



Role of Blood Urea Nitrogen and Serum Creatinine in Disease: An Observational Retrospective Study from India's Northernmost State, Kashmir Valley

Tahseen Bilal Rather¹, G A Bhat¹, Irfan Rashid¹, Sayima Farooq¹, Mir Zubair Ahmad¹, Asgar Ali¹, Asif Ahmad¹, Abid-u-satar¹, Altaf Hussain Khan² and Syed Mudassar^{1*}

¹Department of Clinical Biochemistry, SKIMS, Srinagar, Kashmir, India

²Department of Microbiology, SKIMS, Srinagar, Kashmir, India

*Corresponding Author: Syed Mudassar, Professor and Head, Department of Clinical Biochemistry, SKIMS, Srinagar, Kashmir, India.

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Abstract

Background: Urea and creatinine are protein metabolites that can be used to evaluate renal function. More importantly, the ratio of blood urea nitrogen (BUN) to creatinine (Cr) is a more valuable measure in predicting many diseases than urea and creatinine alone.

Aim: The purpose of this study was to document the serum urea and creatinine levels, as well as their ratio, in our study population and to investigate their impact on our study population.

Methods: In this retrospective observational study, 3181 subjects of all ages were recruited for kidney function test analysis (KFT). The fully automatic Biochemistry analyser (Beckman coulter 5800) was used for Biochemistry analysis. Both urea and creatinine were measured enzymatically.

Results: The median serum urea and creatinine levels documented in mg/dl were as 41 (IQR = 49) and 0.95 (IQR = 0.80). Further, a statistically significant association was found between gender and age group with both urea and creatinine (p value < 0.001). We also found a strong positive correlation between serum urea and creatinine levels, $r = 0.69$ (p < 0.001). Further, a weak to moderate positive correlation was noted between urea and age, $r = 0.50$ (p value < 0.001) and a weak positive correlation was also observed for creatinine and age, $r = 0.40$ (p-value < 0.001). We also found a high BUN/Cr ratio in males (37:1) and females (40:1). Further, the ratio was also higher in different age groups. Participants < 20 years old presented a ratio of 65:1, however those between 20-40 years old retained a ratio of 33:1, whereas individuals >40 years old showed a ratio of 40:1.

Conclusion: Our findings show that blood levels of both urea and creatinine were within the reference range; nevertheless, the increased serum urea nitrogen to creatinine ratio may be useful in evaluating renal and heart associated problems.

Keywords: Urea; Creatinine; Acute Kidney Injury; Kashmir; COVID-19

Introduction

Among many other non-communicable diseases, renal disease is one of the well-known growing global health problem, which includes various sub-types like acute kidney injury (AKI), chronic

kidney disease (CKD) and nephrotic syndrome [1,2]. CKD is common with an incidence rate of about 9–13% in the general adult population [3]. In USA the leading cause of CKD is diabetes mellitus (DM) accounting for a total of 38% of prevalence of end-stage renal disease (ESRD), respectively [4,5]. In India renal diseases is

on the rise. In one of the study, the prevalence of early stage CKD in healthy central government employees was reported [6]. In Kashmir the burden of renal disease is on rise with a substantial number of population individuals getting affected by renal disease. In 2016, a study found the significant prevalence of urinary tract and renal disease in the young children of Kashmir [7]. Another study reported the pregnancy related AKI in Kashmir valley [8]. Various laboratory parameters are in use to assess renal function. Out of all these serum urea and creatinine (Cr) are most commonly used [9]. Serum creatinine concentration is recommended as the most reliable and appropriate single measure for the detection of the renal function as endogenous serum creatinine levels usually remains constant with negligible variance. Blood urea nitrogen (BUN) varies with diet, the level of renal function, amount of protein breakdown, rate of urine flow and quantity of dietary protein intake. Serum urea which represents alterations in nitrogen load as well as renal function, may better indicate the level of clinical illness [10,11]. Urea and creatinine are nitrogenous catabolic end products. Urea is increased in infections and fever, Cushing's syndrome, thyrotoxicosis, congestive heart failure, patients with renal disease which are bedridden and inactive and have low muscle mass [9]. The normal BUN/Cr ratio (BCR) ranges from 10:1 to 20:1 [12]. Various studies have also reported that BUN/Cr ratio is a valuable parameter than SUN or Cr alone in predicting the progression of patients with Acute Heart Failure as well as in predicting the severity of COVID-19 because they are cost-effective and easy to apply [13,14].

Considering the growing global burden of kidney related disorders, availability of limited data sources, also increasing trend of renal disease and presently Covid-19 explosion in our population [15,16], this study was aimed to document the normal serum levels of urea and creatinine, their ratio, their comparison with the international levels, and to see whether there exists a correlation between the two parameters. The study was conducted in the valleys primary tertiary care hospital, Sheri- Kashmir Institute of Medical Sciences, Soura Srinagar (SKIMS).

Materials and Methods

In this observational retrospective study, all the subjects hailing from different corners of the Kashmir valley were enlisted who visited SKIMS for clinical advice and were directed for various

Biochemical investigations from various sections of the institute (OPD/IPD departments). A total of 23367 subjects were suggested for Biochemistry testing in addition to other test parameters such as haematology, endocrinology, microbiology etc. Among all such parameters, kidney function test was recommended for 3181 patients. A fully automated analyser (Beckman Coulter, AU5800) with a capacity of 2000 tests per hour was used to analyse all biochemistry parameters. The normal range of urea nitrogen serum varies according to various methods used. In our study population it ranges from 15 to 45 mg/dl [17]. Serum creatinine varies with the subject's body muscle mass and with the calculation method used. For the adult male, the normal range is 0.6 to 1.2 mg/dl, or 53 to 106 $\mu\text{mol/L}$ by the kinetic or enzymatic method, and 0.8 to 1.5 mg/dl, or 70 to 133 $\mu\text{mol/L}$ by the older manual Jaffe reaction [18]. For the adult female, having low muscle mass generally, the normal range is 0.5 to 1.1 mg/dl, or 44 to 97 $\mu\text{mol/L}$ by the enzymatic method. The normal SUN/Cr ratio is 8:1 to 10:1 [19]. Serum creatinine level was measured by Jaffe's reaction [18], while as blood urea nitrogen (BUN) was estimated by enzymatic method given by Talke and Shubert [17]. The institute's barcode system removes any likelihood of proxy, as previously data analysed from various patients on previous visits was discarded.

Results

Statistical analysis was done by using Spssv26. The median age of the participants was 53 years. Out of 858 participants, 478 (55.71%) were males and 380 (44.28%) were females. 61 (7%) subjects had age < 20, whereas 215 (25%) were those between 20-40 years old and 582 (68%) belonged to age group >40. The overall median serum urea and creatinine level documented in mg/dl were as 41 (IQR = 49) and 0.95 (IQR = 0.80), males had high median urea and creatinine levels (46, 1.07) than females (38, 0.82). The serum urea and creatinine levels in different age groups were recorded as, <20 (25, 0.37), 20-40 (27, 0.78) and >40 (50.5, 1.08). On further analysis we noted a significant association of gender with both urea and creatinine (p value < 0.001). A comparison between different age groups with urea and creatinine, also yielded a statistically significant association (p value < 0.001). Further, a moderate to strong positive correlation was also observed between the two lab parameters $r = 0.68$ (p value < 0.001). Additionally, also a weak and moderate positive correlation was sighted between creatinine and urea with age, ($r = 0.377$, $r = 0.477$, p -value < 0.001).

We also found a high BUN/Cr ratio in males (37:1) and females (40:1). Further, the ratio was also higher in different age groups. Participants < 20 years old presented a ratio of 65:1, however those between 20-40 years old retained a ratio of 33:1, whereas individuals >40 years old showed a ratio of 40:1.

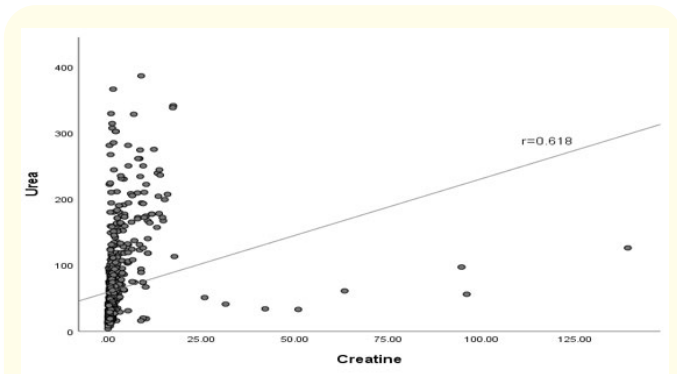


Figure 1: Depicting correlation between BUN and Cr.

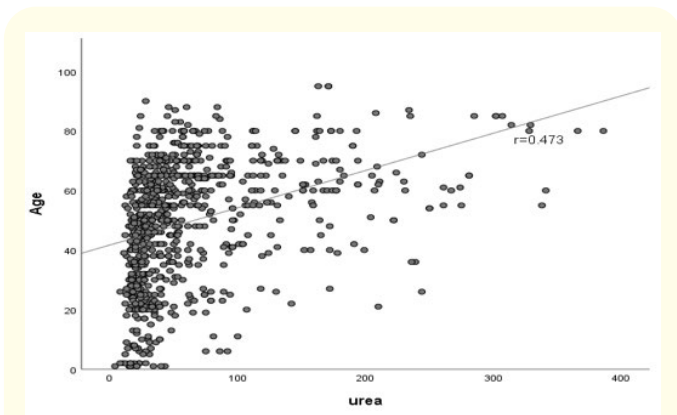


Figure 2: Showing correlation between urea and age.

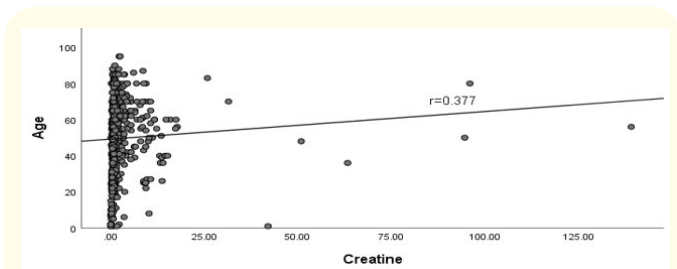


Figure 3: Represents relation between age and creatinine.

Variable	Reference range (mg/dl)	N	Median (IQR)
Urea	15-45	858	41.61(49)
Creatinine	0.5-1.5	858	0.95(0.80)

Table 1: Reference and mean serum urea and creatinine level in study population.

Urea	N	Mean Rank	P-Value
Gender			
M	478	465.39	<0.001
F	380	384.36	
Age			
(i) <20	61	122.02	0.068
20-40	215	143.17	
(ii) 20-40	215	270.84	<0.001
>40	582	446.34	
(iii) <20	61	156.41	<0.001
>40	582	339.36	
Creatinine			
Gender			
M	478	475.19	<0.001
F	380	372.03	
Age			
(i) <20	61	86.14	<0.001
20-40	215	153.36	<0.001
(ii) 20-40	215	300.42	
>40	582	435.42	<0.001
(iii) <20	61	136.63	
>40	582	341.43	

Table 2: Comparison of urea and creatinine with gender and different age groups in study population.

Discussion and Conclusion

Serum urea and serum creatinine are two very important lab parameters used to assess renal function. For several decades, creatinine has been used as a gold standard to measure kidney function and to manage patients with CKD and AKI [20]. Serum urea levels also predominantly increase in the advanced states of kidney diseases. The reference range of serum creatinine and urea levels for the 858 subjects were 0.95 mg/dL and 41 mg/dL respectively. These results are quite consistent with reference values (creatinine 0.8-1.3 mg/dL, urea 22.36- 33.16 mg/dL) that were adopted internationally by Medscape [10,21]. although

median serum levels of these parameters in our population were in the normal reference range, but their levels were approaching threshold upper limit. Similar results were documented by various researchers in previous studies [22,23]. Males with increasing age had higher levels of urea and Cr as compared to females and younger population (p value <0.001), fairly similar results were offered by earlier studies worldwide [24,25]. Another important finding was the significant increase in median BUN/Cr ratio. BUN levels ten times greater than serum creatinine levels have been reported in patients with advanced renal failure who are in a steady state without catabolic stress [11,26,27]. We also noted a strong positive correlation ($r = 0.68$) between the two parameters. These findings are in agreement with the earlier results reported in previous studies around the globe [28].

The study does, however, have certain limitations, including the fact that we were unsure of the illness condition of the patients.

In conclusion our findings show that the serum levels of both urea and creatinine were in reference range, the higher serum urea nitrogen to creatinine ratio may be helpful to evaluate kidney and heart related disorders in this disadvantageous subpopulation.

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