International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

Original Research Article.

A Comparative Study of Serum Uric Acid, Blood Urea, Serum Creatinine And Serum Uric Acid to Creatinine Ratio in Pre and Post-Menopausal Women with and without Diabetes Mellitus

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ABSTRACT

Background: The effects of high levels of serum uric acid is closely related to diabetes and its chronic complications. Among women, menopause and older age might additively influence the elevated probability of diabetes. Elevated serum uric acid is recognized as a risk factor for kidney disease in addition to causing gout, cardiovascular diseases, metabolic syndrome, insulin resistance, and diabetes.

Objectives: To study the levels of serum uric acid, urea, creatinine and uric acid to creatinine ratio in postmenopausal women with and without diabetes.

Materials and Methods: Total of 92 subjects including 37 non-diabetic, 15 diabetic premenopausal women and 15 non-diabetic and 25 diabetic postmenopausal women without any major medical illness were included for the study. Fasting blood samples were collected and analyzed for glucose, uric acid, urea and creatinine by semi-auto analyzer using commercial kits. Values were reported as mean ± standard deviation. The data were analysed by one-way ANOVA with Tukey-Kramer Post Hoc test using SPSS version 20 and p value of < 0.05 was taken as statistically significant at 95% confidence interval.

Results: Serum uric acid, urea and creatinine and UA/Cr ratio were significantly increased in postmenopausal women with and without diabetes compared to premenopausal women without diabetes as well as premenopausal women with diabetes.

Conclusions: UA/Cr ratio in postmenopausal women with and without diabetes seems to be a better marker to evaluate the high risk of CKD and CVD.

Keywords: Menopause, Diabetes, Uric Acid, Urea, Creatinine.

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Article History:

Received: 07-12-2021, **Revised:** 03-01-2022, **Accepted:** 28-01-2022

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2022.8.1.003	

INTRODUCTION

Menopause and ageing are associated with changes in circulating gonadal steroid hormones. As this is happening, the levels of the estrogen and progesterone hormones are changing as well. These fluctuations in the estrogens can affect the blood glucose levels, leading to diabetes mellitus (DM). Estrogen helps to optimize insulin. Premenopausal women have increased insulin sensitivity, however, after menopause, this advantage disappears due in part to the reduction of estrogen in the body.[1] Reduced estrogen levels can lead to insulin resistance, which is when the body does not respond to insulin well and blood sugar increases. The postmenopausal state was significantly associated with the presence of dysglycemia independently of normal aging, although the increased probability in postmenopausal women did not equal that in men. Among women, menopause and older age might additively influence the elevated probability of dysglycemia.[1]

Increased glucose levels have deleterious effects on several organs. Diabetic kidney disease develops in approximately 40% of patients who are diabetic and is the leading cause of CKD worldwide. As kidneys fail, the blood urea nitrogen (BUN) levels will rise as well as the level of creatinine, in the blood.

Elevated serum uric acid (SUA) is increasingly recognized as a risk factor for kidney disease in adults with diabetes. In addition to causing gout, many studies have shown that hyperuricemia is also closely related to cardiovascular diseases, metabolic syndrome,

insulin resistance, and diabetes.[2,3] It was reported that increase in metabolic syndrome and serum uric acid to creatinine ratio (UA/Cr) was observed in postmenopausal women.[4]

Several mechanisms describe the role of uric acid on diabetes and its chronic complications. Increased uric acid levels have been implicated in inflammation[5], oxidative stress[6], endothelial dysfunction[7], inhibiting insulin pathway[8], intra renal hemodynamic dysfunction[9], vascular, glomerular, and tubular injuries[10,11], and loss of nephron mass.[12,13] All these could explain an etiological relationship between elevated serum uric acid and vascular disease in T2D and how elevated serum uric acid may accelerate progression of CKD and CVD. About 30 percent of patients with Type 1 (juvenile onset) diabetes and 10 to 40 percent of those with Type 2 (adult onset) diabetes eventually will suffer from kidney failure. In this study we aimed to study the levels of serum uric acid, blood urea, serum creatinine and along with serum uric acid to creatinine ratio in postmenopausal women with and without diabetes.

MATERIALS AND METHODS

Samples: The postmenopausal women selected were those with a history of natural menopause, who had cessation of menstruation for a minimum of one year, and premenopausal women who were studied were those who had regular menstruation. In the present study the total number of participants were 92. The age group of pre-menopausal group of women was between 25 – 50 and for the post-menopausal women it is between 45 – 75. The first group consisted of 37 premenopausal women without diabetes, and second group consisted of 15 premenopausal women with diabetes, third group had 15 postmenopausal women without diabetes and fourth group consisted of 25 postmenopausal women with diabetes.

Inclusion and Exclusion Criterion: Diabetic and non-diabetic women in the study were selected depending on the exclusion criterion. Women with any type of hormonal abnormality, cardiac problems, pregnancy, hormonal therapy, heavy exercise, and familial hypertriglyceridemia were excluded.

Sample Collection: After an overnight fasting for 12 -14 hours, sample was collected from the subjects. About 5 ml of venous blood was drawn under aseptic precaution in a sterile plain vacutainer from selected subjects. Sample for glucose estimation was separately taken in fluoride, oxalate vial and remaining sample is collected into a plane vial. Glucose is estimated in plasma whereas urea, uric acid and creatinine were estimated in serum. As soon as the sample is collected, serum is separated, and estimations were done on the same day.

Assay Method: Assay of samples for various estimations was done using Erba-chem-5 plus2 semi-automated analyser. The quality control was checked using control sera of two levels. Glucose was estimated by GOD/PAP method[14,15] creatinine by modified Jaffe's method[16,17], urea by urease method[18,19] and uric acid by uricase method.[20,21] Results were reported as mean + standard deviation (SD). The data were analysed by one-way ANOVA with Tukey-Kramer Post Hoc test using SPSS version 20 and p value of < 0.05 was taken as statistically significant at 95% confidence interval.

Ethical Considerations: Sample was collected after taking written/oral consent from the subjects. This project has been approved by the ethical committee of Shadan Institute of Medical Sciences.

Table 1: Number and age of subjects in study groups

Study groups	No of Subjects	Age range (Mean ± SD)
Premenopausal women without diabetes	37	29 – 54 (39.2 ± 6.6)
Premenopausal women with diabetes	15	32 - 49 (39.5 ± 5.7)
Postmenopausal women without diabetes	15	45 - 62 (52.4 ± 5.8)
Postmenopausal women with diabetes	25	50 - 75 (58.8 ± 7.9)
Total number of subjects	92	29 - 75*

*Minimum and Maximum years of age

Table 2: Fasting Blood Glucose Serum Uric acid, Blood Urea, Serum Creatinine and UA/Cr ratio in the study groups

Study groups	Fasting Blood Glucose	Serum Uric acid	Blood Urea	Serum Creatinine	Serum UA/Cr ratio
Premenopausal women without diabetes	95.2 ± 14.1	4.13 ± 0.95	19.9 ± 3.38	1.01 ± 0.22	4.02 ± 0.85
Premenopausal women with diabetes	151.7 ± 32.9*	4.63 ± 0.94	23.1 ± 4.40	1.05 ± 0.14	4.15 ± 0.60
Postmenopausal women without diabetes	92.3 ± 12.4@	5.98 ± 0.56*@	25.3 ± 4.91*	1.25 ± 0.16*	4.99 ± 0.72*@
Postmenopausal women with diabetes	154.9 ± 61.4*#	6.46 ± 1.09*@	27.5 ± 10.3*	1.44 ± 0.48*@	5.03 ± 0.76*@

Statistical analysis done by one-way ANOVA with Tukey-Kramer Post Hoc test

Values are Mean ± SD; statistically significant = p< 0.05

*Statistically significant when compared to premenopausal women without diabetes;

@Statistically significant when compared to premenopausal women with diabetes;

#Statistically significant when compared to postmenopausal women without diabetes

RESULTS

Table 1 gives the number and age of subjects in study groups. Premenopausal women without diabetes group were with 37 number of subjects having 39.2 ± 6.6 mean ± standard deviation years of age and premenopausal women with diabetes group was with 15 subjects having 39.5 ± 5.7, Postmenopausal women without diabetes group was 15 number of subjects having 51.0 ± 7.7 mean ± standard deviation years of age and postmenopausal women with diabetes group was 58.8 ± 7.9. Overall, the subjects were from 29 to 75 years of age.

Fasting Blood Glucose, serum uric acid, blood urea, serum creatinine and serum uric acid to Creatinine ratio (UA/Cr) in the study groups were shown in Table 2. The analysis of results by ANOVA indicated the statistically significant mean values ($p<0.05$) for all the parameters. Fasting blood glucose levels were clearly showed an increased level in pre- and post-menopausal women with diabetes. Serum uric acid, blood urea, serum creatinine and UA/Cr were statistically not significant between the diabetic and non-diabetic subjects of premenopausal women. Serum uric acid levels and UA/Cr ratio of postmenopausal women with and without diabetes were significantly high when compared to diabetic or non-diabetic premenopausal women. Blood urea of postmenopausal women with and without diabetes was significantly high when compared to non-diabetic premenopausal women. Serum creatinine levels were significantly high in postmenopausal women with and without diabetes when compared to non-diabetic premenopausal women. It was also noted that serum creatinine levels were significantly high in postmenopausal women with diabetes when compared to diabetic premenopausal women.

DISCUSSION

High blood glucose can damage the blood vessels in the kidneys. When the blood vessels are damaged, they work less as well. Many people with diabetes also develop high blood pressure, which can also damage their kidneys. Most people with diabetic kidney disease do not have symptoms. The only way to know if they have diabetic kidney disease is to get the kidney function checked. Serum urea, creatinine and uric acid form the main markers of kidney function. Diabetes was found to be a bigger cause (62.3%) of CKD than what has been reported thus far in India. At present association of diabetic-CKD with HT was recorded higher (78.7%) in India.

Menopause contributes to renal dysfunction in women, which is generally attributed to estrogen withdrawal. In addition to decreased estrogen level, serum follicle-stimulating hormone (FSH) level increases after menopause. A high circulating FSH level is an independent risk factor for renal dysfunction in women after menopause. Additionally, aging may aggravate the association of high FSH levels with reduced renal function in post-menopausal women. The incidence of renal disease associated with both type 1 and type 2 DM is far greater in diabetic compared with nondiabetic women, both pre- and postmenopausal.[22,23]

Experimental studies also indicate that estrogen receptor α is abnormally regulated in the diabetic kidney.[24,25] Silbiger and Neugarten appreciate that sex hormones may directly influence many processes involved in the pathogenesis of renal diseases progression. It was however mentioned that the incidence and the progression rate of a kidney disease is higher in diabetic females as compared to non-diabetic females. They consider that several mechanisms could be involved.[26] Uric acid is a last by product of purine metabolism and its increased levels have been associated with insulin resistance and in Type-2 Diabetes Mellitus. The relation between Type-2 DM and increased serum uric acid level has been observed.[27] A higher SUA level was associated with an increased prevalence of CVD and DKD and a variety of diabetic complications in men and postmenopausal women with T2DM.[28] Some studies have shown serum uric acid to creatinine ratio might be a better predictor of incident chronic kidney disease in type 2 diabetes mellitus patients.[29,30]

The present study sought to evaluate the association between UA/Cr ratio and renal disease progression in pre and postmenopausal women with and without diabetes.

Our results have clearly showed that there is a significant increase in uric acid, urea and creatinine along with UA/Cr ratio in postmenopausal women with and without diabetes compared to nondiabetic premenopausal women.

Another interesting result is that there is a significant increase in the ratio of UA/Cr ratio in postmenopausal women with and without diabetes compared to premenopausal women with and without diabetes. Thus, this ratio could be of importance in assessing the kidney function of postmenopausal women compared to serum creatinine or serum uric acid alone. The study was concluded that the observed increased serum uric acid, urea and creatinine and UA/Cr ratio in postmenopausal women with and without diabetes are at high risk of CKD and CVD. UA/Cr ratio seems to be a better marker to evaluate the high risk group CKD and CVD of individuals.

ACKNOWLEDGEMENTS

The authors are grateful to Managing Director and Dean for providing the facilities and constant encouragement for the study. Authors also wish to thank Mrs. Pulikanti Vennela, student, West Virginia School of Osteopathic Medicine, West Virginia, USA for her help in statistical analysis of results for this manuscript.

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Source of Support: Nil.

Conflict of Interest: None Declared.

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Cite this article as: Ameetha Rani V, Mohammed Siddique Ahmed Khan, Swamy M, Jagannatham S. A Comparative Study of Serum Uric Acid, Blood Urea, Serum Creatinine And Serum Uric Acid to Creatinine Ratio in Pre and Post-Menopausal Women with and without Diabetes Mellitus. Int J Med Res Prof. 2022 Jan; 8(1): 11-14. DOI:10.21276/ijmrp.2022.8.1.003