Original Article

A Study of Serum Creatinine and Urea in Adult Female Individuals and their Correlations with BMI

Safina Akhter[1], Chandra Rani Sarkar[2], ATM Zoadur Rahim Zahid[3], Neaz Ahmed[4]

1. Assistant Professor
   Department of Physiology
   Rangpur Medical College
2. Professor and Head
   Department of Physiology
   Rangpur Medical College
3. Professor and Head
   Department of Physiology
   Dinajpur Medical College
4. Assistant Professor and Ex-Head
   Department of Biochemistry
   Rangpur Medical College

Correspondence to:
Safina Akhter
Assistant Professor
Department of Physiology
Rangpur Medical College
Mobile: 01710044837
E-mail: itssabahsafina@gmail.com

Abstract

Background:
The World Health Organization has announced overweight and obesity as a global epidemic that has strong associations with renal function impairment.

Objectives:
To evaluate the serum creatinine and urea status in adult female individuals with previous normal renal function and to observe the correlation of serum creatinine and urea with body mass index (BMI).

Methods:
This cross-sectional analytical study was conducted in the Department of Physiology, Rangpur Medical College, Rangpur. After briefing about the objectives, adult female subjects who met the inclusion and exclusion criteria were enrolled in the study with permission. The study included 90 subjects who were divided into three groups- apparently healthy adult females with normal weight (Group-A), apparently healthy overweight adult females (Group-B), and apparently healthy obese adult females (Group-C). The subjects were selected from different areas of Rangpur city. Their body mass index, serum creatinine, and urea were measured. For statistical analysis, one way ANOVA (post-Hoc) test and Pearson's correlation coefficient test were performed as applicable by computer-based SPSS-25.0 for windows. Regarding the interpretation of results, $p \leq 0.05$ was accepted as significant.

Results:
The mean serum creatinine level was significantly ($p \leq 0.001$) higher in overweight and obese female adults than in normal-weight female adults. It was also significantly ($p \leq 0.05$) higher in obese female adults than in overweight female adults. Again, the mean serum urea level was significantly ($p \leq 0.05$) higher in overweight female adults than normal-weight female adults and in obese female adults than in overweight female adults. It was also significantly ($p \leq 0.001$) higher in obese female adults than in normal-weight female adults. This study also found highly significant ($p \leq 0.001$) positive correlation of serum creatinine ($r=0.499$) and urea ($r=0.396$) with body mass index.

Conclusion:
Serum creatinine and urea were elevated in overweight and obese female adults and both parameters were positively correlated with BMI. Regular body mass index screening is recommended to assess body weight easily and effectively.

Keywords: Obesity, Overweight, Serum Creatinine, Serum Urea, Body Mass Index.

Introduction:

Body mass index (BMI) is a measure of body fat based on height and weight that applies to adult men and women.[1] The regional office of the World Health Organization for the Western Pacific Region, The International Association for The Study of Obesity, And The International Obesity Task Force have categorized normal weight as BMI 18.5 to 22.9 kg/m^2, overweight as BMI 23 to 24.9 kg/m^2 and obesity as BMI 25 kg/m^2 or higher for

the Asian adults.[2] When body weight is >20% above average, mortality rises 20% in men and 10% in women. Obese people with BMI greater than 30 kg/m^2 have a greater risk of dying earlier than non-obese.[3] In 2016, more than 1.9 billion adults aged 18 years and older were overweight worldwide, of these over 650 million were obese.[4] The rate of being overweight or obese climbed from 7% in 1980 to 17% in 2013 for Bangladeshi adults.[5] Overweight and obesity are the fifth leading preventable cause of death worldwide.[6] WHO estimated that 4.5 million deaths worldwide in 2013 were attributable to complications caused by overweight and obesity.[7] Overweight and obesity are leading nutritional disorders.[3] These are the conditions of abnormal or excessive fat accumulation to the extent that health may be impaired. An energy imbalance between consumed and expended calories is the fundamental cause of obesity.[4] Nowadays this effect has been attributed to dietary changes and reduced physical activities. The risk associated with obesity is determined by the amount of fat as well as fat distribution.[2] Adverse health outcomes associated with overweight and obesity range from non-fatal debilitating diseases to increased risk of mortality.[8] The World Kidney Day 2017 promoted education on the harmful consequences of obesity and its association with kidney diseases.[9] Increased BMI is directly associated with increased chronic kidney disease (CKD). The adult prevalence of CKD is 13% and still growing. A higher BMI is associated with increased prevalence and incidence of nephrolithiasis.[10] 10% of all kidney cancers are attributable to excess body weight. It is also evident that weight loss improves kidney function in obese subjects.[9] Creatinine is the cyclic anhydrase of creatine that is produced as the final product of the decomposition of phosphocreatine. Under normal conditions, the daily creatinine production is apparently quite constant and depends on body size.[11] Concentration of serum creatinine has long been the most widely used and commonly accepted measure of renal function in clinical medicine.[12] Elevated blood urea nitrogen represents an independent marker of renal dysfunction. A study in India suggested that the rise of serum creatinine and urea should be regarded as a precursor of renal function loss in overweight and obesity.[13] The renal consequences of excess body weight may begin at an early stage of obesity before the clinical manifestations become apparent.[13] This study has been designed to assess serum creatinine and urea in adult female individuals and to observe the correlation of these parameters with BMI, which would emphasize screening of overweight and obese female adults on the basis of BMI to prevent associated renal complications.

Methods:

This cross-sectional analytical study was conducted from January 2019 to December 2019 in the Department of Physiology, Rangpur Medical College, Rangpur. The Rangpur Medical college ethical committee and thesis protocol review committee approved the study protocol. A total number of 90 female adults aged from 20-45 years from different areas of Rangpur city, who fulfilled the inclusion and exclusion criteria were included by numbering. The purposive sampling technique was used for the selection of study subjects. After the selection of subjects, the objectives and procedures of the study were explained in detail and their informed written consent was taken in easily understandable Bengali phrases. A standard questionnaire was filled up after taking history and thorough clinical examinations.All the study subjects were divided into three groups on the basis of their body mass index, among them, 30 normal-weight female adults were denoted as group A (BMI 18.5-22.9 kg/m^2), 30 overweight female adults were denoted as group B (BMI 23-24.9 kg/m^2) and 30 obese female adults were denoted as group C (BMI 25 kg/m^2 or higher). The subjects in each group were matched in their age and socio-economic condition. Adult female individuals with previous abnormal renal function in the form of acute or chronic kidney diseases or abnormal serum creatinine level, history of diabetes mellitus, hypertension, liver disease, tobacco and alcohol abuse, endocrine disorders (thyroid, adrenal diseases, etc.),psychiatric disorder (depression), taking neurotoxic drugs, pregnancy, and lactation were taken as exclusion criteria.

Measurement of body mass index (BMI):[14]

The height and weight of each individual were measured by measuring tape and medical weighing machine respectively. Body mass index was calculated as the body weight in kilograms divided by the square of height in meters.

BMI = Weight in kilograms / Square of height in meters (kg/m^2)

Collection of blood and sample processing:
All study subjects were advised to be in an overnight (8-10 hrs) fasting state. Then they were attended the next day at 8.00 am at the Department of Physiology, Rangpur Medical College, Rangpur. 5 ml of fasting venous blood was collected from the antecubital vein from each subject under all aseptic precautions by a disposable syringe. Needles were detached from the nozzle and blood was immediately transferred into a de-ionized test tube with a gentle push to avoid hemolysis. The test tubes containing blood were kept in a standing position till the formation of a clot. Serum was separated by centrifuging the blood at 3000 mp for 5 minutes. The clear supernatant was taken and kept in ependorffs. Biochemical tests for serum creatinine and serum urea were carried out as early as possible by enzymatic colorimetric method at the Department of Biochemistry, Rangpur Medical College, Rangpur. Normal level of serum creatinine and urea were 0.5-1.1 mg/dl[15] and 15 - 40 mg/dl[16] respectively.

Statistical analysis:
All data were recorded systematically in a preformed history sheet and statistical analysis was done by computer using SPSS–25.0 version for windows. Comparison of serum creatinine and urea between study groups was done by one-way ANOVA (post-Hoc) test. To observe the correlation of serum creatinine and urea with BMI in the whole study group, Pearson's correlation coefficient test was done. Regarding the interpretation of results, ≤0.05 level of probability (p) was accepted as significant.

Results:
Table-I showed the mean ± SD of age, height, weight, and BMI of a total of 90 adult females. The mean ± SD of age was 28.10 ± 9.09 years in group A, 33.20 ± 8.34 years in group B, and 33.87 ± 8.23 years in group C. The mean ± SD of height were 1.56 ± 0.05 m in group A, 1.61 ± 0.07 m in group B, and 1.54 ± 0.07 m in group C. The mean ± SD of weight was 51.73 ± 5.63 kg in group A, 62.83 ± 5.43 kg in group B, and 68.20 ± 7.93 kg in group C. The mean ± SD of BMI was 21.30 ± 1.69 kg/m2 in group A, 24.31 ± 0.51 kg/m2 in group B, and 29.00 ± 3.70 kg/m2 in group C.

Table-I: Mean ± SD of age, height, weight, and BMI of the study subjects in group A, group B, and group C

Parameters	Mean ± SD		
	Group A	Group B	Group C
Age (years)	28.10 ± 9.09	33.20 ± 8.34	33.87 ± 8.23
Height (m)	1.56 ± 0.05	1.61 ± 0.07	1.54 ± 0.07
Weight (kg)	51.73 ± 5.63	62.83 ± 5.43	68.20 ± 7.93
BMI (Kg/m^2	21.30 ± 1.69	24.31 ± 0.51	29.00 ± 3.70

Table-II showed a statistical analysis of the mean ± SD of age, height, weight, and BMI between different groups. There was no significant difference in age between the groups. The mean height was significantly (p≤0.05) higher in group B than in group A and significantly (p≤0.01) higher in group C than in group B. The mean weight was significantly (p≤0.001) higher in group B than group A and significantly (p≤0.05) higher in group C than group B. The mean BMI was significantly (p≤ 0.001) higher in group B than in group A and in group C than in group B.

Table-II: Mean ± SD of age, height, weight, and BMI of the study subjects in group A, group B, and group C

Groups	p-value			
	Age	Height	Weight	BMI
A/B (n=30)/(n=30)	0.225NS	0.035*	0.000***	0.000***
A/C(n=30)/(n=30)	0.120NS	.717NS	0.000***	0.000***
B/C(n=30)/(n=30)	1.000NS	0.003**	0.039*	0.000***

***=p ≤ 0.001 **=p ≤ 0.01
*=p ≤ 0.05 NS=p >0.05

Table-III showed a statistical analysis of the mean±SD of serum creatinine and serum urea between different groups. The mean±SD serum creatinine were 0.71 ± 0.27 mg/dl in group A, 0.99 ± 0.13 mg/dl in group B and 1.15±0.23 mg/dl in group C. The mean serum creatinine was significantly (p≤0.001) higher in group B and group C than in group A. Again, it was significantly (p≤ 0.05) higher in group C than group B. The mean±SD serum urea was 14.72±5.38 mg/dl in group A, 19.25±6.02 mg/dl in group B, and 25.52±9.54 mg/dl in group C. The mean serum

urea was significantly (p≤0.05) higher in group B than in group A and in group C than in group B. Again, it was significantly (p≤0.001) higher in group C than in group A.

Table- III: Statistical analysis of mean ± SD of serum creatinine and serum urea of study subjects between different groups

Groups	Mean ± SD	P-value
Serum creatinine (mg/dl)		
A / B (n=30)/(n=30)	0.71±0.27 / 0.99±0.13	0.000***
A / C (n=30)/(n=30)	0.71±0.27 / 1.15±0.23	0.000***
B / C (n=30) / (n=30)	0.99±0.13 / 1.15±0.23	0.025*
Serum urea (mg/dl)		
A / B (n=30) / (n=30)	14.72±5.38 / 19.25±6.02	0.037*
A / C (n=30) / (n=30)	14.72±5.38 / 25.52±9.54	0.000***
B / C (n=30) / (n=30)	19.25±6.02 / 25.52±9.54	0.041*

*** = p ≤ 0.001, * = p ≤ 0.05

Table-IV and Figure-1 & 2 showed the relationship between serum creatinine and serum urea with BMI in the whole study group. Serum creatinine was positively correlated with BMI, considering serum creatinine as dependent and BMI as the independent variable. The correlation coefficient was statistically highly (p ≤ 0.001) significant, (r = 0.499). Serum urea was positively correlated with BMI, considering serum urea as dependent and BMI as the independent variable. The correlation coefficient was statistically highly (p ≤ 0.001) significant, (r = 0.396).

Table- IV: Relationship of serum creatinine and serum urea with body mass index (BMI) in the whole study group (n=90)

Variable	Correlation with	Correlation coefficient (r-value)	p-value
Serum creatinine	BMI	0.499	.000 ***
Serum urea	BMI	0.396	.000 ***

Statistical analysis was done by Pearson's correlation coefficient test.
*** = p ≤ 0.001

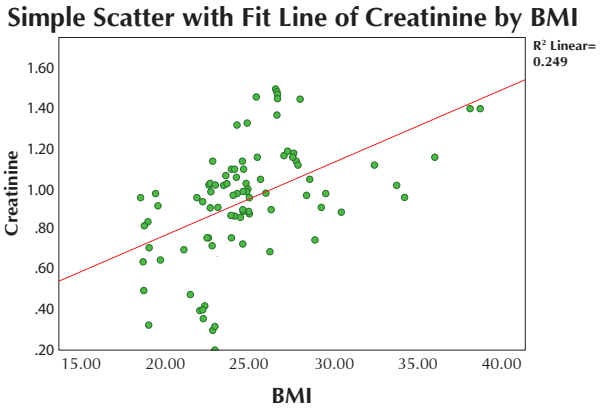

Figure-1: Correlation of serum creatinine with BMI in the whole study group.

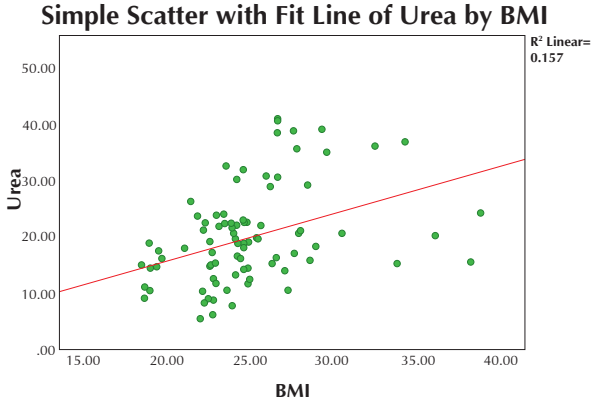

Figure-2: Correlation of serum urea with BMI in the whole study group.

Discussion:

This cross-sectional analytical study was carried out to observe the status of serum creatinine and urea in adult female individuals and to observe the relationship of serum creatinine and urea with BMI. In this study, the mean serum creatinine was significantly (p≤0.001) higher in overweight and obese than normal weight female adults. It was also significantly (p≤0.05) higher in obese than overweight female adults. These findings are in agreement with those of several studies.[11,12,13,17] This study also showed that the mean serum urea was significantly (p≤0.05) higher in overweight than normal weight female adults and in obese than overweight female adults. It was also significantly (p≤0.001) higher in obese than normal weight female adults, which is also similar to the reports by others.[13] Increased body weight results in complex metabolic abnormalities that bring

harmful effects on kidney function. It is suggested that some of these harmful consequences are mediated through diabetes mellitus and hypertension, as the risk of these comorbid conditions is increased by overweight and obesity.[9,18] The literature review suggested several mechanisms for the elevation of serum creatinine and urea in obese individuals. This may be a result of elevated blood pressure due to increased body weight. It causes structural changes and increased metabolic demands by the kidneys. These alterations result in renal hyperfiltration followed by renal damage and loss of nephrons by glomerulosclerosis. Eventually, the renal tubules may become ischemic and gradually atrophic. These changes result in increased blood levels of creatinine and urea.[13] Creatinine production is proportional to the body weight, and importantly the muscle mass. The creatinine clearance increases sequentially with an increase in body weight (muscle mass, body fat, and water) due to increased production and volume of distribution of creatinine along with glomerular hyperfiltration.[11] The correlation between creatinine and BMI is not only connected to the muscle mass, but also to the body fat content of the subjects.[12] High body fat is related to early inflammatory processes associated with increased renal perfusion and hyperfiltration. Ectopic fat deposition around kidneys and associated compression may initially increase the loop of Henle sodium chloride reabsorption, reducing sodium chloride delivery to the macula densa. Via tubuloglomerular feedback, it reduces afferent arteriolar resistance and increases renal blood flow, GFR, and rennin secretion. Adipocytokines like resistin, adiponectin, and leptin are also associated with glomerular hyperfiltration.[17] Adiposity has direct impacts on kidneys induced by its endocrine activity. Adipose tissue produces various adipokines like adiponectin, leptin, and resistin. These adipokines are responsible for inflammation, oxidative stress, abnormal lipid metabolism, activation of the rennin-angiotensin-aldosterone system, insulin resistance, and increased production of insulin. As a result, specific pathological changes occur in the kidneys. There is increased deposition of renal sinus fat and development of glomerular hypertension and hyperfiltration.[9,10] Increased fat mass also causes increased production of pro-inflammatory cytokines including tumor necrosis factor-alpha (TNFα), CRP, and interleukin 6. CRP is a marker of renal injury and a risk marker of renal function loss.[17] Obesity changes the renal hemodynamics which promotes progressive kidney disease. These changes begin in the early stage of obesity before overt renal manifestations are clinically apparent. Elevated serum creatinine and urea may represent an independent marker of renal dysfunction in overweight and obese individuals.[13]

Conclusion:

The result of this study suggested that increased body mass index is correlated with elevated serum creatinine and urea in adult female individuals. As body weight increases, modifications in the renal system also increases. These changes may precede the development of overt clinical disease and may be responsible for maintaining the obese state. These findings highlight the importance of recognizing overweight individuals as an at-risk population. This might help in early diagnosis and could be used to prevent further complications associated with overweight and obesity. Regular body mass index screening is recommended to assess body weight easily and effectively.

References:

1. National Heart Lung and Blood Institute. Aim for a healthy weight.https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm. [Accessed 12th June 2022]
2. World Health Organization. Regional Office for the Western Pacific. International Obesity Task Force. The Asia-Pacific perspective: redefining obesity and its treatment.2000. https://apps.who. int/iris/handle/ 10665/206936. [Accessed 12th June 2022].
3. Choi JW, Pai SH, Kim SK. Associations between total body fat and serum lipid concentrations in obese human adolescents. Ann Clin Lab Sci. 2002 Summer;32(3):271-8.
4. World Health Organization. Obesity and overweight. https://www.who. int/ news-room/-fact-sheets/detail/obesity-and-overweight. [Accessed 10th June 2022].
5. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C,et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014 Aug 30;384(9945):766-81. doi: 10.1016/S0140-6736(14)60460-8.
6. Amira CO, Sokunbi DOB, Sokunbi A. The prevalence of obesity and its relationship with hyper-

tention in an urban community: data from world kidney day screening programme. Int J Med Biomed Res 2012;1(2):104-110. doi: http://dx.doi.org/ 10.14194/ijmbr.124.

7. Helble M, Francisco K. The imminent obesity crisis in Asia and the Pacific: first cost estimates. Asian Development Bank Institute. ADBI Working Paper Series 2017; 743: 1-29. https://www.adb.org/publications/imminent-obesity-crisis- asia-and-pacific-first-cost- estimates. [Accessed 10th June 2022].
8. Nanan DJ. The obesity pandemic--implications for Pakistan. J Pak Med Assoc. 2002 Aug;52(8):342-6.
9. Kovesdy CP, Furth SL, Zoccali C; World Kidney Day Steering Committee. Obesity and kidney disease: Hidden consequences of the epidemic. J Ren Care. 2017 Mar;43(1):3-10. doi: 10.1111/-jorc.12194.
10. Burton JO, Gray LJ, Webb DR, Davies MJ, Khunti K, Crasto W, et al. Association of anthropometric obesity measures with chronic kidney disease risk in a non-diabetic patient population. Nephrol Dial Transplant. 2012 May;27(5):1860-6. doi: 10.1093/ ndt/gfr574.
11. Gerchman F, Tong J, Utzschneider KM, Zraika S, Udayasankar J, McNeely MJ, et al. Body mass index is associated with increased creatinine clearance by a mechanism independent of body fat distribution. J Clin Endocrinol Metab. 2009 Oct;94(10):3781-8. doi: 10.1210/jc.2008-2508.
12. Banfi G, Del Fabbro M, Lippi G. Relation between serum creatinine and body mass index in elite athletes of different sport disciplines. Br J Sports Med. 2006 Aug;40(8):675-8; discussion 678. doi: 10.1136/ bjsm. 2006. 026658.
13. Khan HN, Pergulwar A, Siddiqui AM, Shinde AR. Estimation of serum urea, creatinine and uric acid in obese subjects. International Journal of Innovative Research in Medical Science.2017; 2(8): 1201-1203. doi:https://doi. org/ 10. 23958/ijirms/vol02-i08/18.
14. Guyton AC, Hall JE. The urinary system: Functional anatomy and urine formation by the kidneys, Glomerular filtration, renal blood flow, and their control, Overview of the circulation; Biophysics of pressure, flow, and resistance, Role of the kidneys in long-term control of arterial pressure and in hypertension: the integrated system for arterial pressure regulation. Dietary balances; regulation of feeding; obesity and starvation; vitamins and minerals. In: Hall JE. Guyton and Hall Text Book of Medical Physiology. 13 th ed. Philadelphia Pennsylvania: Saunders publications; 2016. 174, 180-3, 241-3, 323-33, 335-43, 889-95.
15. Hosten AO. BUN and Creatinine. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd ed. Boston: Butterworths; 1990. Chapter 193. https://pubmed.ncbi.nlm.nih.gov/21250147/. [Accessed 16th June 2022].
16. Goddard J, Turner AN, Newby DE, Grubb NR, Bradbury A. Investigation of renal and urinary tract disease, Cardiovascular disease. In: Walker BR, Colledge NR, Ralston SH, Penman ID, eds. Davidson's principle and practice of Medicine.22nd. Edinburg: Churchill Livingstone Elsevier; 2014. 466-71,607.
17. Fouad M, Ismail MI, Gaballah A, Reyad E, ELdeeb S. Prevalence of obesity and risk of chronic kidney disease among young adults in Egypt. Indian J Nephrol. 2016 Nov-Dec;26(6):413-418. doi: 10.4103/0971-4065. 172597.
18. Hall ME, do Carmo JM, da Silva AA, Juncos LA, Wang Z, Hall JE. Obesity, hypertension, and chronic kidney disease. Int J Nephrol Renovasc Dis. 2014 Feb 18;7:75-88. doi: 10.2147/IJNRD.S39739.