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Blood Q Creatinine Based on Sex and Age in Healthy Indonesian Geriatrics

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ABSTRACT

Median blood creatinine (Qcr) is necessary for an accurate evaluation of geriatric renal function. Nonetheless, there is a significant void in existing literature concerning creatinine reference data unique to the elderly. To improve diagnostic precision and clinical decision-making in this susceptible group, this study developed a corresponding Q model for serum creatinine in geriatric patients stratified by age and sex. To determine the Qcr serum and reference range creatinine concentrations, 913 healthy elderly patients (452 males and 461 females) undergoing routine examinations at clinical laboratories were studied. Creatinine concentration reference intervals were divided into 3 age groups, namely: 60-69 years, 70-79 years, and >80 years. The median and percentiles p2.5 (lower reference limit/LRL) and p97.5 (upper reference limit/URL) were determined by the study. The study determined the Qcr serum creatinine and reference values for the elderly, stratified by age and sex. There were no significant differences observed in creatinine level across the age group, either in males or females. Males exhibited higher creatinine compared to females ($p < 0.05$). These recently developed, age- and sex-stratified Qcr values are an invaluable tool for clinical laboratories, enabling more precise, tailored care for elderly patients with renal issues and enabling clinicians to more accurately assess geriatric renal function.

Keywords: Creatinine, reference interval, kidney function, non-communicable disease

INTRODUCTION

The prevalence of chronic kidney disease (CKD) is forty percent higher in geriatrics, making it a serious and expanding health concern in older populations.[1] To date, there have been high cases of end-stage renal disease (ESRD) in the elderly that have increased by more than four times (20 percent).[2,3] Chronic inflammation, cognitive impairment, anorexia, and other factors may contribute to the complex pathophysiology of CKD in the elderly.[4] There is strong evidence that older adults with CKD are at a high risk of serious consequences, such as hospitalizations, ESRD, cardiovascular events, and even death. Therefore, it is critical to identify and treat kidney injury as soon as possible to slow the progression of CKD and eventually prevent the development of ESRD.[5]

Accurate evaluation of geriatric renal function is essential for kidney disease early detection and treatment.[6] Creatinine is a well-known indicator for evaluating kidney function. It has been shown that this endogenous marker is very helpful in identifying kidney diseases. Therefore, it is essential to establish reliable blood creatinine reference ranges that are age and sex specific. Clinicians can mitigate potential nephrotoxicity from medical interventions by using the serum creatinine reference range as a critical trigger for additional diagnostic evaluation and therapeutic intervention. These interventions could involve optimizing hydration status and closely monitoring the administration of medications.[3] In addition to being useful for identifying kidney damage, serum creatinine levels are essential for managing CKD and drug dosage because they allow for the estimation of GFR (eGFR) and allow for more individualized patient care.[7-9] The median creatinine (Qcr) has been widely used to normalize the significant factors affecting creatinine, including race, muscle mass, and geography. Seven factors were identified that significantly correlate with SCr reference values: latitude, annual sunshine duration, annual average temperature, annual average relative humidity, annual precipitation, annual temperature range, and topsoil (silt) cation exchange capacity.[10] Therefore, Qcr acts as a benchmark for understanding creatinine levels, particularly when looking at kidney function and eGFR using race-free formulas based on creatinine. Hence, the objective of this study is to establish reference intervals and Qcr

for blood creatinine levels and Qcr by utilizing data from geriatrics.

METHODS

Study Population

The following criteria were used to collect data from participants in Pramita Laboratorium's elderly routine screening program (PROLANIS) in 2023-2024: they had to be older than 60 and have undergone a creatinine test. People who had a history of diabetes or were sent from the diabetes clinic, had a history of kidney disease, kidney failure, or extremity amputation were excluded, as were those who were referred from the Nephrology Clinic or sent by their nephrologist. Laboratory information systems were used to obtain the creatinine concentration data in retrospect. The research was carried out in compliance with the 2013 revision of the Declaration of Helsinki. The Institutional Review Board of Dr. Soetomo Academic General Hospital (No. 2546/121/2/XI/2023) agreed to this study. Due to the retrospective nature of our study, the Ethics Committee waived the requirement for consent. During and after data collection, the authors did not have access to personal information.

Serum creatinine examination

The concentration of creatinine in the blood was determined by enzymatic methods using an automated chemistry analyzer (Architect Abbott, USA). An IDMS calibrator (calibrator number 08P65/6K30, Abbott, USA) was used to track each test. To guarantee internal quality control in the creatinine measurement, two levels of Lyphochek-assayed chemical quality control materials (Bio-Rad, Hercules, CA, USA) were carried out twice daily. The serum creatinine test's within-laboratory precision and coefficient of correlation (CV) were 1.19% and 0. 67% at QC levels 1 and 2, respectively, during the study period. The laboratory participated in the external proficiency testing program (BBLK) of the Indonesian Association of Quality Assurance for Clinical Laboratory in 2023-2024, and all of the results were positive (Z-scores ranging from 0.14 to 1.09).

Statistical Analysis

The Kolmogorov-Smirnov test was used to perform normality tests on blood creatinine concentration data at a significant level of p <0.05. Creatinine concentration reference intervals were divided into 3 age groups based on a previous study, namely: 60-69 years, 70-79 years, and >80 years.[11] The number of male participants was 170 for the age group 60-69, 132 for 70-79, and 151 for those over 80. For females, the participant counts were 146 for ages 60-69, 146 for 70-79, and 169 for ages over 80. We used Box-Cox transformation and Tukey's method (1977) to remove outliers from each age group in a dataset of 460 males and 465 females. This allowed us to calculate or estimate the reference interval for each age group, yielding 453 (49.5 percent) males and 461 (50.5 %) females. In order to identify outliers, the lower and upper quartiles-which represent the data set's 25th (Q1) and 75th (Q3) percentiles, respectively-must be determined. Q1 minus 1 point 5 times the interquartile range (IQR) represents the lower boundary, while Q3 plus 1 point 5 times the IQR represents the upper boundary. Any data point that lies outside of the defined boundaries either above the upper boundary or below the lower boundary is referred to as an outlier.[12] For continuous variables, the data were displayed as the median and interquartile range (IQR). The median and percentiles p2.5 (lower reference limit/LRL) and p97.5 (upper reference limit/URL) were determined by the study. Age group differences were evaluated using the Mann-Whitney U test, which was significant if p <0.05. Version 20.218 of the MedCalc® software for Windows was used to perform statistical analyses.

RESULTS AND DISCUSSIONS

The Qcr levels for males and females were 1.02 mg/dL and 0.71 mg/dL, respectively, and did not differ significantly between age groups. Male and female Qcr levels differed significantly (p <0.001). We established serum creatinine reference values for geriatrics based on age and sex, which were 0.70-1.6 mg/dL for males and 0.49-1.04 mg/dL for females (Table 1 and Figure 1).

Serum creatinine is regularly tested in clinical chemistry labs worldwide.[8] Despite its drawbacks, this endogenous marker test is less expensive than other markers used to evaluate kidney function.[13] Creatinine serum concentration measurement is very helpful in diagnosing CKD, determining the right dosages for treatment, and evaluating kidney damage.[14-16] As a result, creating age and sex specific reference values for blood creatinine especially in the geriatric population is essential. This study fills this urgent gap by offering clinicians and labs crucial information for interpreting geriatric creatinine levels. An essential first line marker for possible renal dysfunction isthese recently defined reference intervals. The significance of these reference values

Table 1. Characteristic demographic and median creatinine level across age and sex groups.

Variable	60-69 years	70-79 years	>80 years	Total	*p* value
Male n(%)	170 (37%)	132 (30%)	151 (33%)	453	0.46$
BMI median (IQR)	27 (26-28)	25.5(25-27)	25 (25-26)		
Creatinine (mg/d L) Median (IQR)	1.01 (0.89-1.14)	1.04 (0.90-1.16)	1.01 (0.89-1.18)	1.02 (0.89–1.16)	0.55*
Reference range (p2.5-p97.5)				0.70-1.60	
Female n(%)	146 (32%)	146 (32%)	169 (36%)	461	0.88$
BMI median (IQR)	25 (25-26)	27 (26-28)	26 (25-27)		
Creatinine (mg/dL) Median (IQR)	0.72 (0.63-0.81)	0.71 (0.60-0.82)	0.71 (0.60-0.81)	0.71 (0.61-0.81)	0.60*
Reference range (p2.5-p97.5)				0.49-1.04	
Creatinine Male vs Female (mg/dL)	1.02 (0.89-1.16) vs 0.71 (0.61-0.81)				0.001#
n (%)	913				0.98*
Male	452 (49.5%)				
Female	461 (50.5%)				
Age years (median, IQR)					0.57*
Male	74 (65-83)				
Female	73 (66-80)				
BMI (95%CI)					0.69*
Male	26.88 (26.37-27.41)				
Female	25.43 (25.13-25.84)				

Note: *Kruskal-Wallis, # Mann-Whitney Test, $Friedman Test

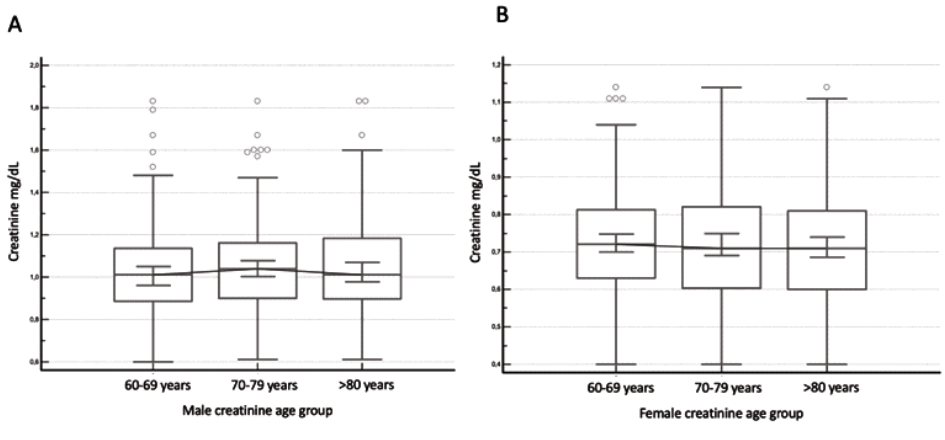

Figure 1. Male (A) and Female (B) box plot median creatinine (mg/dL)

for early detection and intervention is highlighted by the fact that even creatinine elevations that fall within population derived "normal" ranges may signal the beginning of renal compromise.[17]

There is a substantial clinical and laboratory gap due to the glaring lack of geriatric Qcr data for people up to 60 years old. Since the creatinine level is influenced by factors such as muscle mass, sex, age, race, etc., the Qcr may vary among populations.[17] The Qcr is significant because it serves as a benchmark for interpreting creatinine levels, especially when considering kidney function and glomerular filtration rate (eGFR) estimation using creatinine-based formulas.[18] Serum creatinine can be rescaled using the "Q" values, which are obtained from median creatinine curves. This increases the

precision of eGFR estimations, particularly in diverse populations. By rescaling or normalizing serum creatinine measurements, these values enable more precise comparison and interpretation among various people and populations.[16,19,20] The significance of median Q lies in its ability to improve eGFR estimation by correcting differences in serum creatinine (SCr) caused by age, sex, muscle mass, and race-all of which can have an impact on creatinine production. As a result, eGFR equations-which are frequently used to evaluate kidney function-are more reliable. The eGFR equations to be used accurately, SCr must be standardized using Qcr values.[16,19] Therefore, determining the Qcr model is advantageous since it can be applied as a determinant in the creatinine-based race-free estimated glomerular filtration rate (eGFR) formula. The European Kidney Function Consortium (EKFC), Lund-Malmo, Full Age Spectrum (FAS) and Berlin Initiative Study (BIS) are a few formulas that use normalized creatinine. Even among geriatrics, this formula is frequently utilized. For instance, it has been demonstrated that EKFC is better than the well-known CKD-EPI 2021 formula, even when applied to American population.[21]

Creatinine levels vary significantly between sex groups. Creatinine level variations may be influenced by a number of factors, including age, gender, and ethnicity.[17] Since creatinine levels are crucial for assessing renal function, interpreting blood creatinine levels must be done with care, particularly in older adults, because of the influence of variables like age and muscle mass variations.[22] Textbooks, research journals, and national references are some of the sources of the reference range used in laboratory procedures; in the absence of these, the laboratory typically uses data from manufacturers. The insert kit for the Abbott enzymatic examination used in this study only showed the normal range for adults; it did not show the normal range for elderly people. For this reason, doctors and labs can greatly benefit from this reference interval research. A common obstacle in geriatric research is obtaining data specifically from healthy older adults, which presented difficulties for this study even though laboratory validation of reference intervals, as Ozardo explains, is essential.[23] Larger sample sizes are required to further refine these intervals, as evidenced by the notable inter-age group variability that has been observed. Despite possible inherent drawbacks, the indirect methodologies used here to establish reference intervals provide a practical and statistically sound method when dealing with large data.

The Qcr in adults has been extensively researched[24]; however, its occurrence in geriatric, particularly in multi-regions like Indonesia, is still unknown. In populations with a wide range of ethnicities, such as Indonesia (300 ethnicities and inter-ethnic marriages), it is imperative to establish a Qcr that can be used to apply the eGFR formula regardless of the individual's race.

LIMITATION

Authors were unable to minimize the potential influence of factors affecting creatinine levels due to the limited exclusion of data, such as the status of geriatric individuals as professional bodybuilders, athletes, or those with eating problems that may affect muscle mass and subsequently affect creatinine values.

CONCLUSIONS AND SUGGESTIONS

Geriatric reference intervals and associated Qcr levels were established through the stratification of clinical laboratory data by age and sex. These recently developed, sex and age specific reference values and Qcr give clinical labs an essential tool that enables physicians to evaluate geriatric renal function more precisely. As a result, this improved diagnostic method makes it easier to make accurate and timely diagnoses, which eventually improves the clinical outcomes for elderly patients with renal diseases.

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