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Growth in Children With Chronic Kidney Disease: A Report From the Chronic Kidney Disease in Children Study

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Abstract

Background—Growth failure is common among children with chronic kidney disease (CKD). We examined the relationship of growth parameters with glomerular filtration rate (GFR), CKD diagnosis, sex, and laboratory results in children with CKD.

Methods—Baseline data from 799 children (median age 11.0 years, median GFR 49.9 mL/min/1.73m²) participating in the Chronic Kidney Disease in Children Study were examined. Growth was quantified by age-sex-specific height, weight, body mass index (BMI-age), and height-age-sex-specific BMI (BMI-height-age) standard deviation scores (SDS).

Results—Median height and weight SDS were -0.55 (Inter-quartile Range (IQR): -1.35 to 0.19) and 0.03 (IQR: -0.82 to 0.97), respectively. Girls with non-glomerular CKD were the shortest (median height SDS -0.83 [IQR: -1.62, -0.02]). Compared to those with serum bicarbonate (CO₂) 22 mEq/L, children with CO₂ < 18 mEq/L had height SDS that was on average 0.67 lower (95% Confidence Interval (CI): -1.03 to -0.31). Only 23% of children with height SDS < -1.88 were prescribed growth hormone therapy. Forty-six and 32 percent of children with glomerular and non-glomerular CKD were overweight or obese (BMI-height-age 85th percentile).

Conclusions—Growth outcomes in a contemporary cohort of children with CKD remain suboptimal. Interventions targeting metabolic acidosis and overcoming barriers to rhGH usage may improve growth in this population.

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Keywords

Chronic kidney disease; children; growth; metabolic acidosis

Introduction

Severe growth impairment is highly prevalent among children with chronic kidney disease (CKD), occurring in as many as 35% of this population prior to reaching end stage renal disease [1-3]. Beyond facing serious psychosocial and medical challenges [4, 5], children with CKD complicated by severe growth failure experience excessive mortality [6, 7]. Specifically, children initiating dialysis with height < 1st percentile for age-sex had a two-fold higher risk of death than children with preserved height [8], emphasizing the importance of optimizing overall care and in turn, growth during the early stages of CKD. The etiology of growth failure in CKD is multi-factorial and includes age at CKD onset, residual renal function, metabolic derangements, renal osteodystrophy, and abnormalities of the growth hormone-insulin-like growth factor-1 axis [9-11]. The safety and efficacy of recombinant human growth hormone (rhGH) in children with CKD-associated growth failure is proven [12] and despite the availability of treatment guidelines [2], rhGH remains underutilized in this population [1]. The principle aim of this study was to both describe and identify clinical correlates of growth characteristics (height, weight, and body mass index) in a large cohort of children with mild to moderate CKD. To achieve this, we draw upon the baseline data from the Chronic Kidney Disease in Children (CKiD) Study.

Materials and Methods

Study Design and Population

From January 2005 through May 2013, 837 children with mild to moderate CKD have been enrolled in CKiD, a multicenter, prospective cohort study comprised of 53 tertiary care pediatric nephrology programs across the United States and Canada. Details of the CKiD Study design have been previously published [13]. The study design and conduct for CKiD was approved by an Institutional Review Board at each of the 53 participating centers. Height and weight were determined as the mean of two independent measurements via stadiometer and standing scale. Age-sex-specific height, weight, and body mass index (BMI-age) standard deviation scores (SDS) were calculated using CDC growth charts with US normative data [14]; SDS indicate the number of standard deviations the participant is above (positive SDS) or below (negative SDS) the expected mean value for their age and sex. Current clinical practice guidelines recommend that BMI be expressed relative to height-age in children with CKD [15]. Accordingly, height-age-sex-specific BMI (BMI-height-age) SDS was also calculated by using the age at which the child's observed height would be at the 50th percentile for height. For children with height deficits, height-age will be less than the true chronological age and therefore tend to yield BMI-height-age SDS greater than BMI-age SDS, particularly in children older than 5 years. Because the CDC provides height-ages for children 24 to 240 months old, when calculating BMI-height-age SDS scores we excluded 36 boys and 31 girls who had a height below the median for a 2 year old or above the median of a 20 year old for their gender. Pubertal (Tanner) stage was

obtained by physician assessment. Underlying CKD diagnosis was determined by the site nephrologist and reviewed and adjudicated by two members of the CKiD Steering Committee; duration of disease was obtained by parental report. Plasma disappearance of iohexol (GE Healthcare, Amersham Division, Princeton NJ) was used to measure GFR (iGFR), details of which have been previously published [16]. Serum bicarbonate (CO₂), phosphate, and albumin were centrally measured using an enzymatic method on the Bayer Advia 2400 analyzer (Siemens Diagnostics, Tarrytown, NY). Inflammation was assessed centrally via wide-range C-reactive protein (CRP). Complete blood counts were measured locally.

Of the 837 children enrolled between January 2005 and May 2013, baseline height SDS was missing in 15 (2%) children, and baseline weight SDS was missing in one child (<1%). In these cases, we used height and weight SDS from the next available visit. Furthermore, baseline iGFR could not be determined in 60 (8%) children; in these instances, we used published equations to estimate GFR [17]. This analysis includes 799 children (95%) who had data available for GFR, height SDS, and weight SDS. Our primary analyses of laboratory markers contained a total of 749 (94%) children who had complete data available on CO₂, hemoglobin, albumin, and phosphate. Data on laboratory markers at the second visit were used in place of missing data at the baseline visit in 109 (15% of 749) children. Because CRP was available in only 59% of participants, we did not include it in our primary multivariate analyses.

Statistical Analyses

Overall differences between two groups (>2 groups) with respect to median values of continuous characteristics were assessed using Wilcoxon rank sum tests (Kruskal-Wallis tests). The overall association between categorical variables was assessed using either Pearson X² tests or Fisher's Exact tests. Trends in median age-sex-specific height and weight SDS across age categories were assessed using the Jonckheere-Terpstra test. Linear regression was used to quantify the association between both age-sex-specific height and weight SDS and GFR in four sex-CKD diagnosis strata. Multivariable linear regression models were used to quantify the relationship age-sex-specific height and weight SDS had with laboratory markers of CO₂, hemoglobin, albumin, and phosphate, while controlling for sex, CKD diagnosis, recombinant human growth hormone usage, and GFR. Categorizations of laboratory markers were based on clinically relevant values. Two sided P-values < 0.05 were considered statistically significant.

Results

Cohort Characteristics

Demographic and clinical characteristics of the 799 children are shown in Table 1. The study population had a median age of 11.0 yrs; 63% were male, and 67% were Caucasian. The median baseline GFR was 49.9 mL/min/1.73m² (interquartile range [IQR]: 36.8 to 66.9). Non-glomerular diseases accounted for 75% of the underlying diagnoses (see footnote to Table 1 for CKD diagnoses), and the percentage of lifetime with CKD was greater in children with non-glomerular CKD (median of 99%) compared to children with glomerular

CKD (median of 30%). Compared with normative data from children living in the United States (US), CKiD participants were substantially shorter (median age-sex-specific SDS = -0.55; IQR: -1.35, 0.19); 12% exhibited severe short stature (age-sex-specific height SDS -1.88 [3rd percentile]). Parental heights of children in the CKiD cohort were comparable to parental heights in NHANES (maternal height was 163.9 cm (IQR: 158.8 to 167.5cm) in CKiD and 163.3 cm in NHANES; paternal height was 176.5 cm (IQR: 171.9 to 180.4 cm) in CKiD and 177.3 cm in NHANES). Though shorter, CKiD participants on average had normal weights for their age and sex (median age-sex-specific SDS = 0.03, IQR: -0.82, 0.97), resulting in increased BMI-age (median SDS= 0.46, IQR: -0.35, 1.33); 15% were overweight (BMI-age percentile 85 to <95), and 18% were obese (BMI-age percentile 95). Based upon BMI-height-age (median SDS=0.56, IQR: -0.19, 1.43), 17% and 20% were overweight and obese, respectively. Edema was present in 8 (1%) children with non-glomerular disease and in 23 (11%) of those with glomerular disease ($P<0.001$).

Age-Sex-Specific Height and Weight SDS by Sex and Age

Descriptive statistics for age-sex-specific height SDS by sex and eight age strata are displayed in Table 2. Overall, females (median height SDS: -0.68, IQR: -1.46 to 0.13) had a greater height deficit than males (median: -0.49, IQR: -1.30 to 0.24), though the difference was not statistically significant ($P= 0.065$). Males <5 years of age had significantly greater height deficit than males 5 years (median height SDS= -0.71 vs -0.44; $P= 0.029$). Among females, there was no trend across age strata.

Table 3 shows descriptive statistics for age-sex-specific weight SDS by sex and age. Overall, males (median: 0.06, IQR: -0.78 to 0.95) and females (median: -0.06, IQR: -0.92 to 0.97) had similar weight SDS; they differed significantly only between 9 and <11 years of age. Higher weight SDS was associated with older ages among both males ($P_{\text{trend}} < 0.001$) and females ($P_{\text{trend}} < 0.001$).

Age-sex-specific Height SDS by Primary CKD Diagnosis and Renal Function

Compared to children with non-glomerular CKD, the median age-sex-specific height SDS of children with glomerular CKD indicated significantly less deficit (-0.33 vs -0.62; $P= 0.003$). The median age-sex-specific height SDS of females with glomerular disease (-0.25, IQR: -1.06 to 0.58), males with glomerular disease (-0.49, IQR: -1.14 to 0.35) and males with non-glomerular disease (-0.49, IQR: -1.33 to 0.22) were similar ($P= 0.150$). The median age-sex-specific height SDS of females with non-glomerular CKD (-0.83, IQR: -1.62 to -0.02) was significantly lower than each of the other three groups ($P < 0.001$).

Given poorer growth noted among children with non-glomerular CKD, particularly girls within this group, we analyzed the relationship between GFR and age-sex-specific height SDS by both CKD diagnosis and sex. Among those with glomerular CKD, each 10 mL/min per 1.73 m² decrease in GFR was associated with a 0.12 (95% CI: 0.04 to 0.20) lower age-sex-specific height SDS in 112 males and a 0.16 (95% CI: 0.07 to 0.26) lower age-sex-specific height SDS in 91 females. Similarly, in the 393 males and 203 females with non-glomerular CKD, a 10 mL/min per 1.73 m² decrease in GFR was associated with an average decrease in height SDS of 0.14 (95% CI: 0.09 to 0.19) and 0.12 SDS (95% CI: 0.05 to 0.20),

respectively. Hence, the effect of GFR on age-sex-specific height SDS was similar in all four sex-CKD diagnosis strata.

Weight and BMI SDS by Primary CKD Diagnosis and Renal Function

Compared to children with non-glomerular CKD, the median age-sex-specific weight SDS of children with glomerular CKD was significantly higher (0.53 vs. -0.13; $P<0.001$); this relationship was observed in both boys (0.24 vs. -0.05; $P<0.001$) and girls (0.63 vs. -0.32, $P<0.001$). Expressed as BMI-age, 18% of children with glomerular CKD were overweight and 27% were obese (median SDS= 0.91, IQR: -0.10, 1.73), both higher than the corresponding percentages observed in children with non-glomerular CKD (15% overweight and 15% obese; median SDS= 0.31, IQR: -0.41, 1.19). Expressed as BMI-height-age, 17% and 29% of children with glomerular CKD (median SDS= 0.88, IQR: 0.18, 1.76) and 16% and 16% of children with non-glomerular CKD (median SDS= 0.46, IQR: -0.26, 1.29) were overweight and obese, respectively. Given the trend of increased weight SDS with older age in this cohort and the expected changes in body composition during childhood (BMI declining after birth and generally increasing after age 5 years), we examined BMI-height-age of children >5 years of age; 18% and 29% of children with glomerular CKD (N=174; median SDS= 0.88, IQR: 0.18, 1.76) and 17% and 18% of children with non-glomerular CKD (N=465; median SDS= 0.49, IQR: -0.25, 1.37) were overweight and obese, respectively.

We analyzed the relationship between GFR and age-sex-specific weight SDS by both CKD diagnosis and sex. Each 10 mL/min/1.73 m² decrease in GFR was associated with lower weight SDS in males (0.09 SDS lower; 95% CI: -0.01 to 0.20) and females (0.15 SDS lower; 95% CI: 0.04 to 0.27) with glomerular CKD as well as in males (0.13 SDS lower; 95% CI: 0.07 to 0.19) and females (0.13 SDS lower; 95% CI: 0.05 to 0.22) with non-glomerular CKD. There was no significant effect modification of CKD etiology or sex on the relationship between GFR and weight SDS.

Usage of rhGH, Steroids, and Enteral Feeding

Nine percent of the entire cohort and 23% of children with severe short stature (< 3rd percentile for height) were prescribed rhGH. Among children with non-glomerular disease, the percentage of girls (11%) and boys (11%) prescribed rhGH was similar. Likewise, the percentage of girls (4%) and boys (3%) with glomerular CKD who were prescribed rhGH was similar. When compared to children with glomerular disease, children with non-glomerular CKD were significantly more likely to be prescribed rhGH ($P<0.001$). Of children with severe short stature, the percentage prescribed rhGH was similar between girls (23%) and boys (24%). Furthermore, the percentage of children with severe short stature prescribed rhGH was similar among glomerular and non-glomerular groups, regardless of gender ($P=0.569$).

Within 30 days of the baseline visit, prescribed steroids were taken in 27% of children with glomerular CKD compared with 1% of children with non-glomerular diagnoses ($P<0.001$). Among those with glomerular CKD, the median height SDS of children who were prescribed steroids daily (-0.28, IQR: -0.69, 0.90; N=29), less than daily (-0.11, IQR: -1.06,

0.51; N=26), and not prescribed steroids (-0.46, IQR: -1.18, 0.24; N=148) was similar ($P=0.348$). The median weight SDS among glomerular children who took prescribed steroids daily, less than daily, and not prescribed steroids was 1.07 (IQR: 0.04, 2.23), 1.18 (IQR: 0.19, 2.10), and 0.28 (IQR: -0.43, 1.38), respectively. Glomerular children who took prescribed steroids, daily or less than daily, had significantly higher weights than children who were not prescribed steroids ($P=0.007$).

Four percent of the cohort were provided enteral feeding at baseline, and there was no significant difference in enteral feeding by diagnosis or gender. Surprisingly, of the children receiving enteral feedings, only 17% were under 3 years of age and 31% were under 5 years of age. Those receiving enteral feeding experienced significantly greater deficits in both height ($p<0.001$) and weight ($p<0.001$) SDS. Specifically, children on enteral feedings had median height and weight SDS of -1.34 (-2.00, -0.44) and -0.86 (-2.06, 0.22) respectively, whereas children that were not receiving enteral feedings had a median height and weight SDS of -0.52 (-1.31, 0.23) and 0.05 (-0.77, 0.98), respectively.

Age-sex-specific Height and Weight SDS and Laboratory Parameters

Using two multivariate linear regression models, we quantified the relationship that age-sex-specific height SDS and weight SDS had with serum CO₂, hemoglobin, albumin, and phosphate while controlling for sex, CKD diagnosis, rhGH usage, and GFR (Table 4). Baseline growth characteristics were worse in children with metabolic acidosis. Specifically, children with serum CO₂ < 18 mEq/L had height and weight SDS that were on average 0.67 (95% CI: 0.31 to 1.03) and 0.40 lower (95% CI: -0.02 to 0.81), respectively, than children with serum CO₂ ≥ 22 mEq/L. Children with serum CO₂ < 18 mEq/L had an average height SDS that was significantly lower than children with CO₂ ≥ 18 to <22 mEq/L ($p=0.006$), but there was no significant difference in weight. Anemia, low serum albumin, and elevated serum phosphate were not significantly associated with height or weight SDS. In two multivariate analyses that included CRP and all of the variables included in Table 4, among the 443 children with CRP data available, we did not find any significant differences in height and weight SDS in children with CRP >10mg/L compared to children with CRP ≤ 10mg/L (normal range). Only 1% of the cohort had hyponatremia (serum Na <135 mEq/L) and therefore serum sodium was not included in this analysis.

Discussion

The CKiD patient population is particularly well studied with measured GFR, accurate evaluation of height and weight, and regular metabolic assessments. As such, they have provided the opportunity to expand on the data pertaining to growth in patients with CKD that has previously been published. Deficits in height were a frequent finding among our large cohort of North American children with mild to moderate CKD. Twelve percent of the children in this analysis had severe short stature (height SDS ≤ -1.88) at the time of their baseline CKiD visit. Though alarming, this compares favorably with the linear growth of children enrolled in the NAPRTCS chronic renal insufficiency registry during the decade preceding January 2004 when 31% of children with an estimated GFR >25 mL/min/1.73 m² had a height SDS < -1.88 [18].

Previous studies have identified children with CKD during infancy and early childhood to be particularly vulnerable to growth failure [18, 19], and a recent study has demonstrated abnormal birth history to be associated with poorer growth in children with both glomerular and non-glomerular disease [20]. In the CKiD cohort, children with non-glomerular disease, encompassing congenital disorders of the genitourinary tract, had lower height and weight SDS than children with glomerular disease; this outcome likely reflects the longer duration of disease experienced by children with non-glomerular disease. Older age was associated with improved height outcomes among boys, but not among girls. In fact, although gender has not previously been associated with worse growth outcomes [18, 21], our results identified gender as an important correlate of baseline growth; girls with non-glomerular disease proved to be the most severely impacted with respect to linear growth. The overall difference in stature we noted between children with glomerular and non-glomerular CKD was, in fact, due to the greater deficit in stature of girls with non-glomerular CKD. The factors associated with worse height outcomes in these girls is unclear. Girls with non-glomerular CKD and severe short stature did not have a higher prevalence of moderate to severe metabolic acidosis or a lower percentage prescribed rhGH than other children with severe short stature; because only 12% of the cohort had severe short stature it was difficult to better explain these null findings. Though the percentage of girls and boys with non-glomerular disease prescribed rhGH was similar, adherence among these girls may have been lower given societal acceptance and potential subjective satisfaction of shorter stature among girls. When adherence to rhGH was examined in children with primarily non-CKD related growth disorders (< %5 with CKD), adherence was found to be significantly better among boys in one study [22] but not different among genders in another [23]. It is notable that the height of boys with non-glomerular disease was comparable to children with glomerular disease, despite the significantly longer duration of disease experienced by these boys. This finding may be, in part, attributable to a higher percentage of boys with non-glomerular disease prescribed rhGH (11%) when compared to children with glomerular disease (3-4%).

Consistent with previous studies, our results demonstrate the level of estimated renal function to be an important independent variable correlating with growth outcomes in children with CKD [18, 24, 25]. What has not previously been published is our finding that for each 10/mL/min/1.73m² decrease in GFR, there was an average decrease of 0.14 SDS in height for the overall cohort (and an average decrease of 0.12 SDS after excluding those who were prescribed rhGH); the quantification of this association will be further studied longitudinally in the CKiD cohort.

A recent analysis of the CKiD cohort identified participants with mild-moderate CKD to be at increased risk for a variety of laboratory abnormalities, including metabolic acidosis [25]. Among children with normal renal function and renal tubular acidosis, metabolic acidosis has been clearly associated with growth retardation, which improved with alkali therapy [26, 27]. The current National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines recommend providing alkali supplementation to maintain serum CO₂ 20 mEq/L among children less than two years old and 22 mEq/L in children older than two years [14]. Multivariate analysis of the NAPRTCS database did not reveal an association between metabolic acidosis and severe growth delay [18]. In contrast, although mild metabolic

acidosis (CO_2 18 to < 22 mEq/L) was not associated with worse growth outcomes in CKiD, moderate to severe metabolic acidosis (CO_2 <18 mEq/L) was associated with a significantly lower height SDS. The association of metabolic acidosis and poorer height outcomes found in CKiD but not in NAPRTCs may be due to differences in data analysis, particularly with respect to the height outcome chosen. The NAPRTCs study evaluated the association of metabolic acidosis and severe short stature (height SDS < -1.88) a binary outcome, whereas our analysis evaluated the effect of metabolic acidosis on height SDS treated as a continuous outcome. Remarkably, two thirds of children in this analysis who presented with serum CO_2 < 18 mEq/L were not prescribed alkali supplements. Our data would predict significant growth benefits of this inexpensive and easily administered therapy. Though milder degrees of metabolic acidosis were not associated with significant differences in baseline growth, the potential for other negative consequences of metabolic acidosis, including bone disease and more progressive decline in renal function, must be considered [28].

It is notable that 77% of children in CKiD with severe short stature were not prescribed rhGH at their baseline visit despite studies demonstrating efficacy [12, 29, 30], the availability of published guidelines [2], and treatment that was provided at academic medical centers. A prior multicenter study of children with CKD and height below the 5th percentile demonstrated that boys were twice as likely as girls to be treated with rhGH [31], while in our cohort, an equal proportion of girls and boys with severe short stature were prescribed rhGH. Obstacles to rhGH usage include medical and psychosocial factors with secondary hyperparathyroidism, family refusal, and non-compliance being among the most commonly reported [31]. Self-reported nonadherence to rhGH, as defined by missing at least one dose within 7 days, was 25% among the CKiD cohort [32]. Furthermore, the challenges of obtaining insurance approval and anticipation of pre-emptive transplantation may result in significant delay or failure of initiation of rhGH therapy. A recent study has demonstrated height gains and rhGH use to be associated with significant improvements in parent-reported physical and social functioning of children with CKD, and these results may facilitate parental acceptance of this therapy [33]. Analysis of practice patterns of pediatric nephrologists pertaining to the assessment and treatment of growth delay is currently being conducted by CKiD and may identify opportunities to increase appropriate utilization of rhGH.

Anemia has been associated with shorter stature in children with CKD, though data is limited and controversial [3, 18]. The data obtained from our large patient cohort did not reveal an association between anemia and poor growth, largely negating any further consideration of any such correlation in patients with only mild anemia. Consistent with other reports, multivariate analysis of serum albumin, phosphate, and CRP also revealed no association with baseline growth outcomes in the CKiD cohort [3, 18, 24]

Relative to deficits of stature, the weight of children participating in CKiD was generally preserved, a finding consistent with previous reports describing growth outcomes in children with CKD [34, 35]. This analysis identified weight to be significantly associated with underlying CKD diagnosis, whereby the median weight SDS of children with glomerular CKD was higher than expected for their age and sex and significantly higher than the weight

SDS of children with non-glomerular disease. The disproportionate effect on growth parameters was associated with a high prevalence of elevated BMI-age, a known risk factor for cardiovascular disease [36] and future end-stage renal disease [37]. Thirty three percent of the CKiD cohort was overweight or obese, similar to the prevalence reported in children and adolescents in the general population of the US [38], and nearly half of the children with glomerular disease were overweight (18%) or obese (27%). BMI varies with age and pubertal status, increasing in normal children after age five years due to changes in body composition and proportions. Children with CKD are short and sexually immature [25], and thus guidelines recommend that BMI might best be expressed relative to height-age in children in this population [15]. It has been suggested that this measure more effectively compares children with CKD to healthy children of the same height and stage of sexual development [39]. The median BMI-age and BMI-height-age SDS of children with glomerular disease was similar (0.91 vs 0.88), though the latter was higher in children with nonglomerular disease (0.31 vs 0.46) which has not been previously reported. The difference likely relates to the longer duration of disease and shorter stature of children with nonglomerular disease. There are, of course, limitations to using BMI-height-age as an assessment of growth in children, such as when short stature is disproportionate to the degree of delay in sexual maturation or when sexual maturation is complete. In addition, BMI-height-age has not been adequately studied in children with CKD who are less than 5 years of age.

The shorter duration of CKD and higher prevalence of edema may be factors associated with the higher frequency of increased weight seen in children with glomerular disease when compared to children with non-glomerular disease. Data regarding steroid therapy, prescribed more frequently in children with glomerular disease, accounted for treatment within 30 days of the baseline visit and not prior therapy. This limitation precludes a valid assessment of the association of steroid usage and growth in this cohort, though this therapy was associated with significantly greater weight among children with glomerular disease. Data regarding dietary intake was not available.

Though this analysis of growth outcomes of the CKiD cohort has numerous strengths, including cohort size and accurate measurements of growth parameters and GFR, limitations must be acknowledged. This is a cross-sectional analysis, and the longitudinal study of this cohort will be of great import to determine clinical correlates of abnormal growth and to identify potential interventions. The population enrolled may differ from the general population of children with CKD and subject the data to selection bias. Furthermore, nutritional intake was not available for analysis and may limit the generalizability of these findings.

In summary, growth abnormalities were highly prevalent in the CKiD cohort, including a high prevalence of overweight and obesity among children with glomerular disease. Poorer linear growth was associated with moderate to severe metabolic acidosis, and the majority of children with this degree of acidosis were not on alkali therapy. Furthermore, less than 25% of children with severe short stature were prescribed rhGH. One would predict that greater utilization of alkali therapy and rhGH to address two modifiable risk factors for growth impairment could yield improved growth outcomes. This is the first report to provide a

quantitative relationship between decrement in GFR and negative impact on height outcomes. Longitudinal follow-up of the CKiD cohort will permit further evaluation of this important CKD related parameter.

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Table 1
Baseline characteristics, n=799

Characteristic	% or Median (IQR)
Male	63%
Age, years	11.0 (7.6 to 14.6)
Race	
Caucasian	67%
African American	17%
Other	8%
More than one race	8%
Hispanic Ethnicity ^a	14%
Tanner Stage ^a	
Stage I	56%
Stage II	10%
Stage III	9%
Stage IV	15%
Stage V	10%
Age-sex-specific Height SDS ^b	-0.55 (-1.35 to 0.19)
Age-sex-specific Weight SDS ^b	0.03 (-0.82 to 0.97)
Age-sex-specific Body Mass Index SDS ^{a,b}	0.46 (-0.35 to 1.33)
Height-age-sex-specific Body Mass Index SDS ^{a,b}	0.56 (-0.19 to 1.43)
GFR, mL/min per 1.73 m ²	49.9 (36.8 to 66.9)
Glomerular CKD Diagnosis ^c Duration of CKD among Glomerular children ^a , yrs	25% 3.5 (1.5 to 6.5)
% of life with CKD ^a	30% (12% to 60%)
Non-Glomerular CKD Diagnosis ^d Duration of CKD among Non-Glomerular children ^a , yrs	75% 7.1 (3.5 to 10.8)
% of life with CKD ^a	99% (63% to 100%)
Growth hormone use	9%
Of 98 with a age-sex-specific height SDS <-1.88	23%
Corticosteroid use	8%

^aHispanic ethnicity data missing for 11 children, Tanner Stage missing for 11 children, age-sex-height-specific body mass index SDS missing for 67 children, CKD duration missing for 7 children with glomerular CKD and 13 children with non-glomerular CKD.

^bAge-sex-specific and age-sex-height-specific SDS using CDC growth charts with US normative data.

^cGlomerular diagnoses (N=203): focal segmental glomerulosclerosis (31%), hemolytic uremic syndrome (19%), systemic immunological disease (10%), familial nephritis (7%), chronic glomerulonephritis (7%), other (26%).

^dNon-glomerular diagnoses (N=596): obstructive uropathy (24%), aplastic/hypoplastic/dysplastic kidneys (23%), reflux nephropathy (19%), polycystic kidney disease (autosomal recessive) (4%), renal infarction (4%) other (26%).

Table 2
Median and inter-quartile range of baseline age-sex-specific height SDS by sex and eight different age strata among 799 CKiD study participants

Age	Males (N= 505)		Females (N= 294)	
	N (%)	Height SDS	N (%)	Height SDS
1 - < 3	28 (6%)	-0.71 (-1.46, -0.21)	15 (5%)	-0.63 (-1.42, 0.13)
3 - <5	54 (11%)	-0.75 (-1.48, -0.03)	17 (6%)	-0.28 (-1.25, 0.16)
5 - <7	44 (9%)	-0.56 (-1.42, 0.04)	26 (9%)	-1.16 (-1.82, -0.68)
7 - <9	64 (13%)	-0.57 (-1.50, 0.29)	37 (13%)	-0.83 (-1.31, -0.26)
9 - <11	67 (13%)	-0.36 (-1.18, 0.32)	47 (16%)	-0.78 (-1.63, -0.05)
11 - <13	65 (13%)	-0.59 (-1.31, 0.06)	39 (13%)	-0.76 (-1.67, 0.76)
13 - <15	78 (15%)	-0.26 (-1.18, 0.69)	50 (17%)	-0.63 (-1.65, 0.17)
15 - <18	105 (21%)	-0.36 (-1.00, 0.25)	63 (21%)	-0.31 (-1.06, 0.47)
Overall	505 (100%)	-0.49 (01.30, 0.24)	294 (100%)	-0.68 (-1.46, 0.13)

Table 3
Median and inter-quartile range of baseline age-sex-specific weight SDS by sex and eight different age strata among 799 CKiD study participants

Age	Males (N=505)		Females (N=294)	
	N (%)	Weight SDS	N (%)	Weight SDS
1 - < 3	28 (6%)	-0.84 (-1.62, -0.19)	15 (5%)	-0.75 (-1.69, 0.20)
3 - <5	54 (11%)	-0.18 (-0.80, 0.59)	17 (6%)	-0.20 (-0.78, 0.03)
5 - <7	44 (9%)	-0.45 (-1.05, 0.15)	26 (9%)	-0.98 (-1.32, 0.57)
7 - <9	64 (13%)	0.21 (-0.94, 1.24)	37 (13%)	-0.13 (-0.56, 0.78)
9 - <11	67 (13%)	0.21 (-0.53, 1.16)	47 (16%)	-0.29 (-1.03, 0.62)
11 - <13	65 (13%)	0.09 (-0.67, 0.88)	39 (13%)	0.04 (-1.22, 1.28)
13 - <15	78 (15%)	0.22 (-0.88, 1.24)	50 (17%)	0.69 (-0.43, 1.39)
15 - <18	105 (21%)	0.22 (-0.35, 1.05)	63 (21%)	0.11 (-0.48, 1.38)
Overall	505 (100%)	0.06 (-0.78, 0.95)	294 (100%)	-0.06 (-0.92, 0.97)

Table 4

Multivariate Baseline Relationships of age-sex-specific height and weight SDS with carbon dioxide, hemoglobin, albumin, and phosphate in 749 children in the CKiD study; controlling for sex, CKD diagnosis, recombinant human growth hormone usage and GFR.

Characteristic	N (%)	Average Effect (95% CI) on age-sex-specific height SDS	Average Effect (95% CI) on age-sex-specific weight SDS
Carbon Dioxide			
< 18 mEq/L	40 (5%)	-0.67 (-1.03, -0.31)	-0.40 (-0.81, 0.02)
18 to < 22 mEq/L	158 (21%)	-0.14 (-0.34, 0.05)	-0.08 (-0.31, 0.15)
22 mEq/L	551 (74%)	0 (reference)	0 (reference)
Hemoglobin			
< 10 g/dL	26 (3%)	-0.18 (-0.62, 0.26)	-0.10 (-0.61, 0.41)
10 to < 12 g/dL	199 (27%)	-0.15 (-0.34, 0.04)	-0.26 (-0.48, -0.05)
12 g/dL	524 (70%)	0 (reference)	0 (reference)
Albumin			
< 3 g/dL	22 (3%)	-0.18 (-0.66, 0.31)	-0.15 (-0.71, 0.42)
3 g/dL	727 (97%)	0 (reference)	0 (reference)
Phosphate ^a			
Elevated	116 (15%)	0.00 (-0.23, 0.22)	0.11 (-0.15, 0.37)
Not Elevated	633 (85%)	0 (reference)	0 (reference)

^aElevated phosphate levels are age-based as follows:

1 to 5 years of age : > 6.5 mg/dL

6 to 12 years of age : > 5.8 mg/dL

13 to 20 years of age: > 4.5 mg/dL