Published in final edited form as:
Hypertension. 2008 October ; 52(4): 631–637. doi:10.1161/HYPERTENSIONAHA.108.110635.

Blood Pressure in Children with Chronic Kidney Disease: A Report from the Chronic Kidney Disease in Children Study

Joseph T Flynn[1], **Mark Mitsnefes**[2], **Christopher Pierce**[3], **Steven R Cole**[3], **Rulan S Parekh**[4], **Susan L Furth**[4], **Bradley A Warady**[5], and **for the CKiD Study Group**[6]

[1]Children's Hospital and Regional Medical Center, Seattle, WA

[2]Children's Hospital Medical Center, Cincinnati, OH

[3]Johns Hopkins University School of Public Health, Baltimore, MD

[4]Johns Hopkins University School of Medicine, Baltimore, MD

[5]Children's Mercy Hospital, Kansas City, MO

Abstract

To characterize the distribution of blood pressure (BP), prevalence and risk factors for hypertension in pediatric chronic kidney disease (CKD), we conducted a cross-sectional analysis of baseline BP's in 432 children (mean age 11y; 60% male; mean glomerular filtration rate [GFR] 44 ml/min/1.73m^2) enrolled in the Chronic Kidney Disease in Children cohort study. BP's were obtained using an aneroid sphygmomanometer. GFR was measured by iohexol disappearance. Elevated BP was defined as BP≥90th percentile for age, gender and height. Hypertension was defined as BP≥95th percentile or as self-reported hypertension plus current treatment with antihypertensive medications.

For systolic BP, 14% were hypertensive and 11% were pre-hypertensive (BP 90-95th percentile); 68% of subjects with elevated SBP were taking antihypertensive medications. For diastolic BP, 14% were hypertensive, and 9% were pre-hypertensive; 53% of subjects with elevated DBP were taking antihypertensive medications. 54% of subjects had either systolic or diastolic BP≥95th percentile or a history of hypertension plus current antihypertensive use.

Characteristics associated with elevated BP included black race, shorter duration of CKD, absence of antihypertensive medication use, and elevated serum potassium. Among subjects receiving antihypertensive treatment, uncontrolled BP was associated with male sex, shorter CKD duration and absence of ACE inhibitor or ARB use.

37% of children with CKD had either elevated systolic or diastolic BP, and 39% of these were not receiving antihypertensives, indicating that hypertension in pediatric CKD may be frequently under- or even un-treated. Treatment with ACE inhibitors or ARB's may improve BP control in these patients.

Keywords

kidney disease; children; adolescents; hypertension; blood pressure; ACE inhibitors

Address for correspondence: Joseph T. Flynn, MD. MS, Division of Nephrology, A-7931, Children's Hospital & Regional Medical Center, 4800 Sand Point Way NE, Seattle, WA 98105, Phone: 206.987.2524, Fax : 206.987.2636, joseph.flynn@seattlechildrens.org.
[6]please see http://hyper.ahajournals.org

Conflicts of interest: None

Introduction

Few studies have characterized the prevalence of hypertension or quantified the association between the degree of hypertension and progressive kidney damage in children. Data from the 2006 report of the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) reveal that 39% of children enrolled in its chronic renal insufficiency registry since its inception were being treated with anti-hypertensive medications at enrollment[1]. The prevalence of hypertension in children with CKD may be underestimated in this report due to the lack of a blood pressure (BP)-based definition of hypertension and standardized BP measurements. Indeed, an earlier analysis of BP in the NAPRTCS database estimated the prevalence of hypertension among children with CKD as being closer to 50%[2], and demonstrated that renal function in hypertensive children with CKD deteriorated significantly more rapidly than in normotensive children. These data suggest that a significant level of untreated hypertension is present in pediatric patients with CKD and raises the possibility that improved BP control may be one method of slowing the progression of CKD in this population.

We examined baseline BP data collected on participants in the Chronic Kidney Disease in Children (CKiD) Study, a multi-center observational cohort study currently underway in the United States and Canada. We had two specific aims in the present analysis: 1) to describe the distribution of BP, hypertension and antihypertensive medication use in a large cohort of children with CKD; and 2) to identify demographic and clinical characteristics associated with elevated BP or uncontrolled blood pressure in this population.

Methods

Study Population and Design

The CKiD study is an observational cohort study of CKD in children being conducted at 43 pediatric nephrology centers in North America in response to National Institutes of Health RFA DK-03-012 entitled “Prospective Study of Chronic Kidney Disease in Children”[3,4]. The CKiD study protocol has been reviewed and approved by the Institutional Review Boards of each participating center (For list of participating centers and investigators please see http://hyper.ahajournals.org, Table S1).

Eligibility criteria for enrollment in CKiD include: age 1-16 years, estimated Schwartz formula[5] GFR 30 – 90 ml/min/1.73m^2, and signed written informed consent by a parent or guardian, plus signed assent according to local requirements. Exclusion criteria include: solid organ, bone marrow or stem cell transplant, dialysis within the 3 months prior to enrollment, cancer/leukemia or HIV treatment within the past year, pregnancy within the past year, inability to complete protocol procedures, enrollment in a randomized clinical trial in which treatment is masked, or plans to move away from the participating center in the near future.

The present study is a cross-sectional analysis of baseline information for the first 432 children enrolled in CKiD as of February 2008 with complete demographic information, medical history (hypertension history, antihypertensive medication use, and CKD etiology), and measured iohexol GFR and BP.

Measurements

Blood Pressure—CKiD participants have casual BP measurements obtained in the right arm by auscultation at study entry (baseline), then annually thereafter. All participating sites have been provided the same aneroid sphygmomanometer (Mabis MedicKit 5, Mabis Healthcare, Waukegan, IL) by the CKiD Clinical Coordinating Centers (CCC's). The CCC's

also provide standardized training and certification in the auscultatory BP measurement protocol described below to all study personnel responsible for casual BP measurement. Recertification in auscultatory BP measurement technique and calibration of each center's aneroid device takes place annually.

At each study visit, prior to BP determination, arm circumference is measured (in centimeters) with a plastic measuring tape at the midpoint of the upper arm between the amicron and olecranon and a cuff is then selected so that the length of the cuff bladder is equal to 80-100% of the arm circumference[6]. Following cuff selection, the peak inflation pressure is determined by inflating the cuff to 60 mmHg and then gradually continuing to inflate in increments of 10 mmHg until the radial pulse is no longer felt – thereby determining the pulse obliteration pressure. An additional 30 mmHg is added to this value and recorded as the peak inflation pressure. The cuff is then inflated to this value for all BP measurements at that study visit.

After 5 minutes of rest, BP measurement begins. Participants are instructed to refrain from caffeine intake, smoking, and exercise at least one half hour prior to and until completion of BP measurement. They are also instructed to refrain from playing video games, using a cell phone, or other activities that may affect BP until all measurements are obtained. First, pulse is measured by palpation of the radial artery. Then three BP measurements at 30-second intervals are obtained by auscultation of the brachial artery, using the first Korotkoff sound for systolic BP (SBP) and the fifth Korotkoff sound for diastolic BP (DBP). The average of the 3 BP measurements is recorded as the participant's BP for the study visit. Participants' BP's so obtained at the baseline visit are included in the present study.

Other variables—GFR was determined by plasma iohexol disappearance curves with four time points at 10, 30, 120, and 300 minutes after infusion of 5 mL of iohexol; details of the GFR assessment methods have been previously published[7].

Blood and urine samples are collected at the time of the study visit and analyzed at the central laboratory (University of Rochester, Rochester, NY). Biochemical parameters in this analysis include electrolytes, BUN, serum creatinine, serum albumin, urine protein and urine creatinine. In addition, a complete blood count is obtained locally.

Demographic and medical history information is collected at the baseline study visit using standardized forms. Variables of interest for this analysis include age, gender, self-reported race/ethnicity, height, weight, underlying CKD diagnosis (please see http://hyper.ahajournals.org, Table S2), CKD duration, history of hypertension, use of antihypertensive medications, birth history, and family history of hypertension. From this information, other variables of interest were calculated, including body mass index (BMI) and age and gender-specific height, weight and BMI percentiles using standard growth charts for United States children[8].

Definitions—Participant's BP's in CKiD are classified according to the National High Blood Pressure Education Program (NHBPEP) Fourth Report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents[6]: BP readings <90th percentile are categorized as *normotensive*, those ≥90th and <95th percentiles *as pre-hypertensive*, and those ≥95th percentile as *hypertensive*. Measurements in the pre-hypertensive and hypertensive range are defined as *elevated blood pressure*.

The presence of *hypertension* was defined as having hypertensive range BP (systolic or diastolic) or a self-report of a history of high BP plus current treatment with antihypertensive medications. Additionally, *controlled blood pressure* was defined as a

current use of antihypertensive medication, with BP below the 90th percentile and a self-reported history of hypertension; *uncontrolled blood pressure* was defined as BP (systolic or diastolic) ≥90th percentile and current use of antihypertensive medication.

For all analyses, participants are classified as having either glomerular or non-glomerular CKD (see Appendix). Obesity is defined as BMI ≥95th percentile for age and gender[8]. Low birth weight is birth weight <2500g and birth at <36 weeks gestation is defined as being premature. Nephrotic-range proteinuria is defined as a calculated urine protein:creatinine ratio (Up/c) of >2.0 (mg/dL:mg/dL); significant proteinuria as a calculated Up/c of 0.2-2.0. Hypoalbuminemia is defined as a serum albumin level of <4 g/dL.

Statistical analysis—Continuous variables in this report are described as means and standard deviations; categorical variables are described as frequencies and percentages. To assess the relationship of clinical and demographic characteristics with measured BP, means and standard deviations for continuous variables as well as percentages and frequencies for categorical variables were calculated for each level of BP – normotensive, pre-hypertensive and hypertensive. Linear trends across the three levels of BP were determined by regressing respective characteristics against the median BP index for each BP level. BP index – systolic and diastolic, respectively - was calculated by dividing an individual's measured BP by the 95th percentile BP for their age, sex and height. Linear regression was used for continuous variables; logistic regression was used for categorical variables. P-values were reported to summarize the strength of the trend. P-values < 0.05 were considered significant.

Unadjusted and adjusted prevalence ratios (PR) for elevated BP were calculated using a modified Poisson regression[9]. This regression modeled the probability of the outcome (e.g., elevated BP) on a set of risk factors. These models were used rather than logistic models due to the relatively high prevalence of elevated BP and hypertension in the study population[10].

To assess the effectiveness of BP control in children being treated for high BP, a separate analysis was performed, limited to those CKiD participants receiving antihypertensive therapy. For this analysis, clinical and demographic characteristics of individuals with uncontrolled BP were compared to those with controlled BP using percentages for categorical variables and mean ± standard deviation for continuous variables. Similar regression methodology as described above was used to estimate the relative prevalence of uncontrolled BP associated with known risk factors. All analyses were performed using SAS 9.1 statistical software (SAS Institute, Cary, NC).

Results

Cohort characteristics

Subjects' demographic and clinical characteristics are summarized in Table 1. The majority were male, white, and most had non-glomerular forms of CKD. A significant minority of participants were premature at birth or reported a low birth weight. As expected for children with CKD[11], participants tended to be short with preserved weight; relatively few were obese.

Prevalence of hypertension and pre-hypertension (Table 2)

SBP was ≥95th percentile in 14% of subjects and was in the pre-hypertensive range (90-95th percentile) in another 11%. DBP was ≥95th percentile in 14% and was in the pre-hypertensive range in 9%. A history of hypertension was self-reported by 47% of subjects while 64% were currently taking antihypertensive medications. Combining all subjects with

hypertensive-range BP – systolic or diastolic – or a history of hypertension plus current antihypertensive use yielded a 54% prevalence of hypertension overall.

Characteristics associated with elevated blood pressure

Various demographic, anthropometric, clinical and laboratory characteristics of the subjects were examined to determine their relationship, if any, with elevated BP. Results are displayed in Table 3. Black race, glomerular CKD, shorter duration of CKD, obesity, self-reported history of hypertension and elevated serum potassium were the only characteristics significantly associated with the presence of elevated SBP in the univariate analysis; nephrotic-range proteinuria demonstrated borderline, albeit non-significant, associations with elevated SBP (Table 3a). Younger age, black race, shorter duration of CKD and nephrotic-range proteinuria were associated with elevated DBP (Table 3b).

After adjusting for potential confounders (age, race, GFR, CKD diagnosis, duration of CKD, proteinuria, antihypertensive use, obesity and serum potassium), black children were 63% more likely (PR: 1.63 95% CI 1.13-2.37) to have elevated SBP and 79% more likely (PR: 1.79, 95% CI 1.21-2.63) to have elevated DBP compared to non-black children. Elevated serum potassium was the only other characteristic independently associated with elevated SBP (PR: 1.07, 95% 1.01-1.14 per 0.2 mmol/L increase in serum potassium). Longer duration of CKD (PR: 0.85, 95% CI 0.74-0.99, per 3 year increase) and current antihypertensive medication use (PR: 0.63, 95% 0.42-0.93) were both independently associated with a decreased prevalence of elevated DBP.

To further explore the relationship between serum potassium and elevated SBP, we examined ACE inhibitor and ARB use. Serum potassium was significantly higher in the participants receiving ACE inhibitors or ARB's (n=220) compared to those who were not receiving these agents (n=184), 4.41±0.48 vs. 4.62±0.54 mmol/L, $P<0.01$. After controlling for SBP stage (normotensive, pre-hypertensive, hypertensive) both ACE/ARB use and SBP stage were independently associated with elevated potassium levels ($p<0.01$ and $p=0.04$, respectively).

Controlled vs. Uncontrolled blood pressure

Among 275 children receiving antihypertensive medications, 98 had SBP or DBP ≥90^{th} percentile and were classified as having uncontrolled BP. The remaining 177 treated children had SBP and DBP <90^{th} percentile. Of these, 73 reported no history of hypertension and were thus considered to be taking antihypertensive medications for reasons other than hypertension (for example, proteinuria); the remaining 104 children identified themselves as having a diagnosis of hypertension and were classified as having controlled BP. Further analysis was restricted to the 202 children currently receiving antihypertensive medication and classified as having controlled or uncontrolled BP (Tables 4 and 5).

Most demographic and clinical characteristics were similar when comparing those with uncontrolled and controlled BP (Table 4), although those with uncontrolled BP were more likely to be male, of black race, and to have a shorter mean duration of CKD, and were less likely to be receiving an angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) compared to those with controlled BP. In contrast, a higher percentage of participants with uncontrolled BP were obese and were being treated with either calcium channel blockers (CCB's) or another non-ACEi/ARB antihypertensive. Interestingly, the percentage of subjects without a history of hypertension who were taking ACEi/ARB's for other reasons was roughly similar to the percentage reported in Table 4 for subjects with controlled BP (data not shown).

In the unadjusted analysis, longer CKD duration and current ACE inhibitor or ARB use were significantly associated with controlled BP while obesity, male sex, and black race were significantly associated with uncontrolled BP (see table 5).Neither age, GFR, diagnosis, nor nephrotic -range proteinuria were significantly associated with a failure to control BP. After adjusting for multiple variables, male sex and shorter duration of CKD showed statistically significant associations with prevalent uncontrolled BP, while ACEi/ ARB use remained independently associated with controlled BP.

Discussion

This cross-sectional analysis of BP in a large population of children with CKD demonstrates that despite ample data on the role of BP elevation in the progression of renal insufficiency in adults, hypertension is frequently present in clinical practice. Furthermore, despite recommendations from consensus organizations for strict BP control in pediatric patients with CKD[6,12], these data indicate that hypertension is under-treated or even untreated in a significant number of children with renal insufficiency, mirroring what has recently been reported in adults[13].

The role of hypertension in progression of CKD is well established in adults. Long-term prospective studies, most notably the Multiple Risk Factor Intervention Trial and the Modification of Diet in Renal Disease (MDRD) study, have demonstrated that hypertension is one of the most important clinical risk factors for the development and progression of CKD[14,15]. One comparable pediatric study suggests that hypertension likely influences progression of CKD in children as well. In a prospective, multicenter trial of the effects of dietary protein restriction in children with GFR between 15 and 60 mL/min/1.73m^2, Wingen et al [16] showed that although adherence to a low-protein diet for 3 years did not affect the rate of decline in creatinine clearance, SBP exceeding 120 mmHg and urinary protein excretion >50 mg/kg body weight per day were both independent predictors of an increased rate of decline in creatinine clearance. The longitudinal design of CKiD, which includes repeated measures of both iohexol GFR and BP, will allow us to examine whether this will also prove to be the case in the CKiD cohort.

A recent analysis of the North American Pediatric Renal Trials and Collaborative Studies' chronic renal insufficiency database also demonstrated that hypertension plays a role in progression of CKD in children[2]. In this study, the rate of progression of CKD in children with hypertension was compared to that in normotensive children. The time to end point was defined as the time between registry enrollment and progression to initiation of renal replacement therapy, or a 10 mL/min/1.73 m^2 decline in estimated glomerular filtration rate from baseline, whichever happened first. Hypertensive children, who comprised 48% of children enrolled in the registry, reached one of the defined end points significantly sooner than did normotensive patients. The rate of CKD progression was significantly greater for those with higher SBP, older age, and eGFR <50 mL/min/1.73 m^2. The authors concluded that hypertension is a highly significant and independent predictor for progression of CKD in children.

Since hypertension is a treatable condition, both of these studies imply that intervention may prevent or delay CKD progression. Despite this, it is notable that up to one quarter of participants enrolled in CKiD had BP ≥90th percentile at baseline. This finding stands in stark contrast with current recommendations for lower BP goals in children[6,12] and adults[12,17] with CKD, and also demonstrates that despite data indicating that most pediatric nephrologists intend to target a lower goal BP in children with kidney disease than in those without kidney disease[18], in clinical practice this goal is frequently not attained.

Nephrotic range proteinuria was significantly associated with elevated diastolic BP in this cohort, and there was a trend toward an association with elevated systolic BP as well, although this did not reach significance. Proteinuria accompanies many forms of hypertensive kidney disease in children, especially glomerulonephritis and hemolytic-uremic syndrome. Many patients with these forms of hypertensive kidney disease are treated with multiple antihypertensive agents to achieve BP control. Thus, it is not surprising that CKiD participants with nephrotic range proteinuria were more likely to have elevated BP compared to those without proteinuria. In this context it is important to note that proteinuria is also a significant marker of CKD progression as seen in the study of Wingen et al[16]. Reduction of proteinuria has been advocated as a primary goal in the treatment of CKD as well as in hypertensive patients with CKD[19].

Also of note is that African American children in this study had a significantly higher risk of elevated SBP and DBP at entry into CKiD, even after adjustment for age, cause and duration of CKD, GFR, level of proteinuria, obesity, serum potassium level, and anti-hypertensive use. As the burden of CKD and ESRD is particularly high in the African American population[20], aggressive BP control in this group should be a top priority of CKD care providers.

Progression of CKD in hypertensive patients has been attributed to many inter-related mechanisms, with the renin-angiotensin system (RAS) playing a central role[21]. Systemic or local angiotensin II induces efferent arterioloar vasoconstriction, thereby increasing the intraglomerular pressure, which in turn leads to hyperfiltration and proteinuria which itself further activates the local RAS. For this reason, agents that interrupt the RAS have been advocated as optimal agents for treatment of hypertension in proteinuric CKD[12,21]. The increased prevalence of uncontrolled BP in CKiD participants not receiving ACEi or ARB's in our sub-analysis of individuals on anti-hypertensive therapy, is therefore one of the important findings of this study. It is also significant that use of calcium channel blockers (CCB's) was more common in CKiD participants with uncontrolled BP. Dihydropyridine CCB's in particular have been shown to increase proteinuria[22], and in some large-scale trials in adults, poorer outcomes have been seen in subjects treated with CCB's compared to those treated with agents affecting the RAS[17]. Seen in this context, the findings of the present study appear to support preferential use of ACEi or ARB's over CCB's in treatment of hypertension in children with CKD: among those treated with anti-hypertensive agents, the use of ACEi/ARB's was strongly suggestive of a protective effect against uncontrolled BP.

Serum potassium was found to be associated with both elevated systolic and diastolic blood pressure, and was significantly higher in participants receiving ACEi or ARB's. However, since both ACEi/ARB use and SBP stage were independently associated with elevated potassium, use of these medications does not appear to be a complete explanation for the association between serum potassium and elevated BP. It is possible either that (1) individuals with high BP were more difficult to control, and therefore received higher doses of ACEi/ARB, leading to a higher serum potassium, or alternatively (2) those with higher serum potassium were less likely to be treated with ACEi/ARB and therefore had higher BP. Given the cross-sectional analysis of the present study design, we cannot distinguish between these potential explanations.

Limitations of this study include its cross-sectional design, which does not permit inference of cause and effect. Additionally, we only analyzed one set of casual BP readings taken at a single sitting. BP in childhood is known to be labile, even in those with secondary hypertension[23]. Thus, there remains the possibility that measurement error influences our results. Manual BP determination has well-known limitations, including observer bias, terminal digit preference, interobserver variability and white coat effect[24]. To minimize

these known potential biases, meticulous training in proper BP measurement technique and use of standardized equipment and measurement protocols have been established at all CKiD centers. While some inter-center variability may be present, we feel that the standardized training procedures significantly minimize this potential source of bias. Cardiovascular assessments scheduled for later points in CKiD include ambulatory BP monitoring, which should improve the precision of classifying participant's BP's[25].

The CKiD study also has important strengths, including its large sample size, precise measurement of GFR by iohexol clearance[7], and standardized demographic, clinical and laboratory measures. By adhering to the most recent consensus recommendations for BP measurement in children[6], we have avoided the potential errors inherent in other methods of BP determination[26]. We feel that these features of the CKiD study design significantly enhance the significance of our findings.

Perspectives

Hypertension is a frequent co-morbidity in both adults and children with CKD, and contributes to CKD progression in many patients. These data demonstrate that despite awareness of the importance of hypertension and BP control in CKD, many pediatric patients with CKD have either poorly controlled or undiagnosed - and therefore untreated - hypertension. Our finding that patients receiving ACE inhibitors or ARB's were less likely to have uncontrolled hypertension points the way for development of strategies to improve the treatment of hypertension in children and adolescents with CKD, which in turn offers the potential to reduce cardiovascular risk and possibly ameliorate the progression of CKD in this vulnerable patient population. Finally, as the participants in the CKiD Study enter longitudinal follow-up, repeated measurements of iohexol GFR and BP will provide the opportunity to examine the effect of elevated BP on CKD progression in children and adolescents.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Data in this manuscript were collected by the Chronic Kidney Disease in children prospective cohort study (CKiD) with clinical coordinating centers (Principal Investigators) at Children's Mercy Hospital and the University of Missouri – Kansas City (Bradley Warady, MD) and Johns Hopkins School of Medicine (Susan Furth, MD, Ph.D.), and data coordinating center (Principal Investigator) at the Johns Hopkins Bloomberg School of Public Health (Alvaro Muñoz, Ph.D.). The CKiD website is located at http://www.statepi.jhsph.edu/ckid.

Sources of Funding: The CKiD is funded by the National Institute of Diabetes and Digestive and Kidney Diseases, with additional funding from the National Institute of Neurological Disorders and Stroke, the National Institute of Child Health and Human Development, and the National Heart, Lung, and Blood Institute (UO1-DK-66143, UO1-DK-66174, and UO1-DK-66116).

References

1. North American Pediatric Renal Trials and Collaborative Studies: 2006 Annual Report. Emmes Corporation; Rockville, MD: 2006.
2. Mitsnefes M, Ho PL, McEnery PT. Hypertension and progression of chronic renal insufficiency in children: A report of the North American Pediatric Renal Transplant Cooperative Study (NAPRTICS). J Am Soc Nephrol. 2003; 14:2618–2622. [PubMed: 14514740]
3. National Institute of Diabetes and Digestive and Kidney Diseases. [Last accessed: January 16, 2008] RFA DK-03-012. Prospective Study of Chronic Kidney Disease in Children. November 22. 2002 Available at: http://grants.nih.gov/grants/guide/rfa-files/RFA-DK-03-012.html

4. Furth SL, Cole SR, Moxey-Mims M, Kaskel F, Mak R, Schwartz G, Wong C, Muñoz A, Warady BA. Design and methods of the Chronic Kidney Disease in Children (CKiD) prospective cohort study. Clin J Am Soc Nephrol. 2006; 1:1006–1015. [PubMed: 17699320]
5. Schwartz GJ, Brion LP, Spitzer A. The use of plasma creatinine concentration for estimating glomerular filtration rate in infants, children, and adolescents. Pediatr Clin North Am. 1987; 34:571–590. [PubMed: 3588043]
6. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004; 114:555–576. [PubMed: 15286277]
7. Schwartz GJ, Furth S, Cole SR, Warady B, Muñoz A. Glomerular filtration rate via plasma iohexol disappearance: Pilot study for chronic kidney disease in children. Kidney Int. 2006; 69:2070–2077. [PubMed: 16612328]
8. National Center for Health Statistics. [Last accessed: January 16, 2008] CDC Growth Charts. 2000. Available at: http://www.cdc.gov/growthcharts/
9. Zou G. A modified poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004; 159:702–706. [PubMed: 15033648]
10. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA. 1998; 280:1690–1691. [PubMed: 9832001]
11. Furth SL. Growth and nutrition in children with chronic kidney disease. Adv Chronic Kidney Dis. 2005; 12:366–371. [PubMed: 16198275]
12. National Kidney Foundation Kidney Disease Outcomes Quality Initiative. [Last accessed: May 27, 2008] K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. Available at: http://www.kidney.org/professionals/KDOQI/guidelines_bp/index.htm
13. Peralta CA, Hicks LS, Chertow GM, Ayanian JZ, Vittinghoff E, Lin F, Shlipak MG. Control of hypertension in adults with chronic kidney disease in the United States. Hypertension. 2005; 45:1119–1124. [PubMed: 15851626]
14. Peterson JC, Adler S, Burkart JM, Greene T, Hebert LA, Hunsicker LG, King AJ, Klahr S, Massry SG, Seifter JL. Blood pressure control, proteinuria, and the progression of renal disease. The Modification of Diet in Renal Disease Study. Ann Intern Med. 1995; 123:754–762. [PubMed: 7574193]
15. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Ford CE, Shulman NB, Stamler J. Blood pressure and end-stage renal disease in men. N Eng J Med. 1996; 334:13–18.
16. Wingen AM, Fabian-Bach C, Schaefer F, Mehls O. Randomised multicentre study of a low-protein diet on the progression of chronic renal failure in children. Lancet. 1997; 349:1117–1123. [PubMed: 9113009]
17. Bakris GL, Williams M, Dworkin L, Elliot WJ, Epstein M, Toto R, Tuttle K, Douglas J, Hsueh W, Sowers J. Preserving renal function in adults with hypertension and diabetes: A consensus approach. Am J Kidney Dis. 2000; 36:646–661. [PubMed: 10977801]
18. Woroniecki RP, Flynn JT. How are hypertensive children evaluated and managed? A survey of North American pediatric nephrologists. Pediatr Nephrol. 2005; 20:791–797. [PubMed: 15809834]
19. Palmer BF. Proteinuria as a therapeutic target in patients with chronic kidney disease. Am J Nephrol. 2007; 27:287–293. [PubMed: 17457028]
20. Martins D, Tareen N, Norris KC. The epidemiology of end-stage renal disease among African Americans. Am J Med Sci. 2002; 323:65–71. [PubMed: 11863081]
21. Soergel M, Schaefer F. Effect of hypertension on the progression of chronic renal failure in children. Am J Hypertens. 2002; 15(2 Pt 2):53S–56S. [PubMed: 11866231]
22. Flynn JT, Pasko DA. Calcium channel blockers: pharmacology and place in therapy of pediatric hypertension. Pediatr Nephrol. 2000; 15:302–316. [PubMed: 11149130]
23. Ogborn MR, Crocker JFS. Investigation of pediatric hypertension. Use of a tailored protocol. Am J Dis Child. 1987; 141:1205–1209. [PubMed: 3673973]
24. Parati G, Bilo G, Mancia G. Blood pressure measurement in research and clinical practice: recent evidence. Curr Opin Nephrol Hypertens. 2004; 13:343–357. [PubMed: 15073495]

25. Wühl E, Hadtstein C, Mehls O, Schaefer F. Escape Trial Group. Home, clinic, and ambulatory blood pressure monitoring in children with chronic renal failure. Pediatr Res. 2004; 55:492–497. [PubMed: 14630977]

26. Butani L, Morganstern BZ. Are pitfalls of oscillometric blood pressure measurements preventable in children? Pediatr Nephrol. 2003; 18:313–318. [PubMed: 12755148]

Table 1

Demographic, anthropometric and clinical characteristics of CKiD Study participants at baseline, N=432

Characteristic	Mean ± SD or % (n)
Age, years	11 ± 4
Male	60% (260)
Race	
Caucasian	69% (298)
African American	16% (67)
Other	15% (66)
Hispanic Ethnicity	14% (59)
Weight percentile	47 ± 33
Height percentile	32 ± 29
BMI percentile	60 ± 30
% Obese, BMI>95th percentile	17% (72)
Low birth weight, <2500 g	20% (83)
Premature birth, <36 weeks	24% (100)
Iohexol GFR, mL/min/1.73 m^2	44 ± 15
Glomerular CKD	22% (93)
Duration of CKD, years	7 ± 5

Abbreviations used in table: BMI, body mass index; CKD, chronic kidney disease; GFR, glomerular filtration rate

Table 2
Blood pressure status of CKiD Study participants, N=432

Characteristic	Mean ± SD or % (n)
Systolic BP, mmHg	107 ± 13
Systolic BP Status	
SBP <90th percentile	75% (322)
SBP ≥90th - <95th percentile	11% (49)
SBP ≥95th percentile	14% (61)
Diastolic BP, mmHg	66 ± 11
Diastolic BP Status	
DBP <90th percentile	77% (332)
DBP ≥90th - <95th percentile	9% (41)
DBP ≥95th percentile	14% (59)
Current use of antihypertensive medication	64% (275)
Among children with SBP>90th percentile	68%
Among children with DBP>90th percentile	53%
Self-reported hypertension	47% (201)
Parental history of hypertension	28% (122)

Abbreviations used in table: BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure

Table 3

Table 3a. Characteristics of study population by SBP category, N=432

	Systolic Blood Pressure*			
Characteristic†	**<90th percentile (n=322)**	**≥90th - <95th percentiles (n=49)**	**≥95th percentile (n=61)**	**P-value for linear trend**
Age, years	11 ± 4	11 ± 4	10 ± 4	0.38
Male	59% (190)	69% (34)	59% (36)	0.56
Black race	13% (41)	24% (12)	23% (14)	0.01
Hispanic Ethnicity	14% (43)	14% (7)	15% (9)	0.75
Glomerular diagnosis	19% (61)	31% (15)	28% (17)	0.04
Duration of CKD, years	7 ± 5	6 ± 5	5 ± 4	<0.01
Iohexol GFR, ml/min/1.73m^2	45 ± 15	43 ± 16	43 ± 14	0.26
BMI percentile	59 ± 30	61 ± 32	67 ± 29	0.08
Obese, BMI >95th percentile	15% (47)	20% (10)	26% (15)	0.03
Low birth weight, <2500g	21% (65)	18% (8)	16% (10)	0.35
Premature birth, <36 weeks	23% (73)	23% (11)	27% (16)	0.61
Parental history of hypertension	27% (88)	27% (13)	34% (21)	0.36
Self-reported history of hypertension	42% (134)	61% (30)	61% (37)	<0.01
Proteinuria				
Significant, Up/c 0.2-2	60% (177)	67% (32)	60% (35)	0.11‡
Nephrotic, Up/c >2	13% (37)	17% (8)	17% (10)	0.06‡
Sodium (mmol/L)	140 ± 2	139 ± 2	139 ± 2	0.14
Potassium (mmol/L)	4.5 ± 0.5	4.8 ± 0.6	4.5 ± 0.5	0.05

Table 3b. Characteristics of study population by DBP category, N=432

	Diastolic Blood Pressure*			
Characteristic†	**<90th percentile (n=332)**	**≥90th - <95th percentiles (n=41)**	**≥95th percentile (n=59)**	**P-value for linear trend**
Age, years	11 ± 4	10 ± 5	9 ± 4	<0.01
Male	58% (193)	68% (28)	66% (39)	0.14
Black race	12% (41)	27% (11)	25% (15)	<0.01
Hispanic Ethnicity	13% (44)	20% (8)	12% (7)	0.88
Glomerular diagnosis	22% (73)	22% (9)	19% (11)	0.61
Duration of CKD, years	7 ± 5	6 ± 5	6 ± 4	<0.01
Iohexol GFR, ml/min/.73m^2	45 ± 15	45 ± 18	42 ± 13	0.27
BMI percentile	59 ± 30	69 ± 29	64 ± 31	0.07
Obese, BMI >95th percentile	15% (51)	23% (9)	21% (12)	0.17
Low birth weight, <2500g	20% (63)	24% (9)	19% (11)	0.93
Premature birth, <36 weeks	24% (80)	23% (9)	19% (11)	0.37
Parental history of hypertension	28% (92)	32% (13)	29% (17)	0.72
Self-reported history of hypertension	45% (151)	56% (23)	46% (27)	0.59
Proteinuria				

Table 3b. Characteristics of study population by DBP category, N=432

	Diastolic Blood Pressure*			
Characteristic†	**<90th percentile (n=332)**	**≥90th - <95th percentiles (n=41)**	**≥95th percentile (n=59)**	**P-value for linear trend**
Significant, Up/c 0.2-2	62% (187)	67% (26)	54% (31)	0.38‡
Nephrotic, Up/c >2	12% (37)	13% (5)	23% (13)	0.03‡
Sodium (mmol/L)	140 ± 2	140 ± 2	139 ± 2	0.86
Potassium (mmol/L)	4.5 ± 0.5	4.6 ± 0.5	4.5 ± 0.4	0.90

Abbreviations used in table: BMI, body mass index; CKD, chronic kidney disease; GFR: glomerular filtration rate

*Based on causal BP measurement at baseline visit and categorized according to reference 6.

†Mean ± SD or percent (n);

‡Compared to normal range Up/c (<0.2)

Table 4

Demographic and clinical characteristics of participants receiving antihypertensive medications with controlled and uncontrolled blood pressure, N=202*

Characteristic†	Blood Pressure Status		
	Uncontrolled BP N=98	Controlled BP N=104	P (Chi-Square)
Age, years	11 ± 4	11 ± 3	0.72
Male	68% (67)	51% (53)	0.01
Black race	22% (22)	10% (10)	0.02
Hispanic ethnicity	19% (18)	12% (12)	0.16
Obese, BMI≥95th %ile	28% (27)	17% (17)	0.06
Glomerular CKD	34% (33)	26% (27)	0.23
Iohexol GFR, mL/min/1.73 m^2	44 ± 16	44 ±16	0.99
CKD duration, years	6 ± 4	8 ± 4	<0.01
Premature birth (Gestational age<36 weeks)	24% (23)	31% (31)	0.29
Low birth weight (<2500 g)	18% (17)	27% (26)	0.17
Proteinuria			0.33
Significant, 0.2 ≤ Up/c < 2.0	59% (55)	56% (54)	
Nephrotic, Up/c ≥ 2.0	19% (18)	16% (16)	
Parental history of hypertension	31% (30)	29% (30)	0.78
Antihypertensive Use			
ACEi/ARB	76% (74)	88% (92)	0.02
Calcium Channel Blockers	33% (32)	16% (17)	<0.01
Other	35% (34)	21% (22)	0.03
≥2 Antihypertensive medications	44% (43)	33% (34)	0.10

Abbreviations used in table: ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CKD, chronic kidney disease; GFR, glomerular filtration rate

*73 children with SBP and DBP<90th %ile receiving antihypertensive medications but not reporting a diagnosis of high blood pressure were excluded from this analysis.

†Data expressed as percentages (number), or as mean ± SD

Table 5

Prevalence ratios of uncontrolled blood pressure among those receiving antihypertensive medications for select demographic and clinical characteristics, N=202

	Prevalence Ratio (PR) and 95% CI of uncontrolled blood pressure	
Characteristic	**Unadjusted**	**Adjusted***
Age, per 4 years	0.97 [0.84,1.13]	1.00 [0.87,1.15]
Male	1.48 [1.07,2.03]	1.54 [1.14,2.08]
Race, Black vs. Non-black	1.54 [1.15,2.05]	1.15 [0.84,1.58]
Obese, BMI≥95th percentile	1.36 [1.01,1.82]	1.26 [0.93,1.72]
Iohexol GFR, per 10% decrease	1.00 [0.96,1.04]	1.01 [0.96,1.05]
Glomerular CKD	1.20 [0.90,1.61]	1.03 [0.74,1.42]
Duration of CKD, per 3 years	0.87 [0.78,0.97]	0.88 [0.78,0.98]
Nephrotic Proteinuria, Up/c ≥ 2.0	1.11 [0.78,1.58]	1.00 [0.69,1.44]
ACEi/ARB use	0.67 [0.50,0.89]	0.72 [0.52,0.99]

Abbreviations used in table: ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CKD, chronic kidney disease; GFR, glomerular filtration rate

*Adjusted for all variables listed in the table.