# **Original Research**

# Hyperuricemia And Its Association With Hypertension: Risk Factors And Management

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#### Abstract

Background: The present study was conducted for assessing hyperuricemia and its association with hypertension.

**Materials & methods:** All the 200 patients were divided into two study groups as follows: Group A: Subjects with serum uric acid levels more than 5 mg/dL and Group B: Subjects with serum uric acid levels of less than or equal to 5 mg/dL. Comparison was made among the two study groups in terms of hypertension complications. Definition of very high risk was done as per cardiovascular disease prevention guidelines of the European Society of Cardiology. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.

**Results:** There were 105 subjects with serum uric acid levels more than 5 mg/dL (Group A) and 95 subjects with serum uric acid levels of less than or equal to 5 mg/dL (Group B). Obese and male gender were significantly higher among subjects of group A.While assessing the hypertension related complications, heart failure was found to be significant factor associated with group A.While assessing the hypertension treatment, beta blockers and diuretics were found to be significant treatment factor associated with group A.

**Conclusion:** Enhanced uric acid concentration further increases the risk of organ complications. Therefore, early hyperuricemia treatment and serum uric acid level monitoring should be done for preventing multiple organ complications. **Key words:** Hyperuricemia, Hypertension, Inflammatory reactions

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#### Introduction

Hyperuricemia is defined as an elevated serum uric acid level, usually greater than 6 mg/dL in women and 7 mg/dL in men. Elevated serum uric acid is present in an estimated 38 million Americans, and the incidence is increasing worldwide as developing countries adopt more Western diets and lifestyles. Most people with this condition will not have obvious clinical manifestations. however, it is unclear what the long-term effects of hyperuricemia are on overall cardiovascular health, renal function, and overall morbidity. Hyperuricemia results from increased uric acid production, decreased excretion, or a combination of both processes.<sup>1, 2</sup>Ageand sex-specific norms for serum UA are generally accepted as 3.5 to 7.0 mg/dl (208-416 µmol/l) in men and postmenopausal women, and 2.6-5.7 mg/dl (155-339 µmol/l) in premenopausal women. These values have been determined based on UA solubility capacity. Above the threshold of 6.8 mg/dl the risk of serum UA crystallization increases significantly. The

observed differences between sexes have been attributed to estrogen's stimulating effect on UA renal excretion. Hyperuricemia can be classified as symptomatic (when accompanied by symptoms of gout, urolithiasis or acute urate nephropathy), or asymptomatic.<sup>3-</sup> <sup>6</sup>Recent studies have consistently concluded that hyperuricemia may be an independent risk factor for hypertension. Although it seems possible that high uric acid levels are a mere consequence of disease, high uric acid levels always precede the development of hypertension. Hypertension has become increasingly prevalent worldwide, and uric acid levels are rising in correlation.<sup>6</sup> Hence; the present study was conducted for assessing hyperuricemia and its association with hypertension.

#### Materials & methods

The present study was conducted for assessing hyperuricemia and its association with hypertension. A total of 200 subjects with chronic coronary disease (CCD) were enrolled. Complete demographic and clinical details of all the patients was obtained. All the 200 patients were divided into two study groups as follows: Group A: Subjects with serum uric acid levels more than 5 mg/dL and Group B: Subjects with serum uric acid levels of less than or equal to 5 mg/dL. Biochemical and hematological variables among the two study groups were compared. Comparison was made among the two study groups in terms of hypertension complications. Definition of very high risk was done as per cardiovascular disease prevention guidelines of the European Society of Cardiology. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS

software. Univariate analysis was done for evaluation of level of significance.

#### Results

A total of 200 patients were enrolled. There were 105 subjects with serum uric acid levels more than 5 mg/dL (Group A) and 95 subjects with serum uric acid levels of less than or equal to 5 mg/dL (Group B). Obese and male gender were significantly higher among subjects of group A. While assessing the hypertension related complications, heart failure was found to be significant factor associated with group A. While assessing the hypertension treatment, beta blockers and diuretics were found to be significant treatment factor associated with group A.

Table 1:	Comparison	of demogra	phic and gene	eral data
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Variable	Group A (n=105)	Group B (n=95)	OR	p-value
Obesity (BMI > $30 \text{ Kg/m}^2$ )	83	62	1.365	0.001*
Male gender	81	53	1.93	0.000*
Hyperuremic treatment	23	18	1.023	0.771
Diabetes mellitus	39	32	0.928	0.823
Dyslipidemia	41	34	0.813	0.342
Asthma	8	5	0.412	0.812
Thyroid abnormality	13	10	0.729	0.691

### \*: Significant

 Table 2: Hypertension related complications

Variable		Group A (n=105)	Group B (n=95)	OR	p-value
Left	Concentric	38	35	1.023	0.413
ventricular	Eccentric	29	25	0.846	0.845
hypertrophy	Total	38	35	0.981	0.338
Peripheral	Carotid artery stenosis	46	40	0.639	0.415
artery	Limb ischemia	39	36	0.284	0.871
disease	Total	20	19	0.313	0.228
Stroke history		39	34	0.122	0.959
Albuminuria		21	15	0.712	0.825
Heart failure		49	21	2.135	0.001*
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\*: Significant

 Table 3: Hypertension treatment

Hypertension treatment	Group A (n=105)	Group B (n=95)	OR	p-value
Angiotensin-converting enzyme inhibitors	81	77	0.395	0.283
Angiotensin receptor blockers	23	19	0.710	0.118
Calcium channel blockers	48	43	0.228	0.691
Beta blockers	95	71	2.845	0.000*
Diuretics	61	39	2.137	0.001*

\*: Significant

#### Discussion

Uric acid is a by-product of amino acid metabolism, and the breakdown of amino acids produces uric acid in the liver. Moreover, the breakdown of purines releases uric acid in small quantities. Uric acid in human urine and the blood may form sharp crystals and bring about an increased risk of gout. Hyperuricemia mainly caused by metabolic disorders of purine and closely associated with the increases in the risk of cardiovascular disease, kidney disease, diabetes, obesity can be congenital or acquired. Hyperuricemia is the main factor that leads to long-term systemic inflammation in patients with gout.

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Inflammatory reactions in patients with asymptomatic hyperuricemia induced by urate can contribute to the development of obesity, chronic kidney disease, diabetes mellitus, and hypertension. Hyperuricemia may occur when there are high levels of uric acid in the blood due to excess production, or more commonly, inefficient excretion of uric acid.<sup>8-10</sup>Hence; the present study was conducted for assessing hyperuricemia and its association with hypertension. A total of 200 patients were enrolled. There were 105 subjects with serum uric acid levels more than 5 mg/dL (Group A) and 95 subjects with serum uric acid levels of less than or equal to 5 mg/dL (Group B). Obese and male gender were significantly higher among subjects of group A.The study of epidemiological aspects of hyperuricemia shows that doctors often underestimate the problem of hyperuricemia in patients with a high risk of cardiovascular disease. Due to increased comorbidity, moderate hyperuricemia has associations with increased cardiovascular mortality. A 5-year Japanese cohort study indicated that hyperuricemia is an independent risk factor for developing hypertension, especially in children and adolescents. Uric acid associated with proinflammatory immune effects can not only contribute to microvascular iniurv within the intracellular environment but also conduce to increased blood pressure.<sup>11-13</sup>In 2011, Grayson and colleagues published a systematic review of 55,607 patients in 18 prospective cohort studies. They identified that for every 1 mg/dL (60 µmol/L) increase in UA levels, the pooled relative risk for incident hypertension was 1.13 after accounting for potential confounders. This risk was more pronounced in females and younger individuals. Another cohort study of 15,143 subjects identified a similar risk for incident prehypertension with a 9% increased risk for those with SUA levels in the fourth quintile of the population, and 17% risk for those with levels in the fifth quintile, compared with those in the bottom quintile.<sup>14, 15</sup>In the present study, while assessing the hypertension related complications, heart failure was found to be significant factor associated with group A.While assessing the hypertension treatment, beta blockers and diuretics were found to be significant treatment factor associated with group A. The potential effect of uric acid concentrations over 5 mg/dL on the incidence of hypertension complications among patients with very high cardiovascular risk was assessed in a previous study conducted by Muszyński P et al. A total of 705 patients with hypertension and very high cardiovascular risk were selected and included in the analysis. The patients were divided and compared according to serum uric acid levels. The study showed a higher occurrence of heart failure, atrial fibrillation and chronic kidney diseaseamong individuals with serum uric acid levels over 5 mg/dL, males and those with a  $BMI > 25 \text{ kg/m}^2$ . These findings suggest that even

serum uric acid concentrations over 5 mg/dL may affect the prevalence of hypertension-related complications among patients with very high cardiovascular risk.<sup>16</sup>From a clinical point of view, this relationship between SUA and hypertension was explored in 125 teenagers for screening of SUA levels and evaluation of hypertension. The study population consisted of children with essential, secondary, or white-coat hypertension. Forty normotensive controls were recruited from the same clinic. Serum uric acid levels were found to directly correlate with systolic and diastolic blood pressures in controls and in subjects with primary hypertension (but not in subjects with secondary hypertension), independently of renal function. Such a correlation suggested a role for hyperuricemia in the early pathogenesis of primary hypertension. In their study, SUA concentrations > 5.5mg/dL had a positive predictive value of 82% for primary hypertension.<sup>17-20</sup>

#### Conclusion

Enhanced uric acid concentration further increases the risk of organ complications. Therefore, early hyperuricemia treatment and s UA level monitoring should be done for preventing multiple organ complications.

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