

Association of The Uric Acid-To-High-Density Lipoprotein Cholesterol Ratio with Coronary Artery Disease in Patients Younger Than 45 Years Presenting with Stable Chest Pain

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ABSTRACT

Objective: To investigate the frequency of coronary artery disease in patients younger than 45 years presenting with stable chest pain and then to compare the uric acid to HDL ratio in patients with and without coronary artery disease.

Study Design: Cross-sectional survey.

Place and Duration of Study: Armed Forces Institute of Cardiology & National Institute of Heart Diseases, Rawalpindi, Pakistan, from Jul to Nov 2025.

Methodology: After meeting the selection criteria, a total of 200 patients were enrolled. Patients underwent coronary angiography. Based on the findings, they were categorized into two groups: with coronary artery disease or without coronary artery disease. The angiographic procedure was performed by a single team of cardiologists with assistance from the researcher, under local anesthesia. Blood samples were collected using a 3 cc disposable syringe to assess the uric acid-to-HDL ratio.

Results: In this study, 143(71.5%) were male, 163(81.5%) were hypertensive, and 75(37.5%) were diabetic. Regarding the outcome variable, CAD was detected in 125(62.5%) patients. The median uric acid to HDL ratio was 0.34 (IQR: 0.16) in patients with CAD, compared to 0.08 (IQR: 0.03) in those without CAD ($p<0.001$).

Conclusion: It can be concluded that the frequency of coronary artery disease was 62.5% among patients younger than 45 years presenting with stable chest pain, and the uric acid to HDL ratio showed a significant association with coronary artery disease.

Keywords: Coronary Artery Disease, Uric Acid to HDL Ratio, Younger Patients.

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INTRODUCTION

Globally, coronary artery disease (CAD) is the primary cause of mortality. One of the risk factors for atherosclerosis is hyperlipidemia.¹ In addition to carrying cholesterol from the surrounding tissue to the liver for recycling and preventing the recruitment of monocytes and the production of endothelial adhesion molecules in the artery wall, HDL protects against LDL oxidation.² HDL directly affects monocytes to suppress the inflammatory response. It controls thrombosis, vasomotor activity, and vascular inflammation and possesses antioxidant qualities.³

The last byproduct of purine base metabolism is uric acid. Diabetes mellitus, coronary artery disease, renal disease, and hypertension are all at risk due to elevated uric acid production and decreased excretion.⁴ There are several contributing reasons to elevated blood uric acid levels, including

environmental variables like body mass index and purine-rich diets such as meat, fish, alcohol, and legumes.⁵ Elevated serum uric acid in patients with coronary artery disease results from diuretic use, reduced GFR, hyperinsulinemia, and alcohol consumption.⁶ The ratio of uric acid to HDL is a new emerging parameter in coronary artery disease.⁷ An increased uric acid to HDL ratio can be caused by elevated uric acid levels or decreased HDL levels.⁸ Studies have shown that an elevated uric acid to HDL ratio is associated with coronary artery ectasia and cardiovascular events. An elevated ratio is also associated with poor collateral circulation.⁹

The goal of this research is to investigate the frequency of coronary artery disease in cases younger than 45 years presenting with stable chest pain and then to compare the uric acid to HDL ratio in cases with and without coronary artery disease. The incidence of obesity, dyslipidemia, and hyperuricemia is increasing drastically in the young population due to lifestyle modifications. The literature shows that an increased uric acid to HDL ratio has a significant

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impact on the development of CAD. But limited data have also been reported, as only one study has been done in this regard. Therefore, we have planned this study to confirm whether the ratio is high in the local population. This study not only helps physicians to predict the potential risk of coronary artery disease in asymptomatic patients but also provides an effective way for young doctors to wisely and judiciously utilize baseline investigations in a resource-limited setup.

METHODOLOGY

This cross-sectional survey was conducted at Armed Forces Institute of Cardiology & National Institute of Heart Diseases, Rawalpindi, Pakistan, from Jul to Nov 2025 with approval of the Ethical Review Committee (IERB # 5/23 dated 27 April 2023). The calculated sample size for this study was 200 patients. The confidence interval for this sample size calculation was 95% having 6.5% margin of error. For this calculation, the proportion of coronary artery disease was taken as 68.5% in patients with stable chest pain.¹⁰

Inclusion Criteria: The patients having age ≤ 45 years of age of both genders with stable chest pain already undergoing coronary angiography were fall in inclusion criteria. In this study, stable angina was known as common type of angina or angina pectoris, and is a symptom of myocardial ischemia. Stable angina was characterized by chest uneasiness or angina equivalent that was provoked with exertion and alleviated at rest or with nitroglycerin and < 1 mm rise in ST-segment on electrocardiography.¹⁰

Exclusion Criteria: Patients with unstable angina, STEMI, or NSTEMI (on clinical examination), non-ischemic dilated cardiomyopathy, valvular heart diseases (on medical record), and renal failure (creatinine > 1.8 mg/dl or on dialysis) were fall in exclusion criteria.

Ethical review board approval and informed consent was taken from attendants. Demographic profile, including name, age, gender, obesity (BMI > 30 kg/m²), history of diabetes (HbA1c $> 6.5\%$), hypertension (BP $\geq 140/90$ mmHg), smoking (> 5 pack years), alcoholism (> 20 ml/day), any other addiction, family history of coronary artery disease, life style (sedentary if > 8 sitting hours, active if > 8 hours of body working or doing gym/sports), was noted. Then patients underwent coronary angiography, and the presence of $> 50\%$ plaque formation was assessed. Patients were labeled as having coronary artery disease or without coronary artery disease, and two

groups were formed at this point. Coronary angiography was done by a single cardiologist's team with assistance from a researcher under local anesthesia. Blood samples were taken in a 3cc disposable syringe and were sent to the pathology laboratory of the hospital, and the uric acid-to-HDL ratio was noted. Coronary artery disease was labelled if $> 50\%$ atherosclerotic plaque was present in the vessel lumen detected on coronary angiography. Similarly, the uric acid-to-HDL ratio was assessed by dividing serum uric acid by serum HDL level, and the ratio obtained was noted. A predesigned questionnaire was used to gather the data.

Data analysis was performed in Statistical Package for Social Sciences (SPSS) version-25. Normality of data was checked by the Shapiro-Wilk test. Numeric variables like age, uric acid, HDL level, and uric acid to HDL ratio were presented as median with interquartile range (IQR). Categorical variables like gender, obesity, diabetes, hypertension, smoking, alcoholism, any other addiction, family history of coronary artery disease, artery involved, and lifestyle were presented as frequencies, and percentages were calculated. Median uric acid to HDL ratio was compared in patients with and without CAD by using the Mann-Whitney U test. A p -value ≤ 0.05 was considered significant.

RESULTS

A total of 200 cases were enrolled in this study. The median age was 36.00 (IQR: 10) years, with 143 (71.5%) being male. Obesity was present in 168 (84%) cases, hypertension in 163 (81.5%), and diabetes mellitus in 75 (37.5%). Regarding lifestyle factors, 96 (48%) cases were smokers, 18 (9%) reported alcohol use, and 15 (7.5%) had other addictions. A family history of coronary artery disease (CAD) was observed in 159 (79.5%) cases. A sedentary lifestyle was noted in 126 (63%) cases, while 67 (33.5%) had an active lifestyle. Table-I.

With respect to the outcome variable, CAD was identified in 125 (62.5%) patients. Figure-1.

Among these, left anterior descending (LAD) artery involvement was found in 34 (27.2%), left main stem (LMS) in 44 (35.2%), left circumflex (LCX) in 35 (28%), and right coronary artery (RCA) in 12 (9.6%) patients. In this study, patients with CAD had a median uric acid level of 10.80 (IQR: 4.5) mg/dl, whereas those without CAD had a median uric acid level of 4.60 (IQR: 1.1) mg/dl. This difference was highly significant ($p < 0.001$). Patients with CAD had a

median HDL level of 31.00 (IQR: 9) mg/dl, whereas those without CAD had a median HDL level of 60.00 (IQR: 15) mg/dl. This difference was highly significant ($p<0.001$). In this study, patients with CAD had a median uric acid-to-HDL ratio of 0.34 (IQR: 0.16), whereas those without CAD had a median ratio of 0.08 (IQR: 0.03). This difference was highly significant ($p<0.001$). Table-II.

Table-I: Basic Demographic Parameters of Enrolled Patients (n = 200)

Demographic Parameters		Values
Median Age (Years)		36.00(IQR: 10)
Gender	Male	143(71.5%)
	Female	57(28.5%)
Obese		168(84.0%)
Hypertension		163(81.5%)
Diabetes Mellitus		75(37.5%)
Smoking		96(48.0%)
Alcoholism		18(9.0%)
Any other addiction		15(7.5%)
Family history of Coronary Artery Disease		159(79.5%)
Lifestyle	Active	67(33.5%)
	Sedentary	126(63.0%)
	Gym/Exercise	7(3.5%)

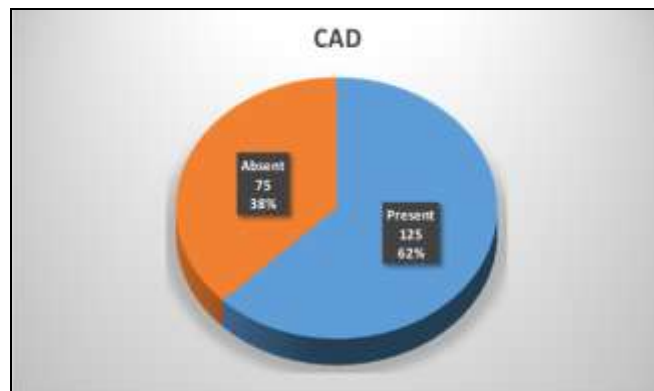


Figure-1: Coronary artery disease detected on angiography (n = 200)

In this research, coronary artery disease (CAD) was noted in 66 cases (67.3%) aged ≤ 35 years, compared to 59 patients (57.8%) aged >35 years ($p=0.165$). Among males, CAD was present in 93 patients (65%), whereas among females it was seen in 32 patients (56.1%) ($p=0.241$). In obese patients, CAD was reported in 107 patients (63.7%), while in non-obese patients it was present in 18 patients (56.2%) ($p=0.426$). Similarly, CAD was identified in 103 hypertensive patients (63.2%) compared to 22 non-hypertensive patients (59.5%) ($p=0.672$). In diabetic patients, CAD was found in 44 cases (58.7%), whereas

in non-diabetics it was present in 81 cases (64.8%) ($p=0.386$). Among smokers, CAD was reported in 64 patients (66.7%), while in non-smokers it was seen in 61 patients (58.7%) ($p=0.242$). With respect to family history, CAD was present in 96 patients (60.4%) without family history, while among those with a family history it was observed in 29 patients (70.7%) ($p=0.222$). Regarding lifestyle, CAD was documented in 83 patients (65.9%) with a sedentary lifestyle, in 38 patients (56.7%) with an active lifestyle, and in 4 patients (57.1%) who reported regular gym/exercise activity ($p=0.335$). Table-III.

Table-II: Angiographic Findings and Laboratory Parameters of Patients with and Without Coronary Artery Disease (n = 200)

Artery Involved	CAD		p-value
	Present n=125	Absent n=75	
LAD	34 (27.2%)	Nil	--
LMS	44 (35.2%)	Nil	
LCX	35 (28%)	Nil	
RCA	12 (9.6%)	Nil	
Uric Acid Level	10.80 (IQR: 4.5)	4.60 (IQR: 1.1)	<0.0001
HDL Level	31.00 (IQR: 9)	60.00 (IQR: 15)	<0.0001
Uric acid to HDL ratio	0.34 (IQR: 0.16)	0.08 (IQR: 0.03)	<0.0001

*LAD - LAD: Left Anterior Descending artery, LMS - Left Main Stem, LCX - Left Circumflex artery, RCA - Right Coronary Artery, HDL-High-density lipoproteins

Table-III: Association of CAD with Age, Gender, Obesity, Comorbid Conditions, and Other Factors (n = 200)

Variables of Study		CAD		Total	p-value
		Present n=125	Absent n=75		
Age Group	≤ 35	66 (67.3%)	32 (32.7%)	98	0.165
	>35	59 (57.8%)	43 (42.2%)	102	
Gender	Male	93 (65.0%)	50 (35.0%)	143	0.241
	Female	32 (56.1%)	25 (43.9%)	57	
Obesity	Obese	107 (63.7%)	61 (36.3%)	168	0.426
	Non-obese	18 (56.2%)	14 (43.8%)	32	
Hypertension	Yes	103 (63.2%)	60 (36.8%)	163	0.672
	No	22 (59.5%)	15 (40.5%)	37	
Diabetes Mellitus	Yes	44 (58.7%)	31 (41.3%)	75	0.386
	No	81 (64.8%)	44 (35.2%)	125	
Smoking	Yes	64 (66.7%)	32 (33.3%)	96	0.242
	No	61 (58.7%)	43 (41.3%)	104	
Alcoholism	Yes	15 (83.3%)	3 (16.7%)	18	0.056
	No	110 (60.4%)	72 (39.6%)	182	
Any other addiction	Yes	11 (73.3%)	4 (26.7%)	15	0.368
	No	114 (61.6%)	71 (38.4%)	185	
Family History of CAD	Present	96 (60.4%)	63 (39.6%)	159	0.222
	Absent	29 (70.7%)	12 (29.3%)	41	
Lifestyle	Active	38 (56.7%)	29 (43.3%)	67	0.335
	Sedentary	83 (65.9%)	43 (34.1%)	126	
	Gym/Exercise	4 (57.1%)	3 (42.9%)	7	

*CAD – Coronary Artery Disease

DISCUSSION

In this study, CAD was detected in 125(62.5%) patients, and the median uric acid to HDL ratio was significantly higher in CAD patients, i.e., 0.34 (IQR:

0.16), as compared to those without CAD, i.e., 0.08 (IQR: 0.03).

The emergence of CAD in younger patients, especially those with acute coronary syndrome (ACS), presents unique challenges and requires a thorough understanding of its patterns and underlying factors. Historically, CAD in the young was often linked to congenital anomalies or rare genetic disorders.¹¹ Recent data indicated a complex mix of genetic predisposition, lifestyle factors, and environmental influences, leading to a notable increase in CAD incidence in younger populations. The impact of CAD in the young is extensive, affecting not just individual health but also imposing societal and economic burdens.¹²

A study by Roth *et al.*, indicates that hyperuricaemia is linked to cardiovascular disease (CVD) due to confounding variables such as obesity, hypertension, diuretic usage, and insulin resistance; the precise significance of uric acid in predicting cardiovascular mortality is still up for discussion.¹³ Globally, cardiovascular disease (CVD) is now one of the main causes of complications and death, which has also been reported by Enomoto *et al.*¹⁴

Rehman *et al.*, found that the majority of patients were men, making up about 65% of the group. Twenty percent of research participants had a family history of CAD, and forty percent had a documented history of smoking. Nearly 50% of the patients had hypertension, which was the most common risk factor.¹⁵ Hyperlipidemia (30%) and diabetes (20%) were next in line.⁷ Balouch *et al.*, demonstrated in their study that the majority of patients (79.1%) had a diagnosis of ST-elevation myocardial infarction (STEMI), with anterior wall MI being the most prevalent form (57.3%). Single vascular diseases (SVD) affected 70% of the patients, with the left anterior descending artery (LAD) being the most frequently affected vessel (53.6%). 6.4% of patients had non-obstructive CAD, while nine (4.1%) had severe left main disease.¹²

Anwar *et al.*, conducted a study and found that, out of 894 patients who underwent angiography, 612 (68.5%) had critical coronary artery disease.¹⁶ They also observed that the uric acid-to-HDL ratio (0.2016 ± 0.094 vs. 0.1461 ± 0.05 , $p < 0.01$) was significantly higher in the case group. Thus, an easy-to-use metric for predicting the existence, severity, and extent of coronary artery disease prior to invasive examination is the uric acid to HDL ratio.¹⁷

In terms of secondary outcomes of the study, similar findings were observed by Kawabara *et al.*, who showed that ST-elevation myocardial infarction (STEMI) was diagnosed in the majority of patients (79.1%), with anterior wall MI being the most common kind (57.3%).¹⁸ Seventy percent of the patients had single vascular disorders (SVD), with the left anterior descending artery (LAD) being the most often impacted vessel (53.6%). Nine patients (4.1%) had severe left main disease, and 6.4% had non-obstructive CAD. Chang *et al.*, also demonstrated that the presence of atherogenic dyslipidemia in CAD patients might be associated with serum uric acid, TC/HDL, and LDL/HDL ratios as objective indicators.¹⁹ Another study by Li *et al.*, further showed that individuals with hemodynamically severe coronary lesions have a substantially elevated uric acid to high-density lipoprotein cholesterol ratio. Serum uric acid levels and the risk of CVD have been linked in the current study.²⁰

These findings highlight the potential relevance of the uric acid-to-high-density lipoprotein cholesterol ratio as an accessible marker associated with coronary artery disease in younger patients presenting with stable chest pain.

LIMITATIONS OF STUDY

The single-center design and relatively small sample size may limit the generalizability of the findings. The observational design precludes establishing causality, while potential confounding by other cardiovascular risk factors cannot be excluded. Larger multicenter prospective studies are recommended to validate these findings.

CONCLUSION

Coronary artery disease was frequently observed among patients younger than 45 years presenting with stable chest pain, with a prevalence of 62.5% in the studied population. The uric acid-to-high-density lipoprotein cholesterol ratio demonstrated a statistically significant association with coronary artery disease, suggesting its potential utility as an accessible biochemical marker for identifying younger patients at increased likelihood of coronary artery disease. Further prospective, multicenter studies are warranted to validate these findings and determine the clinical applicability of this ratio in the early risk stratification of coronary artery disease in younger adults.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AS & AAC: Data acquisition, data analysis, critical review, approval of the final version to be published.

UI & IA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

JA & SK: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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