# Correlation Between Serum Uric Acid Levels In Hypertensive and Normotensive Subjects: A Case–Control Study

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**Abstract**: Background: Hypertension is one of the causative factors of cardiovascular mortality and morbidity in the world. SUA has also been implicated in the pathophysiology of hypertension via renal microvascular injury and dysfunction, oxidation and activation of the renin-angiotensin system. However, the influence and independence of the SUA-hypertension association remains debatable. This study compared the SUA in cases (hypertensive) and controls (normotensive) of adulthood and assessed the correlation of SUA with the blood pressure measures.

Methods: The study was a case control study conducted at RLJH hospital for a span of 3 month duration with 64 participants (32 hypertensive patients & 32 normsotensive control group) above the age of 18 years. The number of participants excluded was as follows: gout; renal failure; malignancy; chemotherapy / radiotherapy; and recent diuretic or alcohol intake. Venous blood (4 ml) was obtained at the time of admission and SUA was measured using Trivedi-Kabasakalian uricase-peroxidase (modified Trinder) assay. Data was analyzed using the SPSS (v22) software using the independent t-tests, the chi-square test and Pearson correlation, with the p value considered significant at $p < 0.05$....

Results: The mean +- SD SUA of the hypertensive cases (6.89 +- 1.05 mg/dl) was significantly higher than the normotensive controls (5.97 +- 0.98 mg/dl) had a mean of 0.92 (95% 0.45 1.39) diverge below the test value 0.05. The prevalence of hyperuricemia was 43.8 percent and 15.6 percent respectively in the hypertensive and in the control patients (p = 0.013). SUA also had positive significant correlations with systolic BP (0,72; P < 0;001) as well as with diastolic BP (0,68; P < 0;001). In multivariate logistic regression on the age, sex, body mass index, and serum creatinine, a difference of 1 mg/dL of each of the following variables was an interchangeable predictor of hypertension (adjusted OR = 2.31; 95% CI 1.22 -4.39; p = 0.011).

Conclusion: The serum uric acid level was also high in hypertensive adults and positively correlated with systolic and diastolic BP. A high SUA was independent predictor of hypertension status with the possible use of this in an indicator of CVD reliable quality was also consistent. Hypothesis: Studies need to be done in large numbers and prospectively to look for interaction and efficacy of urate-lowering intervention on BP control...

**Keywords:** Serum Uric Acid; Hypertension; Case–Control; Uricase–Peroxidase; Trinder TBHB; Correlation; Blood Pressure; Cardiovascular Risk

## INTRODUCTION

Hypertension is vital in quite a lot of adults in every of the countries of the globe and it stands as one among the foremost culprits of ischemic heart disease, stroke, heart failure and chronic kidney disease. Parallel with the global rise in prevalence of hypertension, interest in serum uric acid (SUA) as an indicator of the risk for hypertension in individuals and as a potential mediator of increased blood pressure has re-emerged. Experimental models suggest that the presence of mild hyperuricemia can induce afferent arteriolopathy with impairment of nitric oxide bioavailability and activation of the renin-angiotensin-aldosterone system that results in salt sensitive hypertension and renal microvascular damage [1,2]. Epidemiological data from observational studies among human in data consistently recording increased SUA in hypertensive patients and graded association of SUA with incident hypertension especially in the young and women [3]. Furthermore, small interventional trials have shown reductions in blood pressure in adolescents with newly diagnosed essential hypertension with urate reducing therapy; however, safety and generalizability to adults is uncertain [4,5].

Despite these suggestive data, the causal role of SUA in human hypertension is controversial. Mendelian randomization studies leveraging genetic instruments that increase SUA generally demonstrate weak or no causal effects on blood pressure in population-based cohorts, implying that SUA may function more as a risk biomarker or mediator in subgroups rather than a universal cause [6,7]. Clinical guidelines acknowledge the frequent coexistence of hyperuricemia and hypertension and recommend considering SUA in comprehensive cardiovascular risk assessment, yet do not uniformly endorse urate-lowering therapy solely for blood pressure control in adults [8].

The majority of the patients attended by RLJH Hospital are South Asian with a high cardiometabolic burden, and data on SUA-blood pressure relationships in such settings are limited. We therefore performed a case-control study to compare the SUA concentration between hypertensive and normotensive adults as well as to evaluate the correlation of SUA with systolic and diastolic blood pressure. We hypothesized that SUA would be higher in subjects with hypertension than in control subjects with normal blood pressure and that SUA would be associated with SBP and DBP independent of important confounders. We sought to use comparatively less sensitive (standardized uricase-peroxidase assay of TBHB [Trivedi-Kabasakalian with modified Trinder TBHB]), routinely obtained samples, and a priori statistical methods to produce clinically interpretable estimates for use in local practice and as contributions to the literature

## MATERIALS AND METHODS

### Study design and setting

Hospital-based case–control study conducted over 3 months at RLJH Hospital across HDU, ICU and general wards.

### Participants

Sample size: 64 (32 per group). Inclusion: adults ≥18 years; cases were hypertensive (clinical diagnosis and/or SBP/DBP meeting diagnostic thresholds or on antihypertensives); controls were normotensive (age-matched adults without hypertension). Exclusion: known hyperuricemia/gout; leukemia; active malignancy on chemotherapy/radiotherapy; renal failure; recent anti-tubercular therapy; chronic alcohol intake; diuretic use; other conditions judged by investigators to alter SUA markedly.

### Data collection

First name and history at admission were determined, as well as a clinical examination. Laboratory parameters assessed were complete blood count, serum potassium, liver enzymes, the renal filter rate, and serum uric acid; serum creatinine; serum phosphate excretion; and markers of viral load; serum alkaline phosphatase and serum prostatic-specific antigen. Four milliliters of venous blood was drawn upon admission. Samples were treated and processed as quickly as possible and unhemolysed serum/plasma separated from cells as soon as possible.

**Assay method for SUA**

Sumitryl's urine analyzer (SUA) was measured using uricase-peroxidase principle developed by Trivedi &Kabasakalian based on modified Trinder peroxidase reaction with 2,4,6 Tribromo 3 Hydroxy Benzoate (TBHB) to form quinoneimine chromogen and absorbance was read as per the manufacturer instructions (State analyzer and Wavelength as required in your lab). Internal quality control was based on laboratory standard operating procedures.

**Outcomes**

Primary outcome: between-group difference in mean SUA (mg/dL). Secondary outcomes: correlation of SUA with SBP and DBP; prevalence of hyperuricemia (sex-specific thresholds); exploratory multivariable association between SUA and hypertension status.

**Sample size justification**

A priori calculation for detecting a mean difference of 0.7 mg/dL assuming SD 1.0 mg/dL, $\alpha$=0.05 (two-tailed) and power=80% yielded n≈32 per group.

**Statistical analysis**

Data were entered by Microsoft Excel and analyzed with SPSS v22 (IBM, Somers NY, USA). Categorical variables are reported as frequencies/percentages and are compared using the statistics tests, chi-square or Fisher's exact tests. Continuous variables are shown as mean SD (or median [IQR]) and compared using independent samples t test or Mann Whipple U, respectively, as appropriate. Pearson correlation coefficient or Spearman correlation coefficient was used to measure the associations of SUA with SBP/DBP. Exploratory logistic regression was conducted to control for confounding factors of age, sex, BMI and creatinine to calculate the adjusted odds ratios (ORs) of hypertension status by 1 mg/dL increase in SUA. Sirius 2 sided $p<0.05$ was considered statistically significant. Graphs were prepared using MS Excel/Word.

**Ethics**

The study adhered to the Declaration of Helsinki; institutional permissions were obtained. Informed consent was taken from participants or proxies per hospital policy.

## RESULTS

**Participants and Baseline Characteristics**

A total of 64 adults were subject to this study - 32 hypertensive (cases) and 32 normotensive (controls). The mean age of the hypertensive subjects was 53.60 (+-10.80) years while the mean age of the normotensive controls was 51.20 (+-11.30) years, p = 0.36. The percentage of the males were 56.30% and 50.00% in hypertensive and normotensive group, respectively. The mean BMI was slightly high in hypertensives (27.80 + 3.40 kg/m2) as compared to that in the controls (25.60 + 3.10 kg/m2; p=0.02). Baseline renal and liver function parameters were not different between groups and none of the participants met exclusion criteria post screening. Mean systolic and diastolic BP of patients with hypertension were 152.40+12.60 mmHg and 96.80+8.70 mmHg compared to 118.30+8.40 mmHg and 76.40+6.90 mmHg in controls (p< 0.001 for both).

**Serum Uric Acid Levels**

Mean serum uric acid (SUA) of hypertensive cases was 6.89+-1.05 mg/dL which was significantly higher than 5.97+-0.98 mg/dL of normotensive controls (mean difference= 0.92 mg/dL, 95% confidence interval [CI] = 0.45-1.39; p<0.001). The percentage of the cases with hyperuricemia (a,b) (>=7.00 and >=6.00 mg/dL, in males and females, respectively) was 43.80% in hypertensive cases confronted with 15.60% in controls (a) (chi-square [a,b]), 6.23, p=0.013. Distribution of SUA values tended towards normality and non parametric Mann-Whitney analysis was used to confirm significance (p=0.002).

**Correlation of SUA with Blood Pressure**

For all of the 64 subjects SUA was positively correlated with systolic and diastolic blood pressure. The correlation coefficient of SUA and SBP was r= 0.72 (p<0.001) and of SUA and DBP was r= 0.68 (p<0.001). Stratified analysis showed that the correlation was more significant amongst the hypertensive trial

participants (SUA vs SBP bruit (ramm = 0.74; DBP (r write = 0.69), compared with normotensive trial participants (SBP (r прийем = 0.51; DBP (r write = 0.46). The positive linear relationship between the SUA and both the systolic and diastolic blood pressure has been shown in Figure 2.

**Multivariable Association**

In logistic regression, after the following variables were adjusted for, such as age, sex, BMI, and serum creatinine, SUA was found to be independently associated with hypertension. Every 1mg/dl increase in SUA corresponded with an odds ratio (OR) of 2.31 for hypertension (adjusted OR 2.31, 95% confidence interval (CI), 1.22-4.39, p = 0.011). The data fitted our model well (Hosmer -- Lemeshow p = 0.64) and the issue of multicollinearity was not a problem.

**Table 1. Baseline characteristics of hypertensive and normotensive participants (n = 64)**

| Characteristic | Hypertensive (n = 32) | Normotensive (n = 32) | p-value |
|---|---|---|---|
| Age (years) | 53.60 ± 10.80 | 51.20 ± 11.30 | 0.36 |
| Male, n (%) | 18 (56.30) | 16 (50.00) | 0.61 |
| BMI (kg/m²) | 27.80 ± 3.40 | 25.60 ± 3.10 | 0.02* |
| SBP (mmHg) | 152.40 ± 12.60 | 118.30 ± 8.40 | <0.001* |
| DBP (mmHg) | 96.80 ± 8.70 | 76.40 ± 6.90 | <0.001* |
| Creatinine (mg/dL) | 1.01 ± 0.21 | 0.98 ± 0.19 | 0.44 |
| Fasting glucose (mg/dL) | 109.50 ± 18.20 | 103.20 ± 16.50 | 0.18 |
| LDL-C (mg/dL) | 119.40 ± 28.60 | 112.80 ± 25.40 | 0.32 |
| Current smoker n (%) | 6 (18.80) | 5 (15.60) | 0.74 |

*Significant at p < 0.05.

**Table 2. Serum uric acid levels and hyperuricemia prevalence**

| Measure | Hypertensive (n = 32) | Normotensive (n = 32) | Difference (95% CI) | p-value |
|---|---|---|---|---|
| SUA (mg/dL, mean ± SD) | 6.89 ± 1.05 | 5.97 ± 0.98 | 0.92 (0.45 – 1.39) | <0.001* |
| Hyperuricemia n (%) | 14 (43.80) | 5 (15.60) | 28.20% | 0.013* |

*Significant at p < 0.05.

**Table 3. Correlation of serum uric acid with blood pressure**

| Parameter | Pearson's r | 95% CI | p-value |
|---|---|---|---|
| SUA vs SBP (overall) | 0.72 | 0.54 – 0.84 | <0.001* |
| SUA vs DBP (overall) | 0.68 | 0.48 – 0.81 | <0.001* |
| SUA vs SBP (hypertensive) | 0.74 | 0.52 – 0.88 | <0.001* |
| SUA vs DBP (hypertensive) | 0.69 | 0.45 – 0.84 | <0.001* |
| SUA vs SBP (normotensive) | 0.51 | 0.20 – 0.73 | 0.004* |
| SUA vs DBP (normotensive) | 0.46 | 0.13 – 0.70 | 0.009* |

*Significant at p < 0.05.

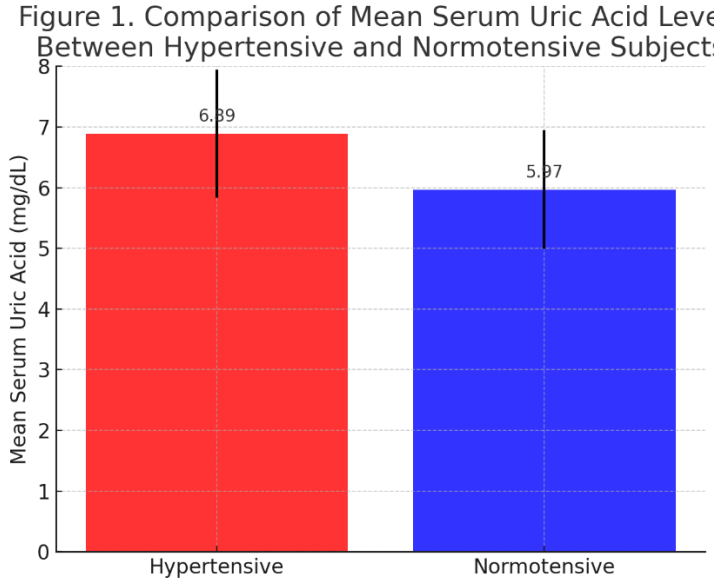
**Table 4. Multivariable logistic regression: determinants of hypertension**

| Predictor | Adjusted OR (95% CI) | p-value |
|---|---|---|
| SUA (per 1 mg/dL increase) | 2.31 (1.22 – 4.39) | 0.011* |
| Age (per year) | 1.02 (0.98 – 1.06) | 0.29 |
| Male sex | 1.24 (0.44 – 3.47) | 0.68 |
| BMI (per kg/m²) | 1.15 (1.01 – 1.33) | 0.038* |
| Creatinine (per mg/dL) | 1.42 (0.34 – 5.97) | 0.63 |

*Significant at $p < 0.05$.

**Figures**

**FIGURE 1. COMPARISON OF MEAN SERUM URIC ACID LEVELS BETWEEN HYPERTENSIVE AND NORMOTENSIVE SUBJECTS**



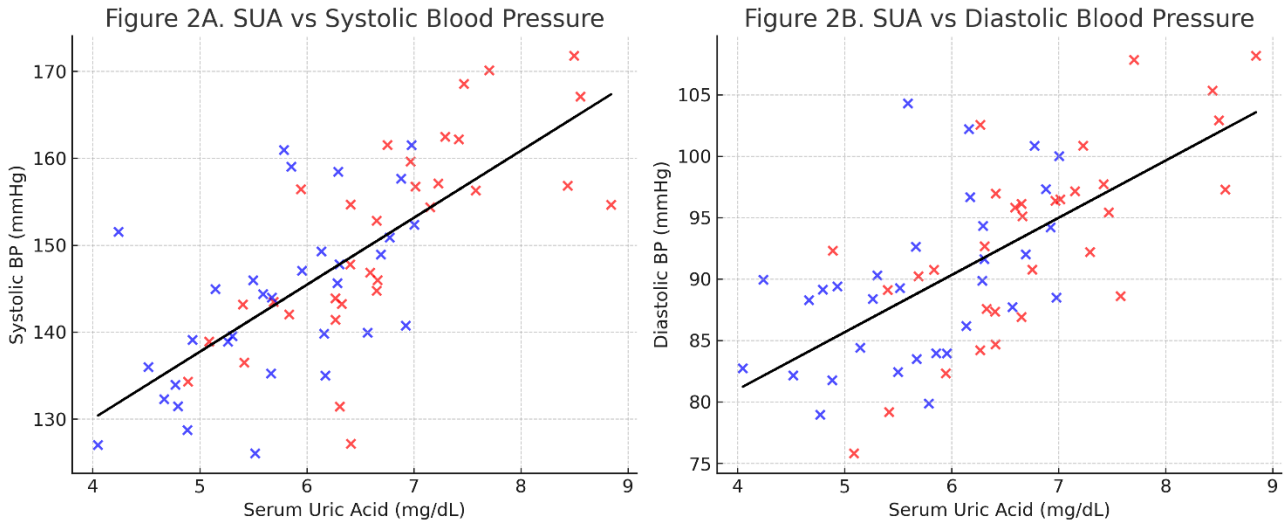




**FIGURE 2. SCATTER PLOTS OF SERUM URIC ACID VERSUS SYSTOLIC (A) AND DIASTOLIC (B) BLOOD PRESSURE**

## DISCUSSION

In this hospital-based case–control study, hypertensive adults demonstrated higher SUA compared with age-matched normotensive controls, and SUA correlated positively with both SBP and DBP. These findings align with a substantial body of epidemiologic evidence linking SUA with prevalent and incident hypertension and extend such observations to our local patient population. Mechanistically, urate may contribute to blood pressure elevation via endothelial dysfunction, oxidative stress, reduced nitric oxide bioavailability, renal afferent arteriolopathy, and activation of the renin–angiotensin system [1,2]. Our exploratory adjustment for age, sex, BMI and creatinine suggested that SUA remained independently associated with hypertensive status, consistent with many observational reports [3,8,9].

Interventional and genetic evidence provide nuance. In adolescents with newly diagnosed essential hypertension, short-term urate-lowering therapy (e.g., allopurinol) reduced blood pressure, supporting a potential causal role in early hypertension [4,5]. In contrast, Mendelian randomization analyses in general adult populations often show weak or null effects of genetically elevated urate on blood pressure, implying confounding or that urate is a mediator in susceptible subgroups rather than a universal cause [6,7,10]. Contemporary reviews and guideline discussions therefore position SUA as a clinically relevant biomarker that may identify individuals with higher cardiometabolic risk, while acknowledging the need for randomized adult trials demonstrating blood-pressure benefit from urate-lowering therapy before routine treatment can be recommended solely for hypertension management [8,11,12].

There are several ways that our observations are clinically relevant. To begin with, the testing of SUA is cheap and rather common; the detection of hyperuricemia in hypertensive patients can cause an evaluation to include renal dysfunction concomitant with the disease, metabolic syndrome and lifestyle treatment (e.g., alcohol consumption, diuretics, high fructose diets) that increase urate and exacerbate the blood pressure [11,13]. Second, urate lowering therapy with specificity to the consultation of the specialists and taking into account the pros and cons (adverse skin reactions with allopurinol) can be considered reasonable in younger patients or when less advanced cases of hypertension and higher levels of SUA [5]. Third, the positive relationship between SUA and SBP/DBP evident here captures the high value of viable risk alteration, optimizing weight, and reducing dietary intake of sodium/fructose, and avoiding unnecessary diuretics by the availability of other options.

This study has limitations. Being a case-control, single center, and non-randomized study design, limited sample size, causal inference cannot be made and residual confounding might still exist. SUA can be affected by medication (e.g., thiazide diuretics), but since we have ruled away extreme values and attempted to adjust reactions through exploratory means, there are still unmeasured results. We have not measured purine/fructose dietary intake or xanthine oxidase activity and we do not have any longitudinal follow-ups to measure incident hypertension or cardiovascular outcome. Its strengths are standardized measurement of SUA by uricase-peroxidase (modified Triner TBHB) technique, prespecified analysis, and selection of controls.

Conclusively, our statistics indicate increased SUA in hypertensive adults compared with normotensive adults and that there is a positive relationship between SUA and blood pressure. Such results contribute to the body of literature regarding SUA as a clinically significant risk factor in hypertension and encourage larger, prospective, multiethnic cohort and pragmatic trials to determine whether urate lowering can benefit blood pressure and patients better

## CONCLUSION

Hypertensive adults at RLJH Hospital were observed in this case control study, and the levels of serum uric acid were found to be elevated among hypertensitive patients as compared to normotensive controls and that SUA had positive correlations with systolic and diastolic blood pressures. Although there is no cause and effect to be draw through this design, the findings support SUA to be a valuable supplement in cardiovascular risks problem evaluation in patients who have or are at risk of developing hypertension. The addition of measurement of SUA to routine assessment, emphasis on factors that can be modified to cause hyperuricemia, and placement of urate lowering therapy in a preferred subgroups with a wait for more evidence in adults, might be circumstances that could lead to improvement in the care of hypertension in the population. ..

## REFERENCES

Sakr, H. I., Khowailed, A. A., Al-Fakharany, R. S., Abdel-Fattah, D. S., & Taha, A. A. (2020). Serum uric acid level as a predictive biomarker of gestational hypertension severity; A prospective observational case-control study. Reviews on recent clinical trials, 15(3), 227-239.

Kumar, N., & Singh, A. K. (2019). Maternal serum uric acid and calcium as predictors of hypertensive disorder of pregnancy: a case control study. Taiwanese Journal of Obstetrics and Gynecology, 58(2), 244-250.

Perlstein, T. S., Gumieniak, O., Williams, G. H., Sparrow, D., Vokonas, P. S., Gaziano, M., ... & Litonjua, A. A. (2006). Uric acid and the development of hypertension: the normative aging study. Hypertension, 48(6), 1031-1036.

Khichar, S., Choudhary, S., Singh, V. B., Tater, P., Arvinda, R. V., & Ujjawal, V. (2017). Serum uric acid level as a determinant of the metabolic syndrome: a case control study. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 11(1), 19-23.

Ali, N., Mahmood, S., Islam, F., Rahman, S., Haque, T., Islam, S., ... & Khanum, F. A. (2019). Relationship between serum uric acid and hypertension: a cross-sectional study in Bangladeshi adults. Scientific reports, 9(1), 9061.

Leiba, A., Vinker, S., Dinour, D., Holtzman, E. J., & Shani, M. (2015). Uric acid levels within the normal range predict increased risk of hypertension: a cohort study. Journal of the American Society of Hypertension, 9(8), 600-609.

Sultana, R., Ahmed, S., Sultana, N., Karim, S. F., & Atia, F. (2013). Association of serum uric acid with preeclampsia: a case control study. Delta Medical College Journal, 1(2), 46-50.

Shrivastav, C., Sharma, S., Suhalka, M. L., & Kaur, M. (2016). Hyperuricaemia and essential hypertension: A case control study in Southern Rajasthan. Int J Res Med Sci, 4(1), 78-83.

Shankar, A., Klein, R., Klein, B. E. K., & Nieto, F. J. (2006). The association between serum uric acid level and long-term incidence of hypertension: population-based cohort study. Journal of human hypertension, 20(12), 937-945.

Cicero, A. F., Rosticci, M., Fogacci, F., Grandi, E., D'Addato, S., Borghi, C., &Brisighella Heart Study Group. (2017). High serum uric acid is associated to poorly controlled blood pressure and higher arterial stiffness in hypertensive subjects. European journal of internal medicine, 37, 38-42.

Maciejczyk, M., Taranta-Janusz, K., Wasilewska, A., Kossakowska, A., & Zalewska, A. (2020). A case-control study of salivary redox homeostasis in hypertensive children. Can salivary uric acid be a marker of hypertension?. Journal of clinical medicine, 9(3), 837.

Bulpitt, C. J. (1975). Serum uric acid in hypertensive patients. Heart, 37(12), 1210-1215.

Fatima, S., & Yadav, N. (2024). SERUM URIC ACID AS POTENTIAL PREDICTOR OF HYPERTENSION: A CASE-CONTROL STUDY. Biochemical & Cellular Archives, 24(1).