

CYSTATIN C, AGE AND GENDER IN HEALTHY AFRICAN BLACK ADULTS :

IVORIAN EXEMPLE

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Abstract

Background: On account of the limitations of creatinine, attention has focused in recent years on cystatin C, a small protein, to be the best marker of renal function evaluation. However data by race, particularly among African black populations are rare or missing.

Aim of this study was to determine in general Ivorian population, usual values of serum cystatin C according to age and gender.

Material and Methods: The study included 150 black healthy adult subjects, successively recruited at the National Blood Transfusion Center (CNTS) of Abidjan. Serum cystatin C was determined using particle-enhanced immunoassay method (PETIA).

Results: Serum cystatine C ranged from 0.43 to 1.45 mg/L with a confidence interval 0.87 to 0.91 mg/L. The averages are 0,92 +/- 0,12 mg/L in men versus 0,87 +/- 0,16 mg/L in women.

After 50 years, concentrations are 0,94 +/- 0,19 mg/L in women.

Conclusion: It appears that the values of serum cystatin found in Ivorian black peoples vary by age and gender. They are different from standards described in Caucasians .

Key words: cystatin C, black African, Ivorian

Introduction.

The evaluation of glomerular filtration rate (GFR) is indispensable to diagnosis of Chronic kidney disease (CKD). Several studies have shown that estimation of GFR using creatinine as the endogenous marker has many limitations - plasma creatinine follows partial tubular excretion with overestimation of GFR. Its production is highly variable, depending on muscle mass and is also subject to the interactions related to the measurement technique - In order to substitute creatinine, cystatin C, has been recently described as a new endogenous marker. Indeed plasma concentration of Cystatin C appears closely correlated with GFR [2,3]; Cystatin C (Cys C) is a non-glycosylated polypeptide produced by all nucleated cells in the human body. After being filtered without restriction by the glomeruli, CysC is entirely reabsorbed by the proximal tubules, where it is almost entirely catabolized. [1]. Moreover some studies have even described Cystatin C as a cardiovascular risk prediction biomarker particularly in the elderly [4, 5.6].

However, to our knowledge, none of the studies concerning this topic included black Africans, particularly Ivorians to date. Also, before considering Cys C use in the African black people for the estimation of GFR formulas or as cardiovascular marker, we should study the characteristics of Cys C in general African population.

Aim of this study was to determine in a healthy population of black Africans, the serum concentration of cystatin C and its possible physiological variations.

Materials and methods

Patient samples

The study involved 150 healthy alleged Ivorian black adults of both sexes (aged at least 18 years). They have been successfully recruited to the national blood transfusion center in Abidjan (Ivory Coast) from voluntary blood donors regularly monitored clinically and biologically. Health was appreciated by a medical examination on the day of recruitment, to eliminate acute and chronic diseases such as diabetes and high blood pressure. Biologically, people with a positive test for HIV, syphilis, hepatitis B or C were excluded. High blood urea, creatinine, bilirubin or triglycerides, and the presence of urinary stigmata nephropathy were also exclusion criteria. Each participant agreed to participate in the study after being instructed about to the protocol of the study. The study was approved by the National Ethics Committee . Blood samples were performed on fasted on gel tubes without anticoagulant. Then, the sera were obtained after centrifugation at 3500 r / min for 5 min.

Analytical method

Serum cystatin was determined by immunoturbidimetric method of particle-enhanced immunoassay technique (PETIA) [7]. We used the automatic analyzer Cobas Integra 400 plus (Roche Laboratories) with the time-quantR reagents Cystatin C gen: 2. The coefficients of variation range from 12% to 19%. Interference described to date with technical PETIA are an underestimate of cystatin C in serum bilirubin greater than 100 mg / L or higher serum triglycerides 15 g / L. These conditions were the exclusion criteria in our cohort.

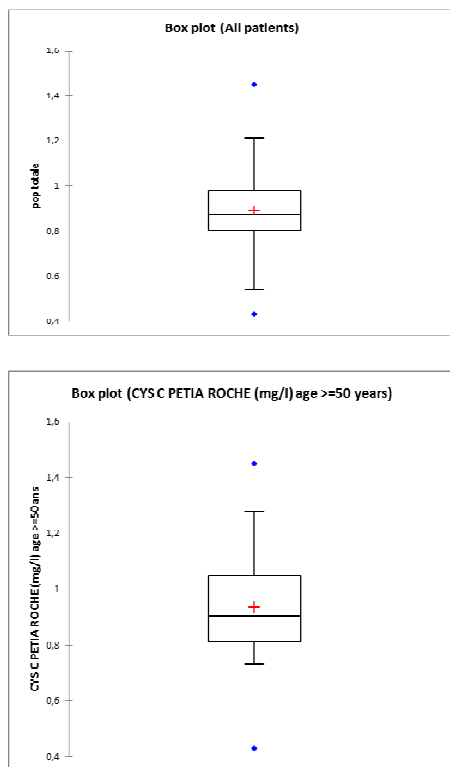
Statistical analysis

Statistical analyzes were performed with SPSS 21. The Shapiro-Wilk test was used to verify the normality of the distribution of values of cystatin. The variables were expressed as mean

+/- standard deviation. The results were compared using the Student t-test to the standards established in Caucasian populations with the same principle of immunoturbidimetric assay. [7]. We regard $p < 0,05$ as statistically significant.

Results

The mean age of subjects was 37 years, ranging from 18-65 years. The majority of the study subjects were female (sex ratio male / female: 0.66). The subjects under 50 years old accounted for 80% of the population study. The values of serum Cystatin C showed a normal distribution and ranged from 0.43 to 1.45 mg / L. (table1, figure 1).



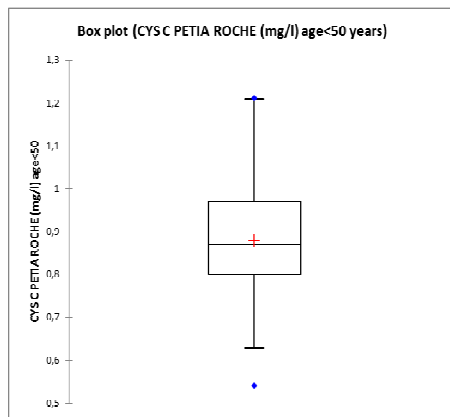


Figure 1 : Serum cystatine according age.

Table 1 : Characteristics of the population

Parameters	Value
Women , n (%)	90 (60%)
Age (mean +/-SD), years	37 +/- 11
Âge < 50 years, n (%)	120 (80%)
Âge >= 50 years , n (%)	30 (20%)

Mean serum cystatin was 0.89 ± 0.14 mg / L with a confidence interval 0.87 to 0.91 mg / L for the entire study population; ~~The coefficients of variation range from 12 to 19.~~ The age of the subjects has an influence on serum cystatin. Subjects aged 50 yeras and older have a significantly higher serum cystatin ($p = .02$) than younger (0.95 ± 0.19 mg / l vs 0.88 ± 0.13 mg / l). There was also a significant difference between the concentrations of serum cystatine about sex ($p = .049$). Table 2 shows the biological data.

Table 2: Serum cystatin C (mg/L) according to age and sex

Parameters (number)	Average +/- SD	Median (2,5–97,5 percentiles)	p
All (n = 150)	0,89 +/- 0.14	0,88 (0,8 – 0,980)	
Male (n = 60)	0,92 +/- 0,12	0,89 (0,82 – 0,99)	0,049
Female (n = 90)	0,87 +/- 0,16	0,87 (0,76 – 0,97)	
Age < 50 years (n = 120)	0,88 +/- 0,13*	0,87 (0,80 – 0,97)	0,022
Age >= 50 years (n = 30)	0,94 +/- 0,19	0,91 (0,81 – 1,05)	
Male <50 years (n = 54)	0,91 +/- 0,12**	0,88 (0,81 – 0,98)	0,010
Female < 50 years (n = 68)	0,85 +/- 0,13	0,85 (0,75 – 0,94)	

SD = standard deviation

* = values lower than those of the subject under 50 years old

** = values higher than those of women of the same age group

Discussion

Influence of race and ethnicity

The average values of cystatin C found in our series differ from those described in several studies in Caucasian populations [8, 9, 10]. Among several studies describing the reference values of cystatin C, we selected those using the immunoturbidimetry and based on rigorous analytical criteria while respecting the minimum sampling such as the study of Norlund [8]. Indeed this study meets current recommendations for reference values [11]. So even if they are not yet standardized, the serum cystatin reference values for PETIA assays may be considered to vary from 0.70 to 1.21 mg / l (before age 50) and 0.84 to 1.55 mg / l (after 50 years) [8]. More recently in Nigeria, Okonkwo [12] on black African population found average values of cystatin C similar to ours. This observation is in favor of authors under which cystatin C concentrations vary by race (13,14). The production and metabolism of cystatin could be related to race and ethnicity. As mentioned by Groesbeck and al. in their study in the US, it is possible for people of different races to have underlying genetic factors that alter the physiologic production and/or elimination of cystatin C. It may also be that this

represents differences in physiologic GFR by race/ethnicity [13]. Several previous studies have already shown the variability of reference values of some parameters according to race [15,16, 17]. In this sense, the work of Edjème and al. [15] showed a difference of Lpa limit value between African and Caucasian in relation with a change of this lipoprotein polymorphism between white and black people.

Influence of age

Variability age of cystatine C level found in our study has been reported by several authors [18,19, 20]. The most recent studies [21,22] described higher values in the newborn compared with adults, regardless of gender, height and weight of the child. According to these authors, physiologically high serum cystatin at birth, decreases to reach values adults at the age of 4 years [18] or even a year. [21] Some authors have even described in United States, a variation of cystatin C level during adolescence. According to them the variation in cystatin C levels is affected by growth and metabolic demands in adolescents [13]. The fact that cystatin C is not dependent, or significantly less than creatinine, muscle mass [21,23] is in pediatrics, an important theoretical advantage. Several studies have demonstrated the ability of cystatin C to detect renal failure pediatric earlier than creatinine or the estimation formulas of the GFR based on creatinine in particular that of Schwartz [24,25,26]. Also we can predict the value of cystatin C in the early detection of renal failure in black African children, although it is important to realize confirmatory studies on the child population.

In adults the majority of studies have confirmed a significant increase ($p < 0.05$) concentrations of cystatin C after 50 years old [8,18, 27,28,29,30, 31]. Also, a rise of 0.045 mg/L every ten years was even reported by some authors [34]. This elevation can theoretically be related to renal factors including poor kidney function depending on age [18, 33,34]. Extra-renal factors [35] with a relative decrease in muscle mass in the elderly were discussed.

Indeed contrary to earlier studies of Vinge [23], other authors like MacDonald [36] and Knight [19] showed that serum cystatin was partly related to muscle mass even though this dependence is significantly lower than that observed with creatinine.

Influence of gender

Unlike the study of Weinert [37], we found in subjects less than 50 years, lower cystatin values in women compared to men. This effect of gender on serum cystatine C has been reported in many recent studies for both PENIA and PETIA method [8,13,18,29,20,38] but the reasons for this difference are not yet clearly established. According Groesbeck [13], differences in cystatin C production may account for the lower serum cystatin C levels in girls. Higher extrarenal elimination, different hormonal variations, or factors that are present in female individuals and interfere with the cystatin C assay may also account for the difference by gender. Galteau and Knight [18,19], reported that this gender difference disappeared beyond 60 years. We have not been able to study this assertion because of the small size of this age group in our sample.

Conclusion

This study shows in Ivorian general population (black African), a variation of cystatin C according to age and gender. Concentrations are higher in patients older than 60 and in men. Otherwise, cystatin C appears to be influenced by race because the Ivorian values are similar to those of Nigerian, but differs from those of Caucasian.

We should now consider studies on larger numbers to determine reference values in healthy black African people (adults and children) and changes in pathological situations including nephrology and transplants, inflammatory processes, cardiovascular diseases and cancers where the interest of this marker is widely reported [39].

Conflict of interest: neither

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