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Original Research Article

Correlation of Serum Uric Acid with Vascular Reactivity and Blood Pressure in Young Adults: A Cross-Sectional Study

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Abstract

Background: Serum uric acid (SUA) has emerged as a potential biomarker associated with endothelial dysfunction, impaired vascular reactivity, and elevated blood pressure even in otherwise healthy young adults. Experimental and epidemiological evidence suggests that uric acid may contribute to oxidative stress, reduced nitric oxide bioavailability, vascular smooth muscle proliferation, and activation of the renin-angiotensin system, thereby influencing vascular tone and blood pressure regulation. The relationship between SUA and early vascular changes in young adults remains clinically important because endothelial dysfunction often precedes overt hypertension and cardiovascular disease.

Objective: To evaluate the correlation of serum uric acid with vascular reactivity and blood pressure among apparently healthy young adults aged 18–30 years.

Materials and Methods: This cross-sectional observational study included 180 young adults (90 males and 90 females) aged 18–30 years. Serum uric acid was measured by the uricase-peroxidase method. Blood pressure was recorded according to standardized guidelines. Vascular reactivity was assessed using brachial artery flow-mediated dilation (FMD) measured by high-resolution ultrasonography after forearm occlusion. Correlations between SUA, FMD, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were analyzed using Pearson correlation and multivariable linear regression.

Results: The mean age of participants was 22.4 ± 3.1 years. Mean SUA was 5.2 ± 1.1 mg/dL, mean SBP was 118.6 ± 9.8 mmHg, mean DBP was 74.2 ± 7.1 mmHg, and mean FMD was 9.8 ± 2.4%. Serum uric acid showed a significant negative correlation with FMD ($r = -0.42$, $p < 0.001$) and positive correlations with SBP ($r = 0.36$, $p < 0.001$) and DBP ($r = 0.31$, $p < 0.001$). After adjustment for age, sex, body mass index, fasting glucose, and lipid profile, SUA remained an independent predictor of impaired vascular reactivity ($\beta = -0.34$, $p < 0.001$) and higher systolic blood pressure ($\beta = 0.27$, $p = 0.002$).

Conclusion: Higher serum uric acid levels were associated with reduced vascular reactivity and increased blood pressure in young adults. These findings support the hypothesis that elevated uric acid may serve as an early marker of endothelial dysfunction and subclinical cardiovascular risk in apparently healthy young individuals.

Keywords: Serum Uric Acid, Vascular Reactivity, Flow-Mediated Dilation, Endothelial Dysfunction, Blood Pressure, Hypertension, Young Adults.

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Introduction

Cardiovascular disease remains the leading cause of mortality worldwide, and increasing evidence suggests that the pathophysiological processes leading to hypertension and atherosclerosis begin early in life. Endothelial dysfunction, characterized by impaired endothelium-dependent vasodilation, is considered one of the earliest detectable abnormalities in the development of cardiovascular disease. Assessment of vascular reactivity provides a non-invasive means of evaluating endothelial function and identifying individuals at increased cardiovascular risk before structural vascular changes become clinically apparent. Serum uric acid, the final product of purine metabolism in humans, has traditionally been regarded as a marker of gout and renal dysfunction. In recent decades, however, uric acid has attracted considerable attention as a possible mediator of hypertension, endothelial dysfunction, metabolic syndrome, and cardiovascular disease. Experimental studies have demonstrated that uric acid can induce oxidative stress, reduce nitric oxide

synthesis, stimulate inflammatory pathways, and promote vascular smooth muscle cell proliferation. These mechanisms may impair endothelial function and alter vascular responsiveness, thereby contributing to elevated blood pressure.

The relationship between serum uric acid and hypertension is particularly relevant in young adults. Unlike older individuals, in whom hypertension is often influenced by multiple comorbidities and long-standing vascular disease, young adults provide an opportunity to examine early vascular alterations with relatively fewer confounding factors. Several epidemiological studies have reported that elevated uric acid predicts the development of hypertension in adolescents and young adults. Hyperuricemia has been associated with increased arterial stiffness, reduced endothelial-dependent vasodilation, and heightened sympathetic activity, suggesting a direct role in blood pressure regulation.

Vascular reactivity can be assessed by several physiological methods, among which brachial artery flow-mediated dilation (FMD) is one of the most widely accepted non-invasive techniques. FMD reflects nitric oxide-mediated endothelial function and correlates with future cardiovascular events. A reduction in FMD indicates impaired endothelial responsiveness and may precede clinically detectable hypertension. Investigating the association between serum uric acid and FMD in young adults may therefore provide insights into the early mechanisms linking metabolic and vascular dysfunction.

In addition to endothelial dysfunction, uric acid may influence blood pressure through activation of the renin-angiotensin-aldosterone system, renal microvascular disease, increased sodium reabsorption, and reduced nitric oxide availability within the renal circulation. These effects can increase systemic vascular resistance and contribute to both systolic and diastolic blood pressure elevation. Importantly, intervention studies have shown that uric acid-lowering therapy can reduce blood pressure in hyperuricemic adolescents, supporting a potential causal relationship in the early stages of hypertension.

Despite growing evidence, data regarding the correlation of serum uric acid with vascular reactivity and blood pressure in apparently healthy young adults remain limited, particularly in the Indian population. Understanding this relationship may help identify young individuals at increased cardiovascular risk and may support the use of serum uric acid as a simple and inexpensive biomarker for early vascular dysfunction.

Aim of the Study: To determine the correlation of serum uric acid with vascular reactivity and blood pressure among apparently healthy young adults aged 18–30 years.

Objectives

1. To estimate serum uric acid levels in apparently healthy young adults.
2. To assess vascular reactivity using brachial artery flow-mediated dilation.
3. To measure systolic and diastolic blood pressure using standardized techniques.
4. To evaluate the correlation between serum uric acid and vascular reactivity.
5. To evaluate the correlation between serum uric acid and systolic and diastolic blood pressure.
6. To determine whether serum uric acid independently predicts impaired vascular reactivity and elevated blood pressure after adjustment for potential confounding variables.

Research Hypothesis: Higher serum uric acid levels are associated with impaired vascular reactivity and higher blood pressure in apparently healthy young adults.

Materials and Methods

Study Design and Setting: This cross-sectional observational study conducted in the Department of Physiology in collaboration with the Department of Biochemistry of a tertiary care teaching hospital. The study period was assumed to extend over 12 months.

Study Population: Apparently healthy young adults aged 18–30 years were recruited from undergraduate and postgraduate students, interns, hospital staff, and volunteers from the local community through convenience sampling.

Sample Size: The sample size was estimated using the formula for correlation studies:

$n = (Z\alpha + Z\beta)^2 / C^2 + 3$

Where:

- $Z\alpha = 1.96$ for a 95% confidence level,
- $Z\beta = 0.84$ for 80% power,
- $C = 0.5 \times \ln[(1+r)/(1-r)]$,
- Anticipated correlation coefficient (r) between serum uric acid and vascular reactivity = 0.25 based on previous literature.

The calculated minimum sample size was approximately 152 participants. Assuming a 15% non-response or incomplete data rate, a final sample size of 180 participants was considered adequate.

Study Sample: A total of 180 participants were included:

- 90 males
- 90 females

Inclusion Criteria

1. Age between 18 and 30 years
2. Apparently healthy individuals without known chronic illness
3. Body mass index (BMI) between 18.5 and 29.9 kg/m²
4. Willingness to participate and provide written informed consent

Exclusion Criteria

1. Known hypertension, diabetes mellitus, cardiovascular disease, chronic kidney disease, liver disease, thyroid disorders, or gout
2. Current use of antihypertensive drugs, uric acid-lowering therapy, diuretics, corticosteroids, or medications affecting vascular function
3. Smoking or tobacco use in any form
4. Alcohol dependence
5. Pregnancy or lactation
6. Acute febrile illness within the preceding two weeks
7. Participation in vigorous exercise within 24 hours before vascular assessment

Ethical Considerations: The study protocol was approved by the Institutional Ethics Committee of the participating institution. Written informed consent was obtained from all participants prior to enrollment.

Confidentiality of participant information was maintained throughout the study in accordance with the principles of the Declaration of Helsinki (2013 revision).

Study Procedure: Participants were instructed to report to the physiology laboratory between 8:00 AM and 10:00 AM after an overnight fast of 10–12 hours.

They were advised to avoid caffeine-containing beverages, alcohol, antioxidant supplements, and strenuous physical activity for 24 hours prior to the examination.

The following sequence was followed:

1. Recording of demographic details
2. Anthropometric measurements
3. Blood pressure measurement
4. Venous blood sampling
5. Assessment of vascular reactivity by flow-mediated dilation

Demographic and Anthropometric Measurements

- Age and sex were recorded for all participants.
- Height was measured using a wall-mounted stadiometer to the nearest 0.1 cm.
- Weight was measured using a calibrated digital weighing scale to the nearest 0.1 kg.
- Body mass index was calculated as:
- BMI (kg/m²) = Weight (kg) / Height (m²)
- Waist circumference was measured midway between the lower costal margin and the iliac crest at the end of normal expiration.

Blood Pressure Measurement: Blood pressure was measured using a calibrated automated sphygmomanometer following American Heart Association recommendations. [1] Participants rested quietly in the sitting position for 10 minutes before measurement.

Measurements were obtained:

- In the right arm,
- With appropriate cuff size,
- Arm supported at heart level,
- Feet flat on the floor,
- Back supported,
- Without talking during measurement.

Three readings were recorded at 2-minute intervals.The average of the final two readings was considered for analysis.

The following parameters were recorded:

- Systolic blood pressure (SBP) in mmHg
- Diastolic blood pressure (DBP) in mmHg

Collection of Blood Samples: Approximately 5 mL of venous blood was collected from the antecubital vein under aseptic precautions. The sample was allowed to clot and centrifuged at 3000 rpm for 15 minutes to obtain serum. Serum samples were analyzed immediately or stored at −20°C until biochemical analysis.

Estimation of Serum Uric Acid: Serum uric acid was estimated by the enzymatic uricase-peroxidase (PAP) method using an automated clinical chemistry analyzer.

Principle: Uric acid is oxidized by uricase to allantoin and hydrogen peroxide. In the presence of peroxidase, hydrogen peroxide reacts with chromogenic substrates to produce a colored compound. The intensity of the color formed is directly proportional to the serum uric acid concentration. Results were expressed in mg/dL.Quality control sera were run daily to ensure analytical accuracy.

Assessment of Vascular Reactivity: Vascular reactivity was assessed by brachial artery flow-mediated dilation (FMD) using high-resolution B-mode ultrasonography with a 7–12 MHz linear array transducer.

Preparation: Participants rested in the supine position for 15 minutes in a temperature-controlled room (22–24°C). The right brachial artery was imaged longitudinally approximately 5–10 cm above the antecubital fossa.

Baseline Diameter: Baseline arterial diameter was recorded during end-diastole using electrocardiographic gating.

Occlusion Protocol: A blood pressure cuff placed around the forearm was inflated to 50 mmHg above systolic blood pressure (minimum 200 mmHg) for 5 minutesto induce ischemia.

Post-Occlusion Measurement: The cuff was rapidly deflated. The maximum brachial artery diameter occurring 45–90 seconds after cuff release was measured.

Calculation of Flow-Mediated Dilation: FMD (%) = [(Post-occlusion diameter − Baseline diameter) / Baseline diameter] × 100

A lower FMD value was considered indicative of impaired endothelial-dependent vascular reactivity.

Laboratory Variables: The primary variables analyzed were:

- Serum uric acid (mg/dL)
- Flow-mediated dilation (%)
- Systolic blood pressure (mmHg)
- Diastolic blood pressure (mmHg)

Additional variables included:

- Age (years)
- Sex
- BMI (kg/m²)
- Waist circumference (cm)
- Fasting blood glucose (mg/dL)
- Total cholesterol (mg/dL)
- HDL cholesterol (mg/dL)
- LDL cholesterol (mg/dL)
- Triglycerides (mg/dL)

Outcome Measures

Primary Outcome: Correlation between serum uric acid and vascular reactivity (FMD%).

Secondary Outcomes

1. Correlation between serum uric acid and systolic blood pressure.
2. Correlation between serum uric acid and diastolic blood pressure.
3. Independent association of serum uric acid with FMD and blood pressure after adjustment for confounding variables.

Statistical Analysis

- Data were analyzed using IBM SPSS Statistics version 26.0.
- Continuous variables were expressed as mean ± standard deviation (SD).
- Categorical variables were expressed as frequency and percentage.
- Normality of distribution was assessed using the Shapiro-Wilk test.

Comparisons between male and female participants were performed using:

- Independent Student's t-test for normally distributed variables
- Mann-Whitney U test for non-normally distributed variables

Correlation analysis was performed using:

- Pearson correlation coefficient (r) for normally distributed variables
- Spearman rank correlation where appropriate

To identify independent predictors of vascular reactivity and blood pressure, multiple linear regression analysis was performed with adjustment for:

- Age,
- Sex,
- BMI,
- Fasting glucose,
- Total cholesterol,
- HDL cholesterol,
- LDL cholesterol,
- Triglycerides.

A p-value < 0.05 was considered statistically significant.

Data Management: All data were entered into a structured Microsoft Excel spreadsheet and cross-verified for accuracy prior to statistical analysis.

Missing values and outliers were checked before analysis, and only complete datasets were included in the final evaluation.

Observations and Results

A total of 180 apparently healthy young adults aged 18–30 years were included in the study. The study population comprised 90 males (50.0%) and 90 females (50.0%).

All participants completed the study protocol, including anthropometric assessment, blood pressure measurement, serum uric acid estimation, and vascular reactivity assessment by brachial artery flow-mediated dilation (FMD).

Demographic and Anthropometric Characteristics: The mean age of the study population was 22.4 ± 3.1 years. Males had significantly higher body weight, body mass index, waist circumference, and serum uric acid levels than females, whereas females demonstrated slightly higher mean FMD values.

Table 1: Demographic and anthropometric characteristics of study participants (n = 180)

Variable	Males (n = 90)	Females (n = 90)	Total (n = 180)	p-value
Age (years)	22.6 ± 3.2	22.2 ± 3.0	22.4 ± 3.1	0.412
Height (cm)	171.2 ± 6.4	158.7 ± 5.8	164.9 ± 8.5	<0.001
Weight (kg)	68.4 ± 9.1	57.3 ± 8.2	62.8 ± 10.2	<0.001
BMI (kg/m²)	23.3 ± 2.8	22.7 ± 2.9	23.0 ± 2.9	0.128
Waist circumference (cm)	84.1 ± 7.2	76.8 ± 6.9	80.5 ± 7.8	<0.001
Serum uric acid (mg/dL)	5.8 ± 1.0	4.6 ± 0.8	5.2 ± 1.1	<0.001
FMD (%)	9.3 ± 2.3	10.3 ± 2.4	9.8 ± 2.4	0.006

Blood Pressure Profile: The mean systolic blood pressure (SBP) of the study population was 118.6 ± 9.8 mmHg, and the mean diastolic blood pressure (DBP) was 74.2 ± 7.1 mmHg. Males had significantly higher SBP and DBP than females.

Table 2. Blood pressure characteristics of study participants

Parameter	Males (n = 90)	Females (n = 90)	Total (n = 180)	p-value
Systolic BP (mmHg)	121.8 ± 9.4	115.4 ± 9.2	118.6 ± 9.8	<0.001
Diastolic BP (mmHg)	76.1 ± 6.8	72.3 ± 6.9	74.2 ± 7.1	0.001
Mean arterial pressure (mmHg)	91.3 ± 6.7	86.7 ± 6.4	89.0 ± 6.9	<0.001

Distribution of Serum Uric Acid: Participants were categorized according to serum uric acid concentration.

Table 3. Distribution of serum uric acid levels

Serum uric acid (mg/dL)	Number (n)	Percentage (%)
<4.0	28	15.6
4.0–4.9	52	28.9
5.0–5.9	56	31.1
6.0–6.9	30	16.7
≥7.0	14	7.8
Total	**180**	**100.0**

The majority of participants (31.1%) had serum uric acid levels between 5.0 and 5.9 mg/dL.

Vascular Reactivity According to Serum Uric Acid Categories: Mean FMD progressively decreased with increasing serum uric acid concentration.

Table 4. Flow-mediated dilation across serum uric acid categories

Serum uric acid (mg/dL)	Participants (n)	Mean FMD (%)	SD
<4.0	28	11.6	2.0
4.0–4.9	52	10.5	2.1
5.0–5.9	56	9.6	2.2
6.0–6.9	30	8.5	2.0
≥7.0	14	7.3	1.8

One-way ANOVA demonstrated a significant reduction in FMD with increasing serum uric acid levels ($F = 14.82$, $p < 0.001$).

Correlation between Serum Uric Acid and Vascular Reactivity: Pearson correlation analysis revealed a significant negative correlation between serum uric acid and FMD.

Table 5. Correlation between serum uric acid and vascular reactivity

Variable	Correlation coefficient (r)	p-value
Serum uric acid vs FMD	−0.42	<0.001

The scatter plot demonstrated a downward linear trend, indicating that higher serum uric acid concentrations were associated with lower endothelial-dependent vasodilation.

Correlation between Serum Uric Acid and Blood Pressure: Serum uric acid showed significant positive correlations with both systolic and diastolic blood pressure.

Table 6: Correlation between serum uric acid and blood pressure

Variable	Correlation coefficient (r)	p-value
Serum uric acid vs SBP	0.36	<0.001
Serum uric acid vs DBP	0.31	<0.001

The correlation was stronger for systolic blood pressure than for diastolic blood pressure.

Correlation Matrix of Major Study Variables

Table 7: Pearson Correlation Matrix

Variable	SUA	FMD	SBP	DBP	BMI
Serum uric acid (SUA)	1.00	−0.42	0.36	0.31	0.28
Flow-mediated dilation (FMD)	−0.42	1.00	−0.33	−0.27	−0.21
Systolic BP (SBP)	0.36	−0.33	1.00	0.74	0.32
Diastolic BP (DBP)	0.31	−0.27	0.74	1.00	0.29
BMI	0.28	−0.21	0.32	0.29	1.00

All displayed correlations were statistically significant at $p < 0.01$.

Multiple Linear Regression Analysis: A multiple linear regression model was constructed with flow-mediated dilation as the dependent variable.

Table 8: Multiple linear regression analysis for predictors of FMD

Predictor	Standardized β	Standard Error	t-value	p-value
Serum uric acid	**−0.34**	0.09	−4.62	**<0.001**
Age	−0.08	0.04	−1.12	0.264
Male sex	−0.12	0.36	−1.68	0.095
BMI	−0.17	0.05	−2.39	0.018
Fasting glucose	−0.09	0.03	−1.27	0.206
LDL cholesterol	−0.11	0.02	−1.54	0.126

Model statistics: $R^2 = 0.29$, Adjusted $R^2 = 0.27$, $F = 11.74$, $p < 0.001$

Serum uric acid remained the strongest independent predictor of impaired vascular reactivity after adjustment for potential confounding variables.

Multiple Linear Regression Analysis for Systolic Blood Pressure

Table 9: Independent predictors of systolic blood pressure

Predictor	Standardized β	Standard Error	t-value	p-value
Serum uric acid	**0.27**	0.88	3.18	**0.002**
Age	0.14	0.39	1.86	0.064
Male sex	0.19	1.74	2.31	0.022
BMI	0.21	0.25	2.56	0.011
Fasting glucose	0.07	0.16	0.94	0.349
LDL cholesterol	0.10	0.09	1.29	0.198

Model statistics:

- $R^2 = 0.24$
- Adjusted $R^2 = 0.22$
- $F = 9.08$
- $p < 0.001$

Higher serum uric acid was independently associated with higher systolic blood pressure.

Summary of Principal Findings: The present analysis showed that:

1. Serum uric acid levels were significantly higher in males than females.
2. Flow-mediated dilation progressively decreased with increasing serum uric acid concentration.
3. Serum uric acid showed a moderate negative correlation with vascular reactivity ($r = −0.42$).
4. Serum uric acid showed significant positive correlations with systolic ($r = 0.36$) and diastolic ($r = 0.31$) blood pressure.
5. After adjustment for demographic and metabolic variables, serum uric acid remained an independent predictor of impaired vascular reactivity and elevated systolic blood pressure.

These findings support a significant association between higher serum uric acid concentrations, reduced endothelial-dependent vascular reactivity, and increased blood pressure in young adults.

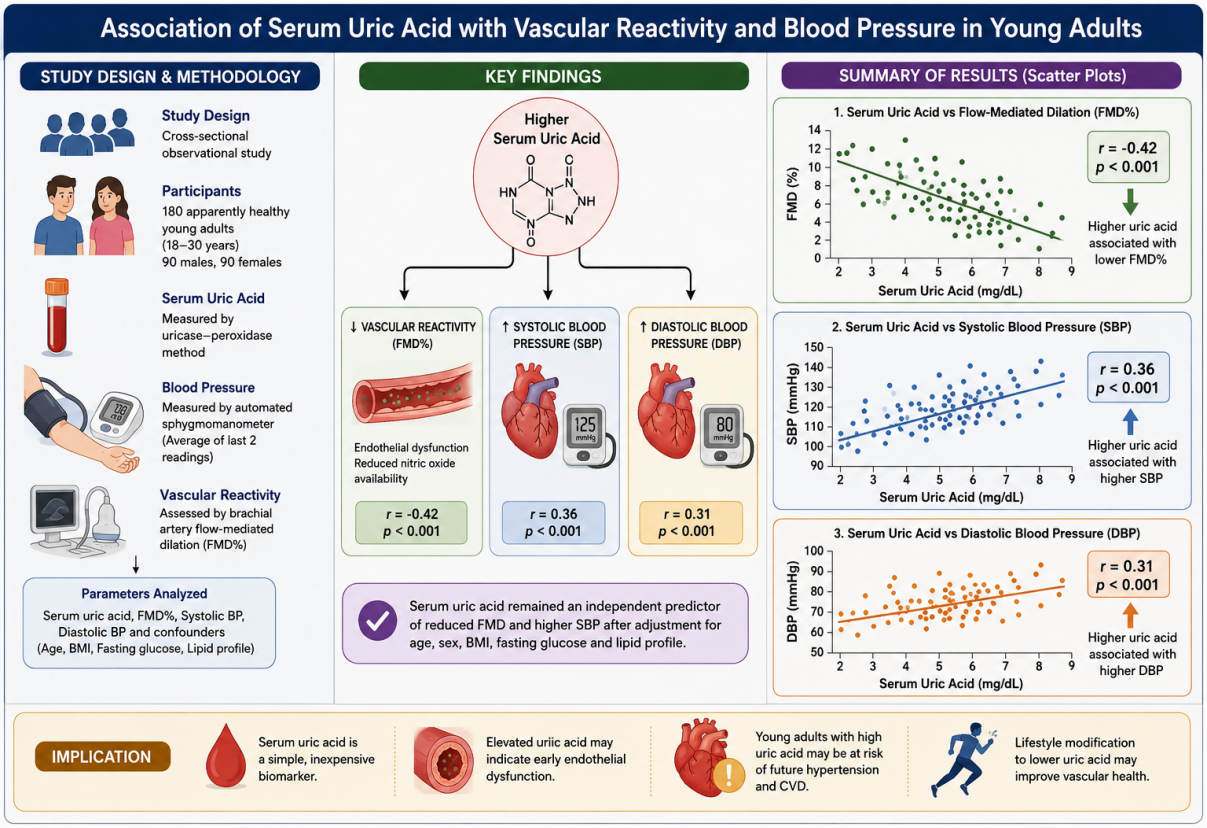

Figure 1: Association of serum uric acid with vascular reactivity and blood pressure in young adults

Discussion

The present cross-sectional study evaluated the relationship between serum uric acid (SUA), vascular reactivity assessed by brachial artery flow-mediated dilation (FMD), and blood pressure among apparently healthy young adults aged 18–30 years. [2] The principal findings were that higher serum uric acid levels were significantly associated with impaired vascular reactivity and elevated systolic and diastolic blood pressure, and that serum uric acid remained an independent predictor of endothelial dysfunction and higher systolic blood pressure after adjustment for age, sex, body mass index, fasting glucose, and lipid parameters. [3]

These findings are consistent with the growing body of evidence suggesting that uric acid is not merely a metabolic end product but also a potential mediator of vascular dysfunction and early cardiovascular risk. [3]

Serum Uric Acid in Young Adults: The mean serum uric acid concentration observed in the present study was 5.2 ± 1.1 mg/dL, with significantly higher values among males compared with females. [4] This sex difference is biologically plausible and has been consistently reported in previous studies. Estrogen enhances renal uric acid excretion through modulation of urate transporters, resulting in relatively lower uric acid concentrations in premenopausal women. [5] In contrast, higher muscle mass, increased purine turnover, and androgen-mediated renal urate handling contribute to higher serum uric acid levels in men.

The distribution of uric acid values in the present study indicated that a substantial proportion of apparently healthy young adults had serum uric acid concentrations in the upper-normal range, emphasizing that metabolic alterations associated with future cardiovascular risk may begin early in life even in the absence of clinically overt disease. [6]

Serum Uric Acid and Vascular Reactivity: The most important finding of this study was the significant negative correlation between serum uric acid and flow-mediated dilation ($r = -0.42$, $p < 0.001$). Participants with higher uric acid concentrations showed progressively lower FMD values, indicating impaired endothelial-dependent vasodilation. [7]

Flow-mediated dilation is a well-established non-invasive marker of endothelial function and primarily reflects nitric oxide (NO)-mediated vasodilatory capacity. [8] Reduced FMD has been associated with increased risk of future hypertension, coronary artery disease, stroke, and cardiovascular mortality. [9] The observed decline in FMD across increasing uric acid categories

suggests that elevated uric acid may contribute to early endothelial dysfunction even before the development of overt hypertension. [10]

Several biological mechanisms may explain this association. Intracellular uric acid stimulates nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, resulting in increased production of reactive oxygen species. [11] Oxidative stress decreases the bioavailability of nitric oxide through direct interaction with superoxide anions, leading to endothelial dysfunction and impaired vasodilation. [12] Uric acid has also been shown to induce endothelial inflammation, expression of C-reactive protein, monocyte chemoattractant protein-1, and vascular cell adhesion molecules, all of which contribute to endothelial injury and reduced vascular responsiveness. [13]

Experimental studies have demonstrated that uric acid enters endothelial cells through specific transporters and activates intracellular signaling pathways that reduce endothelial nitric oxide synthase activity. [14] This reduction in nitric oxide production impairs endothelium-dependent relaxation and promotes vascular stiffness. [15] Furthermore, uric acid stimulates proliferation of vascular smooth muscle cells, contributing to structural vascular remodeling and reduced arterial compliance.

The present findings closely parallel previous clinical investigations showing inverse relationships between serum uric acid and endothelial function measured by FMD, peripheral arterial tonometry, or forearm blood flow responses. [16] The moderate correlation coefficient observed in the present study suggests that uric acid is an important but not exclusive determinant of endothelial function, which is also influenced by obesity, insulin resistance, physical activity, inflammation, and genetic factors. [17]

Serum Uric Acid and Blood Pressure: Serum uric acid showed significant positive correlations with systolic blood pressure ($r = 0.36$)anddiastolic blood pressure ($r = 0.31$). [18] The association was stronger for systolic blood pressure, and serum uric acid remained an independent predictor of systolic blood pressure in multivariable regression analysis.

The relationship between hyperuricemia and hypertension has been extensively investigated over the past two decades. [19] Prospective cohort studies have consistently demonstrated that elevated uric acid predicts the future development of hypertension in adolescents, young adults, and middle-aged populations. [20] The association appears particularly strong in younger individuals, where hypertension is less likely to be influenced by long-standing vascular disease. [21]

Several mechanisms have been proposed. Initially, elevated uric acid causes functional vasoconstriction through reduction of nitric oxide availability and activation of the renin-angiotensin-aldosterone system (RAAS). [22] Increased renin expression and angiotensin II production lead to enhanced vasoconstriction and sodium retention. Over time, uric acid induces renal afferent arteriolopathy and microvascular disease, resulting in persistent sodium-sensitive hypertension. [23] This two-phase model of uric acid-induced hypertension has been supported by experimental animal studies and intervention trials. [24]

The stronger association with systolic blood pressure observed in the present study may reflect early vascular stiffness and reduced arterial compliance, which predominantly influence systolic pressure. 25 In young adults, systolic blood pressure is particularly sensitive to changes in vascular tone and endothelial function.

Independent Association of Serum Uric Acid with Endothelial Dysfunction: One of the strengths of the present study is the use of multiple linear regression analysis, which showed that serum uric acid remained independently associated with impaired FMD ($\beta = -0.34$, $p < 0.001$) even after adjustment for age, sex, BMI, fasting glucose, and lipid profile. [26]

This finding suggests that the relationship between uric acid and endothelial dysfunction is not solely explained by obesity or other metabolic abnormalities. Although body mass index was also associated with reduced FMD, serum uric acid emerged as the strongest predictor in the regression model. [27]

These results support the concept that uric acid may act as an independent cardiovascular risk factor or risk marker in young adults. Whether uric acid is directly causal or reflects underlying metabolic and inflammatory processes remains an area of active investigation. [28]

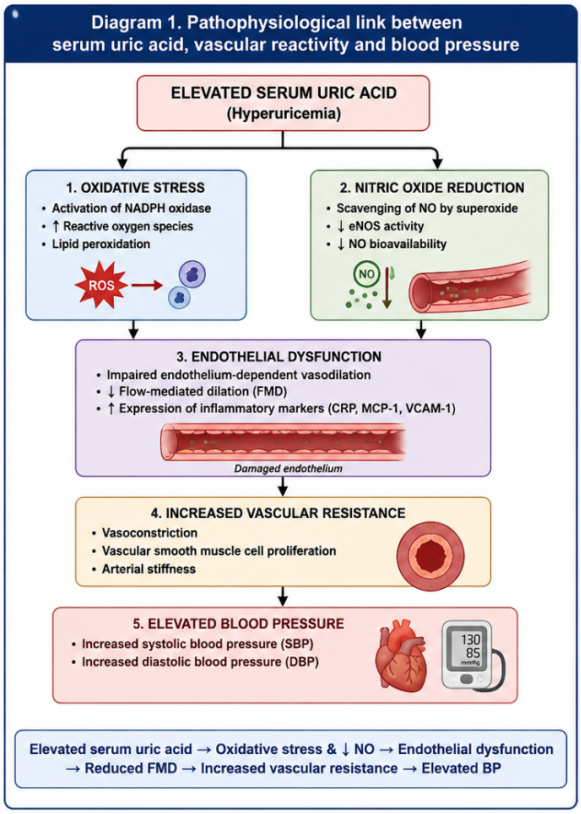

Figure 2: Pathophysiological link between serum uric acid, vascular reactivity and blood pressure

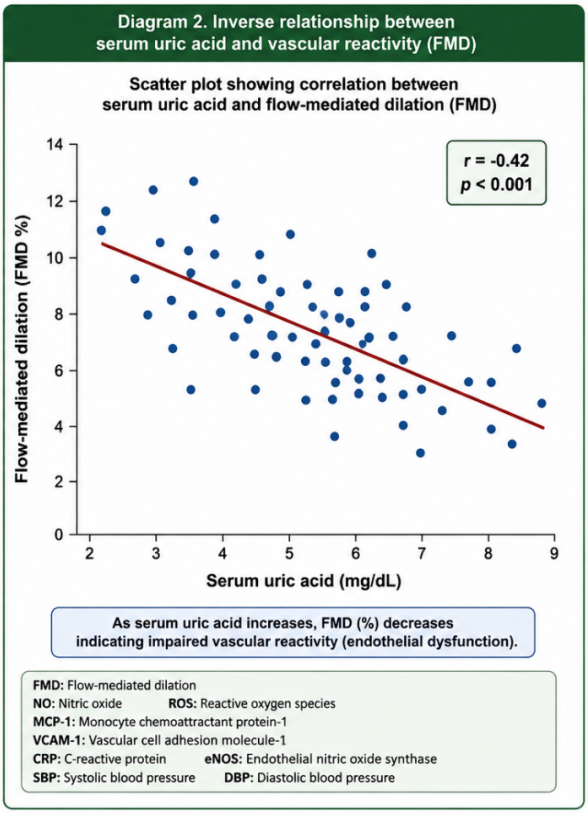

Figure 3: Inverse relationship between serum uric acid and vascular reactivity (FMD)

Comparison with Previous Studies: The findings of the present study are broadly consistent with numerous international studies.

Johnson et al. proposed that uric acid contributes directly to the pathogenesis of hypertension through endothelial dysfunction and renal microvascular injury. [29] Feig et al. demonstrated that uric acid-lowering therapy with allopurinol significantly reduced blood pressure in hyperuricemic adolescents with newly diagnosed hypertension, suggesting a potential causal relationship. [30]

Khosla et al. reported that higher serum uric acid was associated with impaired endothelial function and increased cardiovascular risk. [31] Similar inverse associations between uric acid and flow-mediated dilation have been described in studies involving healthy adults, patients with metabolic syndrome, and individuals with essential hypertension. [32]

Indian studies have also reported significant associations between serum uric acid and blood pressure, obesity, and components of the metabolic syndrome in young adults and medical students. [33] The present study extends these observations by simultaneously examining vascular reactivity and blood pressure, thereby providing a more integrated assessment of early vascular dysfunction. [34]

Clinical Significance: The clinical implications of these findings are important. Young adults are generally considered to be at low short-term cardiovascular risk; however, endothelial dysfunction may precede hypertension by several years. [35] Identification of elevated serum uric acid in apparently healthy young individuals may therefore help identify a subgroup at increased risk for future hypertension and cardiovascular disease.

Serum uric acid estimation is inexpensive, widely available, and routinely performed in clinical laboratories. If confirmed by prospective studies, serum uric acid could serve as a practical biomarker for early vascular risk stratification.

Lifestyle interventions that reduce uric acid levels, including weight reduction, increased physical activity, reduced fructose intake, moderation of purine-rich foods, and avoidance of sugar-sweetened beverages, may improve endothelial function and reduce future cardiovascular risk.

Strengths of the Study: The present study has several strengths:

1. Inclusion of apparently healthy young adults, allowing assessment of early vascular changes before overt disease.

2. Equal representation of male and female participants.
3. Use of flow-mediated dilation, a validated non-invasive measure of endothelial function.
4. Standardized measurement of blood pressure and biochemical parameters.
5. Multivariable regression analysis to adjust for important confounding variables.

Limitations

Certain limitations should be acknowledged.

1. The cross-sectional design precludes establishment of a causal relationship between serum uric acid and vascular dysfunction.
2. The sample was drawn from a single tertiary care institution and may not be fully representative of the general young adult population.
3. Dietary intake, physical activity, socioeconomic status, and genetic determinants of uric acid metabolism were not assessed in detail.
4. Endothelium-independent vasodilation was not measured; therefore, the specific contribution of vascular smooth muscle function could not be evaluated.
5. Longitudinal follow-up was not performed to determine whether participants with higher serum uric acid subsequently developed hypertension.

Future prospective cohort studies and randomized intervention trials using uric acid-lowering therapies may further clarify the causal role of uric acid in endothelial dysfunction and hypertension among young adults.

Overall Interpretation: The present findings showed a moderate but significant inverse association between serum uric acid and vascular reactivity and a positive association between serum uric acid and blood pressure. The persistence of these associations after adjustment for major confounding variables suggests that serum uric acid may be an independent marker of early endothelial dysfunction and cardiovascular risk in young adults. These observations support the growing hypothesis that hyperuricemia may participate in the early pathophysiological pathway linking metabolic abnormalities, endothelial dysfunction, and the development of hypertension. Early identification and modification of elevated serum uric acid may therefore represent a useful strategy for the prevention of future cardiovascular disease in young populations.

Conclusion

The present study showed that serum uric acid was significantly associated with vascular reactivity and blood pressure among apparently healthy young adults.

Higher serum uric acid concentrations showed a moderate negative correlation with brachial artery flow-mediated dilation, indicating impaired endothelial-dependent vascular reactivity, and positive correlations with both systolic and diastolic blood pressure. Importantly, serum uric acid remained anindependent predictor of reduced vascular reactivity and elevated systolic blood pressure even after adjustment for age, sex, body mass index, fasting glucose, and lipid profile.

These findings support the hypothesis that elevated serum uric acid may represent an early marker of endothelial dysfunction and subclinical cardiovascular risk in young adults.

Since endothelial dysfunction precedes the development of overt hypertension and cardiovascular disease, routine assessment of serum uric acid may help identify apparently healthy young individuals who are at increased risk of future cardiovascular events.

Although the cross-sectional design does not establish causality, the observed associations are biologically plausible and consistent with experimental and epidemiological evidence linking uric acid with oxidative stress, nitric oxide depletion, vascular smooth muscle proliferation, and activation of the renin-angiotensin system.

Early lifestyle modification aimed at reducing serum uric acid levels may therefore contribute to preservation of endothelial function and prevention of hypertension in susceptible young adults.

Recommendations for Future Research

1. Prospective longitudinal studies to determine whether elevated serum uric acid predicts incident hypertension and cardiovascular events in young adults.
2. Interventional trials evaluating the effect of uric acid-lowering therapy on endothelial function and blood pressure.
3. Multicenter studies involving larger and ethnically diverse populations.
4. Studies incorporating inflammatory biomarkers, oxidative stress markers, arterial stiffness indices, and ambulatory blood pressure monitoring.

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