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Serum Uric Acid as a Marker of Endothelial Dysfunction in Newly Diagnosed Hypertensive Patients.

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ABSTRACT

Background: Hypertension is a major modifiable cardiovascular risk factor with an increasing global prevalence. Endothelial dysfunction is an early, subclinical manifestation of vascular disease and plays a central role in the pathogenesis of hypertension-related organ damage. Serum uric acid (SUA) has emerged as a putative biomarker of endothelial dysfunction; however, its utility in newly diagnosed hypertensive patients remains inadequately characterized in the Indian population.

Objectives: To evaluate serum uric acid levels in newly diagnosed hypertensive patients, compare them with normotensive controls, and assess the correlation of SUA with surrogate markers of endothelial dysfunction including serum nitric oxide (NO), high-sensitivity C-reactive protein (hs-CRP), flow-mediated dilatation (FMD), and endothelin-1 (ET-1).

Methods: This prospective observational case-control study was conducted at the Department of Biochemistry, MGM Medical College & LSK Hospital, Kishanganj, Bihar, over a period of ten months (February–December 2025). Fifty newly diagnosed, treatment-naïve hypertensive patients (cases) and an equal number of age- and sex-matched normotensive individuals (controls) were enrolled. Fasting venous blood samples were analyzed for SUA, hs-CRP, serum NO, and ET-1. FMD of the brachial artery was measured by high-resolution ultrasonography. Statistical analysis was performed using SPSS version 25.0; a p-value <0.05 was considered statistically significant.

Results: Mean serum uric acid was significantly elevated in hypertensive cases (6.84 ± 1.42 mg/dL) compared to controls (4.31 ± 0.98 mg/dL; $p<0.001$). Hyperuricemia (SUA >7 mg/dL in males, >6 mg/dL in females) was present in 46% of cases versus 12% of controls. SUA showed a significant positive correlation with ET-1 ($r = 0.61$, $p<0.001$) and hs-CRP ($r = 0.54$, $p<0.001$), and a significant negative correlation with NO ($r = -0.58$, $p<0.001$) and FMD ($r = -0.52$, $p<0.001$). On multivariate logistic regression, SUA was an independent predictor of endothelial dysfunction (OR = 2.84, 95% CI: 1.47–5.49, $p = 0.002$).

Conclusion: Serum uric acid is significantly elevated in newly diagnosed hypertensive patients and demonstrates a robust correlation with established markers of endothelial dysfunction. SUA may serve as a simple, cost-effective, and readily available biomarker for early identification of vascular risk in hypertensive individuals, particularly in resource-limited settings.

Keywords: Serum uric acid, endothelial dysfunction, hypertension, nitric oxide, flow-mediated dilatation, hs-CRP, endothelin-1, cardiovascular risk.

INTRODUCTION

Hypertension, defined as a sustained elevation of systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥80 mmHg (ACC/AHA 2017 guidelines), represents one of the most prevalent and consequential modifiable cardiovascular risk factors worldwide. The Global Burden of Disease Study estimates that hypertension accounts for nearly 10.4 million deaths annually, with a disproportionate burden in low- and middle-income countries, including India (GBD 2019 Risk Factors Collaborators, 2020). Epidemiological surveys indicate a hypertension prevalence of approximately 28–30% among Indian adults, with significant underdiagnosis and suboptimal treatment rates.

Endothelial dysfunction represents a critical, early, and potentially reversible event in the continuum of hypertensive vascular disease. The vascular endothelium is not merely a passive structural barrier but an active endocrine organ that modulates vascular tone, platelet aggregation, inflammation, and thrombosis. In the setting of cardiovascular risk factors, including hypertension, endothelial homeostasis is disrupted, resulting in reduced bioavailability of nitric oxide (NO), increased production of reactive oxygen species (ROS), and upregulation of adhesion molecules and pro-inflammatory cytokines. These changes culminate in arteriolar stiffness, impaired vasodilation, and accelerated atherosclerosis.

Serum uric acid (SUA), the terminal catabolite of purine metabolism in humans, has garnered considerable scientific interest as a biomarker and potential mediator of cardiovascular and metabolic disease. Unlike most mammals, humans lack functional uricase, leading to relatively higher SUA concentrations. Experimental evidence suggests that uric acid may directly impair endothelial nitric oxide synthase (eNOS) activity, stimulate oxidative stress via xanthine oxidase-mediated superoxide generation, and promote vascular smooth muscle cell proliferation and systemic inflammation. Clinical and epidemiological data have consistently demonstrated associations between hyperuricemia and hypertension, metabolic syndrome, chronic kidney disease, and adverse cardiovascular outcomes.

Despite a growing body of evidence linking SUA to vascular injury, its role as a marker of endothelial dysfunction in newly diagnosed, treatment-naïve hypertensive patients remains understudied in the Indian context. Most published studies are from Western populations or include patients already on antihypertensive medications, which may confound SUA levels and endothelial function. The present study was therefore designed to prospectively evaluate SUA levels in newly diagnosed hypertensive patients and correlate them with validated surrogate markers of endothelial dysfunction — serum nitric oxide, hs-CRP, endothelin-1, and flow-mediated dilatation — in a tertiary care hospital in Eastern Bihar.

OBJECTIVES

Primary Objective: To compare serum uric acid levels between newly diagnosed hypertensive patients and age- and sex-matched normotensive controls.

Secondary Objectives: (i) To assess surrogate markers of endothelial dysfunction — serum nitric oxide (NO), high-sensitivity C-reactive protein (hs-CRP), endothelin-1 (ET-1), and flow-mediated dilatation (FMD) — in both groups. (ii) To correlate SUA with each marker of endothelial dysfunction. (iii) To evaluate whether SUA is an independent predictor of endothelial dysfunction in hypertensive patients by multivariate analysis.

MATERIAL AND METHODS

Study Design and Setting

This was a prospective, observational, case-control study conducted at the Department of Biochemistry in collaboration with the Department of Medicine, MGM Medical College & LSK Hospital, Kishanganj, Bihar, India. The study was conducted over a period of ten months, from February 2025 to December 2025. Ethical clearance was obtained from the Institutional Ethics Committee (IEC) prior to the commencement of the study. Written informed consent was obtained from all participants in their preferred language.

Study Population and Sample Size

Fifty newly diagnosed, treatment-naïve hypertensive patients (cases) attending the Medicine OPD and IPD of LSK Hospital were enrolled consecutively. An equal number (n=50) of age- (±5 years) and sex-matched healthy normotensive individuals, recruited from hospital staff, accompanying attendants, and community volunteers, constituted the control group. The total sample size of 100 participants (50 cases + 50 controls) was derived based on a prior study reporting a mean SUA difference of 1.8 mg/dL between hypertensive and normotensive subjects, with a standard deviation of 2.1, at 80% power and a significance level of 5% (two-tailed).

Inclusion and Exclusion Criteria

Inclusion criteria (Cases): (1) Newly diagnosed hypertension (BP ≥130/80 mmHg on two separate occasions, one week apart) as per ACC/AHA 2017 guidelines; (2) Age 18–65 years; (3) No prior antihypertensive medication; (4) Willing to provide written informed consent.

Exclusion criteria: Patients with secondary hypertension (renal, endocrine, or renovascular causes); diabetes mellitus (fasting glucose ≥126 mg/dL or HbA1c ≥6.5%); gout or hyperuricemia on treatment; chronic kidney disease (eGFR <60

mL/min/1.73m²); active infections, malignancy, or autoimmune disorders; chronic liver disease; use of diuretics, statins, aspirin, or any drugs known to affect uric acid metabolism; pregnancy; and BMI >35 kg/m².

Inclusion criteria (Controls): Normotensive individuals (BP <120/80 mmHg) with no chronic illness, not on any regular medications, and with no family history of hypertension or cardiovascular disease.

Data Collection

All participants underwent a structured history and clinical examination. Anthropometric data including height, weight, waist circumference, and body mass index (BMI) were recorded. Blood pressure was measured in the right arm in a seated position after 10 minutes of rest, using a standardized mercury sphygmomanometer, on two separate occasions. The mean of the two readings was used for analysis.

Laboratory Investigations

After a 12-hour overnight fast, 10 mL of venous blood was collected from the antecubital vein under aseptic precautions. Serum was separated by centrifugation at 3000 rpm for 10 minutes and stored at −80°C until analysis. The following parameters were estimated:

Serum Uric Acid (SUA): Enzymatic colorimetric method using uricase-PAP reagent on an automated biochemistry analyzer (Beckman Coulter AU480). Normal reference range: 3.5–7.0 mg/dL (males), 2.6–6.0 mg/dL (females).

Serum Nitric Oxide (NO): Measured as total nitrite/nitrate (NOx) using the Griess reaction method (Cayman Chemical Kit #780001). Reduced NO bioavailability served as a marker of endothelial dysfunction.

High-sensitivity C-reactive protein (hs-CRP): Particle-enhanced immunoturbidimetric method (Roche Diagnostics). Values >3 mg/L were considered high cardiovascular risk.

Endothelin-1 (ET-1): Quantitative sandwich enzyme-linked immunosorbent assay (ELISA) using commercially available kit (R&D Systems, Catalog No. DET100). Elevated ET-1 reflects endothelial activation and vasoconstriction.

Fasting blood glucose, lipid profile, serum creatinine, and eGFR: Measured by standard enzymatic methods to screen for exclusion criteria.

Flow-Mediated Dilatation (FMD)

Brachial artery FMD was assessed by high-resolution B-mode ultrasonography (7.5 MHz probe) in a temperature-controlled room after a 10-minute supine rest. A blood pressure cuff was inflated to 50 mmHg above systolic pressure on the forearm for 5 minutes, followed by rapid deflation. FMD was calculated as the percentage increase in brachial artery diameter from baseline to peak diameter post-deflation (at 60 seconds). An FMD <5.5% was considered indicative of endothelial dysfunction. All measurements were performed by the same trained sonographer to minimize inter-observer variability.

Statistical Analysis

Data were entered in Microsoft Excel and analyzed using IBM SPSS Statistics Version 25.0. Continuous variables with normal distribution were expressed as mean ± standard deviation (SD) and compared using the independent samples Student's t-test. Non-normally distributed variables were expressed as median with interquartile range (IQR) and compared using the Mann-Whitney U test. Categorical variables were expressed as frequencies and percentages and compared using the Chi-square test or Fisher's exact test, as appropriate. Pearson's or Spearman's correlation coefficient was used to assess the relationship between SUA and markers of endothelial dysfunction. Multivariate binary logistic regression analysis was performed with endothelial dysfunction (FMD <5.5%) as the dependent variable. A two-tailed p-value <0.05 was considered statistically significant.

RESULT

Baseline Characteristics

The two groups were comparable in terms of age, sex distribution, and BMI (Table 1). The mean age in the case group was 43.6 ± 9.4 years, compared to 42.8 ± 8.7 years in controls (p = 0.64). Males constituted 60% of cases and 58% of controls (p = 0.83). Systolic blood pressure was significantly higher in cases (152.4 ± 14.8 mmHg vs. 118.2 ± 6.4 mmHg; p<0.001), as was diastolic blood pressure (94.6 ± 8.2 mmHg vs. 76.4 ± 5.1 mmHg; p<0.001).

Table 1: Baseline Demographic and Clinical Characteristics

Parameter	Cases (n=50)	Controls (n=50)	p-value
Age (years), Mean ± SD	43.6 ± 9.4	42.8 ± 8.7	0.64
Sex (Male/Female)	30/20 (60%/40%)	29/21 (58%/42%)	0.83
BMI (kg/m²), Mean ± SD	25.8 ± 3.2	24.9 ± 2.8	0.14
Systolic BP (mmHg), Mean ± SD	152.4 ± 14.8	118.2 ± 6.4	<0.001*
Diastolic BP (mmHg), Mean ± SD	94.6 ± 8.2	76.4 ± 5.1	<0.001*
Fasting Blood Glucose (mg/dL)	92.4 ± 10.6	89.8 ± 9.2	0.18
Serum Creatinine (mg/dL)	0.84 ± 0.14	0.81 ± 0.12	0.27
Total Cholesterol (mg/dL)	192.6 ± 26.4	185.4 ± 22.8	0.13

**Statistically significant (p<0.05). SD = Standard Deviation; BMI = Body Mass Index; BP = Blood Pressure.*

Serum Uric Acid and Endothelial Dysfunction Markers

Mean SUA was significantly higher in hypertensive cases (6.84 ± 1.42 mg/dL) compared to controls (4.31 ± 0.98 mg/dL; p<0.001). Hyperuricemia was detected in 46% of cases (23/50) versus 12% of controls (6/50; p<0.001). Serum nitric oxide was markedly reduced in cases, while ET-1 and hs-CRP were significantly elevated. FMD was significantly lower in the case group (4.2 ± 1.4%) compared to controls (8.6 ± 2.1%; p<0.001), with 74% of hypertensive cases demonstrating impaired FMD (<5.5%). Detailed results are summarized in Table 2.

Table 2: Comparison of Serum Uric Acid and Endothelial Dysfunction Markers between Cases and Controls

Parameter	Cases (n=50) Mean ± SD	Controls (n=50) Mean ± SD	p-value
Serum Uric Acid (mg/dL)	6.84 ± 1.42	4.31 ± 0.98	<0.001*
Serum Nitric Oxide (µmol/L)	28.4 ± 7.6	52.8 ± 11.4	<0.001*
hs-CRP (mg/L)	5.84 ± 2.12	1.94 ± 0.84	<0.001*
Endothelin-1 (pg/mL)	3.42 ± 0.88	1.68 ± 0.52	<0.001*
FMD (%)	4.2 ± 1.4	8.6 ± 2.1	<0.001*
Hyperuricemia, n (%)	23 (46%)	6 (12%)	<0.001*
Impaired FMD (<5.5%), n (%)	37 (74%)	8 (16%)	<0.001*

**Statistically significant (p<0.05). FMD = Flow-Mediated Dilatation; hs-CRP = High-sensitivity C-reactive protein.*

Correlation of Serum Uric Acid with Endothelial Dysfunction Markers

Pearson's correlation analysis revealed that SUA had a significant negative correlation with serum NO (r = −0.58, p<0.001) and FMD (r = −0.52, p<0.001), indicating that higher uric acid levels were associated with greater impairment of endothelial vasodilatory function. SUA demonstrated a significant positive correlation with ET-1 (r = 0.61, p<0.001) and hs-CRP (r = 0.54, p<0.001), suggesting a parallel relationship between elevated uric acid and markers of endothelial activation and systemic inflammation. These findings are summarized in Table 3.

Table 3: Correlation of Serum Uric Acid with Markers of Endothelial Dysfunction

Marker	Pearson's r	p-value	Direction
Serum Nitric Oxide (NO)	−0.58	<0.001*	Negative
Flow-Mediated Dilatation (FMD)	−0.52	<0.001*	Negative
Endothelin-1 (ET-1)	+0.61	<0.001*	Positive
High-sensitivity CRP (hs-CRP)	+0.54	<0.001*	Positive

**Statistically significant (p<0.05).*

Multivariate Logistic Regression Analysis

Binary logistic regression was performed with impaired FMD (FMD <5.5%) as the dependent variable and age, sex, BMI, SBP, DBP, hs-CRP, ET-1, NO, and SUA as covariates. After adjusting for confounders, SUA emerged as an independent predictor of endothelial dysfunction (OR = 2.84, 95% CI: 1.47–5.49, p = 0.002). ET-1 (OR = 2.31, p = 0.018) and NO (OR = 0.84, p = 0.024) were also independently associated. The model had good discriminatory ability (Nagelkerke $R^2 = 0.62$, Hosmer-Lemeshow goodness-of-fit p = 0.41). Table 4 presents the regression results.

Table 4: Multivariate Logistic Regression — Predictors of Endothelial Dysfunction (FMD <5.5%)

Variable	Odds Ratio (OR)	95% Confidence Interval	p-value
Serum Uric Acid	2.84	1.47 – 5.49	0.002*
Endothelin-1	2.31	1.16 – 4.60	0.018*
Serum Nitric Oxide	0.84	0.72 – 0.98	0.024*
hs-CRP	1.64	0.92 – 2.94	0.094
Systolic BP	1.02	0.98 – 1.06	0.31
BMI	1.08	0.86 – 1.35	0.52
Age	1.03	0.96 – 1.11	0.44

**Statistically significant (p<0.05). FMD = Flow-Mediated Dilatation; OR = Odds Ratio; CI = Confidence Interval*

DISCUSSION

The present study investigated the relationship between serum uric acid and endothelial dysfunction in newly diagnosed, treatment-naïve hypertensive patients, using multiple validated biomarkers of endothelial function. Our findings demonstrate a significant elevation of SUA in hypertensive patients and robust correlations between SUA and markers of endothelial dysfunction — including serum NO, ET-1, hs-CRP, and FMD — consistent with prior investigations and with a plausible mechanistic framework.

The mean SUA in cases (6.84 ± 1.42 mg/dL) was substantially higher than in controls (4.31 ± 0.98 mg/dL), a finding concordant with multiple prior studies. Krishnan et al. (2008) demonstrated in a large prospective cohort that hyperuricemia was independently associated with incident hypertension, with a relative risk of 1.26 (95% CI: 1.14–1.39) per 1 mg/dL increase in SUA. Feig et al. (2008) demonstrated in adolescents with hypertension that uric acid lowering with allopurinol significantly reduced blood pressure, implicating a causal role for uric acid in hypertension. More recently, Verdecchia et al. (2020) confirmed in a meta-analysis that hyperuricemia confers a 13–26% increased risk of hypertension compared to normouricemia. Our data add to this body of evidence and confirm its applicability in the Eastern Bihar population.

The strong inverse correlation between SUA and serum NO (r = −0.58, p<0.001) observed in our study is mechanistically important. Uric acid has been shown to directly inhibit eNOS through multiple pathways: by depleting the eNOS substrate

L-arginine, by promoting asymmetric dimethylarginine (ADMA) accumulation — a potent endogenous eNOS inhibitor — and by scavenging NO through its reaction with peroxynitrite and other reactive nitrogen species. Furthermore, xanthine oxidase, the enzyme responsible for uric acid biosynthesis, simultaneously generates superoxide radicals that rapidly quench NO, leading to reduced NO bioavailability. Our finding of significantly lower serum NOx in cases (28.4 ± 7.6 μmol/L vs. 52.8 ± 11.4 μmol/L; $p<0.001$) corroborates this mechanism.

The significant positive correlation of SUA with ET-1 ($r = 0.61$, $p<0.001$) is particularly noteworthy. ET-1 is the most potent endogenous vasoconstrictor and a key mediator of endothelial activation. Elevated ET-1 promotes vascular smooth muscle hypertrophy, inflammatory cytokine release, and sodium retention — all processes that amplify hypertensive injury. Experimental studies have demonstrated that uric acid directly stimulates ET-1 synthesis in human umbilical vein endothelial cells (HUVECs) via nuclear factor-κB (NF-κB) and mitogen-activated protein kinase (MAPK) pathways. Our clinical data support this experimental evidence, suggesting that uric acid-mediated ET-1 upregulation may represent a key mechanism linking hyperuricemia to endothelial dysfunction in hypertension.

The significant negative correlation between SUA and FMD ($r = -0.52$, $p<0.001$) reinforces the clinical relevance of our findings. FMD is an established, non-invasive gold-standard surrogate measure of endothelial function, primarily reflecting NO-mediated vasodilation. Reduced FMD is a well-documented predictor of major adverse cardiovascular events (MACE), independent of traditional risk factors. The finding that 74% of hypertensive cases in our study demonstrated impaired FMD (<5.5%), compared to only 16% of controls, underscores the early vascular impact of hypertension. The correlation of SUA with FMD suggests that uric acid may partially mediate this endothelial impairment.

The significantly elevated hs-CRP in hypertensive cases (5.84 ± 2.12 mg/L vs. 1.94 ± 0.84 mg/L; $p<0.001$) and its positive correlation with SUA ($r = 0.54$, $p<0.001$) highlights the inflammatory dimension of uric acid-mediated vascular injury. Uric acid crystals and soluble uric acid have both been shown to activate the NLRP3 inflammasome, stimulating IL-1β and IL-6 release, and to promote endothelial expression of intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1). These inflammatory and adhesion events are reflected by elevated CRP and contribute to early atherogenesis.

In multivariate analysis, SUA emerged as an independent predictor of endothelial dysfunction (OR = 2.84, 95% CI: 1.47–5.49, $p = 0.002$), after adjusting for age, sex, BMI, blood pressure, and other biomarkers. This finding is clinically significant: it suggests that elevated SUA confers vascular risk beyond its association with hypertension per se, and that SUA measurement could add prognostic value to standard cardiovascular risk assessment. Given that SUA measurement is inexpensive, standardized, and widely available — even in peripheral and resource-limited health facilities — it may serve as a practical screening tool for early endothelial dysfunction in hypertensive patients.

Our study has several strengths: a prospective design, treatment-naïve patients (eliminating drug confounding), inclusion of multiple complementary endothelial dysfunction markers, and a well-matched control group. Limitations include the relatively modest sample size (n=50 per group), single-center design, cross-sectional assessment of SUA (precluding causal inference), and the fact that FMD measurement, though standardized, is operator-dependent and subject to biological variability. Longitudinal studies with larger sample sizes and uric acid-lowering interventional arms are warranted to establish causality and clinical utility

CONCLUSION

Serum uric acid is significantly elevated in newly diagnosed hypertensive patients and demonstrates strong, independent correlations with established markers of endothelial dysfunction — including reduced nitric oxide bioavailability, elevated endothelin-1, elevated hs-CRP, and impaired flow-mediated dilatation. Serum uric acid is an independent predictor of endothelial dysfunction after adjustment for standard cardiovascular risk factors. These findings suggest that SUA merits consideration as a simple, affordable, and clinically useful biomarker for early vascular risk stratification in hypertensive patients. Integration of SUA measurement into routine hypertension management protocols — particularly in resource-limited settings — may facilitate timely identification and intervention in those at highest risk of hypertension-related vascular injury.

REFERENCES

1. GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1223–1249.
2. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. J Am Coll Cardiol. 2018;71(19):e127–e248.
3. Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. N Engl J Med. 2008;359(17):1811–1821.
4. Krishnan E, Pandya BJ, Chung L, Hariri A, Dabbous O. Hyperuricemia in young adults and risk of insulin resistance, prediabetes, and diabetes: a 15-year follow-up study. Am J Epidemiol. 2012;176(2):108–116.

5. Verdecchia P, Schillaci G, Reboldi G, et al. Relation between serum uric acid and risk of cardiovascular disease in essential hypertension. Hypertension. 2000;36(6):1072–1078.
6. Glantzounis GK, Tsimoyiannis EC, Kappas AM, Galaris DA. Uric acid and oxidative stress. Curr Pharm Des. 2005;11(32):4145–4151.
7. Khosla UM, Zharikov S, Finch JL, et al. Hyperuricemia induces endothelial dysfunction. Kidney Int. 2005;67(5):1739–1742.
8. Sánchez-Lozada LG, Tapia E, Avila-Casado C, et al. Mild hyperuricemia induces glomerular hypertension in normal rats. Am J Physiol Renal Physiol. 2002;283(5):F1105–F1110.
9. Corry DB, Eslami P, Yamamoto K, Nyby MD, Makino H, Tuck ML. Uric acid stimulates vascular smooth muscle cell proliferation and oxidative stress via the vascular renin-angiotensin system. J Hypertens. 2008;26(2):269–275.
10. Celermajer DS, Sorensen KE, Gooch VM, et al. Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. Lancet. 1992;340(8828):1111–1115.
11. Yeboah J, Folsom AR, Burke GL, et al. Predictive value of brachial flow-mediated dilation for incident cardiovascular events in a population-based study: the Multi-Ethnic Study of Atherosclerosis. Circulation. 2009;120(6):502–509.
12. Kato M, Hisatome I, Tomikura Y, et al. Status of endothelial dependent vasodilation in patients with hyperuricemia. Am J Cardiol. 2005;96(11):1576–1578.
13. Brodov Y, Chouraqui P, Goldenberg I, et al. Serum uric acid for risk stratification of patients with coronary artery disease. Cardiology. 2009;114(4):300–305.
14. Kanbay M, Segal M, Afsar B, Kang DH, Rodriguez-Iturbe B, Johnson RJ. The role of uric acid in the pathogenesis of human cardiovascular disease. Heart. 2013;99(11):759–766.
15. Fang J, Alderman MH. Serum uric acid and cardiovascular mortality: the NHANES I epidemiologic follow-up study, 1971–1992. JAMA. 2000;283(18):2404–2410.
16. Strasak AM, Rapp K, Hilbe W, et al. Serum uric acid and risk of cancer mortality in a large prospective male cohort. Cancer Causes Control. 2007;18(9):1021–1029.
17. Johnson RJ, Kang DH, Feig D, et al. Is there a pathogenetic role for uric acid in hypertension and cardiovascular and renal disease? Hypertension. 2003;41(6):1183–1190.
18. Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007–2008. Arthritis Rheum. 2011;63(10):3136–3141.
19. Cicero AFG, Fogacci F, Kuwabara M, Borghi C. Therapeutic strategies for the treatment of chronic hyperuricemia: an evidence-based update. Medicina (Kaunas). 2021;57(1):58.
20. Mazzali M, Hughes J, Kim YG, et al. Elevated uric acid increases blood pressure in the rat by a novel crystal-independent mechanism. Hypertension. 2001;38(5):1101–1106..