

Study of Serum Uric Acid Level in Acute Coronary Syndrome

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Abstract At present, cardiovascular diseases are global health problems responsible for 17.3 million deaths per year and adding extra burden in developing countries like Nepal. Studies show that serum uric acid (SUA) can result in endothelial dysfunction which can lead to vascular disease like stroke. In this study, we determined serum uric acid levels in patients with acute coronary syndrome (ACS) and assess its risk factors. A cross sectional study was conducted in 82 patients with ACS who fulfilled the inclusion criteria included in the study and their serum uric acid level were investigated. It was found that 51 (62.2%) were males and 31 (37.8%) were females. Mean age in study population was 60.26 ± 11.34 years. Majority of the population belongs to 56-65 years age group. The mean uric acid level of our study population was 6.03 ± 1.50 mg/dl (male = 5.92 ± 1.72 , female = 6.64 ± 1.53). $SUA \geq 7$ mg/dl was maximum in 56-65 years age group and there was no association between age and SUA (P value = 0.146). Over half of the study population were hypertensive i.e. 42 (51.21%) and smoker i.e. 43 (52.43%). It showed association between SUA and ACS (P value = 0.003). Among those having diabetes, maximum have $SUA \geq 7$ mg/dl i.e. 17 (47.22%). Among those having high cholesterol level, male have higher incidence than female with no association between T. Cholesterol and gender (P value = 0.49). The mean value of T. Cholesterol was 189.83 ± 46.81 mg/dl (male = 198.78 ± 55.19 mg/dl, female = 202.30 ± 54.92 mg/dl) with (P value = 0.52). In conclusion, the mean age of ACS patients was 60.26 years, with the peak incidence at the age of 56-65 years. The ACS had male predominance. The potential risk factors of ACS were: Age >56 years (65.83%), male sex (62.2%), dyslipidemia (35.36%), hypertension (51.2%), diabetes mellitus (43.9%), smoking (52.4%) and alcohol consumption (39%). Among these SUA significantly associated with risk factors were- Sex, Diabetes Mellitus, T. Cholesterol. There was association between serum uric acid level and ACS patients. Hypertension and smoking constitutes one of the major risk factor for ACS in study population.

Keywords: Acute coronary syndrome; Alcohol; Diabetes mellitus; HTN; Lipid profile; Smoking

1. Introduction

Cardiovascular disease (CVD) was thought to be the problem of developed countries but today it is a global health problem responsible for 17.3 million deaths per year and adding burden in developing countries like Nepal. However, prevalence of heart diseases is higher in urban areas than rural areas. smoking, dyslipidemia, hypertension, diabetes and

physical inactivity are conventional risk factors. In addition, in men, the risk increases after age 45, while in women, the risk increases after the age 55 [1,2]. Age is strong and independent risk factor. Many risk factors are related to ageing (diabetic mellitus, hypertension, physical inactivity), and appears as one of the most complex risk factor in development of atherosclerosis. Older persons with type 2 diabetes mellitus have double the risk of coronary artery diseases.

Various studies show that uric acid can result in endothelial dysfunction which can lead to vascular disease like chronic artery disease (CAD) and stroke. Evidence based studies suggest that the elevated SUA level may predict an increased risk for acute coronary syndrome (ACS). SUA can also work as pro-oxidant under certain circumstances. Thus, the role of SUA as a risk factor for vascular disease and ACS is controversial and there is little information about it [3, 4].

Uric acid is involved in almost 70% of the free radical scavenging reactions in the human. It is specifically involved in neutralizing peroxy nitrite, hydroxyl, and superoxide radicals [5]. During episodes of ischemic events and oxidative stress due to various causes, the level of local uric acid concentration elevates as a protective mechanism [6]. The role of serum uric acid levels as a risk factor for vascular disease has been predicted with some evidence [7]. Subjects with non-insulin-dependent diabetes mellitus (NIDDM) have a 2-4 folds greater risk of all manifestations of atherosclerotic vascular disease [8]. Theoretically, alterations in this balance may account for hyperuricemia, although clinically defective elimination accounts for most cases of hyperuricemia [9].

In this study, we determined serum uric acid levels in patients with ACS and assess its relationship with ACS risk factors. In addition, we studied the association between serum uric acid level and risk factors of acute coronary syndrome namely hypertension, diabetes mellitus, and adverse lipid profile.

2. Materials and Methods

A cross sectional study was conducted in 82 patients with ACS who fulfilled the inclusion criteria included in the study and their serum uric acid level were investigated. The study was conducted in the Department of Internal Medicine, Universal College of Medical Sciences, Bhairahawa, Nepal. Simple random sampling of the patients with ACS admitted in the medical wards and or medical Intensive care units or present in OPD were taken for the study. Study was conducted from October, 2015 to August, 2017. Informed consent was taken for the study from all the patients. Ethical approval for the study was taken from institutional review board (IRB), UCMS-TH, Bairahawa.

The inclusion criteria were: Patients with Acute Coronary Syndrome evidence with ECG, cardiac enzyme, clinical sign and symptoms and age >30 years of age. Exclusion criteria were: patients with previous history of ACS, chronic renal failure, known cases of gout or show clinical evidences of gout, under medication of thiazide diuretics, with hematological abnormalities like leukemia or other myeloproliferative disorders, and non-compliance of patient.

Blood samples for relevant investigation (complete blood count, renal function test, serum uric acid level, fasting lipid profile, cardiac enzyme) was taken. Chest x-ray and Electrocardiogram was done. All the samples were taken within 24 hours of presentation in hospital. Structural proforma was maintained for the record of all the details about the case.

The information collected regarding all the selected cases were entered in the computer in windows office excel and transferred to SPSS version 20. Data analysis was done. Using this software, frequencies, percentage, mean, standard deviation, independent t - test, Chi-square test and P values were calculated.

3. Results

Out of 82 ACS patients, 51 (62.2%) were males and 31 (37.8%) were females. So, the males were more commonly affected than female. Minority of the population, 36(43.9%) were found to be suffering from DM and 46(56.1%) of the patients were non-diabetic. Majority of population, 42 (51.2%) were found to be suffering from hypertension and 40 (48.8%) of the patients were non-hypertensive. Majority of population, 43 (52.4%) were smokers and 39 (47.6%) of the patients were non-smokers. Majority of population, 50 (61%) were non-alcoholic and 32 (39%) of the patients were alcoholic. Majority of population, 64 (78%) were non-vegetarian and 18 (22%) were vegetarian. Majority of population, 36 (43.9%) were having ST elevation myocardial infarction, 29 (35.4%) were having non-ST elevation myocardial infarction whilst 17 (20.7%) were having unstable angina.

3.1. Association of Uric acid with diagnosis of ACS patients

Table 1 shows that 29 have SUA level between 5-6.9 mg/dl in which maximum 19 (52.77%) were from STEMI, 27 have uric acid ≥ 7 mg/dl among which maximum 16 (55.1%) were from NSTEMI and 26 have uric acid level < 5 mg/dl but there was less variation in this group. There was significant association between SUA and ACS (P value = 0.003).

Table 1. Association of Uric acid with diagnosis of ACS patients

Variables	Diagnosis			Total	P value	
	NSTEMI (%)	STEMI (%)	UA (%)			
SUA (mg/dl)	< 5	8 (27.58%)	9 (25%)	9 (52.94%)	26 (31.70%)	0.003
	5-6.9	5 (17.24%)	19 (52.77%)	5 (29.41%)	29 (35.36%)	
	≥ 7	16 (55.17%)	8 (22.22%)	3 (17.64%)	27 (32.92%)	
Total		29	36	17	82	

3.2. Association of Uric acid with sex of ACS patients

Table 2 shows, out of 51 males, the ones having uric acid level < 5 mg/dl were 11 (21.56%), between 5-6.9mg/dl were 22 (43.13%) and ≥ 7 mg/dl were 18 (35.29%). Similarly, out of 31 females, uric acid level < 5 mg/dl were 15 (48.38%), between 5-6.9mg/dl were 7 (22.58%) and ≥ 7 mg/dl were 9 (29.03%). It also shows evidences for a significant association between SUA and sex of population having ACS (P value = 0.032) in our study.

Table 2. Association of Uric acid with diagnosis of ACS patients

Variables	Diagnosis			Total	P value	
	NSTEMI (%)	STEMI (%)	UA (%)			
SUA (mg/dl)	< 5	8 (27.58%)	9 (25%)	9 (52.94%)	26 (31.70%)	0.003
	5-6.9	5 (17.24%)	19 (52.77%)	5 (29.41%)	29 (35.36%)	
	≥ 7	16 (55.17%)	8 (22.22%)	3 (17.64%)	27 (32.92%)	
Total		29	36	17	82	

3.3. Association of Uric acid with age group of ACS patients

Table 3 shows that, the uric acid level ≥ 7 mg/dl is highest in the age group 56-65 years i.e. 15 (55%) among the population having uric acid level ≥ 7 mg/dl. Similarly, the uric acid level between 5-6.9 mg/dl is highest in the age group 66-75 years i.e. 8 (27.5%) among the population having uric acid level 5-6.5 mg/dl and also the uric acid level < 5 mg/dl is highest in the age group ≤ 45 years i.e. 8 (30.76%) among the population having uric acid level < 5 mg/dl. There was no significant association between SUA and the age group of population having ACS (P value = 0.146) in our study.

Table 3. Association of Uric acid with age group of ACS patients

Variables	Uric Acid (mg/dl)			Total	P value	
	< 5	5-6.9	≥ 7			
Age (yrs)	≤ 45	8 (30.7%)	4 (13.7%)	1 (3.7%)	13 (15.85%)	0.146
	46-55	5 (19.23%)	7 (24.13%)	3 (11.11%)	15 (18.29%)	
	56-65	7 (26.9%)	7 (24.13%)	15 (55.55%)	29 (35.36%)	
	66-75	5 (19.23%)	8 (27.58%)	8 (29.62%)	21 (25.60%)	
	≥ 76	1 (3.8%)	3 (10.34%)	0 (0%)	4 (4.87%)	
Total		26	29	27	82	

3.4. Association of Uric Acid with Dyslipidemia in ACS Patients

Table 4 shows that dyslipidemia is absent in majority of population i.e. is 53 (64.63%) while 29 (35.36%) of them have dyslipidemia. Among those having dyslipidemia, the maximum number i.e.14 (48.27%) falls in the group having SUA level ≥ 7 mg/dl whereas the people having dyslipidemia with SUA acid levels < 5 mg/dl and between 5-6.9 mg/dl are 7 (24.13%) and 8 (27.58%) respectively. There are no association between the uric acid and dyslipidemia (P value = 0.099) in our study.

Table 4. Association of Uric Acid with Dyslipidemia in ACS Patients

Variables	Dyslipidemia		Total	P value	
	Absent	Present			
SUA(mg/dl)	< 5	19 (35.84%)	7 (24.13%)	26 (31.70%)	0.099
	5-6.9	21 (39.62%)	8 (27.58%)	29 (35.36%)	
	≥ 7	13 (24.52%)	14 (48.27%)	27 (32.92%)	
Total		53	29	82	

3.5. Association of Uric Acid with Total Cholesterol in ACS Patient

Table 5 shows, 37 (45.12%) number of population have high total cholesterol ≥ 200 mg/dl and 45 (54.88%) of them have normal total cholesterol < 200 mg/dl. Among those having total cholesterol level ≥ 200 mg/dl, maximum lie in the group having uric acid level ≥ 7 mg/dl and 5-6.9 mg/dl i.e. 18 (48.65%) and 12 (32.43%) respectively. Our study shows evidence of association between the uric acid and total cholesterol (P value = 0.013).

Table 5. Association of Uric Acid with Total Cholesterol in ACS Patient

Variables	T. Cholesterol		Total	P value	
	< 200 mg/dl (Normal)	≥ 200 mg/dl (High)			
SUA(mg/dl)	< 5	19 (42.22%)	7 (18.91%)	26 (31.70%)	0.013
	5-6.9	17 (37.775)	12 (32.43%)	29 (35.36%)	
	≥ 7	9 (20%)	18 (48.64%)	27 (32.92%)	
Total		45	37	82	

3.6. Association of Uric Acid with Diabetes mellitus in ACS Patients

Table 6 shows among the diabetic population most of them belong to group having uric acid level ≥ 7 mg/dl i.e. 17 (47.22%), whereas 10 (27.7%) of them belong to group having uric acid level < 5 mg/dl and 9 (25%) of them belong to 5-6.9 mg/dl. It also shows evidence of significant association between serum uric acid and diabetes mellitus (P value = 0.047).

Table 6. Association of Uric Acid with Diabetes mellitus in ACS Patients

Variables	DM		Total	P value	
	Absent	Present			
SUA (mg/dl)	< 5	16 (34.78%)	10 (27.77%)	26 (31.70%)	0.047
	5-6.9	20 (43.47%)	9 (25%)	29 (35.36%)	
	≥ 7	10 (21.73%)	17 (47.22%)	27 (32.92%)	
Total		46	36	82	

3.7. Association of Uric Acid with Hypertension in ACS Patients

Table 7 shows 42 (51.21%) were hypertensive, most of them among hypertensive belong to group having uric acid level ≥ 7 mg/dl i.e. 18 (42.86%), whereas 13 (30.95%) of them belong to group having uric acid level 5-6.9 mg/dl and 11 (26.19%) of them belonging to < 5 mg/dl. It shows evidence of no significant association between serum uric acid and hypertension (P value = 0.15).

Table 7. Association of Uric Acid with Diabetes mellitus in ACS Patients

Variables	HTN		Total	P value	
	Absent	Present			
SUA(mg/dl)	< 5	15 (37.5%)	11 (26.19%)	26 (31.70%)	0.158
	5-6.9	16 (40%)	13 (30.95%)	29 (35.36%)	
	≥ 7	9 (22.5%)	18 (42.85%)	27 (32.92%)	
Total	40	42	82		

3.8. Association of Uric Acid with smoking in ACS Patients

Table 8 shows among the smokers 43 (52.43%), most of them belong to group having uric acid level 5-6.9 mg/dl i.e. 17 (39.53%), whereas 14 (32.55%) of them belong to group having uric acid level ≥ 7 mg/dl and 12 (27.9%) of them belonging to < 5 mg/dl. It also shows evidence of no significant association between serum uric acid and smoking. (P value = 0.65)

Table 8. Association of Uric Acid with smoking in ACS Patients

Variables	Smoking		Total	P value	
	No	Yes			
SUA(mg/dl)	< 5	14 (35.89%)	12 (27.90%)	26 (31.70%)	0.651
	5-6.9	12 (30.76%)	17 (39.53%)	29 (35.36%)	
	≥ 7	13 (33.33%)	14 (32.55%)	27 (32.92%)	
Total	39	43	82		

3.9. Association of Uric Acid with Alcohol in ACS Patients

Table 9 shows among the alcoholics 32 (39.02%) most of them belong to group having uric acid level ≥ 7 mg/dl i.e. 14 (43.75%), whereas 12 (37.5%) of them belong to group having uric acid level 5-6.9 mg/dl and 6 (18.75%) of them belonging to < 5 mg/dl. It also shows evidence of no significant association between serum uric acid and alcohol (P value = 0.11)

Table 9. Association of Uric Acid with Alcohol in ACS Patients

Variables	Alcohol		Total	P value	
	No	Yes			
SUA (mg/dl)	< 5	20 (40%)	6 (18.75%)	26 (31.70%)	0.110
	5-6.9	17 (34%)	12 (37.5%)	29 (35.36%)	
	≥ 7	13 (26%)	14 (43.75%)	27 (32.92%)	
Total	50	32	82		

3.10. Association of Uric Acid with Dietary Habit in ACS Patients

Table 10 shows, in each group of uric acid level, the frequency of non-vegetarian is more than vegetarian group i.e. 23 (35.9%) of non-vegetarians have uric acid level between 5-6.9 mg/dl whereas 20 (31.25%) have ≥ 7 mg/dl and 21 (32.28%) have < 5 mg/dl. Similarly, amongst the vegetarians, 5 (27.7%) have uric acid levels < 5 mg/dl, 6 (33.3%) have uric acid levels between 5-6.9 mg/dl and 7 (25.9%) have ≥ 7 mg/dl. It also shows evidence of no significant association between serum uric acid and dietary habit (P value = 0.828).

Table 10. Association of Uric Acid with Dietary Habit in ACS Patients

Variables	Dietary Habit			P value	
	Non-Veg	Veg	Total		
SUA(mg/dl)	<5	21 (32.81%)	5 (27.77%)	26 (31.70%)	0.828
	5-6.9	23 (35.93%)	6 (33.33%)	29 (35.36%)	
	≥7	20 (31.25%)	7 (38.88%)	27 (32.92%)	
Total	64	18	82		

4. Discussion

Among the total study population, 36 (43.9%) had STEMI, 29 (35.4%) had NSTEMI and 17 (20.7%) had UA which shows maximum population have MI and least has UA which in agreement with study conducted by Paudel et al where 122 patients (49.6%) had STEMI but in contrast to the same study 26 (10.6%) had NSTEMI and 98 (39.8%) had UA [10]. Likewise, it is in agreement with study done by Khatri et al. which also shows majority 44 (44%) of study population had STEMI [11].

In the present study, results show half number 42 (51.2%) were hypertensive and 40 (48.8%) were non-hypertensive, 36 (43.9%) were diabetic and 46(56.1%) were non-diabetic which is in agreement with study done by Sinan Devenci et al [11] which shows 703 (69%) were hypertensive, 292 (28.9%) were diabetic. Similarly, in the study done by Khatri et al [11] where 68 (68%) were hypertensive and 32 (32%) were non-hypertensive, 19 (19%) were diabetic and maximum were non-diabetic i.e. 81 (81%).

Our study shows 43 (52.4%) were smoker which is in accordance to Man et al [13] which shows 68% patients with ACS were smoker while the other study shows fewer had a smoking history [11,12]. Similarly, 32 (39%) of the study population consume alcohol which is similar to the result of the study conducted by Dali et al where 51 (47.2%) were alcoholic [14]. We can see that higher the level of SUA higher is the frequency of hypertensive patients. However, there is no significant association between SUA and hypertension (P value = 0.15). Also in a study done by Brand et al [15] SUA values were consistently higher in subjects of both sexes who were taking antihypertensive drugs. SUA values correlated with systolic and diastolic blood pressure in both sexes; the relationship was stronger in women than in men for systolic than for diastolic pressure. The SUA relationship with myocardial infarction (MI) was equally strong in both sexes, even correcting for antihypertensive treatment.

In our study it shows, majority of patients, i.e., 29 have SUA level between 5-6.9 mg/dl among which maximum 19 (52.77%) were from STEMI group, 27 have uric acid ≥ 7 mg/dl among which maximum 16 (55.1%) were from NSTEMI group. Mean value of SUA were higher in ACS with its severity undergoing different stages as NSTEMI, STEMI as compared to UA group with less SUA. This result also shows MI patients have higher SUA level than that of UA which is similar to the study by Hasic et al [16] which shows levels of SUA are associated with the type of ACS in the hyperuricemic ACS patients (MI versus UA, 499(458-590) $\mu\text{mol/L}$, 425(400-447) $\mu\text{mol/L}$ respectively with P value = 0.007. Our result also shows significant association between SUA and ACS. In same study done by Hasic et al, if we correlate SUA with total study population it shows Median level of SUA in the ACS patients was 364 (312-437.75) $\mu\text{mol/L}$ and there was significant difference between SUA values depending on the type of ACS in MI patients 357.50 (323.25-498.25) $\mu\text{mol/L}$, UA patients 379 (290.75-414.50) $\mu\text{mol/L}$ and there was no association found (P value = 0.118) which is contrast to our study where majority of the study population fall on MI group and most of them have higher SUA level in comparison to UA group with P value 0.03. In other study done by Lim et al [17] among total study population, 395 patients had CAD. SUA was higher in patients with CAD as compared to those without CAD (5.5 \pm 1.0 vs. 5.2 \pm 1.0 mg/dl, P value = 0.004). In addition, SUA was significantly associated with the severity of CAD (p = 0.002) which shows somehow similar result as our study.

The limitation of this study includes that this is a single center based study so results cannot be generalized, a hospital based study with small sample size and only major factors affecting the SUA level are only considered in this study. The strength of this study includes; this type of study on acute coronary syndrome patients has not been done before in this

region of Nepal. This study deals with not only with SUA level in acute coronary syndrome but also with the risk factors of acute ischemic stroke.

5. Conclusion

It was seen in our study that the mean age of ACS patients was 60.26 years, with the peak incidence at the age of 56-65 years with male predominance. Prevalence of risk factors in ACS in our study were age >56 years (65.83%), male (62.2%), dyslipidemia (35.36%), hypertension (51.2%), diabetes mellitus (43.9%), smoking (52.4%), and alcohol consumption (39%). Among these SUA significantly associated with risk factors; sex, diabetes mellitus and cholesterol. This study showed statistically significant association between serum uric acid level and ACS patients.

6. Abbreviations

SUA: Serum uric acid; ACS: acute coronary syndrome; CVS: Cardiovascular disease; CAD: chronic artery disease; STEMI: non-insulin-dependent diabetes mellitus; NIDDM: non-insulin-dependent diabetes mellitus; MI: myocardial infarction.

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