

# Association of Serum Uric Acid and Microalbuminuria in Prehypertension : A Cross Sectional Study

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## ABSTRACT

**Background:** The relationship between uric acid and microalbuminuria in healthy adults without other cardiovascular risk factors may help to clarify the role of uric acid in cardiovascular disease.

**Objective:** To study and compare the association of serum uric acid levels with microalbuminuria in normotensive and pre-hypertensive subjects without a history of cardiovascular disease or renal dysfunction.

**Materials and Methods:** 350 subjects were included in study. All the routine investigations along with serum uric acid and urinary albumin were conducted. Microalbuminuria was detected by immunoprecipitation in a random urine sample. Serum uric acid level was estimated by Spectrophotometry.

**Results:** The overall prevalence of prehypertension was 38.06% (Males, 39.10% and females, 35.56%). The total prevalence of microalbuminuria was 11.61% (9.9% of normotensives and 14.4% of pre-hypertensives). Hyperuricemia was seen in 10.32% of the total study population. Among normotensives, 9% of males and 8.6% of females and in pre-hypertensive subjects, 14% of males & 9.4% of females had hyperuricemia. Among the pre-hypertensives, those with microalbuminuria had a significantly higher ( $p < 0.001$ ) serum uric acid level ( $7.024 \pm 1.023$  mg/dl) as compared to those without microalbuminuria ( $5.089 \pm 0.965$  mg/dl).

**Conclusion:** This study demonstrates a strong independent association between uric acid level and microalbuminuria in pre-hypertensive subjects without a history of cardiovascular disease, diabetes decreased renal function.

**KEY WORDS:** Microalbuminuria; Uric Acid; Prehypertension; India

## INTRODUCTION

Cardiovascular disease is showing increasing trends in the developing world as the prevalence of risk factors for cardiovascular disease is increasing rapidly in these regions.<sup>[1]</sup> Studies have revealed the association of microalbuminuria and elevated serum uric acid level with cardiovascular disease among patients with diabetes mellitus and hypertension.<sup>[2-10]</sup> The independent association of uric acid with cardiovascular disease appears to be stronger in persons with hypertension than in the general population.<sup>[9,11-13]</sup> Only few studies showed the relationship of these marker in normotensive and pre-hypertensive populations.<sup>[14-16]</sup> In India no such study has been done till date. The relationship between uric acid and microalbuminuria in healthy adults without other cardiovascular risk factors may help to clarify the role of uric acid in cardiovascular disease.

## MATERIALS AND METHODS

This cross sectional study was carried out in department of medicine between 2007 and 2008. 350 subjects were included in study from the relatives of patients attending the medical outpatient department & admitted in medical wards. Out of the 350 subjects, 40 were eliminated from the study due to various reasons like the evidence of gross proteinuria, hematuria, pyuria and an impaired fasting glucose.

*Inclusion criteria:* Non-diabetic and non-hypertensive individuals without cardiovascular or renal disease, age between 21-70 years.

*Exclusion criteria:* Hypertension, Diabetes mellitus, Hypercholesterolemia, other dyslipidemias, Malignancy, Clinical or laboratory evidence of liver and renal disease, h/o urinary tract infection in the previous 3 months, use of NSAIDs during the preceding 72 hours, age >21 years and <70 years.

A detailed systemic examination was performed. Average of 3 readings of blood pressure was

taken over half an hour. Pre hypertension was defined as systolic BP 120-139 mm Hg or diastolic BP 80-89 mm Hg (17). All the routine investigations along with serum uric acid and urinary albumin were conducted. Microalbuminuria (urinary albumin excretion rate of 30-300 mg/day.) was detected by immunoprecipitation in a random urine sample. Serum uric acid level was estimated by Spectrophotometry. (Hyperuricemia was defined as a serum uric acid level of > 7 mg/dl (>420 pmol/L) in males and > 6.5 mg/dl (390 pmol/L) in females). The study was approved by ethical committee of institute.

## Statistical Analysis

All the data were analyzed using appropriate statistical methods. A 'p' value of < 0.05 was taken as representing significance and the value < 0.001 was taken to denote high statistical significance.

## RESULTS

The overall prevalence of prehypertension was 38.06% (Males, 39.10% and females, 35.56%) (table-1). Maximum prevalence of prehypertension was seen in the age group of 61-70 years both in males (47.62%) and females (44.44%). No association was seen between the dietary habits, smoking, BMI and the occurrence of prehypertension. The total prevalence of microalbuminuria was 11.61% (9.9% of normotensives and 14.4% of pre-hypertensives) (table-2). Hyperuricemia was seen in 10.32% of the total study population. Among normotensives, 9% of males and 8.6% of females and in pre-hypertensive subjects, 14% of males & 9.4% of females had hyperuricemia (table-3). Uric acid was correlated to dietary habits (vegetarians and non-vegetarians), and with smoking habits, but difference was not significant statistically ( $p > 0.05$ ). When uric acid levels were compared between the blood pressure groups, pre-hypertensives had a higher mean serum uric acid level ( $5.368 \pm 1.185$ ) than normotensives ( $4.953 \pm 1.150$ ) and this was statistically significant ( $p < 0.01$ ) (table-4). Among the pre-

hypertensives, those with microalbuminuria had a significantly higher ( $p < 0.001$ ) serum uric acid level ( $7.024 \pm 1.023$  mg/dl) as compared to those without microalbuminuria ( $5.089 \pm 0.965$  mg/dl) (table-5). Among the normotensives, no such difference was seen. Serum uric acid levels were significantly higher in males  $5.292 \pm 1.173$  mg/dl compared to females  $4.668 \pm 1.078$  mg/dl ( $p < 0.001$ ). When the subjects were distributed into the uric acid quartiles, we found that in females, the maximum distribution was in the 2<sup>nd</sup> quartile (36.67%) followed by the 4<sup>th</sup> quartile (30%) and the 3<sup>rd</sup> quartile (21.11%). Among males, the highest distribution was seen in the 1<sup>st</sup> quartile (59.09%) followed by the 3<sup>rd</sup> (15.91%) and the 2<sup>nd</sup> (12.73%) quartiles (table-6). When the prevalence of microalbuminuria with respect to various uric acid quartiles was considered. In the normotensive group, a linear trend was seen till the 3<sup>rd</sup> quartile but not in the 4<sup>th</sup> quartile ( $p < 0.05$ ), while a linear trend was seen in pre-hypertensive males ( $p < 0.001$  for interquartile trend). This suggested that the prevalence of microalbuminuria increased proportionally to a rise in serum uric acid level. In the pre-hypertensive females, a linear trend was seen when the first three quartiles were considered, but did not reach statistical significance ( $p > 0.05$ ). There was no association between the prevalence of microalbuminuria and serum uric acid levels among the normotensive females ( $p > 0.05$ ). So, our study suggests that serum uric acid is associated with microalbuminuria even in non-hypertensive subjects, and more so in pre-hypertensives and males.

**Table-1: Distribution of Subjects according to Blood Pressure Groups**

Sex	Normotensives	Pre-hypertensives	Total
Males	134 (69.8)	86 (72.9)	220 (70.97)
Females	58 (30.2)	32 (27.1)	90 (29.03)
Total	192 (100)	118 (100)	310 (100)

$\chi^2 = 0.339$ ;  $df=1$ ;  $p > 0.05$ ; NS. Figures in parenthesis indicate percentage.

**Table-2: Distribution of Subjects according to the Microalbuminuria and Blood Pressure Categories**

Micro-albuminuria	Normo-tensives	Pre-hypertensives	Total
Absent	173 (90.1)	101 (85.6)	274 (88.39)
Present	19 (9.9)	17 (14.4)	36 (11.61)
Total	192 (100)	118 (100)	310 (100)

**Table-3: Distribution of Patients according to Uric Acid Level**

Uric Acid level	Normotensives			Pre-hypertensives		
	Male	Female	Total	Male	Female	Total
Normal	122 (91)	53 (91.4)	175 (91.15)	74 (86)	29 (90.6)	103 (87.29)
Hyperuricemia	12 (9)	5 (8.6)	17 (8.85)	12 (14)	3 (9.4)	15 (12.71)
Total	134	58	192	86	32	118

Figures in parenthesis indicate percentage.

**Table-4: Demographic Characteristics of the Study Population according to the Blood Pressure Categories**

Variables	Normo-tensives	Pre-hypertensives	p value
Age (in years)	40.75 (12.9)	42.36 (13.78)	$> 0.05$
BMI	22.812 (2.6)	22.916 (3.256)	$> 0.05$
Serum glucose (mg/dL)	89.72 (10.72)	91.12 (10.21)	$> 0.05$
Serum uric acid (mg/dL)	4.952 (1.15)	5.368 (1.185)	$< 0.01$
Total cholesterol (mg/dL)	172.383 (31.942)	165.275 (30.452)	$> 0.05$
LDL-C (mg/dL)	98.264 (22.505)	95.319 (30.452)	$> 0.05$
HDL-C (mg/dL)	45.369 (7.975)	45.505 (8.650)	$> 0.05$

Figures in parenthesis indicate percentage. Significance of difference is calculated by application of independent 'T' test (Two tailed).

**Table-5: Study of Various Parameters with the Status of Microalbuminuria in Pre-hypertensives**

Parameters	Microalbuminuria		p Value
	Absent	Present	
Age (in years)	$41.63 \pm 13.95$	$46.71 \pm 12.21$	$> 0.05$
BMI	$22.78 \pm 3.15$	$23.68 \pm 3.79$	$> 0.05$
SBP (mmHg)	$127.49 \pm 3.99$	$132.73 \pm 2.42$	$< 0.001$
DBP (mmHg)	$79.42 \pm 5.35$	$84.34 \pm 1.79$	$< 0.001$
Blood sugar (mg/dl)	$90.69 \pm 10.24$	$93.65 \pm 9.93$	$> 0.05$
Total Cholesterol (mg/dl)	$166.98 \pm 30.94$	$175.96 \pm 26.87$	$> 0.05$
LDL Cholesterol (mg/dl)	$94.239 \pm 21.35$	$101.741 \pm 17.16$	$> 0.05$
HDL Cholesterol (mg/dl)	$45.959 \pm 8.66$	$42.806 \pm 8.31$	$> 0.05$
Serum uric acid (mg/dl)	$5.089 \pm 0.96$	$7.024 \pm 1.02$	$< 0.001$

**Table-6: Distribution of Study Subjects according to Serum Uric Acid Quartiles and Sex**

S. Uric Acid Quartiles	Females No. (%)	Males No. (%)	Total No. (%)
I	11 (12.2)	130 (59.0)	141 (45.4)
II	33 (36.6)	28 (12.7)	61 (19.6)
III	19 (21.1)	35 (15.9)	54 (17.4)
IV	27 (30.0)	27 (12.2)	54 (17.4)
Total	90 (100.0)	220 (100.0)	310 (100.0)

## DISCUSSION

To our knowledge the present study is the first study in this part of country (India) which

demonstrates that serum uric acid level is associated with an increased risk of microalbuminuria in pre-hypertensive subjects. When these subjects were grouped according to their blood pressure status, it was found that the total prevalence of prehypertension was 38.06%. Among males, the prevalence of prehypertension was 39.10% and in females it was 35.56%. When the age wise distribution was considered the maximum prevalence of prehypertension was seen in the age group of 61-70 years both in males (47.62%) and females (44.44%). In one other study the prevalence of prehypertension was found to be 29%.<sup>[14]</sup> No significant association of prehypertension was seen between the dietary habits, BMI. The mean systolic blood pressure was significantly higher ( $p < 0.05$ ) in males ( $119.82 \pm 8.454$  mmHg) as compared to females ( $116.524 \pm 7.614$  mmHg). Similarly, males had a significantly higher ( $p < 0.001$ ) diastolic blood pressure ( $75.249 \pm 5.902$  mmHg) as compared to females ( $71.704 \pm 9.350$  mmHg). The total prevalence of microalbuminuria was found to be 11.61%. 9.9% of normotensives and 14.4% of pre-hypertensives had microalbuminuria. These findings are slightly higher than some other studies.<sup>[14,15]</sup> In the literature, abnormal albuminuria in the general population is reported to range from approximately 7 to 20% depending on variables such as the method and threshold adopted, population studied and age.<sup>[18-21]</sup> Hyperuricemia was seen in 10.32% of the total study population. Among normotensives, 9% of males and 8.6% of females had hyperuricemia. In pre-hypertensive subjects, 14% of males & 9.4% of females had hyperuricemia. These findings are lesser than the previous study.<sup>[14]</sup> When the subjects were distributed into the uric acid quartiles, we found that in females, the maximum distribution was in the 2<sup>nd</sup> quartile (36.67%) followed by the 4<sup>th</sup> quartile (30%) and the 3<sup>rd</sup> quartile (21.11%). Among males, the highest distribution was seen in the 1<sup>st</sup> quartile (59.09%) followed by the 3<sup>rd</sup> (15.91%) and the 2<sup>nd</sup> (12.73%) quartiles. When uric acid levels were compared between the blood pressure groups, pre-hypertensives had a higher mean serum uric acid level ( $5.368 \pm 1.185$ ) than normotensives

( $4.953 \pm 1.150$ ) and this was statistically significant ( $p < 0.01$ ). Among the pre-hypertensives, those with microalbuminuria had a significantly higher ( $p < 0.001$ ) serum uric acid level ( $7.024 \pm 1.023$  mg/dl) as compared to those without microalbuminuria ( $5.089 \pm 0.965$  mg/dl). Among the normotensives, no such difference was seen. When the prevalence of microalbuminuria with respect to various uric acid quartiles was considered, a linear trend was seen in pre-hypertensive males ( $p < 0.001$  for interquartile trend). This suggested that the prevalence of microalbuminuria increased proportionally to a rise in serum uric acid level. In the normotensive group, a linear trend was seen till the 3<sup>rd</sup> quartile but not in the 4<sup>th</sup> quartile ( $p < 0.05$ ). In the pre-hypertensive females, a linear trend was seen when the first three quartiles were considered, but did not reach statistical significance ( $p > 0.05$ ). There was no association between the prevalence of microalbuminuria and serum uric acid levels among the normotensive females ( $p > 0.05$ ). The relations are similar to other studies.<sup>[14,15]</sup> No such response was documented in the normotensive group. So, our study suggests that serum uric acid is associated with microalbuminuria even in non-hypertensive subjects, and more so in pre-hypertensives and males. Interestingly the prevalence of microalbuminuria (14.4%) in pre-hypertensive was approximately similar other study who showed the microalbuminuria (13%) in hypertensive patients. This cross sectional study demonstrates a strong independent association between uric acid level and microalbuminuria in pre-hypertensive subjects without a history of cardiovascular disease, diabetes decreased renal function. Because, it was a cross section study, so, we were unable to examine the impact of hyperuricemia over time. For detecting the impact of hyperuricemia on cardiovascular system a large longitudinal study is required.

## CONCLUSION

This study demonstrates a strong independent association between uric acid level and microalbuminuria in pre-hypertensive subjects

without a history of cardiovascular disease, diabetes decreased renal function.

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