

# Prevalence of Hyperuricemia and Microalbuminuria in Prehypertension.

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## ABSTRACT

**Background:** Many studies in the past have revealed the prevalence of hyperuricemia and microalbuminuria in hypertensive individuals and both are the well known markers of end organ damage. But there are very few studies which have demonstrated the prevalence of hyperuricemia and microalbuminuria in prehypertensive individuals in Indian clinical scenario so that we can identify the prehypertensive individuals at risk of subclinical organ damage by simply measuring these parameters. **Objective:** To study the prevalence of hyperuricemia and microalbuminuria in prehypertension. **Methods:** Study was done on both male and female prehypertensive patients of age more than 18 years and less than 60, admitted in wards and attending OPD under the Department of Medicine, NIMS Hospital, Jaipur. Controls were normotensive patients admitted in wards who were matched for age, sex and confounding factors. **Results:** Hyperuricemia was found in 47(15.67%) patients with prehypertension compared to 29(9.67%) patients with normal BP. Microalbuminuria (quantitative) was found in 51(17%) patients with Prehypertension compared to 31(10.33%) patients with normal BP. The study showed that subjects in prehypertensive group had serum uric acid values distributed more widely in the III<sup>rd</sup> and IV<sup>th</sup> quartiles than in the I<sup>st</sup> and II<sup>nd</sup> quartiles, whereas subjects in control group had serum uric acid values with greater distribution, in the I<sup>st</sup> and II<sup>nd</sup> quartiles than in the III<sup>rd</sup> and IV<sup>th</sup> quartiles. **Conclusion:** We found that microalbuminuria and hyperuricemia are significantly more prevalent among prehypertensive subjects as compared to normotensive subjects so that measurement of these parameters can serve as low cost, accurate & reliable clinical tool to identify prehypertensive patient at higher risk of subclinical target organ damage.

**Keywords:** hyperuricemia, microalbuminuria, prehypertension, normotension.

## INTRODUCTION

Prehypertension appears to be associated with an increased risk of myocardial infarction and coronary artery disease but not stroke.<sup>[1]</sup> So it is a designation to identify individuals at high risk developing cardiovascular complications. So that both patients & clinicians are alerted to this risk & encouraged to intervene & prevent or delay the disease from developing.

According to JNC VII classification (American Medical Association), Prehypertension is defined as either systolic BP 120-139 mm Hg &/or diastolic BP 80-89 mmHg based on "2 or more properly measured seated BP readings on each of 2 or more office visits."<sup>[2]</sup>

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Uric acid is produced by xanthine oxidase from xanthine & hypoxanthine, which in turn are

produced from purine. In humans, the upper end of the normal range is 360 µmol/L (6 mg/dL) for women and 400 µmol/L (7 mg/dL) for men.<sup>[3]</sup>

Recent experimental & clinical studies have implicated increased serum uric acid levels in prehypertension. An elevation in uric acid may be critical initiator of renal mechanism leading to development of essential hypertension via both its ability to cause endothelial dysfunction & rennin activation and by causing intrarenal lesion that mediate the development of salt sensitivity<sup>[4-8]</sup>. Furthermore high uric acid level have been associated with increase generation of free radicals & oxidative stress, which may abolish endothelial cells & vascular smooth muscle cells thus leading to hypertension.<sup>[9]</sup>

Hypertension itself leads to increased serum uric acid by the following mechanisms.

- 1) Increase BP lead to vascular disease & increased renal vascular resistance, both resulting in decrease renal blood flow, which in turn stimulate urate reabsorption.
- 2) Microvascular renal disease lead to local ischemia & release of lactate, which compete

with urate transporter in proximal tubule<sup>[10]</sup>, thus blocking urate excretion.

- 3) Ischemia induces degradation of adenosine to adenine & xanthine whereas an increased generation of xanthine oxidase may be observed. The increase generation of substrate (xanthine) & enzyme (xanthine oxidase) can lead to increase uric acid production.

Microalbuminuria is defined as urinary albumin excretion of 30 to 300 mg/24 hr or urinary albumin to creatinine ratio in the first voided sample in the morning (clean, midstream) greater than 30-300mg/g<sup>[11]</sup> or early morning urine albumin concentration of 20-200 mg/L<sup>[12]</sup> which can be detected by radioimmunoassay, ELISA, or nephelometry (amount of albumin is too small to detect by urinary dipstick or conventional measure of urine protein).<sup>[13,14]</sup>

Third National Nutrition Examination Survey (NHANES 3) in the United States reported that microalbuminuria is very common in diabetic and hypertensive patients, although it is also seen in more than 5% of otherwise healthy subjects<sup>[15]</sup>

“Microalbuminuria accelerates atherosclerosis & also it precedes the decline in GFR. It is one of risk factor for renal disease progression & cardiovascular disease. Presence of microalbuminuria even in the setting of normal GFR is associated with increased cardiovascular risk.”It might be an easily detectable marker of generalized vascular dysfunction. “Pathophysiological mechanism behind microalbuminuria is blood pressure load & increase systemic vascular permeability due to endothelial damage, increase activity of the rennin angiotensin system (RAS) & systemic inflammation.”

Studies have revealed the prevalence of hyperuricemia and microalbuminuria in hypertensive individuals and both are the well known markers of end organ damage. But there are very few studies which have demonstrated the prevalence of hyperuricemia and microalbuminuria in prehypertensive individuals in the Indian clinical

scenario so that we can identify the prehypertensive individuals at risk of subclinical organ damage by simply measuring these parameters.

## MATERIALS AND METHODS

- This study was carried out in the Department of Medicine, NIMS Medical College and Hospital, Shobha Nagar, Jaipur, Rajasthan from July 2014 to September 2015, over the period of 15 months.
- Study was done on both male and female prehypertensive patients of age more than 18 years and less than 60, admitted in wards and attending OPD under the Department of Medicine, NIMS Hospital, Jaipur. Controls were normotensive patients admitted in wards who were matched for age, sex and confounding factors.
- **Type of study:** Cross sectional study
- Complete history regarding name, age, sex, occupation, socioeconomic status, hypertension, diabetes, renal disease, previous history of stroke, smoking, alcohol intake, drug abuse, drug history and complete physical and general examination was done. On the spot urine sample was taken for testing of microalbuminuria. Blood samples was collected by venipuncture, serum was separated and subjected to estimation of following parameters on fully automatic analyzer (Trivitron Nanolab 150) using standard kits and methods.

## RESULTS

Hyperuricemia was found in 47(15.67%) patients with prehypertension compared to 29 (9.67%) patients with normal BP. Thus hyperuricemia was seen in patients of prehypertension which was highly significant as P<0.001.

**Table 1: Serum uric acid Amongst Study Population.**

Sr. Uric Acid	Case		Control		Total	
	No.	%	No.	%	No.	%
High	47	15.67	29	9.67	76	12.67
Low	8	2.67	170	56.67	178	29.67
Normal	245	81.67	101	33.67	346	57.67
Total	300	100.00	300	100.00	600	100.00

Chi-square = 211.632 with 2 degrees of freedom; P < 0.001

**Table 2: Prevalence Of microalbuminuria Amongst Study Population.**

Microalbuminuria	Case		Control		Total	
	No.	%	No.	%	No.	%
Absent	249	83.00	269	89.67	518	86.33
Present	51	17.00	31	10.33	82	13.67
Total	300	100.00	300	100.00	600	100.00

Chi-square = 5.099 with 1 degree of freedom; P = 0.024

Fig.2:Prevalence of serum uric acid among study population

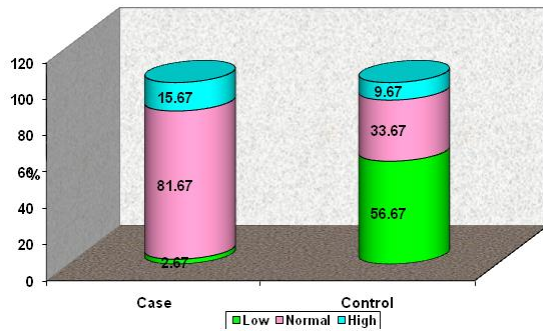


Figure 1: Prevalence of serum uric acid among study population.

Microalbuminuria (quantitative) was found in 51 (17%) patients with Prehypertension compared to 31 (10.33%) patients with normal BP. Thus the

Fig.1:Prevalence of microalbuminuria amongst study population

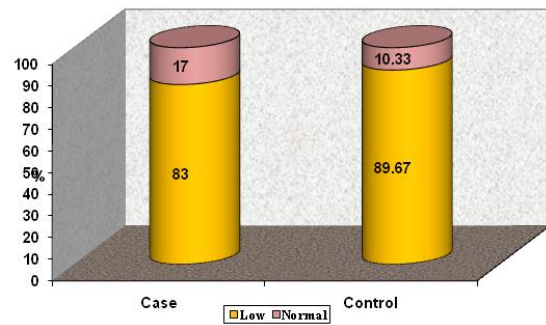


Figure 3: Prevalence of microalbuminuria amongst study population.

occurrence of microalbuminuria in patients of Prehypertension was highly significant as  $P < 0.05$ .

Table 3: Distribution of Study Subjects according to serum uric acid Quartiles.

Sr. Uric Acid (Quartiles)	Case		Control		Total	
	No.	%	No.	%	No.	%
I	4	1.33	147	49.00	151	25.17
II	50	16.67	99	33.00	149	24.83
III	141	47.00	24	8.00	165	27.50
IV	105	35.00	30	10.00	135	22.50
Total	300	100.00	300	100.00	600	100.00

Chi-square = 276.168 with 3 degrees of freedom;  $P < 0.001$

Distribution of Study Subjects according to Serum Uric Acid Quartiles

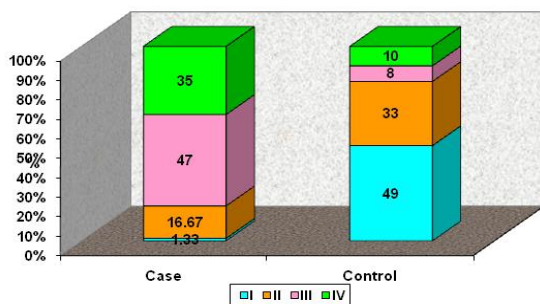


Figure 2: Distribution of Study Subjects according to Serum Uric Acid Quartiles.

The study showed that subjects in prehypertensive group had SERUM URIC ACID values distributed more widely in the III<sup>rd</sup> and IV<sup>th</sup> quartiles than in the I<sup>st</sup> and II<sup>nd</sup> quartiles, whereas subjects in the control group had serum uric acid values with greater distribution, in the I<sup>st</sup> and II<sup>nd</sup> quartiles than in the III<sup>rd</sup> and IV<sup>th</sup> quartiles. It was highly significant as  $p < 0.001$  for interquartile trend.

## DISCUSSION

### Prevalence of Hyperuricemia amongst Prehypertensive Study Group:

In our study, hyperuricemia was found in 47 (15.67%) patients with prehypertension compared to 29 (9.67%) patients with normal BP. Thus hyperuricemia was seen in patients of prehypertension which was highly significant as  $p < 0.001$ .

The study showed that in prehypertensive subjects, hyperuricemia was found in 39 (19.50%) males as compared to 8 (8%) females. The study also showed that there was a statistically significant greater prevalence of hyperuricemia in prehypertensive males as compared to the normotensive males {39 (19.50%) in prehypertensive males; 22 (11%) in normotensive males}; while no such difference was noted between the females of the two groups {8% in prehypertensive females; 7% in normotensive females}.

It was in line with CL Meena et al<sup>[16]</sup>, Jung Eun Lee et al<sup>[17]</sup>.

### Prevalence of microalbuminuria:

According to this study amongst 600 age and sex matched cases and controls, microalbuminuria (quantitative) was found in 51(17%) patients with prehypertension compared to 31(10.33%) patients with normal BP which was highly significant as  $p < 0.05$  Mean urine albumin creatinine ratio (UACR) was  $26.78 \pm 59.24$  in cases compared to 7.55

± 19.85 in controls with p<0.001 which was highly significant.

This is in line with Erhan Tenekecioglu et al<sup>[18]</sup>, CL Meena et al<sup>[16]</sup>, Yasar Yidirim et al<sup>[19]</sup> and Jung Eun Lee et al<sup>[17]</sup>.

**Table 4: Comparison with various previous studies.**

Study	Place &Year of study	Hyperuricemia in cases		Hyperuricemia in controls	
		Male	Female	Male	Female
CL Meena et al	India ; 2013	14%	9.4%	9%	8.6%
Jung Eun Lee et al	Korea ; April 2004 - May 2005	24.8%	1.7%	20%	1.4%
Present study	India ; July 2014 – Sep 2015	19.5%	8%	11%	7%

**Table 5: Comparison with various previous studies.**

Study	Place &Year of study	microalbuminuria in cases		microalbuminuria in controls	
		Male	Female	Male	Female
Erhan Tenekecioglu et al	Turkey ; 2014	25.9 %		10 %	
CL Meena et al	India ; 2013	14.4 %		9.9 %	
Yasar Yidirim et al	Turkey ; 2011-2012	10 %			
Jung Eun Lee et al	Korea ; April 2004 - May 2005	7.9 %		4 %	
Present Study	India ; 2014-15	17%		10.33%	

**Distribution of Study Subjects according to serum uric acid Quartiles**

The study showed that subjects in prehypertensive group had serum uric acid values distributed more widely in the III<sup>rd</sup> and IV<sup>th</sup> quartiles than in the I<sup>st</sup> and II<sup>nd</sup> quartiles, whereas subjects in the control group had serum uric acid values with greater distribution, in the I<sup>st</sup> and II<sup>nd</sup> quartiles than in the III<sup>rd</sup> and IV<sup>th</sup> quartiles. It was highly significant as p<0.001 for interquartile trend.

**CONCLUSION**

The present study showed that microalbuminuria and hyperuricemia was more prevalent in prehypertensive individuals without a history of cardiovascular disease or decreased renal function as compared to normotensive individuals.

Thus, one can expect that measurement of serum uric acid and microalbuminuria can serve as a low cost, accurate & reliable clinical tool to identify prehypertensive patient at higher risk of subclinical target organ damage.

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