

Kidney Function Reference Values in US Adolescents: National Health and Nutrition Examination Survey 1999–2008

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Summary

Background and objectives Few data are available on kidney function in normal US adolescents. This study characterizes the distribution of kidney function measures and associated factors.

Design, setting, participants, & measurements Serum creatinine, cystatin C, and urinary albumin-to-creatinine ratios were measured in US adolescents (aged 12 to 17 years; $n = 5575$) in the cross-sectional National Health and Nutrition Examination Survey 1999–2008. The reference population was defined as healthy adolescents with BP <120/80 mmHg and a Z-score for weight-to-height ≤ 1.645 , without self-reported diabetes or hypertension, not using prescription medications in the preceding 30 days, not pregnant or currently menstruating. Results were analyzed by age, gender, race, ethnicity, body mass index, and BP; estimated GFR (eGFR) was calculated using the original and revised Schwartz formulas.

Results Mean values for eGFR_{Schwartz original formula}, serum creatinine, and serum cystatin C were 147 ml/min/1.73 m², 0.71 mg/dl, 0.82 mg/L, respectively. The median urinary albumin-to-creatinine ratio was 6.8 mg/g creatinine. In the reference population ($n = 2881$), eGFR differed significantly using the two Schwartz formulas; values were higher using the original formula (median values 143 versus 96 ml/min/1.73 m²). Serum creatinine level (0.7 versus 0.72 mg/dl), but not cystatin C level (0.82 versus 0.82 mg/L), was lower in the reference population than in a nonreference population of adolescents.

Conclusions These findings provide important demographic information and highlight the need for confirmatory testing of the revised Schwartz formula by comparison to measured GFR in healthy US adolescents.

Clin J Am Soc Nephrol 6: 1956–1962, 2011. doi: 10.2215/CJN.10311110

Introduction

Measures of kidney function include serum creatinine, cystatin C, and GFR, either measured or estimated. Serum creatinine and cystatin C are endogenous substances used as markers of GFR; cystatin C has been proposed as a superior marker of kidney function (1). Values for measures of kidney function in children are different from values in adults and vary with age. In the absence of precise measurement of GFR using exogenous compounds such as inulin or iothexol, estimation of GFR is thought to provide the best overall measure of kidney function (2). In children, estimated GFR (eGFR) is calculated primarily using the Schwartz formula ($eGFR_{\text{Schwartz}} = kL/\text{Scr}$) (3), where k = an age dependent coefficient, L = length in centimeters, and Scr = serum creatinine level. The Schwartz formula was recently updated for enzymatic serum creatinine concentrations using data obtained in children with chronic kidney disease (the Chronic Kidney Disease in Children [CKiD] study) and a median GFR value of 41.3 ml/min/1.73 m² (4). In the updated Schwartz formula ($eGFR_{\text{CKiD}}$), a con-

stant value is used for k and values for cystatin C and blood urea nitrogen (BUN) are added to the calculation.

Little information is available regarding normal values for kidney function in US adolescents as defined by large-scale, representative, national population studies. Which version of the Schwartz formula should be used to estimate GFR in healthy adolescents is also unknown, as the updated formula has not been validated in healthy children. Whether cystatin C is a better marker for GFR than serum creatinine remains controversial, as large-scale epidemiologic studies have not been performed in healthy children. The National Health and Nutrition Examination Survey (NHANES) is a program of studies from the National Center for Health Statistics within the Centers for Disease Control and Prevention (CDC), designed to monitor the health and nutritional status of adults and children in the United States (5). The program began in the 1960s and has been continuous since 1999. BP, growth, and biochemical data are collected on adolescents and adults. We used

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NHANES 1999 to 2008 data to characterize the distribution of normal kidney function (serum creatinine, cystatin C, eGFR) and associated factors in healthy, noninstitutionalized US adolescents, and to compare estimates of GFR using the original and updated Schwartz formulas in this population.

Materials and Methods

Objectives

Among NHANES participants aged 12 to 17 years between 1999 and 2008, the main objectives of this study were to

1. Enumerate the distribution of serum creatinine, cystatin C, eGFR calculated from serum creatinine and cystatin C, and urinary albumin-to-creatinine ratio (ACR) in an apparently healthy reference population.
2. Quantify the associations of serum creatinine, cystatin C, eGFR calculated from serum creatinine and cystatin C, and urinary ACR in the overall population.

Study Population and Measurements

NHANES is a cross-sectional, multistage, stratified, clustered probability sample of the noninstitutionalized US civilian population performed in two-year cycles. As recommended by the National Center for Health Statistics, the 1999–2000, 2001–2002, 2003–2004, 2005–2006, and 2007–2008 surveys were examined in combination (5). Participants were interviewed at home, and physical examinations and blood and urine collections were performed at mobile examination centers. The kinetic alkaline picrate method was used to measure serum creatinine. As recommended by NHANES, the following formulas were used to standardize the NHANES serum creatinine reported in the laboratory data files for the different biennial cycles (6–8):

$$\text{Standardized creatinine}_{1999-2000} = 1.013 \times (\text{reported creatinine}_{1999-2000}) + 0.147$$

$$\text{Standardized creatinine}_{2001-2002} = \text{reported creatinine}_{2001-2002}$$

$$\text{Standardized creatinine}_{2003-2004} = \text{reported creatinine}_{2003-2004}$$

$$\text{Standardized creatinine}_{2005-2006} = 0.978 \times (\text{reported creatinine}_{2005-2006}) - 0.016$$

$$\text{Standardized creatinine}_{2007-2008} = \text{reported creatinine}_{2007-2008}$$

For 1999–2002 participants, cystatin C levels were measured in stored serum samples for all participants with standardized serum creatinine levels >1.2 mg/dl, all female participants with levels >1.0 mg/dl, and a random sample of 25% of all participants. A particle-enhanced immunonephelometric assay was used to measure cystatin C levels (N Latex Cystatin C; Dade Behring, Deerfield, IL); the range of this assay was 0.23 to 7.25 mg/L, and inter-assay coefficients were 5.05% at 0.97 mg/L and 4.87% at 1.90 mg/L, respectively (9). A solid-phase, noncompetitive, double-antibody, fluorescence immunoassay was used to measure urinary albumin. This assay has a detection limit of 0.3 $\mu\text{g}/\text{ml}$ and interassay coefficients of variation of 10.7% at 1.95 $\mu\text{g}/\text{ml}$, 6.9% at 6.4 $\mu\text{g}/\text{ml}$, 5.9% at 15.07 $\mu\text{g}/\text{ml}$, and 5.5% at 7.54 $\mu\text{g}/\text{ml}$, respectively (10).

The formula of Schwartz and colleagues, employing height (meters) and serum creatinine (mg/dl) was used to

estimate GFR (3,11,12), as follows: $\text{eGFR} = 55 \times \text{height}/\text{serum creatinine}$ in girls and boys age 12 to 13 years and $70 \times \text{height}/\text{serum creatinine}$ in adolescent boys. The CKiD formula (4), employing height (meters), serum creatinine (mg/dl), cystatin C (mg/L), BUN (mg/dl), and gender was also used to estimate GFR, as follows: $\text{eGFR}_{\text{CKiD}} = 39.1 [\text{height}/\text{creatinine}]^{0.516} [1.8/\text{cystatin C}]^{0.294} [30/\text{BUN}]^{0.169} [1.099]^{\text{male}} [\text{height}/1.4]^{0.188}$.

Analysis

Demographic data included age (12 to 13, 14 to 15, 16 to 17 years), gender, race and ethnicity (non-Hispanic Caucasian, African American, Hispanic, other), height, weight, and BP measures. Body mass index (BMI) was calculated as weight (kg) divided by height (m^2). For serum creatinine, $\text{eGFR}_{\text{Schwartz original formula}}$, and ACR, the study population consisted of NHANES participants, 1999 to 2008, aged 12 to 17 years, in whom serum creatinine was measured. For cystatin C and $\text{eGFR}_{\text{CKiD}}$, the study population consisted of NHANES participants, 1999 to 2002, aged 12 to 17 years, in whom serum creatinine and cystatin C were measured. Our sample size was 5575 adolescents who make up the study population.

Fifth, 25th, 50th, 75th, and 95th percentiles for renal function measures were determined from a reference population ($n = 2881$) with the following characteristics: nonobese, BP <120/80 mmHg, no self-reported hypertension or diabetes, not currently pregnant, not currently menstruating, and no use of prescription medications in the preceding month. Obesity is defined as a Z-score for weight-to-height of 1.645 on the CDC growth reference Table 2000. Linear regression was used to quantify associations of renal function measures; because of a nongaussian distribution, urinary ACR values were log-transformed. Analytical procedures recommended by NHANES were followed, and sampling weights for complex survey designs were incorporated in all analyses (5). SUDAAN, v10 (Research Triangle Institute, Research Triangle Park, NC), and SAS, v9.1.3 (Cary, NC), were used for data analysis.

Results are presented as mean \pm 1 SD or medians for urinary ACR. Two-tailed P values <0.05 were considered statistically significant.

Results

Demographic data for the healthy reference and the nonreference adolescent populations are shown in Table 1. Mean values were as follows: age, 14.5 years; height, 1.65 m; weight, 62.8 kg; serum creatinine, 0.71 mg/dl; serum cystatin C, 0.82 mg/L, and eGFR, 147 ml/min/1.73 m^2 by the original Schwartz formula. The median urinary ACR was 6.8 mg/g. The reference population was younger (14.4 *versus* 14.6 years), shorter (1.64 *versus* 1.66 m), and lighter (56.2 *versus* 69.3 kg), with lower serum creatinine values (0.70 *versus* 0.72 mg/dl), a lower proportion of Caucasian participants (58.9% *versus* 65.1%), and a higher proportion of Mexican/Hispanic participants (20.3% *versus* 16.2%).

Figure 1 shows the distributions of serum creatinine (panel A), serum cystatin C (panel B), and urinary ACR (panel C) in the healthy reference population by age, gender, and race/ethnicity. By race/ethnicity, the 50th percen-

Table 1. Characteristics of US adolescents aged 12 to 17 years, NHANES 1999–2008

	All	In Reference Population ^a		P
		Yes, 49.6 (1.2)%	No, 50.4 (1.2)%	
<i>n</i>	5575	2881	2694	
Serum creatinine, mg/dl	0.71 (<0.01)	0.70 (<0.01)	0.72 (<0.01)	<0.07
Serum cystatin C, mg/L (<i>n</i> = 405 ^b)	0.82 (<0.01)	0.82 (0.01)	0.82 (0.01)	1.00
eGFR _{Schwartz} , ml/min/1.73 m ²	147 (1)	147 (1)	147 (1)	0.50
eGFR _{CKiD} , ml/min/1.73 m ² (<i>n</i> = 405 ^b)	99 (1)	98 (1)	99 (2)	0.70
Urinary ACR, mg/g	6.8 [4.51 to 3.3]	7.6 [4.61 to 4.4]	6.3 [4.41 to 1.9]	0.20
Age, years	14.5 (<0.1)	14.4 (0.1)	14.6 (0.1)	0.08
Height, m	1.65 (<0.01)	1.64 (<0.01)	1.66 (<0.01)	<0.01
Weight, kg	62.8 (0.3)	56.2 (0.3)	69.3 (0.6)	<0.01
Body mass index, kg/m ²	22.9 (0.1)	20.8 (0.1)	25.0 (0.2)	
Systolic BP mmHg	109 (<1)	106 (<1)	112 (<1)	
Diastolic BP mmHg	61 (<1)	60 (<1)	61 (<1)	
Female, %	49.3 (1.0)	51.0 (1.4)	47.7 (1.5)	0.10
Race/ethnicity, %				0.05
Caucasian	62.0 (1.8)	58.9 (2.0)	65.1 (2.1)	
African American	14.9 (1.1)	15.4 (1.2)	14.5 (1.2)	
Mexican/Hispanic	18.2 (1.6)	20.3 (1.7)	16.2 (1.7)	
Other	4.9 (0.7)	5.4 (1.0)	4.3 (0.7)	
Obese, ^c %	17.7 (0.8)	0.0	35.1 (1.4)	
Systolic BP ≥120 mmHg, %	13.4 (0.7)	0.0	26.4 (1.2)	
Diastolic BP ≥80 mmHg, %	2.8 (0.4)	0.00	5.6 (0.7)	
Hypertension, %	1.1 (0.2)	0.00	2.1 (0.4)	
Diabetes, %	0.5 (0.1)	0.00	1.0 (0.2)	
Prescription medication last 30 days, %	28.7 (1.1)	0.00	56.9 (1.8)	
Pregnant, %	0.4 (<0.1)	0.00	0.7 (0.1)	
Currently menstruating, %	2.9 (0.4)	0.00	5.8 (0.8)	

Data are presented as means (standard errors), column percentages (standard errors), or median [interquartile range] for urinary ACR. Data are missing as follows: urinary albumin-to-creatinine ratio, *n* = 71; weight, *n* = 14; blood pressure, *n* = 74. ACR, albumin-to-creatinine ratio; eGFR_{CKiD}, estimated GFR calculated with the revised Schwartz formula; eGFR_{Schwartz}, estimated GFR calculated with the original Schwartz formula; NHANES, National Health and Nutrition Examination Survey.

^aThe reference population had the following characteristics: non-obese, BP <120/80 mmHg, no self-reported hypertension or diabetes, not currently pregnant or currently menstruating, not using prescription medications in the preceding 30 days.

^bCystatin C was measured in NHANES 1999–2001.

^cObesity was defined as Z-score for weight-to-height ≥1.645 on the Centers for Disease Control and Prevention growth reference tables in 2000.

tile values of serum creatinine for Caucasians, African Americans, and Mexicans/Hispanics were 0.69, 0.70, and 0.65 mg/dl, respectively. By age, the 50th percentile values for ages 12 to 13, 14 to 15, and 16 to 17 years were 0.59, 0.69, and 0.80 mg/dl, respectively. Serum creatinine increased with age, and values were higher in boys than in girls and in Caucasians and African Americans than in Mexicans/Hispanics. By age, the 50th percentile values of cystatin C for ages 12 to 13, 14 to 15, 16 to 17 years were 0.82, 0.79, and 0.80 mg/L, respectively. Serum cystatin C values were higher in Caucasians than in African Americans and Mexicans/Hispanics and lower in girls than in boys. Urinary ACR values were lower in boys than in girls and decreased with age.

Figure 2, panel A, shows the distribution of eGFR using the original Schwartz formula by age, gender, and race/ethnicity in the healthy reference population. Regarding the 50th percentile for eGFR_{Schwartz original formula}, values were similar in girls and boys, lower with increasing age, lower in African Americans than in Caucasians, and higher in Mexicans/Hispanics than in Caucasians. Figure 2, panel B, shows the distribution of eGFR using the CKiD

Schwartz formula by age, gender, and race/ethnicity in a subset of the healthy reference population (*n* = 220 reference population participants with measured cystatin C levels). Regarding the 50th percentile for eGFR_{CKiD}, values did not significantly differ between girls and boys, values were lower in participants older than 12 to 13 years, and values were lower in Caucasians than in African Americans and Mexicans/Hispanics.

Table 2 shows associations of renal function measures in healthy US adolescents. With unadjusted linear regression analysis, eGFR_{Schwartz original formula} levels are indirectly related with age, female gender, African-American race, BMI, and diastolic BP levels, and directly related with Mexican/Hispanic ethnicity. Except for diastolic BP, these findings persist in adjusted models (Table 3). With unadjusted linear regression analysis (Table 2), eGFR_{CKiD} levels are indirectly related with age and BMI, and directly related with Mexican/Hispanic ethnicity. Except for BMI, these findings persist in adjusted models (Table 3). With unadjusted linear regression analysis (Table 2), cystatin C levels are indirectly related with age, female gender, African-

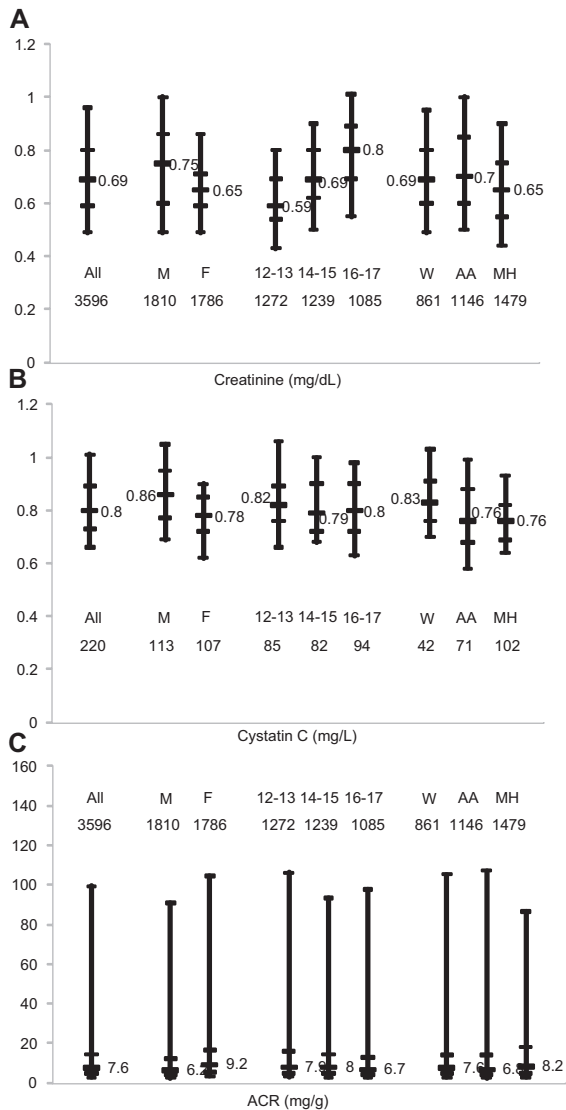


Figure 1. | Fifth, 25th, 50th, 75th, and 95th percentiles of serum creatinine (panel A), cystatin C (panel B), and urinary albumin-to-creatinine ratio (ACR, panel C) in the reference population (All) and in subgroups defined by gender, age in years, and race/ethnicity. AA, African American; F, female; M, male; MH, Mexican/Hispanic; W, white (Caucasian). Numbers included appear below group designations.

American race, and Mexican/Hispanic ethnicity. With adjustment (Table 3), cystatin C levels are indirectly related with age, female gender, African-American race, and Mexican/Hispanic ethnicity, and directly related with BMI. With unadjusted linear regression analysis (Table 2), urinary ACR is indirectly related with age, African-American race, BMI, and systolic BP, and directly related with female gender and diastolic BP. With adjustment (Table 3), urinary ACR is indirectly related with BMI and directly related with female gender, Mexican/Hispanic ethnicity and systolic BP.

Discussion

We have shown that surrogate measures of kidney function in a representative sample of healthy US adolescents differ by age, gender, BMI, BP status, race, and ethnicity.

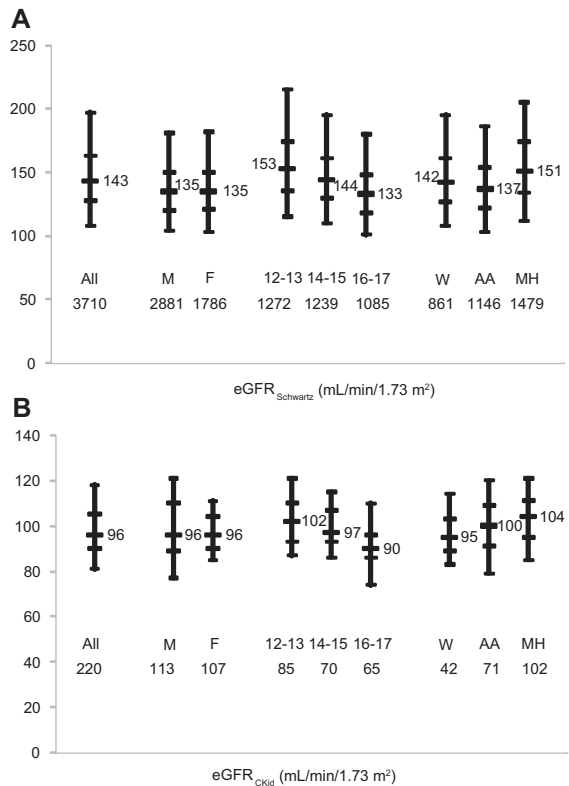


Figure 2. | Fifth, 25th, 50th, 75th, and 95th percentiles of GFR calculated by the original ($GFR_{Schwartz}$, panel A) and revised Schwartz formulas (GFR_{CKiD} , panel B) in the reference population (All) and in subgroups defined by gender, age in years, and race/ethnicity. AA, African American; F, female; M, male; MH, Mexican/Hispanic; W, white (Caucasian). Numbers included appear below group designations.

Results of this analysis show that serum creatinine values increase with age for African-American, Caucasian, and Mexican/Hispanic male and female adolescents. The reason for higher serum creatinine values in adolescent boys compared with girls likely relates to greater muscle mass in adolescent boys. Our results differ from results of an English study that found no influence of gender on serum creatinine results in 59 children aged 9 to 17 years (1). Serum creatinine values were higher in African-American adolescents compared with Caucasians but lower in Mexican/Hispanic adolescents compared with Caucasians. The reasons for racial and ethnic differences in serum creatinine levels are not known. This finding is similar to the finding reported for participants aged 12 to 19 years in NHANES III, 1988–1994 (13). However, the mean serum creatinine values reported in this study are lower than values reported in participants aged 12 to 19 years in NHANES III. Possible explanations are inclusion in the current analysis of a healthy reference population aged 12 to 17 years, use of different analyzers for the serum creatinine assay for 1999 to 2008, and standardization of serum creatinine values.

Estimates of GFR differ significantly between the original Schwartz and the CKiD formulas. With both formulas, mean eGFR at the 50th percentile decreases after age 13 years. With the original formula, mean eGFR at the 50th percentile is higher in boys than in girls. With the CKiD

Table 2. Univariate associations of renal function measures in US adolescents aged 12 to 17 years^a

Characteristics	Renal Function Measures				
	Creatinine	eGFR _{Schwartz}	eGFR _{CKiD}	Cystatin C	Log (ACR) ^b
<i>n</i>	5575	5575	405	405	5504
Age, per 1.5 years	0.07 (<0.01)	-7.13 (0.42)	-2.87 (0.63)	-0.02 (0.01)	-0.05 (0.02)
<i>P</i>	<0.0001	<0.0001	0.0004	0.008	0.004
<i>r</i> ²	0.27	0.08	0.08	0.04	<0.01
Female gender (vs. male)	-0.10 (0.01)	-17.85 (1.01)	-0.86 (1.21)	-0.08 (0.01)	0.36 (0.04)
<i>P</i>	<0.0001	<0.0001	0.5	<0.0001	<0.0001
<i>r</i> ²	0.10	0.10	<0.01	0.12	0.03
Race/ethnicity					
African American (vs. Caucasian)	0.03 (0.01)	-5.38 (1.18)	2.28 (2.16)	-0.05 (0.02)	-0.10 (0.05)
<i>P</i>	<0.0001	<0.0001	0.3	0.01	0.06
Hispanic/Mexican (vs. Caucasian)	-0.05 (0.01)	8.23 (1.71)	5.18 (2.01)	-0.04 (0.01)	0.07 (0.05)
<i>P</i>	<0.0001	<0.0001	0.02	0.007	0.2
Other race (vs. Caucasian)	-0.03 (0.01)	4.29 (3.88)	-1.39 (2.24)	-0.04 (0.0)	-0.13 (0.10)
<i>P</i>	0.04	0.3	0.5	0.003	0.2
<i>r</i> ²	0.02	0.02	0.04	0.04	<0.01
Body mass index, per 3.1 kg/m ²	0.01 (<0.01)	-1.30 (0.38)	-0.78 (0.28)	0.01 (<0.01)	-0.11 (0.01)
<i>P</i>	<0.0001	0.001	0.02	0.06	<0.0001
<i>r</i> ²	0.02	0.01	0.01	0.03	0.03
Systolic BP, per 6.9 mmHg	0.02 (<0.01)	0.47 (0.35)	-0.80 (0.64)	0.01 (<0.01)	-0.03 (0.01)
<i>P</i>	<0.0001	0.2	0.2	0.05	0.02
<i>r</i> ²	0.05	<0.01	0.01	0.05	<0.01
Diastolic BP, per 7.0 mmHg	0.01 (<0.01)	-1.92 (0.38)	-0.36 (0.47)	>-0.01 (<0.01)	0.03 (0.01)
<i>P</i>	0.004	<0.0001	0.5	0.6	0.02
<i>r</i> ²	<0.01	0.01	<0.01	<0.01	<0.01

ACR, albumin-creatinine ratio; eGFR_{CKiD}, estimated GFR calculated with the revised Schwartz formula; eGFR_{Schwartz}, estimated GFR calculated with the original Schwartz formula.

Units: serum creatinine, mg/dl; GFR_{Schwartz}, ml/min/1.73 m²; GFR_{CKiD}, ml/min/1.73 m²; cystatin C, ACR, mg/g.

^aSeparate linear regression models for serum creatinine, GFR_{Schwartz}, GFR_{CKiD}, cystatin C, and log-transformed ACR as dependent variables and age, gender, race/ethnicity, body mass index, systolic BP and diastolic BP as separate candidate explanatory variables. ACR was log-transformed because of non-Gaussian distribution characteristics. Parameter estimates are presented as beta coefficients (standard error). Intervals for continuous variables represent half the interquartile range.

^bThe exponents of the parameter estimates are as follows: -0.05 to 0.95, 0.36 to 1.43, -0.10 to 0.90, 0.07 to 1.07, -0.13 to 0.88, -0.11 to 0.90, -0.03 to 0.97, 0.03 to 1.03.

formula, mean eGFR at the 50th percentile is not significantly different for boys and girls. Also, eGFR_{CKiD} results in values that are significantly lower for both boys and girls than eGFR_{Schwartz original formula} values. Mean eGFR_{CKiD} values at the 5th percentile are less than 90 ml/min/1.73 m² for both male and female healthy adolescents, and are below the normal GFR values established in the Kidney Disease Outcomes Quality Initiative (KDOQI) chronic kidney disease guidelines (14). Additional differences in results using the two formulas include an indirect association with gender and African-American race with eGFR_{Schwartz original formula} but lack of an association with gender with eGFR_{CKiD}. The eGFR_{CKiD} formula is based on data from a cohort of children with chronic kidney disease and does not include data from healthy children. The number of African-American and Hispanic children in the CKiD study is low, at 54 and 48, respectively (15). While the eGFR_{Schwartz original formula} is thought to overestimate GFR, the eGFR_{CKiD} formula may overclassify healthy adolescents as having chronic kidney disease. A recent study in 107 pediatric patients undergoing evaluation for hematopoietic stem cell transplant found significant disagreement between both the original and the revised Schwartz (0.413 x

L/Scr) formulas and the ^{99m}Tc-DTPA in classifying GFR as normal or reduced (*P* < 0.05) (16). One major limitation of our study is lack of formal measures of GFR for comparison with estimates of GFR. Validation studies of the eGFR_{CKiD} formula in healthy children are needed and should include robust percentages of minority populations.

Our cystatin C results are potentially biased in that NHANES measured samples in all male participants with standardized serum creatinine levels >1.2 mg/dl, all female participants with levels >1.0 mg/dl, and a random sample of 25% of all participants age <60 years. Serum cystatin C levels have been previously reported in US adolescents using NHANES data (17). The previous report included participants aged 18 and 19 years. Both this report and our study found that cystatin C was indirectly associated with age and African-American and Mexican/Hispanic race/ethnicity, and both found lower cystatin C levels in girls than in boys. However, in our study, cystatin C was directly associated with BMI. Both studies differ from a European study that found that serum cystatin C levels remained constant in children after 1 year of age and found no association of cystatin C with gender (1).

Table 3. Multivariate associations of renal function measures in US adolescents aged 12 to 17 years^a

	Renal Function Measures				
	Creatinine	GFR _{Schwartz}	GFR _{CKiD}	Cystatin C	Log (ACR) ^b
N	5575	5575	405	405	5504
Age, per 1.5 years	0.07 (<0.01)	-7.09 (0.42)	-2.65 (0.83)	-0.03 (0.01)	-0.02 (0.02)
P	<0.0001	<0.0001	0.007	0.005	0.2
Female gender (vs. male)	-0.10 (0.01)	-17.50 (1.00)	-0.50 (1.28)	-0.08 (0.01)	0.41 (0.05)
P	<0.0001	<0.0001	0.7	<0.0001	<0.0001
Race/ethnicity					
African American (vs. Caucasian)	0.03 (0.01)	-5.99 (1.07)	1.99 (2.00)	-0.06 (0.02)	-0.07 (0.05)
P	<0.0001	<0.0001	0.3	0.0008	0.2
Hispanic/Mexican (vs. Caucasian)	-0.04 (0.01)	7.50 (1.65)	4.94 (1.87)	-0.06 (0.01)	0.11 (0.05)
P	<0.0001	<0.0001	0.02	0.007	0.03
Other race (vs. Caucasian)	-0.02 (0.01)	2.69 (3.24)	-1.74 (2.11)	-0.03 (0.01)	-0.17 (0.09)
P	0.3	0.4	0.4	0.03	0.07
Body mass index, per 3.1 kg/m ²	<0.01 (<0.01)	-0.41 (0.31)	-0.49 (0.39)	0.01 (<0.01)	-0.13 (0.01)
P	0.01	0.2	0.2	0.001	<0.0001
Systolic BP, per 6.9 mmHg	<0.01 (<0.01)	0.59 (0.30)	-0.02 (0.70)	0.01 (0.01)	0.06 (0.02)
P	0.06	0.05	<1.0	0.3	0.001
Diastolic BP, per 7.0 mmHg	<0.01 (<0.01)	-0.38 (0.35)	0.09 (0.43)	<0.01 (0.01)	0.01 (0.01)
P	0.04	0.3	0.8	0.7	0.5
Model r ²	0.40	0.20	0.12	0.26	0.07

ACR, albumin-creatinine ratio; BP, blood pressure; eGFR_{CKiD}, estimated GFR calculated with the revised Schwartz formula; eGFR_{Schwartz}, GFR rate calculated with the original Schwartz formula.

Units: serum creatinine, mg/dl; GFR_{Schwartz}, ml/min/1.73 m²; GFR_{CKiD}, ml/min/1.73 m²; cystatin C, ACR, mg/g.

^aSeparate linear regression models for serum creatinine, GFR_{Schwartz}, GFR_{CKiD}, cystatin C, and log-transformed ACR as dependent variables and age, gender, race/ethnicity, body mass index, systolic BP and diastolic BP jointly considered as candidate explanatory variables. ACR was log-transformed because of non-Gaussian distribution characteristics. Parameter estimates are presented as beta coefficients (standard error). Intervals for continuous variables represent half the interquartile range.

^bThe exponents of the parameter estimates are as follows: -0.02 to 0.98, 0.41 to 1.51, -0.07 to 0.93, 0.11 to 1.12, -0.17 to 0.84, -0.13 to 0.87, 0.06 to 1.06, 0.01 to 1.01.

We found that ACR differs in US adolescents by gender and race, and is indirectly associated with BMI and directly associated with systolic BP. Limited data are available on ACR in healthy children. Previous studies have found ACR to be higher in females than in males (18,19). In our study, ACR at the 50th percentile was higher in Mexican/Hispanic adolescents than in African American and Caucasian adolescents. In contrast, a study of 534 healthy children (62% Caucasian, 19% African American, 7% Hispanic, 12% other) found no significant difference in ACR by race (19). An important new finding of our study is the indirect association between ACR and BMI and the direct association between ACR and systolic BP in healthy US adolescents without obesity or hypertension. High normal urinary albumin levels (10 to 20 mg/L) are associated with cardiovascular risk in apparently healthy adults, and there is a dose-response relationship between urinary albumin concentration and mortality (all-cause and cardiovascular) in the general adult population (20,21). Our findings suggest that the association between ACR and cardiovascular risk may be found in adolescence. In contrast to our findings, a study of urinary albumin excretion in 368 healthy adolescents (mean age 13 ± 1.2 years) found no association between albumin excretion rate (μg/min) and cardiovascular risk factors (systolic BP, BMI, lipids) (22). Consistent with our findings, a study of US young adults demonstrated that mean BMI was higher among those with albuminuria (29.4 kg/m²) than among those without albuminuria (28.3 kg/m², P

< 0.05) (23). As with studies in adults, our study revealed that adolescent males have lower ACR values than adolescent females (17,24). The mean ACR value in adolescents (25.2 ± 2.0 mg/g, 5th to 95th percentile 2.7 to 95.1 mg/g) is higher than in the adult population (12.5 ± 0.4 mg/g, 5th to 95th percentile 1.0 to 46.6 mg/g). The denominator, urine creatinine, potentially confounds ACR data. Studies in adults report greater urinary creatinine excretion in men than in women, and lower urinary creatinine excretion in adults with lower muscular mass, resulting in lower or higher ACRs in participants with similar urinary albumin excretion rates (17,25,26). Further studies are required to determine if “normal” ACR cutoffs should be increased for adolescents and whether different “normal” ranges are required for girls and boys.

We report distributions of serum creatinine, eGFR calculated by two methods, serum cystatin C, and ACR by gender and race/ethnicity in a nationally representative sample of healthy US adolescents aged 12 to 17 years. Given the findings of this study, a validation of the eGFR_{CKiD} formula in a large, diverse, healthy pediatric population is warranted, as is study of the association between ACR, BMI, and systolic BP in adolescents without obesity or hypertension.

Acknowledgments

This study was performed as a deliverable under Contract No. HHSN267200715002C (National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda,

MD). The authors thank United States Renal Data System colleagues Beth Forrest for regulatory assistance, Shane Nygaard for manuscript preparation and submission assistance, and Nan Booth, MSW, MPH, ELS, for editorial assistance.

Disclosures

None.

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Received: November 22, 2010 **Accepted:** April 4, 2011

Published online ahead of print. Publication date available at www.cjasn.org.

See related editorial, "GFR Estimation in Children: Questions and Answers (and Questions)," on pages 1810–1812.

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