

Original research article**Study of correlation of serum uric acid with preclinical target organ dysfunction in newly diagnosed essential hypertension patients****¹Dr. Syed Waseem Khadri, ²Dr. Krupali, ³Dr. Mohmed Samiulla, ⁴Dr. Ravi Kumar**^{1,2}Assistant Professor, Department of General Medicine, ESIC Medical College, Kalaburagi, Karnataka, India³Senior Resident, Department of General Medicine, ESIC Medical College, Kalaburagi, Karnataka, India⁴Senior Resident, Department of General Medicine, Dr. Hedgewar Arogya Sansthan, New Delhi, India**Corresponding Author:**

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Abstract

Hyperuricemia (elevated serum uric acid) has emerged as one of the strongest risk factors for the development of prehypertension, primary hypertension and resistant hypertension. Hyperuricemia also confers increased risk for cardiovascular mortality, especially in women. Hospital based prospective observational study was done on 60 cases for Period of 3 years in the department of General Medicine. Microalbuminuria was present in 81.6% (41/60). 18.3% showed no urine albumin excretion. 83.3% cases showed ECG changes of left ventricular hypertrophy (>5). 70% (42/60) showed Grade II retinal changes. 16.6% (10/60) showed Grade III retinal changes.

Keywords: Microalbuminuria, serum uric acid, hypertension

Introduction

Hypertension (HTN) is the leading cause of preventable deaths and disability worldwide and is a major global risk factor for cardiovascular diseases ^[1]. It has an estimated prevalence of 30-45% in the general population, resulting in an increased burden of heart diseases, vasculopathy, nephropathy and cerebrovascular damage, often with devastating consequences ^[1]. Approximately 90% of patients with HTN have elevated BPs with no known reason and are termed having Essential hypertension (EH) ^[2]. EH defined as an idiopathic chronic elevation of systemic BP ^[2]. This diagnosis is often one of exclusion typically after ruling out other causes of HTN (secondary hypertension). Some causes of secondary HTN include white coat HTN, pulmonary HTN, pregnancy related HTN, Cushing syndrome, renovascular causes, renal parenchymal disease, primary hyperaldosteronism, and pheochromocytoma ^[3]. An elevation in serum uric acid has been associated with an increased risk for the development of hypertension ^[4] and 25% to 50% of hypertensive individuals are hyperuricemic. Hyperuricemia also confers increased risk for cardiovascular mortality, especially in women ^[4, 5]. Recent cross-sectional, cohort, and interventional studies have identified hyperuricemia as an independent risk factor for hypertension ^[6]. In women, especially, the disease risk increases at even lower serum uric acid levels compared to men and requires more attention. Hyperuricemia often accompanies metabolic syndrome, hypertension, diabetes, dyslipidemia, chronic renal disease, and obesity, and the serum uric acid level is known to vary significantly depending on meals, lifestyle, gender, and previous use of diuretics.

Methodology

- The study was approved by the Institutional Ethics Committee.
- Written informed consent was obtained from the all the cases included in the study.
- **Sample Size:** 60 cases.
Calculated using the formula
$$N = Z^2 \times P(1-P) / d^2$$

Where N is the sample size; Z is the statistic corresponding to level of confidence; P is the expected prevalence and d, the precision.

- **Type of Study:** Hospital based prospective observational study.

Inclusion Criteria

1. Patients who are willing to participate in the study.
2. Age between 18 to 61 years.
3. Newly diagnosed essential hypertension patients.

Exclusion Criteria

1. Patients who are unwilling to participate in the study.
2. Patients older than 61 years.
3. Hypertension duration > 6 months.
4. Diabetes mellitus.
5. Cardiac failure.
6. Chronic kidney disease.
7. Patients on diuretics, ACE inhibitors, ARBs.
8. Secondary hypertension.
 - In the Present study we included 60 hypertensive cases with BP > 140/90 mm Hg.
 - Cases were selected randomly.
 - A clinical proforma (questionnaire) was prepared which included present history, past history, Personal history including history of smoking and alcohol and family history of cardiovascular and renal diseases.
 - General and systemic examination was done.
 - Hypertension was defined as a condition when subjects are on current antihypertensive medication or on systolic blood pressure of ≥140 mm Hg or diastolic blood pressure of ≥90.
 - Hyperuricemia is defined as serum uric acid level >7.0 mg/dL in men and ≥6.0 mg/dL in women (77).
 - Target organ damage was defined by the presence of raised serum uric acid levels, Microalbuminuria (urinary albumin excretion: 20-200 mg/L) or Echocardiographic evidence of LV hypertrophy (LVH).

Results

Table 1: Correlation of Average Blood Pressure with URIC Acid Levels

S. No.	Parameter	No. of cases	Mean uric acid levels	SD	t-test
1.	Systolic < 140 and Diastolic < 90 mm of hg	09	5	1.500	p-0.000
2.	Systolic 140-160 or Diastolic 90-100 mm of hg	36	8.28	1.003	
3.	Systolic > 160 or Diastolic > 100 mm of hg	15	8.40	0.632	

- There is a statistically significant difference in mean uric acid levels between Group 1 & Group 2 and Group 1 & Group 3 blood pressures (p-0.000).
- There is no statistically significant difference between Group 2 and Group 3 blood pressures (p-0.919).

Table 2: Correlation of Blood Pressure Control with Target Organ Damage

Characteristic	Target organ damage	Correlation coefficient (p value)
Average Blood pressure	Microalbuminuria	0.657** (p- 0.000)
	LV mass index	0.719** (p- 0.000)
	Carotid IMT	0.339** (p- 0.008)
	Fundus	0.478** (p- 0.000)

**Correlation is significant at 0.01 level

There is positive correlation between average blood pressure and target organ damage. Microalbuminuria (p-0.000), LV mass index (p-0.000) and carotid IMT (p-0.008) and Fundus (p-0.000).

Table 3: Correlation of Components of Metabolic Syndrome with Uric Acid and Target Organ Damage

Characteristic	Uric Acid (cc/p value)	Microalbuminuria (cc/p value)	LV mass index (cc/p value)	Carotid IMT (cc/p value)
BMI	0.160 (p-0.221)	0.649 (p-0.000)**	0.423** (p-0.001)	0.222 (p-0.088)
Waist circumference	0.190 (p- 0.146)	0.328 (p-0.011)*	0.271* (p-0.036)	0.153 (p-0.243)

**Correlation is significant at 0.01 level

* Correlation is significant at 0.05 level

- Correlation is statistically significant between BMI and Microalbuminuria & LV mass index.
- There is statistically significant correlation between Waist circumference and Microalbuminuria & LV mass index.

Table 4: Correlation of Parameters of Target Organ Damage with Uric Acid Levels

Characteristic	No. of cases	Mean uric acid levels	SD	t-test
LV mass Index				
Uric acid	Normal	10	4.90	1.449
	Abnormal	50	8.40	0.670
Carotid IMT				
Uric acid	Normal	12	5.50	1.931
	Abnormal	48	8.40	0.676
Microalbuminuria				
Uric acid	Normal	11	5.27	1.849
	Abnormal	49	8.39	0.671

Statistically significant difference in mean uric acid levels was found with LV mass index, carotid IMT & Microalbuminuria (p<0.000).

Table 5: Correlation of Parameters of Fundus Damage with URIC Acid Levels

S. No.	Parameter	No. of cases	Mean uric acid levels	SD	t-test
1.	GRADE I	08	4.63	1.061	p-0.000
2.	GRADE II	42	8.31	0.950	
3.	GRADE III	10	7.82	0.201	

- There is a statistically significant difference in mean uric acid leaves between Grade 1 & Grade 2 and Grade 1 & Grade 3 fundal changes (p<0.000).
- There is no statistically significant difference between Grade 2 and Grade 3 changes (p<1.000).

Discussion

In the present study 85% cases show ECG changes of left ventricular hypertrophy. Abidemi Jude Fasae *et al.* study [7] observed abnormal ECG in 86.1% of hypertensive patients. In a study conducted by Sandra N Ofori *et al.* study [8] LVH was present in 55.4% of the cases. Electrocardiographic evidence for LVH was found in 10% in the present study, while Echocardiographic evidence was present in 51%.

In the present study Microalbuminuria was present in 78.3% of the hypertensive cases. Whereas in Sandra N Ofori *et al.* study [8] the prevalence of microalbuminuria among the cases was 54.1%. In C Tsioufis *et al.* study [9] the main finding observed that, SUA concentrations in essential hypertensive patients are accompanied by augmented Urinary albumin excretion. But not by increased LV mass index.

Table 6: Comparative Studies Related with Fundus Examination (Patients with hypertensive retinopathy had higher SUA levels)

Keith-Wagener-Barker grading	Xuling Chen et study [10]	Present study
Grade I	58.80%	15%
Grade II	14.81%	68.3%
Grade III	2.34%	16.6%

- In the present study Grade 1 retinopathy was diagnosed in 13.3% cases, grade 2 in 70% cases, and grade 3 in 16.6% cases. Only three subjects were diagnosed as Hypertensive retinopathy grade 4, so these grade 4 subjects were merged with the grade 3 group for analysis. Xuling Chen *et al.* study (72) 75.95% subjects were diagnosed with hypertensive retinopathy. Grade 1 in 58.80%, grade 2 in 14.81%, and grade 3 in 2.34%.

Table 7: Comparison of Present Study with Other Studies

Characteristics	Abidemi Jude Fasae <i>et al.</i> [7]	Fiazee <i>et al.</i> [11]	Kumral Cagli <i>et al.</i> [12]	C Tsioufis <i>et al.</i> [9]	Present study
Age	50.4±12.3 years p vaue- Not significant	47±9 years	57.313.6 years p value-.09	53.05±11.06 years P vaue-NS	41.77 years p value-Not significant
Sex	(0.5:1)	NA	p value -0.50 NS	NS	Not significant (p-0.172)
Pre-menopausal	NA	NA	NA	NA	Not significant (p-0.351)
Family history	NA	NA	NA	NA	Not significant (p-0.743).

Smoking/alcohol	NA	NA	70 (23.3) p value-0.43	37.5 P vaue-NS	Not significant (p-0.637).
BMI	23.3 <0.0001	26.4 ± 3.6	27.22.1 p vaue-<.001	28.7±4.72 P vaue-NS	Correlation is significant at 0.01 level
Average Blood pressure	175±24.0mmHg 106±16.4mmHg SBP-p<0.0001 DBP-p<0.0001		159.0 (148.0- 174.0) p vaue-.03	150 ±19.31 97 ± 11.56 SBP- NS DBP- 0.02	158.25 mmHg 95 mmHg Significant (p-0.000).
Mean uric acid	0.4±0.1mmol/l (p<0.0001)	5.14 mg/dL	5.4 mg/Dl	5.20 mg/dL	7.73 mg/dL
LV mass Index	(p<0.001),	52 + 2.8	NA	111±28 NS	Significant (p-0.000)
Carotid IMT	NA	NA	NA		Significant (p-0.000)
Microalbuminuria	NA	NA	NA	68.16±9.73 0.00	Significant (p-0.000)
Fundus	NA	NA	NA	NA	Significant (p-0.000)

Conclusion

- There is Positive correlation between average blood pressure and target organ damage. Microalbuminuria (p-0.000), LV mass index (p- 0.000) and carotid IMT (p- 0.008) and Fundus (p-0.000).
- Statistically significant difference in mean uric acid levels was found with LV mass index, carotid IMT & Microalbuminuria (p-0.000).
- There is a statistically significant difference in mean uric acid levels between Grade 1 & Grade 2 and Grade 1 & Grade 3 fundal changes (p- 0.000).

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