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# Serum Uric Acid in Hypertension

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**Abstract**

*Introduction:* Hypertension is defined by the presence of persistently elevated blood pressure leading to morphological and functional changes in the heart and systemic arterioles. It is ranked as the third most important risk factor for attributable burden in South East Asia. Elevation of serum uric acid has been found to be associated with subsequent morbidity and mortality in the general population among patient with congestive heart failure, diabetes and hypertensive patients. Our study, thus, aims to compare the association between levels of serum uric acid (SUA) and serum lipid profile between controls and hypertensive patients with or without complications.

*Materials and Methods:* This cross-sectional study was carried out in hypertensive patients attending medicine OPD and admitted in Medicine ward from October 2018 to September 2020. Study population consisted of 65 cases and 65 age and sex matched controls.

*Results:* The study shows that serum uric acid level was significantly higher in hypertensives (6.2 ± 1.2 mg/dl) than that of controls (4.6 ± 1.0 mg/dl). A poor correlation was observed between uric acid level and cholesterol ($R_p$ - 0.195) and LDL ($R_p$ - 0.044) but for triglycerides and HDL, there was fair correlation and the findings were statistically significant.

*Conclusion:* It can be concluded that serum uric acid is a potent biomarker for the risk of hypertension and its complications.

**KEYWORDS:** HDL, Hypertension, LDL, Serum Uric Acid

## INTRODUCTION

Hypertension is defined by the presence of persistently elevated blood pressure leading to morphological and functional changes in the heart and systemic arterioles. The increased afterload on the heart results in left ventricular hypertrophy and the increased pressure in the arterioles resulting in the thickening of their walls and a reduced lumen. The changes increase the risk of stroke, heart failure, renal failure and retinopathy, with a direct relation between the risk and the level of blood pressure. Sometimes it goes undetected until complications arise. [1]

In 2008, worldwide, approximately 40% of adults ≥25 years of age had been diagnosed with hypertension (600 million in 1980 to 1 billion in 2008). [2] Hypertension is ranked the third most important risk factor for attributable burden in South East Asia.[3]

It was observed that hyper-uricemia is commonly associated with obesity, hypertriglyceridemia and hypertension. Elevation of serum uric acid has been

found to be associated with subsequent morbidity and mortality in the general population among patient with congestive heart failure, diabetes and hypertensive patients. [4]

Uric acid is a weak organic acid, the end product of purine nucleotides degradation. [5] Elevated Serum Uric acid (SUA) positively correlates with development and progression of cardiovascular diseases as it stabilizes platelet aggregation and enhances thrombotic tendency. [6] Dyslipidemia is also considered as one of the risk factors linked to serum uric acid. [7] Though many studies in the past have shown an increased level of serum uric acid in hypertensive patients, few have shown its opposite. So, this study was carried out to assess the level of uric acid in the hypertensive population of Manipur for the first time.

## AIMS AND OBJECTS

1. To estimate and compare serum uric acid (SUA) and serum lipid profile between controls and hypertensive patients with or without complications
2. To find out the correlation between uric acid and lipid profile among hypertensive cases

## MATERIALS AND METHODS

It was a cross sectional study carried out in the Department of Biochemistry in collaboration with the Department of Medicine, RIMS, Imphal, Manipur from October 2018 to September 2020. Study population consisted of 65 hypertensive patients attending Medicine OPD and admitted in Medicine ward, RIMS. Another 65 age and sex matched healthy, non-hypertensive individuals were taken as controls.

*Inclusion criteria:*

New onset and recent onset hypertensive patients in the age group between 16 and 65 years were included in the study irrespective of socio-economic status.

*Exclusion criteria:*

- Age < 16 years and > 65 years
- Individuals suffering from Type 1 and Type 2 Diabetes mellitus or metabolic syndrome, gout, endocrine disorders, psoriasis and malignancy
- Long term drug intake - steroids, ATT, diuretics, antimetabolites or chemotherapy drugs

*Method*

Detailed history regarding the duration of disease, age of onset of disease, associated symptoms of complications were taken and recorded. A written consent was taken from all the subjects. Blood pressure was measured according to the routine clinical practice in a supine position with right arm placed horizontally at the heart level. Based on the criteria used by NHNS (1976-80) the individual was diagnosed as having hypertension when the blood pressure is ≥ 140/90 mmHg. Fasting venous blood of about 5 ml was collected from the anterior cubital vein in sterile vial which was allowed to centrifuge at 3000 rpm for 10 minutes to obtain serum for the estimation of SUA and lipid profile. Estimation of Serum Uric Acid was done by Enzymatic colorimetric method as described by Fossati P et al [8] using Randox kit by RX Imola autoanalyser. Serum lipid profile estimation was done by Enzymatic Colorimetric Test kits manufactured by HUMAN Gesellschaft fur Biochemica und Diagnostica Indian branch. Ethical approval from research ethics board, RIMS, Imphal was taken prior to the study. Statistical analysis was done using SPSS version 21. Student's t test was used to test for significance and Pearson's correlation coefficient was used to establish the relationship between serum uric acid and lipid parameters. A Probability value (p value) of <0.05 was considered statistically significant.

## RESULTS

Table 1 shows that maximum of the controls were above 50 years of age (70.8 %), whereas maximum hypertensives fall in the age group between 41 to 50 years (35.4 %). But the finding was statistically insignificant ($p > 0.05$). Mean age of controls was 51.75 ± 9.2 years and that of hypertensive cases was 55.60 ± 8.3 years, which shows that both the group were age matched.

Table 2 shows males constituted 53.8 % of controls and 63.1 % of cases indicating a male dominance. But the difference was statistically insignificant ($p > 0.05$). So, regarding sex, both the groups were comparable.

In table 3 biochemical parameters were presented in mean and standard deviation. Test of significance was performed using t-test. Serum uric acid was higher in hypertensives (6.2 ± 1.2 mg/dl) than that of controls (4.6 ± 1.0 mg/dl). The finding was statistically significant ($p < 0.05$). similarly other biochemical parameters were



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significantly higher in hypertensives except for HDL which was lower.

Figure 1 showing maximum of the hypertensive patients had systolic blood pressure levels under 140 mm of Hg (43.1%) followed by 140- 145 mm of Hg (24.6 %) and maximum diastolic blood pressure levels between 90-95 mm of Hg (47.7 %).

Table 4 showing uric acid level was higher in hypertensives with complications compared to the hypertensives without complications and the finding was statistically significant ($p < 0.05$).

Table 5 shows that there was poor correlation between uric acid level and cholesterol ($R_p$ - 0.195) and LDL ($R_p$ - 0.044) but the findings are statistically insignificant. For triglycerides and HDL there was fair correlation and the findings were statistically significant.

## DISCUSSION

In the present study age wise distribution shows, 35.4% of cases were in the age group of 41-50 years followed by 32.3% in 51- 60 years, 18.5 % in > 60 years and 13.8% in 30-40 years age group. This finding is consistent with the observation of Fishberg AM [9] that the vast majority of hypertension occurs after the age of 40 years. The highest incidence in much older age group in cases is due to a stiff artery that has decreased capacitance and limited recoil and is thus unable to accommodate the changes that occur during cardiac cycle. Furthermore, during systole the arteriosclerotic arterial vessel exhibits limited expansion and fails to buffer effectively the pressures generated by the heart causing an increase in SBP. On the other hand, the loss of recoil during diastole results in reduction of DBP. [10] Renin- angiotensin- aldosterone system decline with age. Plasma renin activity at the age of 60 is 40% to 60% of the levels found in younger individuals. [11] The aging kidney is categorized by progressive development of glomerulosclerosis and interstitial fibrosis, which is associated with a decline in GFR and reduction of other homeostatic mechanisms. [12]

In the current study, 63.1% of the cases and 53.8% of controls were males while 36.9% of cases and 46.2% of controls were females (Table 2). The higher incidence of males in both cases and controls may be due to higher male attendance in the hospitals in addition to female hesitancy to seek early medical advice in the hospital. Also, the lower incidence in females may be partly due to the ability of estrogen to reduce hypertensive effects of Renin- angiotensin system. [13,14] The percentages observed however closely resembles those found by Mishra A et al [15] where 58% of cases and 54% of controls were males as compared to 42% and 46% of females, respectively.

The hypertensive patients have higher mean SUA level (6.2±1.2 mg/dl) as to that of controls (4.6±1.0 mg/dl), which is statistically significant (p value <0.001). The findings are in accordance with the findings of Jawed S et al [16] which shows that SUA was elevated to 6.51±1.45 in cases as compared to 4.72 ± 1.83 in controls. Kashem MA et al [17] studied that the mean SUA level was 5.8 ± 1.5 mg/dl vs 4.5 ± 1.2 mg/dl in cases and control patients respectively with p value < 0.05. A similar conclusion was also obtained by Poudel B et al [18], Ofori SN et al [19] and Loeffler LF et al. [20]

It indicates that the pathophysiology of hypertension involves both inflammatory and oxidative pathways where SUA acts as antioxidant and free radical scavenger. But at an elevated level it can have deleterious effect by promoting atherosclerotic process as pro-oxidant indicating its property of antioxidant-pro-oxidant urate redox shuttle. The mean SUA level of male (6.8± 0.8 mg/dl) and female (5.7±1.1 mg/dl) cases were higher as compared to the values in male and female controls (4.6±1.1 mg/dl) and (4.4±0.7 mg/dl). The results are in agreement with the study done by Emokpae AM et al [21] and Anton FM et al [22] and thought to be related to a higher renal clearance of urate in women, possibly due to their higher plasma estrogen levels.

The SUA level in cases with complications have significantly elevated (7.5±0.9 mg/dl) as compared to patients without complications (6.1±1.1 mg/dl). This finding supports the study done by Ofori SN et al [19] who found that serum uric acid has linear correlation with end organ damage.

Abnormalities in serum lipid and lipoprotein levels (dyslipidemia) are recognized as major modifiable cardiovascular disease risk factors [23] and have been identified as independent risk factors for essential hypertension. It has been documented that the presence of hyperlipidemia substantially worsens the prognosis in hypertensive patients. [24]



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In our study, fasting mean serum cholesterol level in cases is 187.1 ± 50.4 mg/dl, which is significantly elevated as compared to controls (158.9 ±39.9 mg/dl). Mean serum LDL level for the cases is elevated to 122.4± 38.1 mg/dl vs 108.0±34.1 mg/dl in controls with a p value <0.05. The findings are well supported by other studies, like that conducted by Choudhury KN et al [25], Stampfer MI et al [26] and Campos G et al [27]. The mean fasting serum HDL in cases (35.9 ±8.6 mg/dl) is significantly less than that of the controls (40.4±11.9 mg/dl), p value<0.05. This observation agrees with the findings of Pyadala N et al [28] and Choudhury KN et al. [25]

The mean fasting serum triglycerides level in cases (199.7 ± 112.5 mg/dl) is higher as compared to controls (134.3 ± 63.6 mg/dl). The higher level of TG among hypertensives are in consistent with the reports of Kolovou GD et al [29] who reported that the plasma TG conc. increased significantly after fat loading among hypertensives compared to controls due to delayed clearance of plasma triglyserides. The involvement of TG rich lipoproteins in many pathways leading to atherosclerosis have been discussed by many previous workers. [30,31]

A poor correlation was observed between uric acid and cholesterol ($R_p$- 0.195) and LDL ($R_p$- 0.044). The triglyceride level and HDL level have a fair correlation with SUA level and the finding was statistically significant, p value <0.05. Conen D et al [32] and Moriarity JT et al [33] found that the connection between TG and uric acid levels were linear and evident, which is in complete agreement with our findings. The relationship between triglycerides and uric acid level had been attributed to genetic factors. [34,35]

It has been speculated that the synthesis of triglycerides will need NADPH, which resulted in increased uric acid production. [36]

*Limitations of the study:* - The limitation of this study was the small sample size. The sample size obtained mainly from an urban hospital and may not be the representative of all hypertensive patients residing in rural areas.

## CONCLUSION

The study shows that the risk of hypertension increases with increase in age. Hypertensive cases have higher SUA as compared to healthy controls indicating that the pathophysiology of hypertension involves both inflammatory and oxidative pathways and SUA at an elevated level act as a pro-oxidant promoting atherosclerotic process. Serum TC, TG, LDL are elevated in contrast to the lower level of HDL in hypertensive cases. Serum TG and HDL have significantly fair correlation with SUA level. Hypertensive cases with complications have significantly elevated uric acid level as compared to cases without complication. Thus, it can be concluded that serum uric acid is a potent biomarker for the risk of hypertension and its complications. Measurement of SUA for all hypertensive patients is suggested in order to take necessary precautions to prevent the complications.

***Table 1: Age wise distribution of controls and hypertensive cases***

| Age in years | Controls N (%) | Hypertensive cases N (%) | Total N (%) | Chi – square test |
|---|---|---|---|---|
| 30-40 | 4(6.2) | 9(13.8)13(10.0) | | |
| 41-50 | 15(23.1) | 23(35.4) | 38(29.2) | Value= 7.155 |
| 51-60 | 23(35.4) | 21(32.3) | 44(33.8) | df -3 |
| >60 | 23(35.4) | 12 (18.5) | 35(26.9) | P = 0.067 |
| Total | 65(100) | 65(100) | 130(100) | |
| Mean ± SD | 51.75 ± 9.2 | 55.60 ± 8.3 | | |



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***Table 2: Sex distribution of cases and controls***

| Sex | Controls N (%) | Hypertensive cases N (%) | Total N (%) | Chi – square test |
|---|---|---|---|---|
| Female | 30(46.2) | 24(36.9) | 54(41.5) | Value=1.14 |
| Male | 35(53.8) | 41(63.1) | 76(58.5) | df = 1 |
| Total | 65(100.0) | 65(100) | 130 | p = 0.286 |

***Table 3: Comparison of various biochemical parameters between cases and controls***

| Parameters (Biochemical) | Controls Mean ± SD | Cases Mean ± SD | t-test p-value |
|---|---|---|---|
| Uric acid (mg/dl) | 4.6 ± 1.0 | 6.2 ± 1.2 | Value = 8.4<br>df-128<br>p = 0.001 |
| Cholesterol (mg/dl) | 158.9 ± 39.9 | 187.1 ± 50.4 | Value = 3.5<br>df-128<br>p= 0.001 |
| Triglycerides (mg/dl) | 134.3 ± 63.6 | 199.7 ± 112.5 | Value = 4<br>df-128<br>p= 0.000 |
| LDL (mg/dl) | 108.0 ± 34.1 | 122.4 ± 38.1 | Value = 2.2<br>df-128<br>p= 0.025 |
| HDL (mg/dl) | 40.4 ± 11.9 | 35.9 ± 8.6 | Value = 2.459<br>df-128<br>p= 0.015 |

***Table 4: Comparison of uric acid level among hypertensive cases with and without complications***

| Hypertensives | Uric acid level (mg/dl) Mean ± SD | t-test p-value |
|---|---|---|
| With complications (n = 5) | 7.5 ± 0.9 | Value=2.3 |



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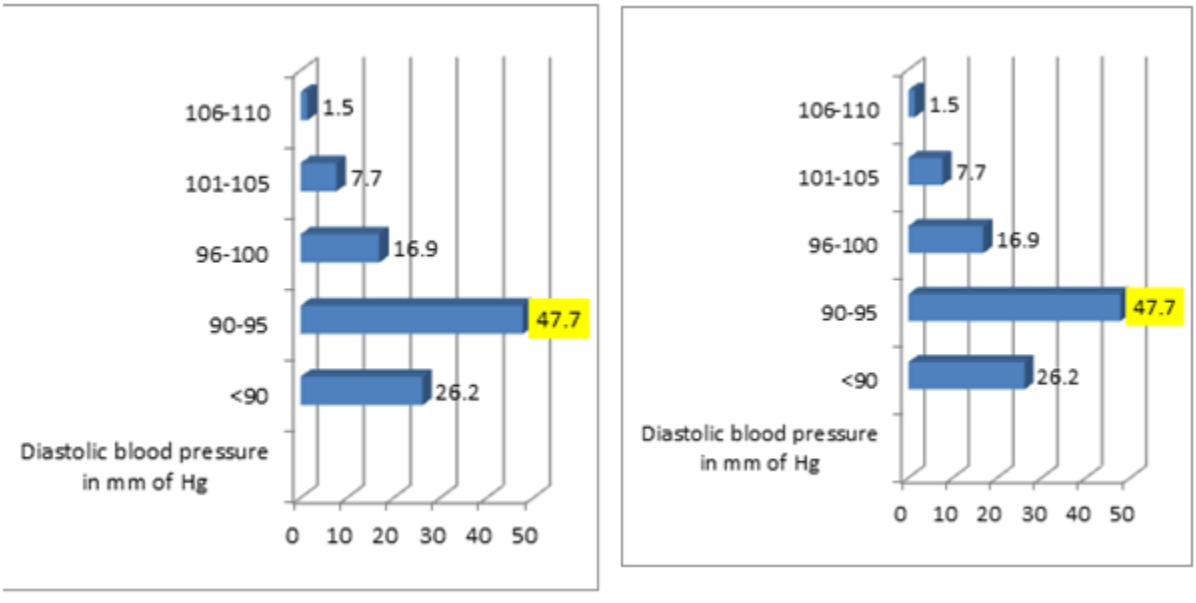
| | | |
|---|---|---|
| | | df - 63<br>p - 0.020 |
| Without complications (n = 60) | 6.1 ± 1.1 | |

***Table 5: Relation between uric acid and lipid profile among hypertensive cases***

| Lipid profile | Uric acid<br>Correlation coefficient<br>p-value |
|---|---|
| Cholesterol | $R_p$- 0.195 p- 0.119 |
| Triglycerides | $R_p$- 0.306 p- 0.013 |
| LDL | $R_p$- 0.044 p- 0.731 |
| HDL | $R_p$- 0.384 p- 0.002 |

**FIGURES**

*Figure 1: Horizontal bar diagram showing distribution of respondents by systolic/diastolic blood pressure in hypertensive cases*



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