria occurred more often in female patients (24.5% of females versus 17.3% of males); however, this did not reach statistical significance (relative risk 1.57, 95% confidence interval [CI] 0.97 to 2.54, P = 0.07). In females, urinary albumin was higher (median 8.6 mg in females versus 6.2 mg in males, P = 0.02), whereas urinary creatinine was not significantly different (median 78.0 mg in females versus 72.0 mg in males, P = 0.30), indicating that the higher prevalence of abnormal ACR in females was not due to lower creatinine. Because population studies have suggested that albumin excretion is greater in younger girls, possible interactions of gender and age were examined (21,22). In the 7- to 12-year age range, females had a higher frequency of abnormal albuminuria than males (26.3% versus 13.3%, P = 0.04); however, in age-stratified analysis, the effect of gender on abnormal albuminuria was NS (odds ratio 1.51, 95% CI 0.92 to 2.47), and there was no interaction between gender and age (Breslow–Day test, P = 0.39).

Hematologic values were obtained retrospectively in 360 patients, excluding 40 patients on chronic transfusion therapy and 10 patients with missing data. Complete blood count (CBC) values were measured on the same date as albuminuria testing in most patients and within 6 months

![Table 1. Patient characteristics of 410 children ages 2 to 21 years with sickle cell disease](image)

<table>
<thead>
<tr>
<th>Hematologic Parameters</th>
<th>HbSS, Sβ0 Thalassemia (n = 261)</th>
<th>HbSC, Sβ+ Thalassemia (n = 149)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>261</td>
<td>149</td>
</tr>
<tr>
<td>Age (years)</td>
<td>11.3 ± 4.6</td>
<td>11.5 ± 4.4</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>134/127</td>
<td>81/68</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>17.8 ± 4.1</td>
<td>19.7 ± 6.3</td>
</tr>
<tr>
<td>Chronic transfusion</td>
<td>39</td>
<td>1</td>
</tr>
<tr>
<td>Hydroxyurea (%)</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.46 ± 0.35</td>
<td>0.57 ± 0.17</td>
</tr>
</tbody>
</table>

Continuous variables are expressed as the mean ± 1 SD (range).

![Table 2. Comparison of age and baseline hematologic parameters in 410 sickle cell patients with and without abnormal albuminuria](image)

<table>
<thead>
<tr>
<th>Hematologic Parameters</th>
<th>Abnormal Albuminuria (≥30 mg/g)</th>
<th>Normal Albuminuria (&lt;30 mg/g)</th>
<th>P</th>
<th>Abnormal Albuminuria (≥30 mg/g)</th>
<th>Normal Albuminuria (&lt;30 mg/g)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>60 (23.0)</td>
<td>201 (77.0)</td>
<td>&lt;0.01</td>
<td>25 (16.8)</td>
<td>124 (83.2)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>13.5 ± 4.4</td>
<td>10.7 ± 4.5</td>
<td>&lt;0.01</td>
<td>12.0 ± 4.3</td>
<td>11.4 ± 4.4</td>
<td>0.53</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>27/33</td>
<td>107/94</td>
<td>0.26</td>
<td>10/15</td>
<td>71/53</td>
<td>0.11</td>
</tr>
<tr>
<td>Chronic transfusions (%)</td>
<td>11 (18.3)</td>
<td>28 (13.9)</td>
<td>0.40</td>
<td>0</td>
<td>1 (0.7)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hydroxyurea (%)</td>
<td>4 (6.7)</td>
<td>13 (6.5)</td>
<td>1.00</td>
<td>0</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>In patients not on chronic transfusions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC (10³/mm³)</td>
<td>11.3 ± 2.6</td>
<td>11.7 ± 3.8</td>
<td>0.31</td>
<td>8.6 ± 3.7</td>
<td>8.1 ± 3.3</td>
<td>0.52</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>8.17 ± 1.47</td>
<td>8.66 ± 1.40</td>
<td>0.04</td>
<td>11.51 ± 1.18</td>
<td>11.30 ± 1.26</td>
<td>0.45</td>
</tr>
<tr>
<td>ARC (10³/mm³)</td>
<td>277 ± 114</td>
<td>292 ± 121</td>
<td>0.43</td>
<td>123 ± 41</td>
<td>129 ± 56</td>
<td>0.48</td>
</tr>
<tr>
<td>platelets (10³/mm³)</td>
<td>427 ± 148</td>
<td>406 ± 127</td>
<td>0.38</td>
<td>288 ± 119</td>
<td>277 ± 117</td>
<td>0.69</td>
</tr>
</tbody>
</table>

Continuous variables are expressed as the mean ± 1 SD. NA, not applicable; WBC, white blood cell count; Hb, hemoglobin; ARC, absolute reticulocyte count.
of albuminuria testing in 90% of patients. In the HbSS/HbSβ group, patients with abnormal albuminuria had significantly lower baseline hemoglobin levels (8.17 versus 8.66 g/dl, \( P = 0.04 \)). In the HbSC/HbSβ⁺ group, no differences in hematologic values were observed between patients with and without abnormal albuminuria. Among chronically transfused HbSS patients, 11 of 39 (28.1%) had abnormal albuminuria, compared with 49 of 222 (22.1%) HbSS/HbSβ0 patients not on chronic transfusions (\( P = 0.40 \)).

Renal Insufficiency

Serum creatinine and height values were available to estimate GFR using the updated Schwartz formula in 190 patients (114 with HbSS/HbSβ and 76 with HbSC/HbSβ⁺); one patient with serum creatinine 0.1 mg/dl was excluded from eGFR estimation. Mean eGFR was 134 ± 39 ml/min per 1.73 m² (range 62 to 273 ml/min per 1.73 m²). Mean eGFR was higher in the HbSS/HbSβ0 group as compared with the HbSC/HbSβ⁺ group (148 ± 39 ml/min per 1.73 m² versus 115 ± 29 ml/min per 1.73 m², \( P < 0.0001 \)). eGFR correlated negatively with age (all patients: \( r = -0.23, P = 0.002 \); HbSS/HbSβ0 patients: \( r = -0.17, P = 0.08 \); HbSC/HbSβ⁺ patients: \( r = -0.29, P = 0.01 \), Figure 1).

Among HbSS patients, GFR correlated positively with ACR (\( r = 0.25, P = 0.007 \)), whereas no significant correlation of ACR and GFR was seen in HbSC/HbSβ⁺ patients (data not shown). In age-stratified analysis, the correlation of GFR with ACR was significant only among HbSS/HbSβ0 children over 6 years old (HbSS/HbSβ0 patients ages 7 to 12 years: \( r = 0.41, P = 0.005 \); ages 13 to 21 years: \( r = 0.30, P = 0.06 \).

CKD was present in 50 of 189 (26.5%) patients: 28 (14.8%) with stage 1 and 22 (11.6%) with stage 2. Characteristics of patients with and without CKD are shown in Table 3. CKD was more prevalent in the HbSC/HbSβ⁺ group (35.5% versus 20.3% in the HbSS/HbSβ0 group). Stage 1 CKD had a similar prevalence in HbSS/HbSβ0 and HbSC/HbSβ⁺ (15.0% and 14.5%, respectively), whereas stage 2 CKD was more prevalent in HbSC/HbSβ⁺ (21.1% versus 5.3% in HbSS/HbSβ0). In both groups, CKD was more prevalent in adolescents (Figure 2). In multivariable logistic regression analysis, CKD was associated with age (\( P = 0.003 \) and HbSC/HbSβ⁺ genotype (odds ratio 2.03 [95% CI 1.04 to 3.97]). Baseline hemoglobin, gender, and chronic transfusions were not significant determinants of CKD.

Discussion

This cohort is the largest study of albuminuria in pediatric SCD patients and is the first study to stage CKD in children with SCD. The significant decrease in GFR and increase in albuminuria with age support the hypothesis that sickle nephropathy is a progressive condition that begins during childhood. In HbSS/Sβ0 and HbSC/HbSβ⁺, GFR was found to decline during the first 2 decades of life. Abnormal albuminuria was more prevalent with older age in the HbSS/Sβ0 group but not in those with HbSC or HbSβ⁺ genotypes; however, stage 2 CKD was more prevalent in the HbSC/HbSβ⁺ patients. For HbSS/Sβ0 children who have higher GFR in early childhood, as GFR declines, a longer period of time is needed to reach GFR < 90 ml/min per 1.73 m² compared with HbSC/HbSβ⁺ patients, and fewer HbSS/Sβ0 patients will reach GFR < 90 ml/min per 1.73 m² during childhood and adolescence despite possibly earlier glomerular damage in HbSS/Sβ0. Thus, although stage 2 CKD may appear to be less prevalent in the HbSS/HbSβ0 group, if CKD were defined by the rate of decrease in GFR, the prevalence would likely be greater.

In the pediatric population, the best noninvasive estimation of GFR is the recently modified Schwartz formula. In previous studies of infants and children with SCD, the modified Schwartz formula has been compared with diethylenetriaminepentaacetic acid clearance, showing a positive correlation although wide variation (9,18). Although the Schwartz GFR correlates with measured GFR, it was derived for use in children with CKD and is known to overestimate GFR when compared with gold standard techniques (23). This positive bias likely is greater in children with SCD because of an above-normal proximal tubular secretion of creatinine and decreased muscle mass (3). Thus, our finding that the Schwartz eGFR was < 90 ml/min per 1.73 m² in 12% of patients may underestimate the number of children with renal insufficiency, and it may be more prudent to examine change in GFR over time to define stages of CKD in sickle cell nephropathy.

![Figure 1](image-url)

Figure 1. | Inverse correlation of estimated GFR with age in (A) HbSS/Sβ0 patients (\( r = -0.19, P = 0.048 \)) and (B) HbSC/HbSβ⁺ patients (\( r = -0.29, P = 0.01 \)).
The prevalence of abnormal albuminuria that we report is consistent with previous studies of albuminuria in smaller pediatric SCD cohorts. McKie et al. found abnormal albuminuria in 19.4% of 191 children with HbSS and observed a significant association of albuminuria with age and lower baseline hemoglobin (15). Alvarez et al. demonstrated abnormal albuminuria in 16.8% of HbSS children and 18% of HbSC children (24). In a smaller pediatric cohort, Becton et al. found abnormal albuminuria in 19.7% of children with HbSS but in 0 of 15 children with HbSC (17). The similar prevalence of albuminuria in these studies compared with our finding of abnormal albuminuria in 23.0% of HbSS/HbSβ0 and 16.8% of HbSC/HbSβ+ children suggests that there is no significant regional variability in albuminuria in the United States.

The findings of this study are limited by the cross-sectional design. Although our findings suggest that albuminuria (stage 1 CKD) and decreased GFR (stage 2 CKD or higher) develop and progress with age, without longitudinal follow-up of individuals, this does not distinguish transient versus persistent, progressive albuminuria. Among healthy children, transient albuminuria occurs at a prevalence as high as 7% (25). Alvarez et al. found that 13 of 38 (34%) children with SCD and ACR/Hb11022 > 30 mg/g had only intermittent albuminuria (16). McKie et al. found that 14 of 38 (34%) normoalbuminuric HbSS children developed abnormal albuminuria over a mean of 2.1 years (15). Thus, serial albuminuria testing is necessary to increase the specificity of detecting progressive glomerulopathy as opposed to transient changes.

In other clinical settings, elevated albuminuria is a marker of vascular damage and glomerulopathy. Modest elevations of ACR, even when <30 mg/g, are associated with cardiovascular disease and death in adults (26–28). The appropriate cutoff value for defining abnormal albuminuria is not known for pediatric SCD. Our study found

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| Table 3. Characteristics of 189 sickle cell patients with and without CKD |

<table>
<thead>
<tr>
<th>All Patients</th>
<th>No CKD</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>189</td>
<td>139 (73.5)</td>
<td>28 (14.8)</td>
<td>22 (11.6)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>11.7 ± 4.6 (2.5 to 21.7)</td>
<td>11.1 ± 4.4</td>
<td>13.1 ± 4.5</td>
<td>13.3 ± 5.3</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>97/92</td>
<td>72/67</td>
<td>10/18</td>
<td>15/7</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>19.1 ± 5.5 (11.5 to 59.4)</td>
<td>18.4 ± 4.2</td>
<td>22.1 ± 9.7</td>
<td>19.7 ± 4.5</td>
</tr>
<tr>
<td>HbSS/Sβ0 genotype (%)</td>
<td>113</td>
<td>90 (79.7)</td>
<td>17 (15.0)</td>
<td>6 (5.3)</td>
</tr>
<tr>
<td>HbSC/Sβ+ genotype (%)</td>
<td>76</td>
<td>49 (64.5)</td>
<td>11 (14.5)</td>
<td>16 (21.1)</td>
</tr>
<tr>
<td>Hb (g/dl) in HbSS/Sβ0</td>
<td>8.9 ± 1.5</td>
<td>8.9 ± 1.4</td>
<td>8.4 ± 1.4</td>
<td>9.9 ± 1.9</td>
</tr>
<tr>
<td>Hb (g/dl) in HbSC/Sβ+</td>
<td>11.5 ± 1.2</td>
<td>11.4 ± 1.0</td>
<td>11.3 ± 1.0</td>
<td>12.2 ± 1.7</td>
</tr>
<tr>
<td>Chronic transfusion therapy (%)</td>
<td>12</td>
<td>10 (83.3)</td>
<td>1 (8.3)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>Hydroxyurea therapy</td>
<td>9</td>
<td>8 (88.9)</td>
<td>0</td>
<td>1 (11.1)</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.48 ± 0.17 (0.2 to 1.2)</td>
<td>0.45 ± 0.13</td>
<td>0.44 ± 0.14</td>
<td>0.77 ± 0.15</td>
</tr>
</tbody>
</table>

Continuous variables are expressed as mean ± 1 SD (range). CKD, chronic kidney disease.

Figure 2. Prevalence and stages of chronic kidney disease (CKD) in HbSS/Sβ0 and HbSC/Sβ+. (A) In HbSS/Sβ0, CKD occurred in 11 of 73 (15.1%) children ages 2 to 12 years versus 12 of 40 (30%) children ages 13 to 21 years (P = 0.06). (B) In HbSC/Sβ+, CKD occurred in 11 of 41 (26.8%) children ages 2 to 12 years versus 16 of 35 (45.7%) children ages 13 to 21 years (P = 0.09).
that SCD children classified as normoalbuminuric have a mean ACR above the values reported for healthy children (29–31). In addition to the 85 patients (20.7%) with ACR > 30 mg/g, another 26 (6.3%) had ACR between 20 and 30 mg/g, which may represent early glomerular injury in this population. Although many children with SCD who have ACR < 30 mg/g are classified as normal, a mildly elevated ACR may indicate renal and glomerular endothelial dysfunction, a precursor to CKD.

CKD and albuminuria occur in children with all genotypes of SCD, with an increasing prevalence with age. Although abnormal albuminuria was greater in HbSS/HbSβ+-stage 2 CKD was more prevalent in HbSC/HbSβ+. A similar rate of decline in GFR with age was seen in HbSS/HbSβ+ and HbSC/HbSβ+. Because of hyperfiltration and a higher GFR in early childhood in HbSS/HbSβ+, we speculate that a longer period of time is needed to reach the low GFR level that defines stage 2 CKD. Future longitudinal studies are necessary to characterize the progression of CKD and albuminuria during childhood and to allow for earlier therapeutic intervention to decrease the morbidity and mortality of CKD in adulthood.

Disclosures

None.

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