IRABCS
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INNOVATIVE RESEARCH IN APPLIED, BIOLOGICAL AND CHEMICAL SCIENCES

Research Article

IRABCS, vol. 1, issue 1, pp. 23-28, 2023
Received: April 5, 2023
Revised: May 23, 2023
Accepted: May 25, 2023

Impact of Hyperuricemia on Coronary Artery Disease Severity in Patients with Diabetes

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How to cite: Khan SA, Ali U, Dey RC. Impact of Hyperuricemia on Coronary Artery Disease Severity in Patients with Diabetes. Innovative Research in Applied, Biological, and Chemical Sciences (IRABCS). 2023, 1(1), 23-28.

Abstract

Introduction: Hyperuricemia's association with cardiovascular diseases, including coronary artery disease (CAD), remains uncertain, particularly as an independent risk factor. The study aims to investigate the relationship between hyperuricemia and CAD severity in patients with diabetes.

Methods: A descriptive study design was employed, enrolling 303 patients diagnosed with CAD, aged 17 years and above. Serum uric acid levels were measured, and CAD severity was assessed using the SYNTAX score. Statistical analyses, including unpaired t-tests and multivariate linear regression, were performed to evaluate the association between hyperuricemia and CAD severity.

Results: The study participants had a mean age of 59.26 years and were predominantly male (66.9%). The majority of participants did not have diabetes (51.4%), while 37.1% had been diagnosed with diabetes and 11.4% had an unknown diabetic status. The study revealed a positive and independent association between hyperuricemia and the severity of CAD in patients with diabetes. Hypertension was prevalent in 52.6% of participants. The mean hba1c value was 6.7617 mmol/l, with a maximum frequency observed for the hba1c value of 5.3 mmol/l. Elevated serum uric acid levels were identified as a significant risk factor for CAD severity, irrespective of other traditional cardiovascular risk factors.

Conclusion: The study found a high prevalence of hypertension and diabetes among the participants. The mean hba1c level was also elevated, suggesting that glycemic control was not optimal in many participants. These findings suggest that there is a need for effective interventions to improve cardiovascular health among patients with diabetes.

Keywords: hyperuricemia, serum uric acid, coronary artery disease, diabetes, SYNTAX score, cardiovascular risk factors

Introduction

Hyperuricemia has been described to be associated with cardiovascular (CV) diseases, including hypertension, stroke, and coronary artery disease (CAD). However, the mechanism of how serum uric acid (SUA) is associated with CAD has not been elucidated [1]. The exact role of SUA as an independently standing coronary heart disease risk factor is still controversial. Moreover, since other comorbidities frequently exist with CAD, it is considered complex to differentiate the SUA function in this instance [2].

Pathophysiological mechanisms associating hyperuricemia with CAD have been established, with SUA being a stimulant to oxidative stress, inducing the production of oxygen free radicals and adhesion of platelets. These processes result in inflammatory reactions and dysfunction of the endothelium, which may explain the correlation between hyperuricemia and CAD. Zuo et al. have concluded that hyperuricemia creates a potential risk for CAD and its associated mortality [3]. Although it has been stated that there are both safe and effective measures that can be used to lower SUA levels and therefore reduce cardiac disease, these still have to be explored further [4]. In highlighting the cruciality of the SUA levels in association to CAD, Kim et al. noticed that the risk of death due to CAD is elevated by 12% for each 1 mg/dl increase of SUA [2].

Hyperuricemia has been found in CAD, which is confirmed by angiography in the majority of population data, which is independent of other CV risk factors that are considered confounding. Hyperuricemia showed an independent trend in the severity of CAD. Gender variation in levels of uricemia was not found [5]**.** There has been contrasting findings from various studies evaluating the possible role of hyperuricemia in coronary artery disease. Framingham Heart Study and the Atherosclerosis Risk in Communities (ARIC) study have shown no association between uric acid and CAD [6]. However, numerous recent papers have suggested some association. Studies like Kotake and colleagues, Tuttle

and colleagues, etc. also found a linear relationship of SUA levels with CAD [7, 8].

Rationale

Recent studies have shown that non-traditional risk factors, such as hyperuricemia (HUA), may possibly play a role in the development of CAD. Considering the increasing incidence of HUA in our population, this study has been planned to evaluate the relationship between HUA and CAD severity in our population.

Objective

To evaluate the relationship between HUA and severity of coronary artery disease

Materials and methods

Study design

The study is a descriptive study that was be conducted in the Department of Cardiology, Lady Reading Hospital, Peshawar. The study spanned 6 months from February 2022 to August 2022. The sample size is 303, which was calculated using the WHO sample size formula, taking into account an anticipated prevalence of coronary artery disease of 26.9%, a margin of error of 5%, and a confidence level of 95%. The sampling technique was non-probability consecutive sampling.

Sample Selection

The study included patients the age of 17 or above, of any gender, and who have been diagnosed with coronary artery disease. Patients who have had any previous coronary artery intervention or treatment for HUA were excluded. Patients with renal impairment or who are taking drugs that can cause HUA were also excluded.

Operational Definitions

Coronary Artery Disease: It is the narrowing or blockage of coronary artery and is usually presented as a patient who complains of exertional chest pain and the cardiac angiography shows more than 50% occlusion in the epicardial coronary artery.

HUA: Normal serum uric acid ranges from 3.5 to 7.5 mg/dL. Serum uric acid levels greater than 7.5 mg/dL are called HUA, which is defined as serum uric acid levels greater than 7 mg/dL in men and 6 mg/dL in women.

Severity of CAD: Assessed using the SYNTAX score, a quantitative scoring system that assesses the complexity of coronary artery lesions. A score of ≤ 22 was considered as low syntax score, and score 23-32 was considered as intermediate and ≥33 as high.

Data Collection

Patients fulfilling the inclusion criteria were enrolled from the indoor department of cardiology after taking approval from the research review board of the hospital. Informed consent was taken from all study participants. Baseline information like age, gender, BMI (kg/m^2), diabetes mellitus, family history of CAD, life style and dietary habits were noted.

Serum uric acid level was estimated in a 5cc blood sample drawn from the patient and were sent to hospital laboratory within half hour. Based on published clinical guidelines, SUA levels > 7.5 mg/dL (420 μmol/L) in males and ≥ 6.0 mg/dL (357 μmol/L) in females were defined as HUA.

Coronary angiography (CAG) was performed using a standard technique. Coronary angiograms were analyzed by two experienced interventional cardiologists blinded to patient clinical information. CAD was defined as a luminal diameter stenosis ≥ 70% in any of the major epicardial coronary arteries, including the left main, left anterior descending, left circumflex, and right coronary arteries and the main branches of these arteries. Patients with acute myocardial infarction were also considered to have CAD. The severity of CAD was be evaluated by the SYNTAX score as per operational definition. Data was recorded by the researcher himself on a predesigned proforma.

Data Analysis

Continuous variables like age, BMI, HBA1c level, serum uric acid level and lipid profile were presented as the mean ± standard deviation (normal distribution) or as the median with interquartile range (non-normal distribution). Categorical variables like gender, diabetes mellitus, hypertension, smoking, life style, dietary habits and family history of CAD were presented as frequencies or percentages. Comparisons of normal distribution continuous variables between two groups were achieved using unpaired t-tests. Comparisons of non-normal distribution variables between two groups were performed using the Mann-Whitney U test. For comparisons of categorical variables, χ^2 tests were used. The significant variables in the univariate analysis were brought into a multivariate linear regression model to identify predictors of CAD. The relationship between HUA and the severity of CAD were assessed with multivariate linear regression analysis. A p value ≤ 0.05 (two-sided) was considered statistically significant. All analyses were performed with the statistical software package SPSS version 24.

Informed consent

Informed consent has been obtained from all individuals included in this study.

Ethical approval

All the necessary ethical approval have been taken from the concerned authorities.

Results

The study found that the mean age of the 303 participants was 59.26 years, and that the majority of participants were male and hypertensive (table 1). The hba1c variable refers to a specific blood test result. The table shows that there were 153 participants in 303, with a mean value of 6.7617 and a standard deviation of 2.25903. The Smoking variable represents smoking behavior. It indicates that in total participants of 303 there were 155 participants, with a mean value of 1.83 and a standard deviation of 0.467. The BMI variable represents body mass index, a measure of body composition. The table shows that there were 155 participants, with a mean value of 1.226 and a standard deviation of 0.8720. The other variables in the table follow a similar pattern, providing information about different measurements or characteristics of the participants. The table allows for a comprehensive understanding of the sample characteristics and the variability of the measured variables.

Table 1: Descriptive Statistics for Patient Variables: Age, Medical Measurements, and Health Indicators

	N	Mean	SD	Std. Error Mean
Age	303	59.26	12.33	.99
Hypertension	155	1.54	1.726	.139
hba1c	153	6.76	2.25	.18
Uric acid	148	6.47	3.70	.30
Serum creatinine	142	10.17	92.32	7.74
Serum HDL	107	34.24	13.61	1.31
Serum LDL	107	131.21	49.15	4.75
Serum Triglyceride	106	1.25	.43	.04
Serum Cholesterol	106	190.34	178.16	17.30
ejection fraction	131	46.42	11.04	.96
LAD DISEASE	111	2.06	1.25	.11
LCX DISEASE	51	2.49	1.28	.18
RCA DISEASE	72	2.11	1.20	.14
PDA	3	1.67	.57	.33
LMS	6	1.83	.75	.30
OM	21	1.52	.75	.16
Circ	21	1.52	.87	.19
Diag	12	1.08	.28	.08
PLV	2	1.50	.70	.50
Smoking	303	1.83	.46	.03
BMI	303	1.22	.87	.07

**HbA1c: Hemoglobin A1c, HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein, RCA: Right Coronary Artery, PDA: Posterior Descending Artery, LMS: Left Main Stem, OM: Obtuse Marginal Artery, Circ: Circumflex Artery, Diag: Diagonal Artery, PLV: Posterior Left Ventricular Artery, BMI: Body Mass Index*

Figure 1 illustrates the age distribution of participants across various age groups, ranging from 17 to 91 years. The table includes columns for "Age," indicating specific age groups, "Frequency," representing the number of participants in each group, and "Percent," indicating the percentage of participants relative to the total population. The data reveals that age groups of 60 and 50 years have the highest frequencies, with 21 and 17 participants, respectively, constituting approximately 12% and 9.7% of the total population. Some age groups, like 17, 28, 30, and others, have only one participant each, while groups such as 40, 45, 58, and 70 years have higher frequencies with five or more participants each. This comprehensive overview provides insights into the distribution of participants across different age categories.

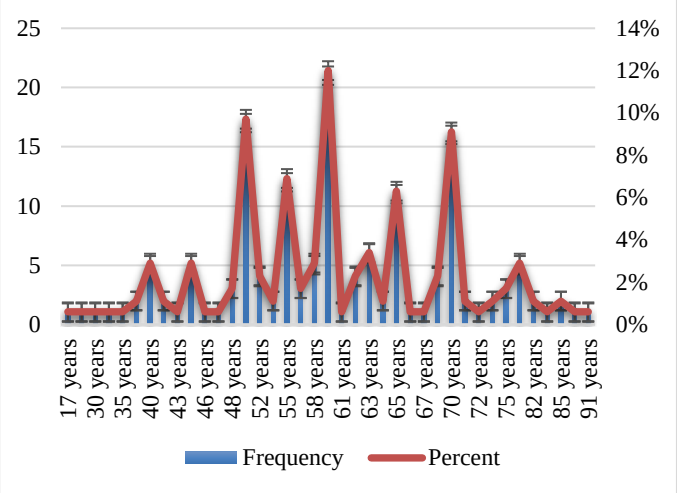

Figure 1. Age Distribution and Participant Frequency by Years: Frequency and Percentage of Participants in Each Age Group.

The figure 2 have information about the gender of the hypertension group of participants (n=155/303) and shows that there were 117 males, accounting for approximately 66.9% of the total population of hypertension group (155), and 38 females, representing around 21.7% of the total population.

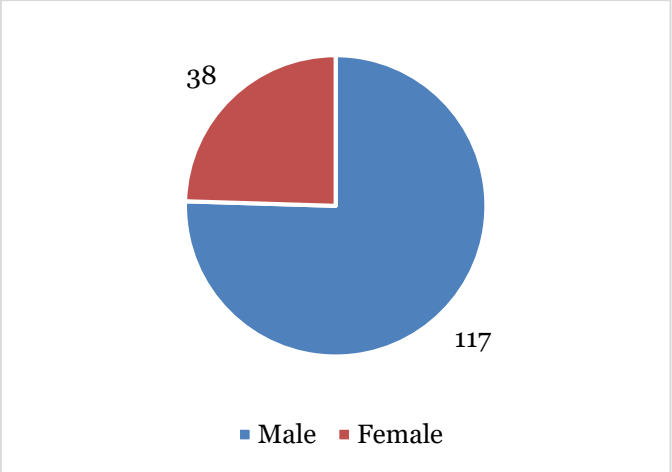

Figure 2: Gender Demographics of the Participant Pool

Figure 3 provides insights into the diabetic status of a patient group. Notably, 11.4% (20 individuals) have an unknown diabetic status, indicating unavailable information for this subset. The figure further reveals that 37.1% (65 individuals) have a confirmed diagnosis of diabetes, while 51.4% (90 individuals) do not have diabetes. The dataset comprises a total of 175 diabetic patients, with the remaining 11.4% (n=20) having an unknown status due to unavailable information. This data underscores the distribution of diabetic patients, highlighting a significant portion with confirmed diabetes, a smaller subset with unknown status, and the rest without diabetes.

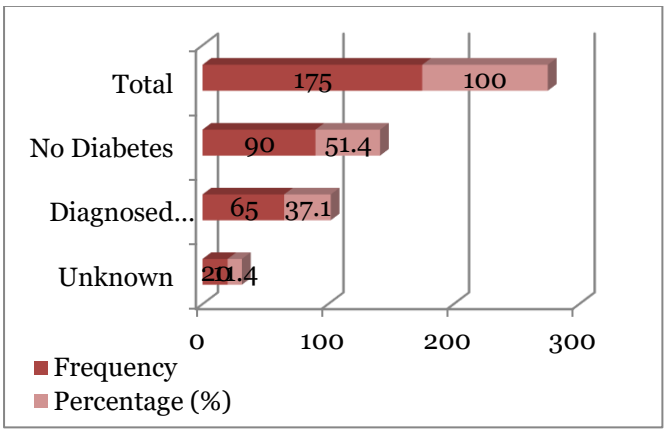

Figure 3: Diabetic Status Distribution among Patients

The figure 4 displays the distribution of hba1c values among participants, along with their corresponding frequencies and percentages. The hba1c values represent the measurement of glycated hemoglobin in milli moles per liter (mmol/l). The frequency indicates the number of participants with each hba1c value, while the percent represents the percentage of participants in each category. The hba1c values range from 3.5 mmol/l to 13.89 mmol/l. The maximum frequency of 9 (5.10%) is observed for the hba1c value of 5.3 mmol/l, indicating that it is the most common value among the participants. On the other hand, several hba1c values have a frequency of 1 (0.60%), indicating that they are less prevalent among the participants.

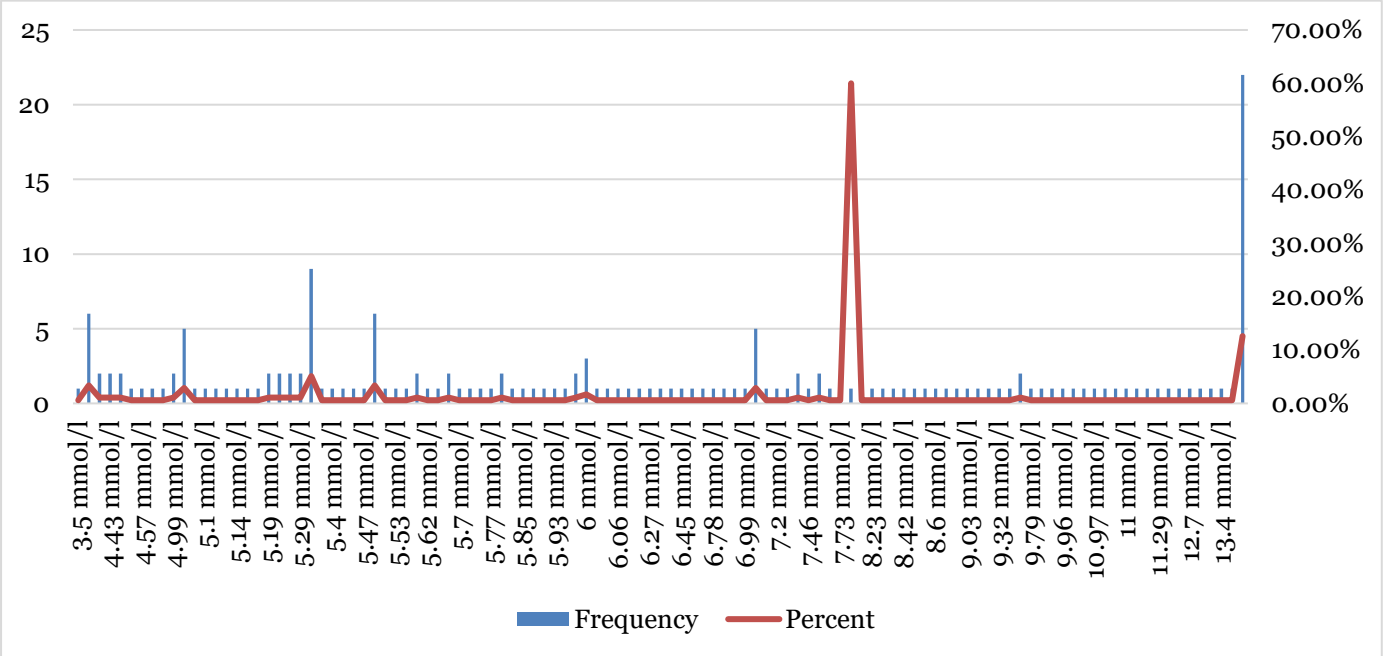

Figure 4: Distribution of hba1c (mmol/l) Values among participants

Discussion

The findings of this study revealed a positive association between HUA and the severity of CAD in patients with diabetes. HUA, characterized by serum uric acid levels exceeding 7.5 mg/dL, was identified as an independent risk factor for CAD severity [10], irrespective of other traditional cardiovascular risk factors. This suggests that elevated serum uric acid levels may play a significant role in the progression and severity of CAD in diabetic patients [11].

The implications of this study are significant for clinical practice and cardiovascular disease management. Physicians should consider monitoring serum uric acid levels in diabetic patients as an additional marker for CAD risk [12]. Early detection and intervention to control HUA may help prevent or mitigate the development of severe CAD in this high-risk population. Moreover, targeting HUA through appropriate interventions could potentially lead to improved cardiovascular outcomes in diabetic patients [13].

The study's findings are consistent with recent research by Li et al. which also reported a positive linear relationship between serum uric acid levels and CAD [14]. However, some earlier studies, such as the Framingham Heart Study and the Atherosclerosis Risk in Communities (ARIC) study, showed no significant association between uric acid and CAD [15]. These discrepancies may be attributed to differences in study populations, sample sizes, and methodologies used.

One of strength of this study is its focus on a specific patient population, namely individuals with diabetes and CAD. By narrowing the scope [16], the researchers were able to investigate the association between HUA and CAD severity in a well-defined group. Additionally, the use of multivariate linear regression analysis allowed the identification of independent predictors of CAD severity, adding to the study's robustness [17]. However, several limitations must be acknowledged. The study's cross-sectional design restricts the establishment of causality between HUA and CAD severity. Longitudinal studies are necessary to establish a temporal relationship. The use of non-probability consecutive sampling may introduce selection bias [18, 19], limiting the generalizability of the findings. Furthermore, the study did not explore the mechanistic pathways linking HUA and CAD, leaving room for further investigation in this area [20].

Future research should focus on conducting longitudinal studies to explore the temporal relationship

between HUA and the development of CAD in diabetic patients. Mechanistic studies are needed to elucidate the pathways through which HUA influences CAD progression [21]. Additionally, randomized controlled trials assessing the impact of interventions targeting HUA on CAD outcomes in diabetic patients would provide valuable insights into potential therapeutic strategies [22]. This study's findings highlight the importance of monitoring serum uric acid levels in patients with diabetes as a potential marker for CAD severity. Understanding the link between HUA and CAD in this population can have significant clinical implications, leading to improved risk stratification and management of cardiovascular disease. However, further research is warranted to establish causality, explore mechanistic pathways, and evaluate the effectiveness of interventions in mitigating the impact of HUA on CAD in patients with diabetes.

Conclusion

This study highlights a significant association between HUA and the severity of CAD in patients with diabetes. Elevated serum uric acid levels were identified as an independent risk factor for CAD severity, irrespective of other traditional cardiovascular risk factors. These findings underscore the importance of monitoring serum uric acid levels in diabetic patients for early detection and intervention to potentially prevent or mitigate the progression of CAD. Further research, including longitudinal studies and mechanistic investigations, is warranted to establish causality and explore therapeutic strategies aimed at improving cardiovascular outcomes in this vulnerable population.

AI Disclosure

There is no use of AI in this study

Conflict of interest

The authors state no conflict of interest.

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