Nigerian Journal of Paediatrics 2001; **28(4)**:119-22

Plasma Creatinine, Age and Body Surface Area in Nigerian Children and Adolescents

OO Oladipo*, MO Ajala*, OA Afonja****

Summary

Oladipo OO, Ajala MO, Afonja OA. Plasma Creatinine, Age and Body Surface Area in Nigerian Children and Adolescents. *Nigerian Journal of Paediatrics* **2001; 28:119.** In a bid to establish reference values for plasma creatinine in children and adolescents using age and body surface area (BSA), 462 apparently healthy Nigerian children/adolescents aged one day to 15 years were studied. They were recruited from well baby clinics, as well as primary and secondary schools. Plasma obtained from venous blood was analyzed for its creatinine in batches, employing the kinetic Jaffe method. There was a positive correlation between age and plasma creatinine ($r = 0.27$, $p<0.001$) and between BSA and plasma creatinine ($r = 0.28$, $p<0.001$). No gender difference was demonstrable. A multiple regression equation was obtained which relates age, BSA and plasma creatinine as follows: $y = 30.97 + 99x_1 + 0.023x_2$ where y = plasma creatinine in mmol/L, x_1 = BSA in M^2, and x_2 = the age in months. Two regression curves related plasma creatinine to age and to BSA. The values obtained should be useful for patient care because each child has his/her own predicted reference value according to the surface area and age; they should also serve as baseline reference values for healthy Nigerian children and adolescents.

Introduction

SERUM creatinine concentration is widely used as an index of renal function and a measure of glomerular filtration rate in adults and children.[1-3] Glomerular filtration rate (GFR) varies inversely with plasma creatinine and directly with surface area.[4] It is therefore, important that it is properly interpreted with appropriate reference values, taking into consideration the variables that affect its concentration. The concept of a constant daily production of muscle creatinine and thus, of serum creatinine in an individual derives from an understanding of the fundamental relationships between creatine, creatinine and muscle mass.[5] It is generally recognized that plasma creatinine concentrations in healthy individuals are directly related to body weight and muscle mass and increase with age. The total muscle mass varies with serum creatinine value,[6] age, sex, weight,[4] race,[7] diet [8,9] and height.[10] Most clinical laboratories in Nigeria provide a single reference range for serum creatinine measurements irrespective of these variables. Children and adolescents are constantly growing at different rates, which will affect the interpretation of their plasma creatinine levels. Intra-individual variations, usually less than 15 per cent, are largely due to dietary fluctuations in the consumption of creatine in meat products.[11,12] The purpose of this study is to derive a relationship between age, body surface area (BSA) and plasma creatinine in Nigerian children and adolescents so as to individualize the reference value for each child taking into consideration the BSA and the age, factors which affect plasma creatinine levels. This will also serve as a baseline for the interpretation of plasma creatinine results obtained in disease.

College of Medicine, University of Lagos
Department of Clinical Pathology
* Lecturer II
**Professor
General Hospital, Lagos Island
Department of Chemical Pathology
*** Consultant

Correspondence: OO Oladipo

Subjects and Methods

Children and adolescents aged between one day and 15 years, and of whom both parents were Nigerians, were recruited from five infant welfare clinics (88), ten primary schools (192) and five secondary schools (182) in the Lagos metropolis. Written consent was obtained from the local government sole administrators, school headmasters and principals as well as parents of the subjects admitted into the study. The schools were selected by random sampling, and consent for participation in the study was granted in respect of the students through consent forms completed by the parents, while oral consent was obtained from the

mothers of the pre-school children attending the infant welfare clinics. The 462 subjects comprising 199 males and 263 females were apparently healthy individuals. Obese, ill, malnourished children, patients with sickle cell disease and those taking any form of medication were excluded from the study. The length/height (metres) and weight (kilogram) of each child were recorded. One to three millilitres of blood were collected from each child in the morning (before 10 a.m.) into heparinized containers. This was to reduce the influence of exercise on the plasma creatinine and to ensure that specimens were obtained at a constant time in the day. The plasma samples obtained from the blood were stored at –20°C. Analysis was carried out in batches within one week of collection. "True plasma creatinine" levels were obtained using a direct kinetic modified Jaffe reaction.[13] Appropriate standards and controls were used for the assay.

The subjects were grouped by age and sex. The EPI-INFO 6.04 package was used for statistical analysis. Student's 't' test was used for comparison of means in the groups. Correlation and regression analyses were carried out to relate plasma creatinine values to age, weight, height and BSA.

Results

The distribution of plasma creatinine values in the population was Gaussian, hence standard deviation was used in the statistical evaluation.

The mean value of plasma creatinine in the subjects was 41.6 (15) μmol/L (range, 18-78 μmol/L), with a reference interval (at 95% confidence interval) of 26.6-56.6. Mean plasma creatinine in infants (aged <12 months) was 40.6 (14.9) μmol/L and this fell gradually and began to rise again, at about 54 months (Table I). This rise was gradual until 180 months (15 years). The mean plasma

Table I

Means (SD) of Body Surface Area, Plasma Creatinine, Weight and Height in Children and Adolescents

Age (mons)	*No of Subjects*	*Plasma Creatinine (μmol/L)*	*Body Surface Area (Metre²)*	*Weight (Kg)*	*Length/Height (Metre)*
<12	78	40.6 (14.9) [25.7 – 55.5]	0.03 (0.008)	5.76 (2.02)	0.58 (0.09)
12-54	52	30.2 (11.6) [18.6 – 41.8]	0.061 (0.016)	12.9 (2.3)	1.07 (0.71)
55-114	110	38.5 (15.6) [22.9 – 54.1]	0.085 (0.013)	21.5 (4.1)	1.21 (0.14)
115-180	222	47.1 (18.4) [28.7 – 65.5]	0.118 (0.02)	35.4 (9.3)	1.44 (0.15)

[ ] = reference interval of plasma creatinine in each age group.

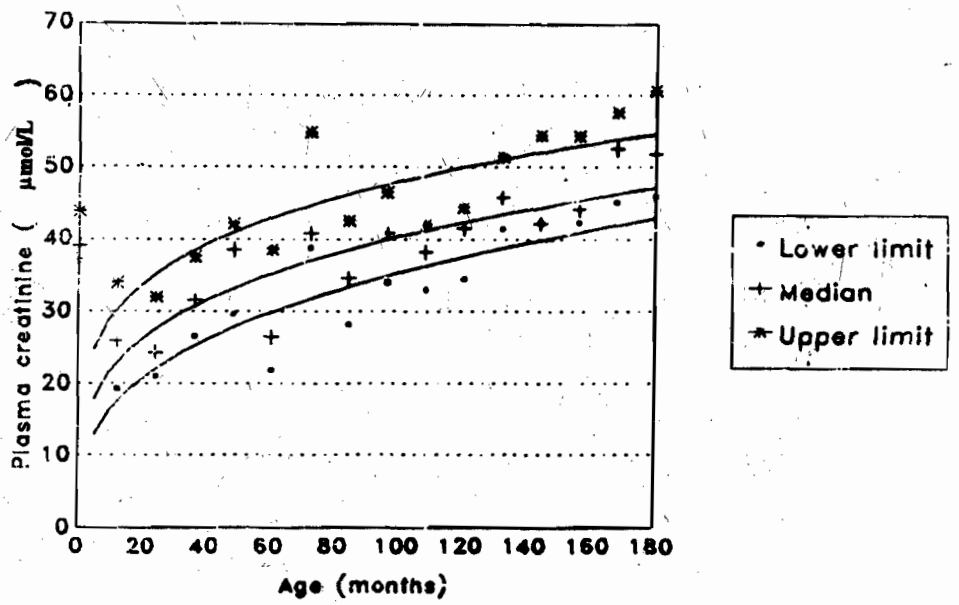

Fig. 1 Normogram of plasma creatinine values by age of subjects. The lower and upper values are the 95% confidence intervals for each age category.

Table II

Correlation Coefficients, P Values and Confidence Intervals of Variables

Variables	*Correlation Coefficient (r)*	*Coefficient of Determination (r^2)*	*P Value*	*95% Confidence Limits*
BSA vs PCr	0.28	0.08	<0.001	0.20 – 0.36
Age vs PCr	0.27	0.07	<0.001	0.19 – 0.36
Height vs PCr	0.17	0.03	<0.001	0.08 – 0.25
Weight vs PCr	0.33	0.11	<0.001	0.24 – 0.41

BSA = Body surface area
PCr = Plasma creatinine

creatinine in males was 42.4 (18) μmol/L while in females, it was 41.5 (16.6) μmol/L (p>0.05).

Height, weight and BSA increased with age (Table I). There was a positive correlation between age and weight, age and height and between age and BSA (Table II). There was also a positive correlation between (1) plasma creatinine and weight and (2) plasma creatinine and height (Table II). There was a positive linear correlation between plasma creatinine and age (r = 0.27, p<0.001) (Table II, Fig 1) and plasma creatinine and body surface area (r = 0.28, p<0.001; Table II; Fig 2). The regression curves in Figs 1 and 2 were drawn using the raw values. Multiple regression analysis was used to develop a relationship between plasma creatinine, BSA and age, using the following equation: $y = 30.97 + 99x_1 + 0.023x_2$ where y = plasma creatinine in μmol/L, x_1 = BSA in M^2, and x_2 = the age in months. The regression coefficients 99 and 0.023 represent the amount of change in the independent variables (age and BSA, respectively) per unit increase in y (plasma creatinine). The 95% confidence intervals for age and BSA were –0.049 – 0.096, and –14.69 – 213.09, respectively while the standard errors were 0.04 and 58.1, respectively. From the equation, it can be inferred that BSA has a stronger influence on the outcome of y than age. From the regression analysis curve (Figs 1 and 2), it is also possible to predict the plasma creatinine from the age or from the surface area.

Discussion

The mean plasma creatinine reported for infants less than 12 months was 40.6 μmol/L and this fell further to 30.2 μmol/L until about 54 months (4.5 years) when it began to rise steadily till age 180 months. A study carried out in Enugu,[14] on 246 healthy children aged 4-14 years revealed a steady rise in the mean plasma creatinine from 46.8 (11.4) μmol/L at four years of age to 60.9 (10.6) μmol/L at 14 years of age. Lower values were obtained in this study with the mean plasma creatinine being 38.5 (15.6) μmol/L at 4.5 years, and rising steadily to 47.6 (18.4)μmol/L at 15 years of age. The range of 18 mmol/L - 78 μmol/L is lower than that obtained in Enugu. The

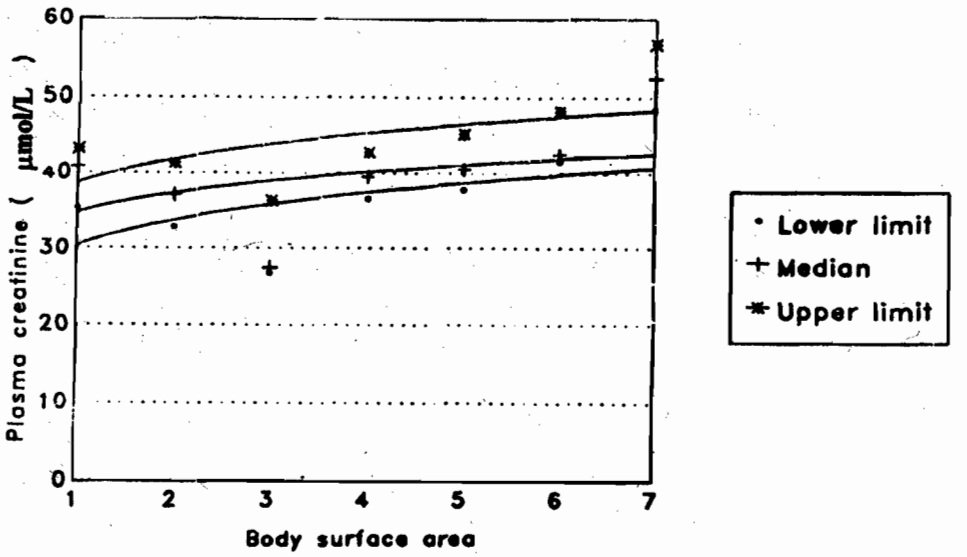

Fig. 2. Normogram of plasma creatinine values by body surface area of subjects. The lower and upper values are the 95% confidence intervals. 1=0.01-0.03; 2=0.031-0.050; 3= 0.05-0.07; 4=0.071-0.090; 5=0.091-0.11; 6 = 0.11-0.13 and 7=0.14 and above.

reason for these lower values may be attributable to the accuracy levels of the methods used; the present study measured "true creatinine" eliminating the quasi creatinine substances. Nicolino *et al*[15] reported a steady rise in plasma creatinine from the age of three months to 12 years of age while Schwartz *et al*[16] reported a steady rise from one year to 20 years. The pattern obtained in this study was different from those of previous studies with a decrease in plasma creatinine levels after 12 months and a steady rise from 54 months. A possible explanation is that meat consumption, which is a major source of dietary creatine, may be low in this age group. Recent studies on Nigerians have shown that creatinine excretion was affected by dietary habits.[17]

Positive correlations were reported between plasma creatinine and age, weight, height and BSA. This is in keeping with the theory that plasma creatinine concentration is proportional to muscle mass that can be estimated from the individual's age, sex and weight. This has formed the basis of the many formulas available for estimation of creatinine clearance from plasma creatinine.[18,19]

This study confirms other findings[14,20,21] that there is no gender difference in plasma creatinine values in children and adolescents. Gender differences have however, been reported after puberty and in adult males who have higher creatinine levels due to increased muscle mass.[21] Doolan *et al*[22] corrected plasma creatinine levels for sex and age using BSA and lean body mass in adults and demonstrated that muscle mass increased with age in them. Similar observations were made in this study in children and adolescents in whom there are corresponding increases in surface area with age. Although in previous studies, the plasma creatinine was not related to age and body surface area in children, our study and those of others[4] show that it is important to consider age and body size in the interpretation of plasma creatinine concentrations.

Since muscle mass increases significantly with growth, plasma creatinine levels must be adjusted for lean weight and height to assess renal function[22] especially as there are differences in muscle mass and therefore plasma creatinine levels between blacks and Caucasians.[7] The relationship between age, surface area and plasma creatinine in this study provides reference values in children taking into consideration the variables affecting the concentration of plasma creatinine and this also helps to assess their renal function.

References

1 Bjornsson TD. Use of serum creatinine concentration to determine renal function. *Clin Pharmacokinetics* 1979; **4**: 200-22.

2 Clermont MJ, Brion LP, Schwatz GJ. Reliability of plasma creatinine measurements in infants and children. *Clin Pediatr* 1986; **25**: 569-72.

3 Kassirer JP. Clinical evaluation of kidney glomerular function. *N Eng J Med* 1971; **285**: 385-9.

4 Perrone R, Nocolaos E, Levey A. Serum creatinine as an index of renal function: new insights into old concepts. *Clin Chem* 1992; **38**: 1935-54.

5 Heymsfield SB, Arteaga C, McManus C, Smith J, Moffit S. Measurement of muscle mass in humans: validity of the 24hour urinary creatinine method. *Am J Clin Nutr* 1983; **37**: 478-94.

6 Heymsfield SB, McManus C, Smith J, Stevens V, Nixon DW. Anthropometric measurement of muscle mass: revised equation for calculating bone free arm muscle area. *Am J Clin Nutr* 1982; **36**: 680-90.

7 Agamah ES, Webber LS, Lawrence M, Wattigney IN, Berenson GS. Serum creatinine and its relation to cardiovascular risk variables in children and young adults in a biracial community. *J Lab Clin Med* 1990; **116**: 327-34.

8 Hoogwerf BJ, Laine DC, Greene E. Urine C-peptide and creatinine (Jaffe method) excretion in healthy young adults on varied diets: sustained effects of varied carbohydrate, protein and meat content. *Am J Clin Nutr* 1986; **43**: 350-60.

9 Bleiler RE, Schedl HP. Creatinine excretion variability and relationship to diet and body size. *J Lab Clin Med* 1972; **59**: 945-55.

10 Schwartz GH, Brion LP, Spitzer A. The use of plasma creatinine for estimating GFR in infants, children and adolescents. *Pediatr Clin N Am* 1987; **34**: 571-90.

11 Edwards OM, Bayliss RS, Millen S. Urinary creatinine excretion as an index of the completeness of 24hour urine collection. *Lancet* 1969; **2**: 115-6.

12 Turner WJ, Cohn S. Total body potassium and 24hour creatinine excretion in healthy males. *Clin Pharm Therapeutics* 1975; **8**: 405-12.

13 Bartels H. Serum kreatininbestimmung ohne entelweissen. *Clin Chim Acta* 1972; **37**: 193-7.

14 Okoro BA, Onwuamaeze IC. Serum creatinine, urea and electrolytes in healthy as well as in children with homozygous sickle cell anaemia in a steady state. *Orient J Med* 1993; **5**: 62-5.

15 Nicolino M, Cochat P, Savaidarian B, David L. Value of blood creatinine in children. *Pediatrics* 1987; **42**: 393-7

16 Schwartz GJ, Haycock GB, Spitzer A. Plasma creatinine and urea concentration in children: normal values for age and sex. *J Pediatr* 1976; **5**: 828-30.

17 Taylor GO, Bamgboye EA, Oyediran ABOO, Longe O. Serum creatinine and prediction formula for creatinine clearance. *Afr J Med med Sci* 1982; **11**: 175-81.

18 Cockroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; **6**: 31-41.

19 Counaham R, Chantler C, Ghazali S. Estimation of GFR from plasma creatinine concentration in children. *Arch Dis Child* 1976; **51**: 875.

20 Jury BR. Serum creatinine concentration in children. Normal values for sex and age. *Austr NZ Med* 1979; **90**: 453-6.

21 Donkerwolke RAMG, Sander PC, van Stebelenburg GJ, Stoop JW, Tiddens HAWN. Serum creatinine values in healthy children. *Acta Pediatr Scand* 1970; **59**: 399-402.

22 Doolan PD, Alpen EL, Theil GB. A clinical appraisal of the plasma concentration and endogenous clearance of creatinine. *Am J Med* 1962; **32**: 65-79.