

## ASSOCIATION OF SERUM URIC ACID WITH LEVEL OF BLOOD PRESSURE IN TYPE 2 DIABETIC PATIENTS

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### ABSTRACT

**Background and Objectives:** Diabetes mellitus (DM) is a chronic disease characterized by insulin deficiency or peripheral resistance resulting in hyperglycemia. Hyperuricemia has been reported with increased risk of renal insufficiency. The objective of the study was to determine the association of uric acid with blood pressure in type 2 diabetic patients.

**Methods:** In this study eighty patients with type 2 diabetes mellitus were included. No patient had history of gout or history of using antihypertensive or uric acid lowering drugs. HbA<sub>1c</sub> was performed on Hemoglobin – Testing System (D-10-Biored Laboratories). Serum uric acid (UA), serum creatinine and plasma glucose were measured on fully automated chemistry analyzer (Metrolab – 2300).

**Results:** The study population consisted of 80 subjects, among them 32 (40%) were male and 48 (60%) were female. Among 80 subjects, the age limit started from 50 years to 68 years with mean of 58.16 ±. Mean HbA<sub>1c</sub> level was 7.63 ± 1.6, mean uric acid level 5.86 ± 0.97 and mean creatinine level was 0.86 ± 0.20. Mean systolic and diastolic blood pressure were 124 ± 11.78 and 82.50 ± 8.49 respectively. Uric acid levels are correlated with blood pressure (systolic and diastolic) in diabetic patients.

**Conclusion:** The present study demonstrated a strong correlation between serum uric acid and systolic and diastolic blood pressure levels in type 2 diabetic patients.

**Key word:** Diabetes Mellitus, Uric acid, Hypertension.

### INTRODUCTION

Diabetes mellitus is a chronic metabolic disease associated with high glucose level in blood which results from defects in insulin secretion, insulin action, or both.<sup>1</sup> According to an estimate of 2014, approximately 387 million people worldwide have diabetes and 90% have type 2 diabetes mellitus.<sup>2</sup>

The patients with diabetes mellitus have a higher incidence of hypertension. This is particularly correct for type 2 diabetes patients. Diabetes characterizes a major risk of cardiovascular disease and nephropathy. This risk is significantly heightened by the co-existence of hypertension. A number of studies in the current years have revealed that tight blood pressure control is indispensable in diabetic patients to have greatest protection against cardiovascular events and the worsening of renal function.<sup>3</sup>

Uric acid (UA), is produced as the final oxidation product of purine catabolism. It is found that it has been associated with several clinical conditions such as diabetes mellitus and atherosclerotic disease. It is recommended in various studies that UA is a significant and independent risk factor for kidney disease, predominantly in patients with hypertension.<sup>4-6</sup> There is a positive correlation between raised serum uric acid

and development of cardiovascular diseases.<sup>7,8</sup> There is an evidence of positive association between serum uric acid and risk of major coronary heart disease events. There is considerable a positive correlation between serum uric acid, hypertension and renal diseases.<sup>9</sup> Moreover, hypertension and raised serum uric acid additionally confound the debates of uric acid role in cardiovascular events and the factors involved in the progression of atherosclerosis. Many clinical studies have been done to evaluate the causative role of uric acid in hypertension.<sup>10</sup>

The relationship between uric acid and hypertension can be defined by at least two mechanisms, molecular mechanisms and elimination pathways of urates. Recent studies propose that uric acid considerably related to kidney disease, predominantly in patients with hypertension. It was revealed that uricase inhibitor produce hyperuricemia, that initiated hypertension and reduced nitric oxide generation in the macula densa. Even though it was found that by inducing nitric oxide generation both hypertension and renal damage are reduced.<sup>11-13</sup> The mechanism by which uric acid may cause organ damage is not fully understood; though, various studies suggest that endothelial dysfunction is a mechanism which may cause uric acid to affect

kidney function and structure.<sup>14-17</sup>

Uric acid has been associated with hypertension in many studies involving different populations but little or no information was found on this association in a Pakistani population. The aim of this cross sectional study was to determine that whether there is an association between serum uric and blood pressure in type 2 diabetic patients.

## METHODS

Before the start of the study, ethical permission was acquired from the University of Health Sciences, Lahore, Pakistan. The study was conducted in the Department of Chemical Pathology, University of Health Sciences Lahore.

Eighty patients of type 2 Diabetes Mellitus were included in the study. The minimum duration of the diabetes was ten years. The patients do not have gout, kidney or cardiovascular disease. These patients were recruited from the diabetic clinic of Jinnah Hospital Lahore.

Patients having nephropathy, taking any hypertensive drugs or taking any drug to lower uric acid level were excluded from the study.

Socio-Demographic data and clinical history were obtained from patients using questionnaires. After informed consent, three readings of systolic blood pressure and the diastolic blood pressure were taken while the patients were seated in a comfortable position and an average of three readings was calculated.

Fasting Blood sample was taken by standardized aseptic conditions for the measurement of plasma glucose, serum creatinine serum uric acid and HbA<sub>1c</sub>.

HbA<sub>1c</sub> was performed on Hemoglobin – Testing System (D-10-Biorad Laboratories).

Serum Uric Acid, serum creatinine and plasma glucose were measured on fully automated chemistry analyzer (Metrolab – 2300).

The data was entered and analyzed by using standard SPSS software version 16 for statistical analysis.

Results were expressed as mean  $\pm$  standard deviation and comparisons were considered significant when two – sided P value was less than 0.05. For association of serum uric acid with levels of blood pressure, the Pearson correlation test was used.

## RESULTS

The study population consisted of 80 subjects, among them 32 (40%) were male and 48 (60%) were female.

Among 80 subjects, the age ranged between 50 to 68 years with mean of  $58.16 \pm 3.866$ . According to descriptive statistics of HbA<sub>1c</sub> of subjects, the values ranged from 5.40 to 11.80 with mean of  $7.63 \pm 1.6$ . Duration of diabetes ranged from 7 years to 15 years with mean of  $9.61 \pm 1.74$  years. Mean uric acid level was  $5.86 \pm 0.97$  and mean creatinine level was  $0.86 \pm 0.20$ . Mean systolic and diastolic blood pressure are  $124 \pm$

$11.78$  and  $82.50 \pm 8.49$  respectively. In this study, there was no significant difference in ser-um uric acid, HbA<sub>1c</sub> or serum creatinine levels between men and women.

According to data, Pearson correlation was applied to get association of uric acid level with other parameters. It was seen that uric acid is correlated with blood pressure (systolic and diastolic) in diabetic patients. It means that in diabetic patients hyperuricemia is associated with hypertension. This data also showed that hyperuricemia is correlated with age.

Uric acid was positively correlated to systolic blood pressure with  $r = 0.538$  and  $P = 0.000$ . It was also found that uric acid was positively correlated to diastolic blood pressure with  $r = 0.472$  and  $P = 0.000$ .

## DISCUSSION

This study was conducted with the determine correlation. This study was conducted to rule out the correlation of serum uric acid with Blood Pressure in Type 2 Diabetic Patients.

In this study it was seen that uric acid is correlated with blood pressure (systolic and diastolic) in diabetic patients. A significant positive correlation was seen between serum Uric Acid and systolic and diastolic blood pressure. Results of this study suggest that there is a strong correlation of serum uric acid with systolic and diastolic blood pressure in diabetic patients and this is comparable to the studies done by Rafieian, et al, Cicero and Taniguchi.<sup>3,18,19</sup> A significant positive correlation was seen between HbA<sub>1c</sub> and systolic ( $r = 0.165$ ,  $P = 0.01$ ) and diastolic blood pressure ( $r = 0.068$ ,  $P = 0.01$ ).<sup>3,20</sup>

The most interesting fact shown by the data was that there is strong correlation between duration of diabetes with systolic pressure ( $r = 0.360$ ,  $p = 0.01$ ), diastolic pressure ( $r = 0.271$ ,  $p = 0.01$ ) and uric acid level ( $r = 0.367$ ,  $p = 0.01$ ). That means that with increase in diabetes duration there are more chances of hyperuricemia and hypertension.<sup>3</sup>

In a study done by Feig DI, it was found that hyperuricemia is associated with hypertension cross-sectionally.<sup>21, 22</sup>

Hyperuricemia was observed in 25 – 60% of untreated hypertensive patients. Higher serum uric acid levels were also found in 89% of children with primary hypertension. In addition, raised uric acid is independently associated with pre hypertension.<sup>21,22</sup>

Syamala et al, from the National Health and Nutrition Examination Survey (NHANES) reported that the multivariable-adjusted odds ratio for prehypertension was 1.96 in subjects with uric acid more than 6 mg/dL comparing to those with uric acid less than 4 mg/dL.<sup>23</sup>

A larger survey that enrolled 14,451 adults free of hypertension confirmed the above findings.<sup>24</sup> These results suggest that uric acid might have a role in the

**Table 1:**

		<i>Uric Acid</i>	<i>Systolic Blood Pressure</i>	<i>Diastolic Blood Pressure</i>	<i>Age</i>	<i>HbA<sub>1c</sub> (%)</i>	<i>Duration of Diabetes (Years)</i>
Uric Acid	Pearson Correlation	1	.538**	.472**	.325**	.011	.367**
	Sig. (2-tailed)		.000	.000	.003	.922	.001
	N	80	80	80	80	80	80
Systolic Blood Pressure	Pearson Correlation	.538**	1	.888**	.301**	.165	.360**
	Sig. (2-tailed)	.000		.000	.007	.143	.001
	N	80	80	80	80	80	80
Diastolic Blood Pressure	Pearson Correlation	.472**	.888**	1	.223*	.068	.271*
	Sig. (2-tailed)	.000	.000		.047	.549	.015
	N	80	80	80	80	80	80
Age	Pearson Correlation	.325**	.301**	.223*	1	-.088	.516**
	Sig. (2-tailed)	.003	.007	.047		.436	.000
	N	80	80	80	80	80	80
HbA <sub>1c</sub> (%)	Pearson Correlation	.011	.165	.068	-.088	1	.166
	Sig. (2-tailed)	.922	.143	.549	.436		.140
	N	80	80	80	80	80	80
Duration of Diabetes (Years)	Pearson Correlation	.367**	.360**	.271*	.516**	.166	1
	Sig. (2-tailed)	.001	.001	.015	.000	.140	
	N	80	80	80	80	80	80

\*\*Correlation is significant at the 0.01 level (2-tailed).

\*Correlation is significant at the 0.05 level (2-tailed).

early pathogenesis of hypertension.

Fang et al. analyzed data from the NHANES I Epidemiologic Follow-up study and concluded that both systolic and diastolic blood pressure were associated with increasing serum uric acid levels in the general population.<sup>25</sup>

In a study done by Verdecchia et al, 1,720 untreated adult hypertensive subjects were recruited and their blood pressure and biochemical parameters were measured the study demonstrated that hypertensive patients with high levels of serum uric acid were associated with higher office and ambulatory systolic blood pressure than those with lower uric acid levels.<sup>26</sup>

The association between hyperuricemia and high blood pressure could be detected even in a clinical

cohort of children with the mean age of 14 years. Jones et al. measured 24-h ambulatory blood pressure and serum uric acid in 104 children referred for possible hypertension.<sup>27</sup> They found that uric acid was significantly associated with 24-h and nocturnal diastolic blood pressure, independent from sex, ethnicity, and body mass index. Uric acid was also significantly associated with increased risk of diastolic hypertension, with an odds ratio of 2.1 after adjusting for confounding factors in these children. Serum uric acid appears to be an important marker of high blood pressure in adults and in children.<sup>27</sup>

Several studies published in the past few years provide more information to support an independent risk relationship between hyperuricemia and the deve-

lopment of hypertension, with full adjustments for multiple confounders.<sup>28-30</sup>

In **conclusion** it is found in this study that serum uric acid is positively correlated with levels of systolic and diastolic blood pressure in type 2 diabetic patients. If the serum uric acid is regularly monitored in these patients, the progress of diabetic nephropathy and cardiovascular events may be delayed in these patients.

#### Authors' Contribution

**NR** has designed the research, performed the tests on the samples, statistical analysis of the data and write the article. **NA** has collected the samples, recorded the blood pressure of the patients and collected the data of the patients. **SG** has checked and corrected the article.

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