

# HYPERURICEMIA: A PREDICTOR OF IN HOSPITAL COMPLICATIONS IN ACUTE CORONARY SYNDROME PATIENTS

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## ABSTRACT

**Background:** Various studies done in the past few decades have shown association of hyperuricemia with the increase in cardiovascular (CV) mortality. **Objective:** To determine the association of hyperuricemia and in hospital complications in acute coronary syndrome patients. **Methodology:** This cohort study was conducted on 154 patients in department of Cardiology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan from 1<sup>st</sup> January to 30<sup>th</sup> June 2017. Hyperuricemia was defined as serum uric acid level  $\geq 7.2$  mg/dl in males and serum uric level  $\geq 6$  mg/dl in females. The data collection was started after getting informed consent of the patients admitted through accident and emergency department. Consecutive patients of acute coronary syndrome were selected and those with hyperuricemia were labeled as exposed (Group I) and those with normouricemia were considered as non-exposed (Group II). The two groups were followed for 7 days and outcome i.e in-hospital complications in terms of conduction defect and heart failure were noted as per operational definition. The data were collected on a proforma like age and sex. Effect modifiers like age, sex, family history of ACS, history of T2DM, history of hypertension, smoking and BMI were stratified to see the impact of these on outcomes. Chi square test were applied to determine the association of hyperuricemia with in hospital complications like conduction defect and heart failure. P value  $\leq 5\%$  was taken as significant. **Results:** Among the total study subjects (n=154), 100(65%) were male and 54(35%) were female. The mean age and BMI of Group I (ACS with hyperuricemia) and Group II (ACS without hyperuricemia) were  $65 \pm 12$  years vs.  $62 \pm 11$  years and BMI  $27 \pm 3.2$  vs  $25 \pm 2.8$  respectively. Out of 154 patients, 28 (18.1%) have conduction defect and only 40(26%) patients suffered heart failure. From these 28 patients with conduction defects, 19 (24.6%) were with ACS and hyperuricemia and 09(11.6%) were with ACS without hyperuricemia. From these 40 patients with heart failure, 33 (42.8%) were with ACS and hyperuricemia and 07 (9%) were with ACS without hyperuricemia. **Conclusion:** This study showed that in-hospital complications were significantly higher in patients with ACS with hyperuricemia as compared to patients with ACS without hyperuricemia.

**Keywords:** Acute coronary syndrome, Hyperuricemia, Cardiovascular disease, Heart failure, Complications, In-hospital.

## INTRODUCTION

Uric acid is the final breakdown product of purine metabolism due to the abnormality in the uricase gene functioning, which results in high serum uric acid levels in the body.<sup>1</sup> High serum uric acid levels are a common finding in patients with high blood pressure, insulin resistance, obesity and Cardiovascular (CV) disease.<sup>2</sup>

It's a debate from many years among clinicians and researchers that uric acid is an interdependent cardiovascular risk factor or no.<sup>3</sup> It was proved and suggested by many that renal vasoconstriction and various most commonly used CV drugs like low dose aspirin and loop diuretics and insulin were associated with decreased urate kidney excretion.<sup>4</sup> However, many studies later on showed that it's more accurate to regard hyperuricemia as a consequence of the already existing cardiovascular risk factors like obesity and insulin resistance than as an independent cardiovascular risk factor.<sup>5,6</sup> Whereas, some studies showed the beneficial effect of the raised uric acid levels on the

human body cells i.e., its antioxidant properties.<sup>2</sup> This controversy caused raised serum uric acid to be no longer regarded as a true independent CV risk factor.<sup>3</sup>

By time with increased knowledge about the role of serum uric acid in the cardiorenal disease, controversy is resurfacing. It was proved later with the advances in medical research that the rising serum uric acid levels predicts the progression of chronic kidney disease,<sup>4</sup> the chances of ischemic stroke,<sup>5</sup> and a recent meta-analysis showed that raised serum uric acid level is associated with hypertension,<sup>6</sup> diabetes mellitus,<sup>7</sup> and metabolic syndrome.<sup>8</sup> Another recent meta-analysis studied the relationship between serum uric acid and acute coronary syndrome (ACS) and showed that serum uric acid level is not an independent risk factor for ischemic heart disease and awareness should be made in the general population as well as among general practitioners that it should not be used for prediction of ACS and high risk for ischemic heart disease.<sup>1,9,10</sup> This study was conducted to determine

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the association between hyperuricemia and in hospital complications like heart failure and conduction defects in acute coronary syndrome patients.

## METHODOLOGY

**Study Design:** Cohort study. **Settings of Study:** Department of Cardiology, Sheikh Zayed Medical College, Rahim Yar Khan. **Study duration:** 1<sup>st</sup> January to 30<sup>th</sup> June 2017. **Sampling technique:** Non-probability consecutive sampling. **Inclusion Criteria:** Patient presenting with ACS, 40 years and above age, both gender. **Exclusion Criteria:** Previous history of myocardial infarction, chronic renal failure patients (A GFR below 15), patients on drugs causing hyperuricemia like diuretics, unstable angina, chest pain >20 min with either Transient ST Segment depression (>0.05 mV) or T-wave inversion (>0.2 mV) during the symptomatic period, hepatic Failure: INR >6.5 (PT>100 seconds)

**Data collection:** The data was started after informed consent of the patients admitted through accident and emergency department. Consecutive patients of acute coronary syndrome were selected and those with hyperuricemia were labeled as exposed (Group I) and those with normouricemia were considered as non-exposed (Group II). The two groups were followed for 7 days and outcome i.e in-hospital complication in terms of conduction defect and heart failure were noted as per operational definition at the end of 7<sup>th</sup> day of admission. The data were collected on a proforma like age and sex, family history of ACS, history of T2DM, history of hypertension, smoking and BMI.

**Data Analysis:** The data was entered and analyzed by using SPSS version 16. The numerical data were presented as mean and standard deviation, like age and BMI. Categorical data was presented as frequencies & percentages like sex, family history of ACS, history of T2DM, history of hypertension, smoking, conduction defect and heart failure in the two groups. Chi square test were applied to determine the association of hyperuricemia with in hospital complications like conduction defect and heart failure. P value  $\leq$  5% were taken as significant. Effect modifiers/confounders like age and sex were stratified to see the impact of these on outcomes. Ethical approval was sought from Institutional Review Board.

## RESULTS

Among the total study subjects (n=154), 100(65%) were male and 54(35%) were female. The mean age of the study subjects was  $60 \pm 12$  years & mean weight of the patients was  $54 \pm 2.3$  & means height of the patients was  $1.65 \pm 0.09$ . In our study most of the patients 50% were in age range 60 years and above followed by 35% patients were in age range 40-50 years and 15% age range of 50-60 years. Out of them 77, 58 patients (37.6%) male and 19(12.3%) female were having hyperuricemia. The mean  $\pm$  SD of age and BMI of Group I (ACS with hyperuricemia) and Group II (ACS without hyperuricemia) were  $65 \pm 12$  vs.  $62 \pm 11$  & BMI  $27 \pm 3.2$  vs  $25 \pm 2.8$  respectively. Out of 154 patients 48(31.1%) were having DM, 95(61.6%) were hypertensive and 51(31.1%) were smokers.

Out of 154 patients, 28(18.1%) has conduction defect and 40(26%) patients suffered heart failure. From the 28 patients with conduction defects, 19(24.6%) were with ACS and hyperuricemia and 09(11.6%) were with ACS without hyperuricemia. From the 40 patients with heart failure, 33(42.8%) were with ACS plus hyperuricemia and 07(9%) were with ACS without hyperuricemia.

**Table I: Baseline characteristics**

Characteristics	ACS with hyperuricemia	ACS without hyperuricemia
Age (Years)	56 $\pm$ 12	62 $\pm$ 11
BMI	27 $\pm$ 3.2	25 $\pm$ 2.8
Gender	Male	58(75.3%)
	Female	19(24.7%)
DM	Yes	39(50.6%)
	No	38(49.4%)
HTN	Yes	65(84.4%)
	No	12(15.6%)
Smoking	Yes	31(40.2%)
	No	46(59.8%)

**Table II: Complications in study population**

Complications	ACS with hyperuricemia	ACS without hyperuricemia	P Value
Conduction defect	Yes	19(24.6%)	0.01
	No	58(75.4%)	
	Total	77 (100%)	
Heart failure	Yes	33(42.8%)	<0.001*
	No	44(57.2%)	
	Total	77 (100%)	

## DISCUSSION

In this study we planned to find out possible association of hyperuricemia and in hospital complications in acute coronary syndrome patients. A previous study has labeled high serum uric acid levels as strong predictor of cardiovascular disease mortality in healthy middle-aged men, independent of variable commonly associated with out or the metabolic syndrome.<sup>8,9,10</sup> This is comparable to our finding in current study where it was noted that those who have ACS with hyperuricemia 75.3% as compared to 44.1% (Without ACS) in hyperuricemia showing that have high serum uric acid levels is significantly associated with ACS.

The frequency of conduction defect among ACS patients in our study was 18%. The frequency of hyperuricemia in our study is lower than the prevalence observed by Jularattanaporn et al<sup>11</sup> which was 42.9%. Prevalence of hyperuricemia in this study was 89(57.7%), greater than in the study of the general population.<sup>12</sup>

In our study most of the patients 50% were in age range 60 years and above followed by 35% patients were in age range 40-50 years. Mean age was 60 years with standard deviation  $\pm$  12 years. Similar results were found in another study done by Abid AR et al<sup>13</sup> in which most of the patients 50% were in age range 60 years and above while 40% patients were found in age range 51-60 years. In our study most of the patients 70% were male and 30% patients were female. Similar results were in another study done by Abid AR et al<sup>13</sup> in which most of the patients 60% were male and 40% patients were female.

The overall incidence of HF complicating ACS in our study was 26%. This rate of HF is lower than reported in some previous studies of HF after AMI,<sup>11,12</sup> but similar to several other ones.<sup>11,13,14</sup> Since there is no definitive diagnostic test for HF, these differences may well be due to varying definitions of HF among studies, exclusion criteria or as in the present study, inclusion of all patients with ACS, or could be due to different delays in seeking care thereby not receiving timely diagnosis or optimal therapies. It was observed that one in four ACS patients from six Middle Eastern countries in the entire GULF RACE cohort had HF.<sup>15</sup> In this study and using only the UAE data from the GULF RACE, we observed that one in five patients with ACS had HF during admission. This high rate of HF

patients with ACS could be due to the high prevalence of DM in the region.<sup>15,16</sup>

Our study shows that 40(26%) patients had heart failure while 74% patients didn't have heart failure. Similar results were found in another study in which 35% patients had heart failure while 65% patients didn't have heart failure.<sup>17</sup> The overall incidence of conduction defects complicating ACS in our study was 18%. While in another study "Admission Serum Uric Acid Levels and In-Hospital Outcomes in Patients with Acute Coronary Syndrome" done by Abu Sadique Abdullah et al<sup>18</sup> at Dhaka Medical College Hospital it was 14.5%. This may be due to little sample size (n=97 vs n=154) in our study conduction defects were more in hyper uricemic group than normouricemic (24.6% vs 11.6%). This finding was also consistent with study of Abu Sadique Abdullah et al<sup>18</sup> where findings were (13.0% vs 1.4%, p=0.017) hyper uricemic group than normouricemic respectively.

## CONCLUSION

This study showed that in-hospital complications like conduction defects and heart failure rate was significantly higher in patients with ACS with hyperuricemia as compared to patients with ACS without hyperuricemia.

## REFERENCES

1. Kim SY, Guevara JP, Kim KM, Choi HK, Heitjan DF, Albert DA. Hyperuricemia and coronary heart disease: a systematic review and meta-analysis. *Arthritis care & research.* 2010;62(2):170-80.2.
2. Nieto FJ, Iribarren C, Gross MD, Comstock GW, Cutler RG. Uric acid and serum antioxidant capacity: a reaction to atherosclerosis? *Atherosclerosis.* 2000;148(1):131-9.
3. Dulleton BF. Uric acid and cardiovascular disease: a renal-cardiac relationship? *Current opinion in nephrology and hypertension.* 2001;10(3):371-5.
4. Kang D-H, Nakagawa T, Feng L, Watanabe S, Han L, Mazzali M, et al. A role for uric acid in the progression of renal disease. *Journal of the American Society of Nephrology.* 2002;13(12):2888-97.
5. Kim SY, Guevara JP, Kim KM, Choi HK, Heitjan DF, Albert DA. Hyperuricemia and risk of stroke: a systematic review and meta analysis. *Arthritis Care & Research.* 2009;61(7):885-92.
6. Grayson PC, Kim SY, lavalley M, Choi HK. Hyperuricemia and incident hypertension: a systematic review and metaanalysis. *Arthritis care & research.* 2011;63(1):102-10.
7. Kodama S, Saito K, Yachi Y, Asumi M, Sugawara A, Totsuka K, et al. Association between serum uric acid and development of type 2 diabetes. *Diabetes care.* 2009;32(9):1737-42.

8. Nakagawa T, Hu H, Zharikov S, Tuttle KR, Short RA, Glushakova O, et al. A causal role for uric acid in fructose-induced metabolic syndrome. *American Journal of Physiology-Renal Physiology*. 2006;290(3):F625-F31.
9. Wheeler JG, Juzwishin KD, Eiriksdottir G, Gudnason V, Danesh J. Serum uric acid and coronary heart disease in 9,458 incident cases and 155,084 controls: prospective study and meta-analysis. *Plos Med*. 2005;2(3):e76.
10. Wannamethee SG. Serum uric acid is not an independent risk factor for coronary heart disease. *Current Hypertension Reports*. 2001;3(3):190-6.
11. Jularattanaporn V, Krittayaphong R, Boonyasirinant T, Udol K, Udompunurak S. Prevalence of hyperuricemia in Thai patients with acute coronary syndrome. *Thai Heart J*. 2008;21:86-92.
12. Uttawichai K, Takahashi M, Kiyoshi S, Hirai K, Kasempitakpong B, Matanasarawoot A, et al. Physical check up and blood data analysis in the Thai elderly of Chaingmai Province, Thailand. *Geriatrics & Gerontology International*. 2004;4(s1):S220-S2.
13. Abid A, Ali L, Mohyuddin T, Naveed S, Tarin S, Azhar M, et al. Acute myocardial infarction; evidence for a sex-age interaction. *Professional Med J*. 2006;13(2):178-85.
14. Spencer FA, Meyer TE, Gore JM, Goldberg RJ. Heterogeneity in the Management and Outcomes of Patients With Acute Myocardial Infarction Complicated by Heart Failure The National Registry of Myocardial Infarction. *Circulation*. 2002;105(22):2605-10.
15. Alsheikh Ali AA, Al Mallah MH, Al Mahmeed W, Albustani N, Al Suwaidi J, Sulaiman K, et al. Heart failure in patients hospitalized with acute coronary syndromes: observations from the Gulf Registry of Acute Coronary Events (Gulf RACE). *European journal of heart failure*. 2009;11(12):1135-42.
16. Khan S, Matiullah YA, Noor L, Ghaffar R, Awan ZA. Frequency of heart failure and its clinical outcome among patients presenting with acute myocardial infarction. *Pak J Physiol*. 2012;8(2):13-19
17. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe: epidemiological update. *European heart journal*. 2013;34(39):3028-34.
18. Abu sadique abdullah, Noortaj Begum, Md.Aminul Haque khan, etal. Admission Serum Uric Acid Levels And In-Hospital Outcomes In Patients With Acute Coronary Syndrome. *J Enam Med Col*. 2015;5(1):15-22.

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