Hormozgan Medical Journal
doi 10.34172/hmj.8355
Hormozgan Med J. 2024;28(4):209-213

Original Article

Severity of Coronary Artery Stenosis in Angiography

Mojgan Hajahmadi Pourrafsanjani[1], Alireza Rostamzadeh[1*], Venus Shahabi Rabari[1], Fatemeh Jahangiri[1]

[1]Department of Cardiology, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran

***Correspondence to**
Alireza Rostamzadeh
Email: rostamzadeh.a@umsu.ac.ir

Abstract

Background: Serum uric acid (SUA), a byproduct of purine metabolism, is linked to coronary artery disease (CAD) development and progression. Elevated SUA levels are considered an independent risk factor for cardiovascular mortality and may indicate endothelial dysfunction. The aim of the study was to evaluate the association of the SUA level with the angiographic severity of CAD.

Methods: This observational cross-sectional descriptive study included 150 patients who had undergone coronary angiography in the Department of Cardiology at Seyed al-Shohadah Hospital in Urmia, Iran, from October 2022 to November 2022. Coronary atherosclerosis, with stenosis > 50% in each coronary artery, was categorized as single-vessel, two-vessel, three-vessel, or normal CAD according to angiography findings. The association of the SUA levels with CAD prevalence, severity, and clinical outcomes was assessed by statistical analyses.

Results: Of 150 patients, the female gender was predominant (n = 96, 64%), and the difference between uric acid levels and gender was statistically significant ($P = 0.049$). Regarding age groups, 58% of the patients were under 65 years (42.5 ± 68.6), and 42% were older than 65 years (41.8 ± 69.1). A significant number of patients were hypertensive (60%). More than half of the studied patients were not affected by diabetes mellitus (68%). Similarly, no significant difference was found in patients with a history of hyperlipidemia (42%, $P = 0.701$). According to the initial diagnosis, 36.7% of the patients had a condition without some degree of coronary involvement. Therefore, 30%, 12%, and 21.3% had single-, two-, and three-vessel coronary obstructions, respectively. When relating these conditions to the levels of obtained uric acid, there was no evidence of difference between the different groups ($P = 0.191$).

Conclusion: The present study suggests that hyperuricemia in patients with conventional cardiovascular risk factors may be associated with more severe CAD and an elevated overall cardiovascular risk.

Keywords: Coronary artery disease, Hyperuricemia, Risk factors, Angiography

Received: November 12, 2023, **Revised:** January 1, 2024 ,**Accepted:** January 13, 2024, **ePublished:** October 30, 2024

Background

Coronary artery disease (CAD) is a pervasive global health concern, accounting for a significant portion of cardiovascular morbidity and mortality (1). Endothelial dysfunction underlies a multitude of cardiovascular disorders arising from genetic, biochemical, and hemodynamic perturbations, which can be modulated by established risk factors, some of which are amenable to modification and control (2). In this context, exploring novel risk factors, such as serum uric acid (SUA) levels, holds substantial clinical significance for enhancing CAD risk stratification and optimizing patient care (3).

Uric acid, the final byproduct of purine metabolism in humans, is regulated by the enzyme xanthine oxidase (4). Some proposed mechanisms for uric acid's pathogenic role in cardiovascular morbidity involve the generation of free radicals, enhanced platelet adhesiveness, and aggregation, all of which contribute to thrombus formation (5). While numerous studies have linked elevated SUA levels to reduced survival in patients with CAD (6, 7), several recent investigations have failed to confirm this association (8). Additionally, high uric acid levels are associated with endothelial dysfunction, antiproliferative effects, altered nitric oxide production, lipid peroxidation, and smooth muscle proliferation (9, 10).

Invasive coronary angiography serves as a valuable imaging tool for assessing the severity of coronary artery narrowing (1). However, its inability to provide pathophysiological information on myocardial ischemia restricts its effectiveness in evaluating stenosis functionally (11). With the advent of technological advancements in noninvasive myocardial perfusion imaging employing single-photon emission computed tomography, current guidelines advocate for its utilization in patients suspected of CAD to assess ischemia (12).

A connection between SUA and cardiovascular disease has been recognized since the 19th century (13). Subsequently, considerable epidemiological evidence has emerged, highlighting the association between uric acid and a range of cardiovascular diseases (14).

Hyperuricemia has also been demonstrated to correlate with cardiovascular risk factors for ischemic heart disease, including male gender, advanced age, diabetes mellitus, hypertension, insulin resistance, hypertriglyceridemia, and metabolic syndrome (15). Furthermore, various studies have consistently established a strong association between SUA levels and adverse outcomes in ischemic heart disease, particularly in patients with heart failure (16).

Given the potential for adverse outcomes in patients undergoing coronary angiography, early diagnosis and modification of risk factors are paramount. Investigating uric acid's role as a risk factor and its relationship to coronary artery disease severity and the number of affected vessels can provide crucial guidance for preventive and therapeutic interventions in these individuals. Therefore, this study aimed to study the association between serum uric acid level with the angiographic severity of CAD.

Methods

After receiving approval from the Research Ethics Committee of Urmia University of Medical Sciences (Approval No. IR.UMSU.REC.1395.170) and obtaining written informed consent from patients, this observational, cross-sectional, descriptive study was conducted in the Department of Cardiology at Seyed al-Shohadah Hospital by considering sample size and amount of more patients one month was considered to take 190 patients. All the eligible patients undergoing angiography and electively admitted to the hospital were included in the study using the convenience sampling method. The inclusion criteria were age less than 18 years, a coronary angiogram clear enough to enable the evaluation of the cause of stress-induced chest pain, and the patient's consent. On the other hand, the exclusion criteria were current pregnancy, cardiomyopathy, previous myocardial infarction or any revascularization procedure, unstable angina pectoris, history of congenital heart disease, renal dysfunction (glomerular filtration rate < 30 mL/min), experience of any SUA-lowering therapy, and history of any uric acid metabolism disorder.

Study participants were divided into two age groups, including those under 65 years old and those 65 years of age and older. All participants underwent coronary angiography, and blood samples were concurrently drawn to measure blood uric acid levels. Subsequent to participant selection, the study's rationale, objectives, and method were meticulously explained, and written informed consent was obtained from each enrolled patient. Demographic information (age and gender), cardiovascular risk factors, diabetes history, hypertension history, and smoking status were gathered for each patient, along with laboratory tests measuring SUA levels. These findings were documented in an information form. Hyperlipidemia was characterized by total cholesterol levels ≥ 200 mg/dL, low-density lipoprotein ≥ 130 mg/dL, triglyceride levels ≥ 200 mg/dL, high-density lipoprotein of ≤ 40 mg/dL, or the use of lipid-lowering drugs. Hypertension was defined as blood pressure > 140/90 mm Hg or the use of antihypertensive medications. Diabetes was diagnosed with the concurrent use of insulin and blood sugar-lowering drugs. Coronary atherosclerosis, with stenosis > 50% in each coronary artery, was categorized as single-vessel, two-vessel, three-vessel, or normal CAD, according to angiography findings. Angiographic data were recorded in the study form. Transthoracic echocardiography was conducted using a GE Vivid S5 cardiac ultrasound machine and a 2.5-MHz phased-array transducer, and the left ventricular ejection fraction was determined using modified Simpson's rule. Investigation tools included a Shimadzu Bransist Alexa C12 (ceiling-mounted angiographic machine, Japan) for coronary angiography and a GE Vivid S5 cardiac ultrasound machine (India) for left ventricular ejection fraction assessment. Eventually, serum fasting uric acid levels were measured using an enzymatic colorimetric method with the enzyme uricase.

Sample Sizing Method

According to a similar study conducted by Nabati et al. in 2013 (17), regarding the level of serum uric acid level and severity of coronary artery involvement in angiography on 181 patients with angina pectoris, elective150 patients referred to Seyed Al-Shohda Hospital for angiography in the women's and men's department were selected by convenience sampling method.

Statistical Analysis

Categorical data were presented as frequencies (percentages), while continuous data were presented as means and standard deviations. Differences between the means were compared by unpaired t-test or the Mann-Whitney U test based on the normal or non-normal distribution, respectively. Either the chi-square test or Fisher's exact test was used for the comparison of categorical variables. The analysis of variance was utilized for quantitative variables, and the Kruskal-Wallis test was employed if defaults were not established. Moreover, ordinal logistic regression analysis was applied to determine the risk factors of coronary disease severity. A P value of <0.05 (two-sided) was considered statistically significant. The obtained data were analyzed with the SPSS statistical software, version 21.0 (Chicago, Illinois, USA).

Results

According to Table 1, of 150 patients, 96 (64%) were female vs. 81 (54%), and the difference between uric acid levels and gender was statistically significant ($P = 0.049$). Regarding age groups, 58% of the patients were under 65 years (42.5 ± 68.6) and 42% were older than 65 years

Table 1. Demographic and Clinical Characteristics of Patients and Comparison With Uric Acid Levels

	N (%) 150 (100%)	Relation With Uric Acid Levels	
		Mean (SD)	*P* Value
Age			
<65	87 (58)	42.5±68.6	0.692
>65	62 (42)	41.8±69.1	
Gender			
Male	96 (64)	5.34±1.49	0.049
Female	81 (54)	5.78±1.37	
Coronary vessel obstruction			
Normal	55 (36.7)	5.26±1.28	0.191
One-vessel coronary obstruction	45 (30)	5.81±1.41	
Two-vessel coronary obstruction	18 (12)	5.67±1.68	
Three-vessel coronary obstruction	32 (21.3)	5.73±1.23	
Diabetes mellitus			
Yes	48 (32)	5.28±1.42	0.073
No	102 (68)	5.71±1.33	
Obesity			
Yes	78 (52)	5.70±1.40	0.241
No	72 (48)	5.44±1.34	
Smoking			
Yes	47 (31.3)	5.76±1.36	0.276
No	103 (68.7)	5.49±1.37	
Hyperlipidemia			
Yes	63 (42)	5.53±1.35	0.701
No	87 (58)	5.61±1.39	
Hypertension			
Yes	90 (60)	5.58±1.49	0.965
No	60 (40)	5.57±1.18	

Note. SD: Standard deviation.

(41.8±69.1). No difference was found with respect to age groups ($P=0.692$, Table 1).

About 60% of patients were hypertensive; when they were related to uric acid levels (5.58±1.49), the difference between the two groups was not significant ($P=0.965$). More than half of the studied patients were not affected by diabetes mellitus (68%), and no difference was found between the groups when they were related to uric acid levels ($P=0.39$). Likewise, no significant difference was observed in patients with a history of hyperlipidemia (42%, $P=0.701$). Finally, as one of the habits related to coronary disease, smoking was found in 31.3% of patients, without a significant difference when related to uric acid ($P=0.276$).

According to the initial diagnosis or clinical presentation, 36.7% of the patients had a condition without some degree of coronary involvement. Hence, 30%, 12%, and 21.3% had single-, two-, and three-vessel coronary obstructions, respectively. There was no evidence of difference between the different groups when relating these conditions to the obtained levels of uric acid ($P=0.191$, Table 1).

Table 2. Odds Ratios of Coronary Vessel Obstruction in Patients With Uric Acid Levels ≥6 and <6 by Ordinal Logistic Regression Analysis

	Coronary Vessel Obstruction			
	Yes	No	OR (95% CI)	*P* Value
Uric acid levels ≥6	33 (34.7%)	14 (25.5%)	1.60 (0.3, 74.27)	
Uric acid levels <6	62 (65.3%)	41 (74.55)		0.238
Total	95 (100%)	55 (100%)		

Note. OR: Odds ratio; CI: Confidence interval.

The chance of coronary vessel obstruction in people with a uric acid level of above 6 was 1.6 times more than that of people with a uric acid level of below 6, which is not statistically significant ($P=0.238$, Table 2).

Discussion

Uric acid is a heterocyclic organic compound with the formula C5H4N4O3, consisting of carbon, nitrogen, oxygen, and hydrogen (17). It is the final metabolic product of purine metabolism in humans, and excessive accumulation can lead to various health issues. Elevated uric acid levels are typically caused by hereditary factors (18). High uric acid levels have been observed in individuals with diabetes, hypertension, obesity, and dyslipidemia (19). The primary finding of our study confirmed a significant association between uric acid levels and the prevalence of CAD. Our findings strongly suggest that hyperuricemia is an independent risk factor for CAD. These results corroborate previously reported findings in the literature. One study demonstrated that individuals with CAD had substantially higher uric acid levels than those without CAD (7.35±1.61 mg/dL vs. 4.08±0.83 mg/dL, $P<0.001$) (20). Another study also reported a statistically significant difference in the mean of uric acid levels between patients with and without CAD (358.23±71.11 µmol/L vs. 251.32±54.92 µmol/L, respectively, $P<0.001$) (21). Conversely, Matsumoto et al (22) found no association between uric acid levels and CAD severity.

Our study's findings contradict those from the existing literature (23,24), demonstrating a higher prevalence and severity of CAD in women compared to men. While the association between hyperuricemia and CAD according to gender remains a contested topic, our results are in line with those of an Iranian study, reporting an independent association between hyperuricemia and a trend toward more severe CAD in men but not in women (25). Furthermore, elevated SUA has been shown to be associated with the presence and severity of CAD in both men and women to an equal degree (26).

Our findings revealed a consistent age-related increase in SUA levels, with a noticeable rise starting during puberty in men. Conversely, women exhibited relatively stable SUA levels until around 50 years old, followed by a

steep increase after menopause (27). This gender disparity is likely attributed to the diminishing uricosuric effect of estrogens (28), which have been shown to downregulate protein levels of the urate reabsorptive transporters Urat1 and Glut9 and the urate efflux transporter Abcg2 (29). Similar findings were reported in Western population-based studies from Ireland (30), Taiwan (31), and a study exclusively for women in the United States (32). However, these factors were not found to be significant in our study.

The coronary angiography data revealed a predominance of triple-vessel disease (21.3%), but no correlation was observed between uric acid levels and the number of affected vessels. Our findings corroborate the results of several other studies. An observational study involving 607 premenopausal women (33) confirmed that patients with higher SUA levels exhibited an increased prevalence of multi-vessel disease. Another study exploring SUA levels and premature CAD (<45 years of age) found that SUA levels exceeding 8 mg/dL were predictive of an elevated risk of three-vessel disease (OR: 2.345, 95% CI: 1.335–4.119), independent of traditional cardiovascular risk factors (34). Duran et al (35) concluded that patients with hyperuricemia had a higher number of diseased vessels. They further indicated that SUA levels were significantly associated with the number of diseased vessels, and SUA was an independent risk factor for multi-vessel disease.

Limitations

This study's limitations included the one-time measurement of SUA levels and the restricted sample size. Additionally, the study's focus on patients undergoing coronary angiography at a single center limits its generalizability to the broader population. Further research could benefit from longitudinal patient follow-ups to assess prognostic implications and investigate the influence of varying uric acid levels.

Conclusion

Overall, hyperuricemia in patients with conventional cardiovascular risk factors may be associated with more severe CAD and an elevated overall cardiovascular risk. Therefore, it is recommended that hyperuricemia be considered when assessing cardiovascular risk in CAD patients. Early identification of high-risk CAD patients could facilitate more intensive management of modifiable cardiovascular risk factors and more frequent diagnostic evaluations in clinical practice.

Acknowledgments

The authors would like to express their gratitude to the Clinical Research Development Unit of Imam Khomeini Hospital, Urmia University of Medical Sciences, for English editing.

Authors' Contribution

Conceptualization, data analysis and writing the original draft, Supervision: Mojgan Hajahmadipourrafsanjan; Methodology: Alireza Rostamzadeh;Investigation and Data collection: Venus ShahabiRabari; Review and editing: Mojgan Hajahmadi Pourrafsanjani, Alireza Rostamzadeh, Venus Shahabi Rabari, Fatemeh Jahangiri.

Competing Interests

The authors report there are no competing interests to declare.

Ethical Approval

This research, including human subjects, complied with all relevant national regulations and institutional policies and is in accordance with the tenets of the Helsinki Declaration (as amended in 2013). In addition, it has been approved by the Ethics Committee of Urmia University of Medical Sciences (with code IR.UMSU.REC.1395.170).

Funding

This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Xu S, Liu L, Yin G, Mohammed AQ, Lv X, Feng C, et al. Prognostic significance of uric acid in patients with obstructive and nonobstructive coronary artery disease undergoing D-SPECT. Clin Interv Aging. 2021;16:1955-65. doi: 10.2147/cia.S339600.
2. Sun HJ, Wu ZY, Nie XW, Bian JS. Role of endothelial dysfunction in cardiovascular diseases: the link between inflammation and hydrogen sulfide. Front Pharmacol. 2019;10:1568. doi: 10.3389/fphar.2019.01568.
3. Virdis A, Masi S, Casiglia E, Tikhonoff V, Cicero AF, Ungar A, et al. Identification of the uric acid thresholds predicting an increased total and cardiovascular mortality over 20 years. Hypertension. 2020;75(2):302-8. doi: 10.1161/hypertensionaha.119.13643.
4. Jayachandran M, Qu S. Harnessing hyperuricemia to atherosclerosis and understanding its mechanistic dependence. Med Res Rev. 2021;41(1):616-29. doi: 10.1002/med.21742.
5. Kivity S, Kopel E, Maor E, Abu-Bachar F, Segev S, Sidi Y, et al. Association of serum uric acid and cardiovascular disease in healthy adults. Am J Cardiol. 2013;111(8):1146-51. doi: 10.1016/j.amjcard.2012.12.034.
6. Wang R, Song Y, Yan Y, Ding Z. Elevated serum uric acid and risk of cardiovascular or all-cause mortality in people with suspected or definite coronary artery disease: a meta-analysis. Atherosclerosis. 2016;254:193-9. doi: 10.1016/j.atherosclerosis.2016.10.006.
7. Ndrepepa G. Uric acid and cardiovascular disease. Clin Chim Acta. 2018;484:150-63. doi: 10.1016/j.cca.2018.05.046.
8. Cheong E, Ryu S, Lee JY, Lee SH, Sung JW, Cho DS, et al. Association between serum uric acid and cardiovascular mortality and all-cause mortality: a cohort study. J Hypertens. 2017;35 Suppl 1:S3-9. doi: 10.1097/hjh.0000000000001330.
9. Borghi C, Cicero AFG. Serum uric acid and cardiometabolic disease: another brick in the wall? Hypertension. 2017;69(6):1011-3. doi: 10.1161/hypertensionaha.117.09081.
10. 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):759-66. doi: 10.1136/heartjnl-2012-302535.
11. Cabac-Pogorevici I, Muk B, Rustamova Y, Kalogeropoulos A, Tzeis S, Vardas P. Ischaemic cardiomyopathy. Pathophysiological insights, diagnostic management and the roles of revascularisation and device treatment. Gaps and dilemmas in the era of advanced technology. Eur J Heart Fail.

2020;22(5):789-99. doi: 10.1002/ejhf.1747.
12. Kunadian V, Chieffo A, Camici PG, Berry C, Escaned J, Maas A, et al. An EAPCI expert consensus document on ischaemia with non-obstructive coronary arteries in collaboration with European Society of Cardiology Working Group on Coronary Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group. Eur Heart J. 2020;41(37):3504-20. doi: 10.1093/eurheartj/ehaa503.
13. Sun Y, Zhang H, Tian W, Shi L, Chen L, Li J, et al. Association between serum uric acid levels and coronary artery disease in different age and gender: a cross-sectional study. Aging Clin Exp Res. 2019;31(12):1783-90. doi: 10.1007/s40520-019-01137-2.
14. Ehsan Qureshi A, Hameed S, Noeman A. Relationship of serum uric Acid level and angiographic severity of coronary artery disease in male patients with acute coronary syndrome. Pak J Med Sci. 2013;29(5):1137-41. doi: 10.12669/pjms.295.4029.
15. Rathmann W, Funkhouser E, Dyer AR, Roseman JM. Relations of hyperuricemia with the various components of the insulin resistance syndrome in young black and white adults: the CARDIA study. Coronary Artery Risk Development in Young Adults. Ann Epidemiol. 1998;8(4):250-61. doi: 10.1016/s1047-2797(97)00204-4.
16. Hamaguchi S, Furumoto T, Tsuchihashi-Makaya M, Goto K, Goto D, Yokota T, et al. Hyperuricemia predicts adverse outcomes in patients with heart failure. Int J Cardiol. 2011;151(2):143-7. doi: 10.1016/j.ijcard.2010.05.002.
17. Al-kadumi AS, Abdulsattar JO, Nabhan KJ. Colorimetric determination of uric acid in live samples. Indian J Forensic Med Toxicol. 2020;14(2):1120-7.
18. Roman YM. The role of uric acid in human health: insights from the uricase gene. J Pers Med. 2023;13(9):1409. doi: 10.3390/jpm13091409.
19. Luo Y, Wu Q, Meng R, Lian F, Jiang C, Hu M, et al. Associations of serum uric acid with cardiovascular disease risk factors: a retrospective cohort study in southeastern China. BMJ Open. 2023;13(9):e073930. doi: 10.1136/bmjopen-2023-073930.
20. Kumbhalkar S, Deotale R. Association between serum uric acid level with presence and severity of coronary artery disease. J Assoc Physicians India. 2019;67(4):29-32.
21. Akanda MA, Choudhury KN, Ali MZ, Naher S, Islam AS, Ali MI. Serum uric acid and its association with coronary artery disease. Cardiovasc J. 2012;5(1):12-7.
22. Matsumoto I, Moriya S, Kurozumi M, Namba T, Takagi Y. Relationship between serum uric acid levels and the incidence of cardiovascular events after percutaneous coronary intervention. J Cardiol. 2021;78(6):550-7. doi: 10.1016/j.jjcc.2021.08.005.
23. Ekici B, Kütük U, Alhan A, Töre HF. The relationship between serum uric acid levels and angiographic severity of coronary heart disease. Kardiol Pol. 2015;73(7):533-8. doi: 10.5603/KP.a2015.0024.
24. Sayed AI. Gender differences in coronary artery disease, clinical characteristics, and angiographic features in the Jazan region, Saudi Arabia. Cureus. 2022;14(10):e30239. doi: 10.7759/cureus.30239.
25. Goodarzynejad H, Sotoudeh Anvari M, Boroumand MA, Karimi A, Abbasi SH, Davoodi G. Hyperuricemia and the presence and severity of coronary artery disease. Lab Med. 2010;41(1):40-5. doi: 10.1309/lmkdb9pbkzgus20t.
26. Sinan Deveci O, Kabakci G, Okutucu S, Tulumen E, Aksoy H, Baris Kaya E, et al. The association between serum uric acid level and coronary artery disease. Int J Clin Pract. 2010;64(7):900-7. doi: 10.1111/j.1742-1241.2009.02263.x.
27. Zitt E, Fischer A, Lhotta K, Concin H, Nagel G. Sex- and age-specific variations, temporal trends and metabolic determinants of serum uric acid concentrations in a large population-based Austrian cohort. Sci Rep. 2020;10(1):7578. doi: 10.1038/s41598-020-64587-z.
28. Kuo CF, Grainge MJ, Zhang W, Doherty M. Global epidemiology of gout: prevalence, incidence and risk factors. Nat Rev Rheumatol. 2015;11(11):649-62. doi: 10.1038/nrrheum.2015.91.
29. Takiue Y, Hosoyamada M, Kimura M, Saito H. The effect of female hormones upon urate transport systems in the mouse kidney. Nucleosides Nucleotides Nucleic Acids. 2011;30(2):113-9. doi: 10.1080/15257770.2010.551645.
30. Arun Kumar AU, Browne LD, Li X, Adeeb F, Perez-Ruiz F, Fraser AD, et al. Temporal trends in hyperuricaemia in the Irish health system from 2006-2014: a cohort study. PLoS One. 2018;13(5):e0198197. doi: 10.1371/journal.pone.0198197.
31. Chuang SY, Lee SC, Hsieh YT, Pan WH. Trends in hyperuricemia and gout prevalence: Nutrition and Health Survey in Taiwan from 1993-1996 to 2005-2008. Asia Pac J Clin Nutr. 2011;20(2):301-8.
32. Krishnan E, Bennett M, Chen L. Aging, not menopause, is associated with higher prevalence of hyperuricemia among older women. Menopause. 2014;21(11):1211-6. doi: 10.1097/gme.0000000000000230.
33. Zhang JW, He LJ, Cao SJ, Yang Q, Yang SW, Zhou YJ. Association of serum uric acid and coronary artery disease in premenopausal women. PLoS One. 2014;9(9):e106130. doi: 10.1371/journal.pone.0106130.
34. Dai XM, Wei L, Ma LL, Chen HY, Zhang ZJ, Ji ZF, et al. Serum uric acid and its relationship with cardiovascular risk profile in Chinese patients with early-onset coronary artery disease. Clin Rheumatol. 2015;34(9):1605-11. doi: 10.1007/s10067-015-2878-1.
35. Duran M, Kalay N, Akpek M, Orscelik O, Elcik D, Ocak A, et al. High levels of serum uric acid predict severity of coronary artery disease in patients with acute coronary syndrome. Angiology. 2012;63(6):448-52. doi: 10.1177/0003319711426868.