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Original Research Article

A Comparative Study of Heart Rate Variability and Serum Uric Acid between Normotensive and Hypertensive Individuals in Tertiary Care

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Abstract

Background: Hypertension constitutes a major global health burden, contributing substantially to cardiovascular, renal, and cerebrovascular morbidity and mortality. Two emerging pathophysiological contributors—autonomic nervous system dysfunction as quantified by Heart Rate Variability (HRV), and elevated serum uric acid, the terminal metabolite of purine catabolism—have been independently implicated in the onset and progression of hypertension, yet their concurrent assessment in a treatment-naive cohort remains underexplored.

Aims and Objectives: To compare HRV parameters and serum uric acid levels between newly diagnosed treatment-naive hypertensive patients and age- and BMI-matched normotensive controls.

Setting and Design: A cross-sectional observational study conducted in the Department of Physiology, P.D.U. Government Medical College and Civil Hospital, Rajkot, Gujarat, India.

Materials and Methods: Sixty age- and BMI-matched individuals aged 30–50 years were enrolled: 30 newly diagnosed untreated hypertensive patients and 30 normotensive volunteers. HRV was recorded using the Polar H9 heart rate sensor with the Elite HRV application. Serum uric acid was determined by Autoanalyzer. Statistical analysis was performed using SPSS v30.0.0. Intergroup comparisons were conducted using the unpaired Student's t-test.

Results: Hypertensives showed significantly elevated serum uric acid (5.84 ± 1.80 mg/dL vs. 4.34 ± 1.05 mg/dL; $p < 0.001$). Mean RR Interval, SDNN, and RMSSD were each significantly lower in the hypertensive group ($p < 0.001$). Frequency-domain analysis revealed significant reductions in LF ($p < 0.001$) and HF ($p = 0.036$); the LF/HF ratio did not differ significantly ($p = 0.122$).

Conclusion: Hypertensive individuals exhibit markedly reduced HRV and elevated serum uric acid, collectively reflecting impaired autonomic regulation and augmented cardiovascular risk. Monitoring these non-invasive biomarkers may facilitate early cardiovascular risk stratification and targeted preventive intervention.

Keywords: Autonomic Nervous System, Heart Rate Variability, Hypertension, Serum Uric Acid.

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Introduction

Hypertension is a multifactorial, chronic non-communicable disease and one of the most significant modifiable risk factors for cardiovascular disease globally. According to the NCD Risk Factor Collaboration, the global age-standardised prevalence of hypertension remains alarmingly high, contributing disproportionately to stroke, coronary artery disease, chronic kidney disease, heart failure, and premature mortality.[1-3]

Clinically, according to the 2018 European Society of Cardiology/European Society of Hypertension (ESC/ESH) guidelines,[4] blood pressure is categorized as optimal (<120/80 mm Hg), normal (120–129/80–84 mm Hg), and high normal (130–139/85–89 mm Hg). Hypertension is graded as Grade 1 (140–159/90–99 mm Hg), Grade 2 (160–179/100–109 mm Hg), and Grade 3 (≥180/≥110 mm Hg). Approximately 90% of cases represent

primary (essential) hypertension, which is idiopathic in nature. Among the central contributors to hypertension, dysregulation of the Autonomic Nervous System (ANS) has emerged as a critical determinant. The ANS governs heart rate, cardiac output, vascular tone, and haemodynamic homeostasis through the integrated and reciprocal actions of its sympathetic and parasympathetic divisions.[5]

Sympathetic overactivity leads to peripheral vasoconstriction, increased cardiac output, and activation of the renin-angiotensin-aldosterone system, elevating systemic blood pressure. Conversely, diminished parasympathetic activity impairs cardiovascular recovery, rendering the system vulnerable to adverse events. ANS dysfunction is thus strongly implicated not only in the pathogenesis of hypertension but also in the development of coronary artery disease, cardiac arrhythmias, and sudden cardiac death.[6]

Heart Rate Variability (HRV) is a well-validated, non-invasive method of assessing autonomic function by quantifying temporal oscillations between consecutive R-R intervals.[7] Time-domain indices—Mean RR Interval, SDNN (Standard Deviation of NN Intervals), and RMSSD (Root Mean Square of Successive Differences)—capture overall autonomic magnitude and vagal modulation. Frequency-domain indices—Low Frequency and High Frequency power—reflect autonomic modulation. HF power primarily represents parasympathetic (vagal) activity, whereas LF power reflects combined sympathetic and parasympathetic influences, including baroreflex-mediated modulation. High HRV is associated with robust parasympathetic dominance and cardiovascular fitness, while low HRV is an independent predictor of adverse outcomes and all-cause mortality.[8]

Serum uric acid—the terminal catabolic product of purine metabolism via xanthine oxidase—has gained attention as a clinically relevant metabolic biomarker.[9] Hyperuricemia is associated with elevated risk of cardiovascular events, peripheral arterial disease, chronic kidney disease, and metabolic syndrome.[10] Mechanistically, elevated uric acid promotes endothelial dysfunction by inhibiting nitric oxide bioavailability, generating reactive oxygen species through xanthine oxidase, activating the renin-angiotensin system, and triggering inflammatory cascades, collectively elevating vascular resistance and blood pressure. Hyperuricemia has been increasingly recognised as an independent risk factor for the de novo development of hypertension.[11,12]

While both autonomic dysregulation and hyperuricemia are established independent cardiovascular risk factors, their simultaneous evaluation and comparison with blood pressure in a treatment-naive hypertensive cohort remains insufficiently studied.[13] The present study was designed to compare HRV parameters and serum uric acid levels in newly diagnosed hypertensive patients and matched normotensive controls at a tertiary care institution.

Materials and Methods

The present investigation was designed as a cross-sectional observational study, conducted in the Department of Physiology at P.D.U. Government Medical College and Civil Hospital, Rajkot, Gujarat, India. The study protocol received formal approval from the Institutional Ethical Committee, and written informed consent was obtained from all participants in accordance with the Declaration of Helsinki principles. A total of 60 individuals aged 30–50 years were enrolled following a systematic age- and BMI-matched approach. The population was divided into two equal groups: Group I comprised 30 newly diagnosed, treatment-naive hypertensive patients recruited from the General Medicine Outpatient Department; Group II comprised 30 normotensive healthy volunteers from the hospital campus.

Figure 1:

A. Inclusion Criteria

Both male and female participants aged 30–50 years were eligible. Hypertensive subjects were required to have a Systolic Blood Pressure (SBP) exceeding 140 mm Hg and/or Diastolic Blood Pressure (DBP) exceeding 90 mm Hg on at least two separate visits, newly diagnosed with no prior antihypertensive pharmacotherapy.

Normotensive controls were required to have SBP below 130 mm Hg and DBP below 85 mm Hg. All

participants were required to be capable of providing voluntary written informed consent.

B. Exclusion Criteria

Individuals outside the age range of 30–50 years and known hypertensives already on antihypertensive medications were excluded. To eliminate confounders that could independently influence HRV or serum uric acid, individuals with a history of the following were excluded: chronic renal dysfunction, gout or treated hyperuricaemia, diabetes mellitus, established cardiac diseases (myocardial infarction, coronary artery disease, and angina pectoris), connective tissue disorders, malignancies, psoriasis, and thyroid dysfunction. Those with chronic alcohol use, or on pharmacological agents known to alter serum uric acid (allopurinol, probenecid, high-dose salicylates) or autonomic function (sympathomimetic, sympatholytic, cholinergic, or anticholinergic agents), were also excluded.

C. Procedure and Data Collection

Blood pressure was measured using a standardised mercury sphygmomanometer in the sitting position after five minutes of rest; the mean of two readings taken two minutes apart was recorded. All enrolled participants underwent both HRV recording and serum uric acid estimation.

HRV was recorded over five minutes in the resting, supine position using the Polar H9 chest-strap heart rate sensor paired via Bluetooth with the Elite HRV mobile application, which computed both time-domain and frequency-domain parameters in real time.[14] The Polar H9 is an ECG-based chest-strap sensor utilising R-wave detection technology comparable to previously validated Polar models such as the H7.[15] Participants remained still and breathed naturally throughout recording. Venous blood samples were collected under aseptic precautions following an overnight fast; serum uric acid was quantitatively determined by the uricase-peroxidase enzymatic colorimetric method on a fully automated biochemistry Autoanalyzer.

D. Statistical Analysis

Data were analysed using IBM SPSS Statistics v30.0.0. Continuous variables were expressed as Mean ± Standard Deviation. Normality was assessed using the Shapiro-Wilk test. The unpaired Student's t-test was used for intergroup comparison of continuous variables. Categorical variables such as sex distribution were analysed using the Chi-square test. A two-tailed p-value < 0.05 was considered statistically significant.

Results

Sixty participants were enrolled (30 per group). Mean age was 36.10 ± 5.35 years in normotensives versus 37.70 ± 4.71 years in hypertensives ($p = 0.22$). Mean BMI was 24.34 ± 2.47 vs. 24.95 ± 3.84 kg/m² ($p = 0.46$), confirming comparability. Sex distribution was comparable between normotensive (17 males, 13 females) and hypertensive groups (18 males, 12 females) (Chi-square test, $p = 0.79$). SBP was significantly higher in hypertensives (148.06 ± 8.79 mm Hg vs. 116.5 ± 9.2 mm Hg; $p < 0.001$), as was DBP (86.4 ± 4.22 vs. 74.8 ± 6.44 mm Hg; $p < 0.001$). Full anthropometric and clinical data are summarised in Table 1.

Table 1: Anthropometric and Clinical Measurements.

Parameter	Normotensives (N=30) Mean ± SD	Hypertensives (N=30) Mean ± SD	P-value
Age (years)	36.10 ± 5.35	37.70 ± 4.71	0.22
Height (cm)	164.17 ± 7.09	165.20 ± 5.44	0.53
Weight (kg)	65.90 ± 10.04	67.97 ± 10.18	0.43
BMI (kg/m²)	24.34 ± 2.47	24.95 ± 3.84	0.46
Systolic BP (mm Hg)	116.5 ± 9.2	148.06 ± 8.79	< 0.001
Diastolic BP (mm Hg)	74.8 ± 6.44	86.4 ± 4.22	< 0.001

Biochemical evaluation demonstrated significantly elevated mean serum uric acid in hypertensives (5.84 ± 1.80 mg/dL) compared to normotensives (4.34 ± 1.05 mg/dL; $p < 0.001$), as shown in Table 2.

Table 2: Serum Uric Acid in Normotensives and Hypertensives.

Parameter	Normotensive Mean ± SD	Hypertensive Mean ± SD	P-value
Serum Uric Acid (mg/dL)	4.34 ± 1.05	5.84 ± 1.80	< 0.001

Time-domain HRV analysis revealed significant differences.

The Mean RR Interval was shorter in hypertensives (789.51 ± 64.05 ms vs. 870.46 ± 64.9 ms; $p < 0.001$). SDNN was reduced (31.65 ± 14.16 ms vs. 51.97 ± 12.64 ms; $p < 0.001$). RMSSD—the primary indicator of cardiac vagal tone—was significantly lower in hypertensives (25.92 ± 11.10 ms vs. 42.6 ± 14.88 ms; $p < 0.001$).

These findings are presented in Table 3.

Table 3: Time Domain HRV Parameters.

Parameter	Normotensive Mean ± SD	Hypertensive Mean ± SD	P-value
Mean RR Interval (ms)	870.46 ± 64.9	789.51 ± 64.05	< 0.001
SDNN (ms)	51.97 ± 12.64	31.65 ± 14.16	< 0.001
RMSSD (ms)	42.6 ± 14.88	25.92 ± 11.10	< 0.001

Frequency-domain analysis corroborated these findings.

LF power was significantly reduced in hypertensives (324.46 ± 138.50 ms² vs. 488.04 ± 181.96 ms²; $p < 0.001$). HF power was also lower (224.94 ± 93.37 ms² vs. 298.86 ± 163.4 ms²; $p = 0.036$). The LF/HF ratio did not differ significantly between normotensives (1.89 ± 0.94) and hypertensives (1.55 ± 0.75; $p = 0.122$).

Data are summarised in Table 4.

Table 4: Frequency Domain HRV Parameters.

Parameter	Normotensive Mean ± SD	Hypertensive Mean ± SD	P-value
Low Frequency (LF) (ms²)	488.04 ± 181.96	324.46 ± 138.50	< 0.001
High Frequency (HF) (ms²)	298.86 ± 163.4	224.94 ± 93.37	0.036
LF/HF Ratio	1.89 ± 0.94	1.55 ± 0.75	0.122

Discussion

The present study demonstrates that newly diagnosed, treatment-naive hypertensive individuals exhibit significantly elevated serum uric acid levels and markedly reduced Heart Rate Variability (HRV) parameters compared to age- and BMI-matched normotensive controls. These findings indicate that both metabolic dysregulation and autonomic imbalance are present even at the earliest stage of essential hypertension.

The significantly higher serum uric acid observed in hypertensives, although within the conventional physiological range, supports growing evidence that even relatively elevated uric acid levels may contribute to the pathogenesis of hypertension. Elevated uric acid contributes to endothelial dysfunction by reducing nitric oxide bioavailability and promoting oxidative stress through xanthine oxidase activity.[9] This process enhances vascular smooth muscle proliferation, stimulates inflammatory signaling pathways, and activates the renin-angiotensin-aldosterone system, ultimately increasing peripheral vascular resistance and sustaining blood pressure elevation. Thus, uric acid may function not merely as a marker, but as a mediator of early vascular changes in hypertension.[11,12]

Time-domain HRV analysis revealed a significantly shorter Mean RR interval and reduced SDNN and RMSSD in hypertensives, reflecting diminished overall autonomic modulation and parasympathetic withdrawal. Reduced SDNN suggests impaired total heart rate variability and has been associated with increased cardiovascular morbidity.[7,8] The marked decline in RMSSD, a robust indicator of vagal tone, indicates reduced cardioprotective parasympathetic influence and relative sympathetic predominance, contributing to impaired baroreflex buffering and cardiovascular instability.[6]

Frequency-domain analysis further confirmed autonomic imbalance. Both LF and HF power were significantly reduced in hypertensives, indicating globally attenuated autonomic modulation with diminished baroreflex-mediated variability and reduced parasympathetic activity.[7] The LF/HF ratio did not differ significantly and was numerically lower in hypertensives. Although earlier interpretations associated sympathetic predominance with an increased LF/HF ratio, contemporary evidence suggests that the LF/HF ratio may not reliably quantify sympathovagal balance, particularly when total spectral power is reduced. When overall spectral power is reduced, the LF/HF ratio may lose discriminatory value, and absolute spectral components may better reflect autonomic impairment.[7,8]

The interaction between hyperuricemia and autonomic dysfunction may represent a self-reinforcing pathophysiological mechanism.[13] Oxidative stress induced by elevated uric acid can impair central and peripheral autonomic regulation, while sympathetic overactivity may reduce renal uric acid excretion, promoting further hyperuricemia. This potential bidirectional interaction may contribute to the progression and maintenance of essential hypertension.

Certain limitations should be acknowledged. The relatively small sample size may limit generalizability. The cross-sectional design precludes causal inference, and single-time HRV recordings may not fully reflect circadian autonomic variations. The study design focused on intergroup comparison and did not evaluate individual-level correlations between blood pressure values and autonomic indices. Larger longitudinal studies are warranted to clarify

temporal relationships between serum uric acid, autonomic dysfunction, and blood pressure elevation.

Conclusion

This study demonstrates that newly diagnosed, treatment-naive hypertensive individuals exhibit significantly reduced Heart Rate Variability—encompassing time-domain indices (Mean RR Interval, SDNN, RMSSD) and frequency-domain measures (LF and HF power)—alongside markedly elevated serum uric acid, compared to age- and BMI-matched normotensive controls.

These findings suggest that impaired cardiac autonomic regulation and heightened metabolic oxidative burden are present even at the earliest, untreated stage of essential hypertension. Both HRV assessment and serum uric acid quantification are non-invasive, cost-effective, and clinically feasible measurements that can be incorporated into routine cardiovascular risk assessment protocols.

Their integration may enhance early identification of high-risk hypertensive patients, facilitate more targeted preventive strategies, and contribute to reduction of hypertension-associated cardiovascular morbidity and mortality.

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