



E-ISSN: 2706-9575

P-ISSN: 2706-9567

IJARM 2021; 3(2): 594-598

Received: 25-07-2021

Accepted: 26-09-2021

**Dr. Anshu Kapoor**

Jr 3, Department of Medicine,  
Subharti Medical College,  
Meerut, Uttar Pradesh, India

**Dr. Saurabh Singhal**

HOD & Professor, Department  
of Medicine, Subharti Medical  
College, Meerut, Uttar  
Pradesh, India

## Serum uric acid level correlation in a patients of CKD with or without metabolic syndrome

**Dr. Anshu Kapoor and Dr. Saurabh Singhal**

**DOI:** <https://doi.org/10.22271/27069567.2021.v3.i2i.365>

### Abstract

**Aim:** To evaluate serum uric acid level correlation in a patient of CKD with or without metabolic syndrome.

**Material and method:** The present prospective observational study was conducted in the department of Medicine at Chatrapati Shivaji Subharti Hospital from 2019 to 2021. The study group comprised of 100 patients, suffering from CKD. Metabolic syndrome was assessed according to International Diabetic Federation. Uric acid was estimated using Uricase method.

**Results:** Out of 100 CKD subjects, 63 were suffering from metabolic syndrome while 37 were free from metabolic syndrome. Maximum subjects were from the age group of >60 years (45%) followed by 51-60 years (37%). Diabetes and hypertension was revealed among 73.02%, 80.95% and 48.65%, 59.46% of the subjects with and without metabolic syndrome respectively. Hyperuricemia was noted among 53.97% and 35.13% of the subjects with and without metabolic syndrome respectively. Mean serum uric acid (mg/dl) in subjects with metabolic syndrome and without metabolic syndrome was  $6.64 \pm 1.58$  and  $6.09 \pm 1.16$  respectively with statistically significant difference as  $p < 0.05$ .

**Conclusion:** The above study shows that serum uric acid levels are significantly elevated in CKD patients with metabolic syndrome. The association of elevated levels of serum uric acid was seen with all the components of metabolic syndrome.

**Keywords:** Uric acid, CKD, Diabetes, metabolic Syndrome

### Introduction

Chronic kidney disease (CKD) is becoming a major global public health concern and its prevalence and incidence are steadily increasing mostly because of the rising burden of type 2 diabetes (T2D) and obesity worldwide<sup>1</sup>. Metabolic Syndrome (Mets) is widely prevalent among patients with CKD and has been reported to play a role in the progression of renal damage<sup>[2, 3]</sup> and development of end stage renal disease (ESRD)<sup>[4]</sup>. Moreover, Mets is increasingly recognized as an important predictor for de novo incidence of CKD, largely based on studies conducted among non diabetic populations from different ethnic groups<sup>[5]</sup>.

The presence of metabolic syndrome is strongly associated with the development of diabetes, hypertension, cardiovascular disease and all-cause mortality. However, recent studies have emphasized that metabolic syndrome also is both associated with and a risk for the development of CKD. For example, in a recent study, the metabolic syndrome was found to be strongly correlated with CKD (defined as GFR <60 ml/min) and microalbuminuria, and the risk increased progressively with the number of criteria constituting the syndrome. In another study of Native Americans without diabetes, a positive relationship was identified between microalbuminuria and features of the metabolic syndrome<sup>[1]</sup>.

Serum UA was incriminated in the pathogenesis of gout and kidney stones. However, for more than 140 years ago, high serum UA (SUA) was proposed in association with other diseases including Htn, CKD and DM<sup>[6]</sup>. As serum UA excretion falls in cases of CKD, compensatory increase in intestinal secretion of serum UA ensues. Whether serum UA is a cause or an association to renal diseases is a question that still waits for a definitive answer<sup>[2]</sup>. Mets is also associated with hyperuricaemia<sup>[7]</sup>, which has been shown by some although not all studies to independently predict the onset and progression of CKD in several clinical settings, including T2D<sup>[8]</sup>. The associations between each individual component of Mets and outcomes have been reported to vary in the literature but are not thought to be sufficient to account for the increased hazard of CKD usually associated with Mets. It has been proposed

**Corresponding Author:**

**Dr. Anshu Kapoor**

Jr 3, Department of Medicine,  
Subharti Medical College,  
Meerut, Uttar Pradesh, India

that the components of Mets may foster the progression of renal damage mainly through the coexistence of several underlying pathological mechanisms such as increased oxidative stress, chronic inflammation, increased fibrogenic activity, and endothelial dysfunction [9]. Nevertheless, a causal relationship has not been proven and more studies are needed to precisely elucidate the mechanisms linking Mets to the development of renal damage.

As the diagnostic techniques and aggressive treatment strategies have developed, renewed attention has been given to elevated SUA levels. The relationship between the serum UA level and development of CKD has been supported by expanding epidemiologic and experimental evidence. Researchers have investigated the role of serum UA not only as a potential marker of renal dysfunction [10], but also as a significant pathogenic factor that is involved in the development of renal disease [11]. Due to scarcity of data available in the studying region, the present study was planned to evaluate serum uric acid level correlation in a patient of CKD with or without metabolic syndrome.

**Material and method:** The present prospective observational study was conducted in the department of Medicine at Chattrapati Shivaji Subharti Hospital from 2019 to 2021. The study group comprised of 100 patients, suffering from CKD. Patients were enrolled in the study after obtaining their written informed and approval from Institutional Ethical Committee.

#### Inclusion criteria:

1. Subjects of both genders with aged >18 years.
2. Metabolic syndrome, according to International Diabetic Federation, patients having:
  - a. Central obesity (waist circumference) more than equal to 90 cm in South Asian male and more than equal to 80 cm in South Asian female.
  - b. With any two of the following:
    - Serum triglyceride >150mg/dl or specific treatment for lipid abnormality.
    - Serum HDL cholesterol <40 mg/dl in males and <50 mg/dl in female or specific treatment for lipid abnormality.
    - Blood pressure (BP) in supine position after 10 minute rest systolic BP more than or equal 130 mm Hg or diastolic BP more than or equal 85 mm of hg or on treatment of previously diagnosed hypertension.
    - Fasting plasma glucose more than equal 100 mg/dl or a preciously diagnosed type 2 diabetes mellitus.
3. Subjects suffering from chronic kidney disease.

#### Exclusion criteria:

1. Subjects with age <18 years.
2. Subjects having cancer,
3. Subjects having hepatic disease or other coexisting illnesses including autoimmune kidney diseases and renal artery stenosis, as well as subjects treated with xanthine

oxidase inhibitors.

#### Estimation of uric acid

**Method:** Uricase method

Principle: Uricase converts serum uric acid to allantoin and hydrogen peroxide. The hydrogen peroxide formed further reacts with phenolic compound and 4-Amino antipyrine by the catalytic action of peroxidase to form a red coloured quinoneimine dye complex. Intensity of the colour formed is directly proportional to the amount of serum uric acid present in the sample.

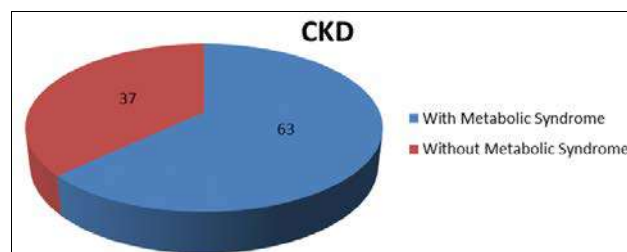
#### Normal values:

Serum Uric Acid (males) = 3.0 to 7.0 mg/dl

Serum Uric Acid (females) = 2.5 to 6.0 mg/dl

**Statistical analysis:** Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using student t-test as well as chi square test and the level of significance was set at  $p < 0.05$ .

**Results:** Out of 100 CKD subjects, 63 were suffering from metabolic syndrome while 37 were free from metabolic syndrome (graph 1).



**Graph 1:** Distribution of CKD subjects according to metabolic syndrome

Out of 100 subjects, there were 69 males and 31 females. 65.22% and 58.07% of the male and female were suffering from metabolic syndrome. When male and female was compared according to metabolic syndrome, it was found to be statistically insignificant as  $p > 0.05$ . Maximum subjects were from the age group of >60 years (45%) followed by 51-60 years (37%). Subjects with metabolic syndrome were more from age group of >50 years as compared to subjects without metabolic syndrome with statistically significant difference as  $p < 0.05$ . Mean age in subjects with metabolic syndrome and without metabolic syndrome was  $58.91 \pm 5.77$  and  $56.29 \pm 6.04$  years respectively (table 1).

**Table 1:** Distribution of CKD subjects according to mean age

Age Group (in years)	With Metabolic Syndrome		Without Metabolic Syndrome		p value
	N=63	%	N=37	%	
18-30	1	20	4	80	0.002*
31-50	4	30.77	9	69.23	
51-60	26	70.27	11	29.73	
>60	32	71.11	13	28.89	
Mean±SD	58.91±5.77		56.29±6.04		0.21

\*: statistically significant

Mean BMI ( $\text{kg/m}^2$ ) in subjects with metabolic syndrome and without metabolic syndrome was  $30.54 \pm 3.25$  and  $27.12 \pm 3.07$  respectively. When mean BMI ( $\text{kg/m}^2$ ) was

compared among subjects with and without metabolic syndrome, it was found to be statistically significant as  $p < 0.05$  (table 2).

**Table 2:** Distribution of CKD subjects according to mean BMI

CKD	BMI ( $\text{kg/m}^2$ )		p value
	Mean	SD	
With Metabolic Syndrome	30.54	3.25	0.024*
Without Metabolic Syndrome	27.12	3.07	
Total	28.99	3.16	

\*: statistically significant

Diabetes and hypertension was revealed among 73.02%, 80.95% and 48.65%, 59.46% of the subjects with and without metabolic syndrome respectively. When diabetes

and hypertension was compared among subjects with and without metabolic syndrome, it was found to be statistically significant as  $p < 0.05$  (table 3).

**Table 3:** Distribution of CKD subjects according to diabetes and hypertension

Variables	With Metabolic Syndrome		Without Metabolic Syndrome		Total		p value
	N=63	%	N=37	%	N	%	
Diabetes	46	73.02	18	48.65	64	64	0.013*
Hypertension	51	80.95	22	59.46	73	73	0.036*

\*: statistically significant

Mean FBS ( $\text{mg/dl}$ ) in subjects with metabolic syndrome and without metabolic syndrome was  $151.36 \pm 12.95$  and  $146.89 \pm 7.47$  respectively. Mean HbA1c (%) in subjects with metabolic syndrome and without metabolic syndrome was  $7.53 \pm 0.81$  and  $7.12 \pm 0.64$  respectively. TC ( $\text{mmol/L}$ )

and TG ( $\text{mmol/L}$ ) was comparatively more in subjects with metabolic syndrome and without metabolic syndrome respectively, however significant difference was found w.r.t. TG only. LDL-C and HDL-C were approximately similar among both the groups (table 4).

**Table 4:** Distribution of CKD subjects according to diabetic and lipid profile

Variables	With Metabolic Syndrome		Without Metabolic Syndrome		Total		p value
	Mean	SD	Mean	SD	Mean	SD	
FBS ( $\text{mg/dl}$ )	151.36	12.95	146.89	7.47	149.28	10.02	0.42
HbA1c (%)	7.53	0.81	7.12	0.64	7.34	0.75	0.27
TC ( $\text{mmol/L}$ )	5.39	0.92	5.34	0.97	5.36	0.95	0.69
LDL-C ( $\text{mmol/L}$ )	2.78	0.81	2.85	0.87	2.83	0.83	0.74
TG ( $\text{mmol/L}$ )	2.54	1.09	2.18	1.22	2.41	1.14	0.027*
HDL-C ( $\text{mmol/L}$ )	1.35	0.77	1.49	0.86	1.40	0.81	0.12

\*: statistically significant

Hyperuricemia was noted among 53.97% and 35.13% of the subjects with and without metabolic syndrome respectively. Mean serum uric acid ( $\text{mg/dl}$ ) in subjects with metabolic syndrome and without metabolic syndrome was  $6.64 \pm 1.58$  and  $6.09 \pm 1.16$  respectively. When mean serum uric acid ( $\text{mg/dl}$ ) was compared among subjects with and without metabolic syndrome, it was found to be statistically significant as  $p < 0.05$  (table 5).

**Table 5:** Comparison of CKD subjects according to serum uric acid

CKD	Serum Uric Acid ( $\text{mg/dl}$ )		p value
	Mean	SD	
With Metabolic Syndrome	6.64	1.58	0.039*
Without Metabolic Syndrome	6.09	1.16	
Total	6.38	1.37	

\*: statistically significant

## Discussion

The complex pathogenesis of CKD has yet to be fully elucidated. Apart from hypertension and diabetes, metabolic syndrome was recently found to be significantly associated with CKD in some studies. Metabolic syndrome is a cluster of metabolic disorders, including abdominal obesity,

elevated blood pressure, glucose intolerance, and dyslipidemia. Hyperuricemia (HUA), the precursor to gout, has also been suggested to be a useful predictor of cardiovascular diseases such as CKD. Many studies have reported an association between elevated SUA and CKD, whereby elevated SUA (Serum Uric Acid) plays a causal role in the pathophysiology of CKD rather than occurring as a consequence of CKD. However, these results were mainly observed in the general population. Epidemiological evidence of this relationship is still limited. Moreover, reports on the association between elevated SUA and CKD that also take into account the number of metabolic syndrome risk factors have also been scant [12].

Out of 100 CKD subjects, 63 were suffering from metabolic syndrome while 37 were free from metabolic syndrome. Haijiang Dai *et al.* [12] in their study reported that in models adjusted for age and sex, subjects with metabolic syndrome had 2.16-fold higher ORs of having CKD than those without. After further adjusting for various confounding factors, subjects with metabolic syndrome had 1.49-fold higher ORs of having CKD than those without ( $P < 0.001$ ). Moreover, the ORs for CKD increased with increasing number of metabolic syndrome. According to a cross-sectional study involving 15,987 individuals, metabolic

syndrome was found to be significantly associated with the prevalence of CKD. Kang *et al.* [13] also demonstrated a 1.53-fold increased ORs for CKD in Koreans with metabolic syndrome based on the general health screening data of 10,253,085 participants. Consistent with these findings, the positive effects of metabolic syndrome on the prevalence of CKD were shown in several studies [14].

Out of 100 subjects, there were 69 males and 31 females. 65.22% and 58.07% of the male and female were suffering from metabolic syndrome. When male and female was compared according to metabolic syndrome, it was found to be statistically insignificant as  $p > 0.05$ . Similar male dominance was reported by Reddy M *et al.* [15] and Haijiang Dai *et al.* [12] in their studies.

Diabetes and hypertension was revealed among 73.02%, 80.95% and 48.65%, 59.46% of the subjects with and without metabolic syndrome respectively. When diabetes and hypertension was compared among subjects with and without metabolic syndrome, it was found to be statistically significant as  $p < 0.05$ . Similarly Reddy M *et al.* [15] in their study metabolic syndrome was significantly associated with hypertension and Diabetes.

TC (mmol/L) and TG (mmol/L) was comparatively more in subjects with metabolic syndrome and without metabolic syndrome respectively, however significant difference was found w.r.t. TG only. LDL-C and HDL-C were approximately similar among both the groups in our study. Reddy M *et al.* [15] in their study showed that serum uric acid concentration is most strongly correlated with serum triglyceride. According to the study conducted by Li Yeng in China shows serum uric acid is markedly associated with metabolic syndrome and its components, in particular serum triglycerides [16]. A previous study showed that increased serum uric acid levels are associated with components of metabolic syndrome, such as hypertriglyceridemia, insulin resistance, elevated blood pressure, and low high-density lipoprotein-cholesterol (HDL-C), but the relationship between serum uric acid and hypertriglyceridemia was the strongest and most stable [15].

Mean serum uric acid (mg/dl) in subjects with metabolic syndrome and without metabolic syndrome was  $6.64 \pm 1.58$  and  $6.09 \pm 1.16$  respectively. When mean serum uric acid (mg/dl) was compared among subjects with and without metabolic syndrome, it was found to be statistically significant as  $p < 0.05$ . Hyperuricemia was noted among 53.97% and 35.13% of the subjects with and without metabolic syndrome respectively in this study. Although the association between SUA and CKD has been explored for a long time, the underlying mechanism is still not completely understood. It has been suggested that SUA induced oxidative stress and endothelial dysfunction may result in the development of both systemic and glomerular hypertension, which would reduce renal blood flow and elevate renal vascular resistance. Uedono *et al.* [17] also found that SUA levels was significantly and independently associated with the vascular resistance at the afferent arteriole. In addition, SUA may stimulate vascular smooth muscle cell proliferation through the activation of the renin-angiotensin system. Lowering serum uric acid in mice with allopurinol was able to improve the proinflammatory effects by reducing ICAM-1 expression in tubular epithelial cells. Moreover, SUA was also able to induce an epithelial-to-mesenchymal transition, with direct effects on the renal tubular cells. However, elucidating the complex

mechanisms between SUA and CKD still requires further research.

Haijiang Dai *et al.* [12] in their study showed that when compared to those without CKD, subjects with CKD exhibited a higher prevalence of HUA and metabolic syndrome, as well as higher uric acid. In a meta-analysis of 15 cohort studies, each 1 mg/dL SUA increment was found to be significantly associated with a 1.22-fold CKD risk in middle-aged participants [17]. Sae-Ron Shin *et al.* [18] in their study revealed that statistically significant correlation between the sUA/creatinine ratio and the presence of MS as well as with each component of MS.

Our study also has some limitations. The primary limitation of this study is that cross-sectional data do not allow us to observe the impact of risk factors over time and distinguish between reason and consequence. In addition, the information on some associated variables such as smoking, drinking habits, renal artery measurements, and so on was prone to underreporting or lacking. Finally, our study has a huge overhang of male participants, which may cause biased outcomes. Given those limitations, further longitudinal cohort studies are needed to observe and analyze the causative relationship of SUA and metabolic syndrome with CKD in the hypertensive patients.

## Conclusion

The above study shows that serum uric acid levels are significantly elevated in CKD patients with metabolic syndrome. The association of elevated levels of serum uric acid was seen with all the components of metabolic syndrome. However further studies are needed to look for serum uric acid lowering therapies which will be of benefit in the management of metabolic syndrome. These results may be relevant to help focusing on better prevention and therapeutic strategies as epidemiological surveys indicate increasing prevalence of CKD among subjects with Mets and hyperuricemia.

## References

1. Gregg EW, Sattar N, Ali MK. The changing face of diabetes complications. *Lancet Diabetes Endocrinol.* 2016;4:537-547.
2. Lee CC, Sun CY, Wu IW, Wang SY, Wu MS. Metabolic syndrome loses its predictive power in late stage chronic kidney disease progression. *Clin Nephrol.* 2011;75:141-49.
3. Kovačs T, Vas T, Kovesdy CP, Kelecsői I, Saági B, Wittmann I, *et al.* Metabolic syndrome and other cardiovascular risk factors associated with the progression of IgA nephropathy. *Clin Kidney J.* 2013;6:95-401.
4. Navaneethan SD, Schold JD, Kirwan JP, Arrigain S, Jolly SE, Poggio ED, *et al.* Metabolic syndrome, ESRD, and death in CKD. *Clin J Am Soc Nephrol.* 2013;8:945-952.
5. Rashidi A, Ghanbarian A, Azizi F. Are patients who have metabolic syndrome without diabetes at risk for developing chronic kidney disease? Evidence based on data from a large cohort screening population. *Clin J Am Soc Nephrol.* 2007;2:976-983.
6. El Din UA, Salem MM, Abdulazim DO. Uric acid in the pathogenesis of metabolic, renal, and cardiovascular diseases: A review. *Journal of advanced research.* 2017;8(5):537-48.

7. Lin WY, Liu CS, Li TC, Lin T, Chen W, Chen CC, *et al.* In addition to insulin resistance and obesity, hyperuricemia is strongly associated with metabolic syndrome using different definitions in Chinese populations: a population-based study (Taichung Community Health Study). *Ann Rheum Dis* 2008;67:432-433.
8. Chonchol M, Shlipak MG, Katz R, Sarnak MJ, Newman AB, Siscovick DS, *et al.* Relationship of uric acid with progression of kidney disease. *Am J Kidney Dis*. 2007;50:239-247.
9. Borghi C, Rosei EA, Bardin T, Dawson J, Dominiczak A, Kielstein JT, *et al.* Serum uric acid and the risk of cardiovascular and renal disease. *J Hypertens*. 2015;33:1729-1741.
10. Sonoda H, Takase H, Dohi Y, Kimura G. Uric acid levels predict future development of chronic kidney disease. *Am J Nephrol*. 2011;33:352-7.
11. Kim IY, Lee DW, Lee SB, Kwak IS. The role of uric acid in kidney fibrosis: experimental evidences for the causal relationship. *Biomed Res Int*. 2014;638-732.
12. Dai H, Lu S, Tang X, *et al.* Combined association of serum uric acid and metabolic syndrome with chronic kidney disease in hypertensive patients. *Kidney and Blood Pressure Research*. 2016;41(4):413-23.
13. Kang DH, Park SK, Lee IK, Johnson RJ. Uric acid-induced C-reactive protein expression: implication on cell proliferation and nitric oxide production of human vascular cells. *Journal of the American Society of Nephrology*. 2005;16:3553–3562.
14. Cirillo P, Sato W, Reungjui S, Heinig M, Gersch M, Sautin Y, Nakagawa T, Johnson RJ. Uric acid, the metabolic syndrome, and renal disease. *Journal of the American Society of Nephrology*. 2006;17(12 suppl 3):S165-8.
15. Reddy M, Rao VV, Kulkarni A, Kumar A, Medappa S. Study of Serum Uric Acid Levels in Patients of Metabolic Syndrome in a Tertiary Care Centre in South India. *J. Evid. Based Med. Healthc*. 2020;7(18):896-899.
16. Chen L, Zhu W, Chen Z, *et al.* Relationship between hyperuricemia and metabolic syndrome. *J Zhejiang Univ Sci B* 2007;8(8):593-598.
17. Uedono H, Tsuda A, Ishimura E, *et al.* Relationship between serum uric acid levels and intrarenal hemodynamic parameters. *Kidney Blood Press Res* 2015;40:315-322.
18. Shin SR, Han AL. Relationship between metabolic syndrome and uric acid to creatinine ratio in Korean adults: Korea National Health and Nutrition Examination Survey 2016. *Korean Journal of Health Promotion*. 2018;18(3):113-8..