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A STUDY OF HYPERURICACIDEMIA AND THE PRESENCE AND SEVERITY OF ACUTE CORONARY SYNDROME IN INDEX MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTER, INDORE (M.P.)

Dr. B. Khanam[1], Dr. M. Imran Khan[2], Dr. Ajay Kumar Singh[3], Dr. Sumit Solanki[4], Dr. S.M. Holkar[5]

Associate Professor [1], PG Resident [2], Assistant Professor [3],PG Resident[4], Professor[5],
Department of General Medicine, Index Medical College, Hospital and Research Center, Indore (M.P.) .

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Corresponding author: Dr. Ajay Kumar Singh
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Abstract

Background: Few studies have assessed the relation of hyperuricacidemia with the acute coronary syndrome (ACS). This study investigated the association between high uric acid levels with the presence and severity of ACS.

Methods: Three hundred and seventy patients having angiographic evidence of atherosclerosis (CAD + case group) compared to 170 patients with no luminal stenosis (n=110) or with <50% luminal stenosis (n=60) at coronary angiography (CAD – control group).

Results: The mean age of the patients was 60 ± 10 years (317 men, 58.7%). Hyperuricacidemia was more likely associated with a trend toward higher vessel scores, indicating a more severe CAD (adjusted OR=1.51, 95% CI=1.09-2.09; P=0.005) in the whole population. A comparison of sex-specific values showed a significant association existed only in men.

Conclusions: Asymptomatic hyperuricacidemia may be associated with the presence and severity of ACS.

Keywords: Hyperuricacidemia, Severity & Acute Coronary Syndrome.

Introduction

The role of serum uric acid in the development of cardiovascular disease has been debated for over 50 years.[1] In some studies, uric acid was found to be an independent risk factor for development of cardiovascular and diseases.[2,3,4] Hyperuricacidemia was postulated to be a risk factor for acute coronary syndrome (ACS).

Aim and Objective

The present study was undertaken to determine whether raised serum uric acid levels

are associated with presence and severity of ACS.

Study Designed: This is an observational study.

Materials and Methods:

After obtaining Institutional Ethical Committee approval and written informed consent from patients, this hospital based on observational study was conducted in 550 cases of either genders having age 50-70 years from period to 1st July 2019 to 31st December 2019 with symptoms related to ACS patients.

All the patients were divided into two groups according to gender.

Exclusion Criteria:

Exclusion criteria were presence of heart failure; malignancy; pregnancy; impaired renal function (serum Cr levels >1.5 mg/dL); gout symptoms; diuretic, antioxidants, or alcohol use as well as taking medications targeted to lower uric acid levels; and antiplatelets and liver disease.

Patients were also excluded if they had a prior coronary revascularization, valvualar heart disease and cardiomyopathies.

Inclusion Criteria

Patients above 50 to 70 years of age of both the genders are included.

Patients consuming tobacco (either smoking, chewing) ,diabetic, hypertensive, family history of ACS and hyperuricacidemia.

Definition of Cad Risk Factors

Patients who currently smoked any kind of tobacco or who had quit smoking less than 1 month prior were considered current smokers.

Hyperlipidemia was defined as plasma total cholesterol level ≥200 mg/dL, LDL-cholesterol level ≥130 mg/dL, triglyceride level ≥200 mg/dL, and HDL-cholesterol level ≤40 mg/dL, or being on lipid lowering drugs at the time of the study with normal values.

Patients were considered to have hypertension if they were diagnosed for the 1st time with arterial pressure of 140/90 mmHg or were being treated with antihypertensive medications.

Patients were considered to have diabetes if they were taking insulin or oral hypoglycemic agents or detected for the 1st time having fasting blood glucose >126 mg/dL .

A positive family history was defined as CAD in a parent or sibling noted under the age of 55 for men and 60 for women in form of sudden cardiac death, cardiac arrest and/on medication for coronary artery disease and surgical intervention for the same.

Patients with hyperuricacidemia were defined as serum uric acid concentrations ≥7.0 mg/dL in men and ≥6.0 mg/dL in women.

The presence and severity of ACS was determined by ECG/2D- ECHO/TROPRNIN I/ CPKMB/LDL and heart failure, malignant dysarrythmias and death after admission into hospital.

ECG - extensive area involved, malignant dysarrythmias.

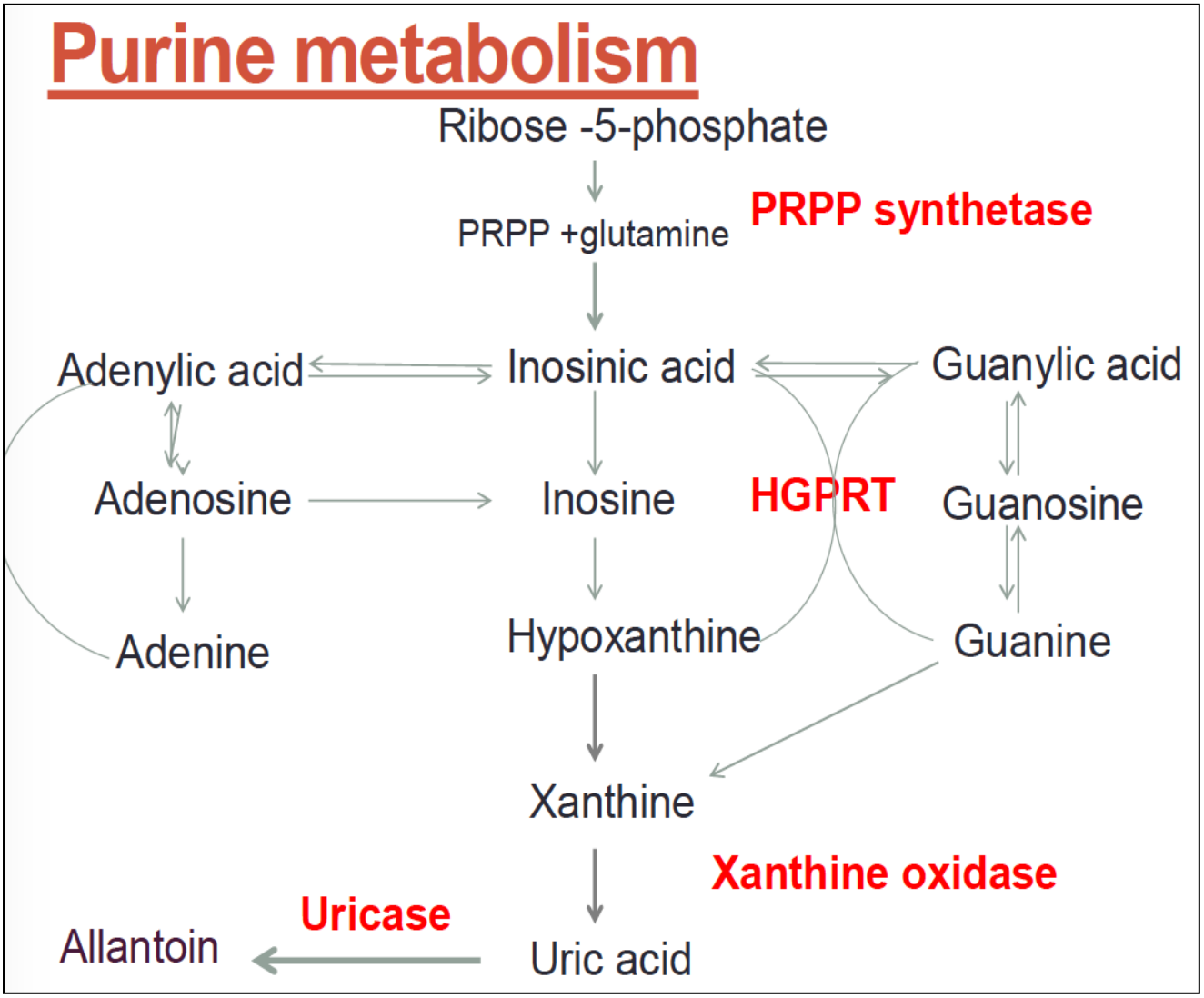
2D ECHO - area of akinesia/dyskinesia and systolic/ diastolic dysfunction grade 3.

Introduction

The aim of this study was to evaluate a number of risk factors of ACS including hyperuric-acidemia to determine the independent predictors of ACS in male and female patients and to explore whether there was a possible association between hyperuricacidemia and the severity of ACS in total and in men and women separately when adjusting for various confounding factors.

The study protocol was approved by the local ethical committee. Written informed consent was obtained from all patients who approved the collection of blood samples for scientific research.

Uric acid, an end product of purine metabolism, was first discovered in 1776.



The mechanism by which uric acid may play a pathogenic role in cardiovascular disease is unclear.

Biochemical Analysis

Peripheral venous blood specimens were collected from an antecubital vein after 10 hours of overnight fasting and at time of admission if fasting hours are more than 6.

Biochemical measurements such as lipid profile and fasting blood sugar (FBS) levels were completed by an auto analyzer from Pathology department and especially for uric acid.

The uric acid concentration was measured in milligrams per deciliter by an enzymatic colorimetric method using uricase and peroxidase from department of Central Pathology**.**

Statistical Method

Results were reported as mean ± standard deviation (SD) for quantitative variables, and categorical variables were presented as absolute frequencies and percentages. Continuous variables were compared by using one-way analysis of variance (ANOVA)

The association between independent predictors with ACS existence as well as its severity was expressed as odds ratios (OR) with a 95% confidence interval (CI)

For the statistical analysis, the statistical software SPSS for Windows (SAS Institute, Cary, NC) were used. All *P* values were 2-tailed, with statistical significance defined by $P \leq 0.05$.

Results

The baseline characteristics of the study population are summarized in **Table 1**.

The mean age of the patients was 60 ±10 years, and 58.7% were men.

Table 1: Baseline Characteristics of the Population studied

The baseline characteristics of the study population are summarized in Table 1.
The mean age of the patients was 60 ±10 years, and 50 were men and 50 were female (total 100 patients).

	All (n=550)	Men (n=321)	Women (n=228)	P-value*
Age (50-70 years)	59.77±9.76	60.21±0.921	61.45±08.10	
Body mass index (kg/m2)	28.79±04.47	27.61±04.28	30.21±04.63	
Waist circumference (cm)	99.40±11.04	97.19±10.14	103.01±10.29	
Height (cm)	162.65±9.36	168.87±6.23	156.79±4.3	
Weight (kg)	75.61±11.41	76.91±12.16	73.31±11.04	
Non-smoker	63	17	46	
Hypertension	56	14	34	
Diabetes	34	14	20	
Hyperlipidemia	74	34	40	
Family history of CAD	26	13	13	
Fasting blood glucos(mg/dL e	128.18±43.90	117.75±40.43	189.0±50.31	
Triglyceride (mg/dL)	196.60±11.72	196.38±108.25	198.13±113.98	
HDL-cholesterol (mg/dL)	41.60±9.48	39.94±8.01	44.61±9.53	
LDL-cholesterol (mg/dL)	118.46±36.81	115.02±33.01	124.83±40.23	
Total cholesterol (mg/dL)	194.77±43.65	189.36±40.15	198.47±51.32	
Uric acid (mg/dL)	7.17±2.32	7.52±2.18	6.22±2.89	

Data are presented as mean ± SD or n%(%). *(P-values for men vs women. CAD, coronary artery disease.
The baseline characteristics of the participants with and without CAD in total and in men and women with uric acidemia individually are presented in **Table 2.**

Table 2: Demographic and Clinical Characteristics of the Patients With or Without Coronary Artery Disease Stratified by gender

	All	**(n = 550)**	**Men**	**(n = 317)**	**Women**	**(n = 223)**
	STEMI (n=370)	NON -STEMI (n=170)	STEMI (n=242)	NON -STEMI (n=75)	STEMI (n=128)	NON -STEMI (n=95)
Age (50-70 years)	61.12± 9.45	56.83 + 9.80	60.15±9.79	56.52 + 10.98	62.95±8.50	57.07±8.82
Body mass index (kg/m2)	28.49 ± 4.55	29.11 ± 4.60	27.73± 4.08	27.56 ± 4.56	29.95 ± 5.05	30.36±4.26
Waist circumference (cm)	99.32 ± 10.87	99.27 ± 11.36	97.51 ± 9.87	96.03 ± 11.13	102.28 ± 11.80	101.84 ± 10.93
Height (cm)	162.91 ± 9.79	161.78 ± 8.73	167.5 7± 7.54	168.47 ± 6.56	153.98 ± 7.03	156.33±6.08
Weight (kg)	75.47 ± 12.51	75.95± 12.23	77.80 ± 11.58	78.25± 13.94	71.02 ± 13.05	74.08 ± 10.33
Hyperuricemia	237 (64.1)	80(47.1)	155(64.0)	36(48.0)	82(64.1)	44(46.3)
Cigarette smoking		FOR TREND TEST				
Current smoker	67(18.1)	20(11.8)	60(24.8)	18(24.0)	7(5.5)	2(2.1)
Ex-smoker	85(23.0)	27(15.9)	78(32.2)	25(33.3)	7(5.5)	2(2.1)
Non-smoker	218(58.9)	123(72.4)	104(43.0)	32(42.7)	114(89.0)	91(95.8)
Hypertension	215(58.1)	88(51.8)	113(46.7)	31(41.3)	102(79.7)	57(60.0)
Diabetes (T_2 + T_1)	142(38.4)	43(25.3)	78(32.2)	14(18.7)	64(50.0)	29(30.5)
Hyperlipidemia	288(77.8)	113(66.5)	178(73.6)	40(53.3)	110(85.9)	73(76.8)
Family history of CAD	104(28.1)	35(20.6)	70(28.9)	12(16.0)	34(26.6)	23(24.2)
Fasting blood glucos(mg/dL)	127.51±54.54	110.44±35.11	119.13± 47.52	99.72± 19.94	143.40 ±63.03	118.98 ±41.75
Triglyceride (mg/dL)	204.14± 119.70	172.83 ±96.37	203.12± 113.24	157.72 ±102.21	206.07± 131.49	184.76±90.26
HDL-cholesterol (mg/dL)	38.74± 9.85	44.67± 10.67	37.18± 8.39	42.69 ±10.07	41.67 ±11.62	46.22 ±10.93
LDL-cholesterol (mg/dL)	115.84± 39.75	115.22±40.32	114.30± 36.79	104.56 ±37.03	118.81 ±44.92	123.45±41.02
Total cholesterol (mg/dL)	192.25 ± 47.85	190.74 ± 44.05	189.72 ± 43.70	175.53 ± 39.72	197.04 ± 54.71	202.74 ±43.78
Uric acid (mg/dL)	7.55± 2.27	6.66 ± 1.97	7.78 ± 2.09	7.13± 1.98	7.13 ± 2.54	6.29 ± 1.90

*P-value <0.05; †P-value <0.01; ‡P-value <0.001.Data are presented as mean ± SD or n (%). STEMI, ST elevation MI = CAD +, coronary artery disease.

Table 3, reveals the predictors for ACS in the tested population and in subgroups stratified by gender.

Table 3:_Predictors of Acute Coronary Syndrome in all Participants and in Men and Women Separately

	All	**Participants**	**Men**		**Women**	
Predictors	OR (95% CI)	P-Value	OR (95% CI)	P-Value	OR (95% CI)	P-Value
Age (years)	1.07 (1.04-1.09)	<0.0001	1.05 (1.02-1.08)	0.0014	1.10 (1.06–1.14)	<0.0001
Male sex	2.60 (1.66-4.06)	<0.0001	-	-	-	-
Hyperuricemia	1.75 (1.15-2.68)	0.0087	-	-	-	-
Hypertension	-	-	-	-	2.54 (1.24-5.23)	0.0100
FH of CAD	1.78 (1.09-2.92)	0.0213	2.43 (1.18-5.03)	0.0148	-	-
FBS (mg/dL)	1.01 (1.01-1.02)	0.0002	1.02 (1.00-1.03)	0.0054	1.01 (1.01-1.02)	0.0002
HDL (mg/dL)	0.95 (0.93-0.97)	<0.0001	0.94 (0.91-0.97)	<0.0001	0.95 (0.92-0.97)	0.0004

CAD, coronary artery disease; CI, confidence interval; FBS, fasting blood glucose; FH, family history; HDL, HDL-cholesterol; OR, odds ratio for the presence of CAD.

Table 4, there was a strongly significant linear trend of higher prevalence of hyperuricacidemia as well as higher concentrations of uric acid with increasing numbers of patients who had (P=0.001 and P<0.001 for the Mantel-Hanzel Test of Linear Trend, respectively), and this trend remained significant by stratifying the study population into men and women.

Table 4: Unadjusted Serum Uric Concentrations and Prevalence of Hyperuriacidemia in Patients With Various Severity of Coronary Artery Disease

	Absent (No complications)	**Mild CAD+MONOFOCAL DYSARRYTHMIA KILLIP 1**	**Moderate MULTIPLE MALIGNANT MULTIPLE DYSARRYTHMIA KILLIP 2**	**Severe[4] EXTENSIVE MI/ MULTIFOCAL DYSARRYTHMIAS KILLIP 3**	**P-value**
All participants	n=110	n=90	n =100	n =180	
Hyperuricemia	50 (45.5)	58 (64.4)	60(60.0)	119(66.1)	0.001
Uric acid (mg/dL)	6.56 ± 2.01	7.43±2.39	7.55±2.35	7.66±2.18	<0.001
Men	n=47	n=54	n =70	n =118	
Hyperuricemia	22 (46.8)	35(64.8)	39(55.7)	81(68.6)	0.014
Uric acid (mg/dL)	7.04 ± 2.04	7.53 ±2.16	7.46±2.02	8.08±2.07	0.030
Women	n=63	n=36	n =30	n =62	
Hyperuricemia	28 (44.4)	23(63.9)	21(70.0)	38(61.3)	0.037
Uric acid (mg/dL)	6.21 ± 1.93	7.05 ± 2.71	7.77±3.01	6.87±2.17	0.032

Data are presented as mean ± SD or n (%).
Using Proportional Odds model, we found that in the whole population, hyperuricacidemia was more likely associated with a trend toward higher vessel scores indicating a more severe ACS (adjusted OR=1.51, 95% CI=1.09-2.09; P=0.005), and a comparison of sex-specific values showed that a significant association existed in men but not in women as seen in **Table 5**.

Table 5: Predictors of Acute Coronary Syndrome Severity in All Participants

	All	**Participants**	**Men**		**Women**	
Predictors	OR (95% CI)	P-Value	OR (95% CI)	P-Value	OR (95% CI)	P-Value
Age (years)	1.05 (1.04-1.07)	<0.0001	1.04(1.02-1.06)	0.0012	1.09 (1.06–1.12)	<0.0001
Male sex	2.21 (1.57-3.12)	<0.0001	-	-	-	-
Hyperuricacidemia	1.51 (1.09-2.09)	0.0052	1.65(1.08-2.52)	0.0232	-	-
Diabetes mellitus	2.13(1.50-3.01)	0.0003	2.19(1.36-3.51)	0.0051	2.22(1.34-3.67)	0.0005
Hypertension	1.49(1.06-2.09)	0.0219	-	-	2.35(1.34-4.10)	0.0039
FH of CAD	1.77(1.23-2.54)	0.0018	1.71(1.06-2.75)	0.0214	-	-
HDL (mg/dL)	0.96(0.95-0.98)	<0.0001	0.95 (0.93-0.97)	<0.0001	0.97 (0.95-0.99)	0.0075

CAD, coronary artery disease; CI, confidence interval; FH, family history; HDL, HDL-cholesterol; OR, odds ratio for ACS severity.

Discussion

Numerous studies have investigated the association between elevated serum uric acid and ACS. The overall prevalence of cardiovascular risk factors including hypertension, diabetes mellitus, tobacco use, cigarette smoking, bidi, tobacco chewing, gutkha, hyperlipidemia, and family history of ACS were high.

The women had a greater prevalence of hypertension, diabetes mellitus,and hyperlipidemia compared to men, but cigarette smoking was much more common in men than in women.

Men and women similarly showed a family history of ACS. Unsurprisingly, serum levels of and uric acid were significantly greater for men than women

Some studies found hyperuricacidemia to be an independent risk factor for ACS.[5,6,7]

Others reported that it was merely confounded by the relation of uric acid with conventional risk factors for ACS including diabetes mellitus, hypertension, and hyperlipidemia

Even though most of the studies investigated the association between uric acid levels with the presence of ACS and its risk factors, studies examining relationships between uric acid levels and severity of ACS are few.[8,9,10,11]

We found an association between hyperuricacidemia and a trend for more severe coronary artery disease in men, but not in women.Such disparity may be due to genetic backgrounds such as family history and lifestyle[12,13,14,15] for e.g. tobacco in serum uric acid levels.

The well recognized risk factors like age, sex, smoking, diabetes, hypertension, dyslipidemia explain only a part of this mortality. Hence a search for other risk factors is the need of the hour. Many studies have found conflicting role of uric acid in patients with cardiovascular diseases.

This study was conducted to assess the association of serum uric acid level with presence and severity of ACS. The main findings of the study were:

(i) The serum uric acid level was higher in patients with ACS compared with patient without ACS;

(ii) The serum uric acid level was associated with the presence and severity of ACS.

We included serum uric acid as continuous variables. The severity of ACS was higher in patients belonging to higher serum uric acid with respect to lower serum uric acid level.

It is well documented that uric acid is also related to risk factors for ACS such as hypertension ,[16,17,18,19] diabetes mellitus,[18,19] metabolic syndrome,[20] dyslipidemia,[21] and obesity [18] are few patients.

Limitations

First, our study was observational in nature, which possibly restricted us in identifying and analyzing all potential confounding factors.

Second, our analyses are based on a single measurement of uric acid, and the changes in uric acid levels over time are likely to occur.

The populations that was selected had some or other comorbid condition such as essential hypertension, diabetes mellitus, sedentary lifestyle, smoking, tobacco chewing.

We could not establish the direct co-relation of ACS with the uric acid level as there were no patients in the age group that was selected and who didn't have any other comorbid conditions/lifestyle modification who had all parameters with a normal and ACS and had hyperuricidemia.

Conclusion

Few patients had diabetes mellitus with essential hypertension and diabetes mellitus with metabolic syndrome.

Diabetes mellitus had more of hypertriglycerides as compared to other comorbid condition. Hypercholestremia had high levels of cholesterol as compare to some hypertensive patients. Tobacco chewers also had smoking habit.

Hyperuricacidemia is also one of the risk factor for ACS , hypertension,diabetes mellitus ,obesity , dyslipidemia are enhancing any pathological condition presenting with ACS.

Uric acid included is one of the parameter to predict or evaluate the risk factor for ACS.

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