Review Article

An Observational Study to Assess Outcome of NSTEMI Patients with Raised Serum Uric Acid Level in a Tertiary Care Hospital of Bangladesh

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Abstract

Background: Non-ST Segment Elevation Myocardial Infarction (NSTEMI) is the commonest form of ACS and a leading global cause of premature morbidity and mortality. Evidences link serum uric acid with short and long-term major adverse outcomes (MACE) in patients with NSTEMI.

Objective: To see in-hospital outcome of NSTEMI patients with raised serum uric acid level.

Methodology: This cross-sectional observational study was conducted in the Department of Cardiology, Sylhet MAG Osmani Medical College Hospital, Sylhet during the period from July, 2017 to June, 2019. Fifty NSTEMI patients with raised serum uric acid (>7mg/dl in male; >6mg/dl in female) level (Group A) and fifty NSTEMI patients with normal serum uric acid level (group B) admitted within 24 hours of symptom onset were consequently enrolled. In-hospital complications and mortality were recorded while continuing standard treatment for the event.

Results: The mean age was 60.82 (SD 9.62) years in group A and 49.90 (SD 10.40) years in group B. The mean age of the patients of group A was significantly higher than patients of Group B (p<0.001). Male preponderance was in both groups (84.0% versus 80.0%; p=0.603). Diabetes mellitus (52.0% versus 22.0%; p=0.002), hypertension (78.0% versus 52.0%; p=0.039) and dyslipidaemia (48.0% versus 12.0%; p=0.001) were more frequent in group A than that of group B. But smoking status (70.0% versus 66.0%; p=0.668), family history of CAD (10.0% versus 26.0%; p=0.476) did not differ significantly. Killip class did not differ significantly between group A and group B (p=0.127). In-hospital mortality was 5 (10.0%) patients in group A and 2 (4.0%) patients in group B; did not reach the level of significance (p>0.05) and complications such as post MI angina, cardiogenic shock, acute left ventricular failure, re-infarction, sinus tachycardia, sinus bradycardia, atrial flutter, atrial fibrillation, bundle branch block, ventricular tachycardia, ventricular fibrillation did not differ significantly between the two groups (p>0.05).

Conclusion: There is no significant difference between in-hospital outcome (mortality and complications) of NSTEMI patients with raised and normal serum uric acid level.

Introduction

The term Acute Coronary Syndrome (ACS) is a unifying construct representing a pathophysiologic and clinical spectrum culminating in acute myocardial ischemia. ACS encompasses Unstable Angina (UA) and ST-segment elevation MI (STEMI) or non-ST-segment elevation MI (NSTEMI) [1].

Myocardial infarction (MI) is one of the most common life threatening diagnoses in emergency hospital admissions.
Most of the complications occur during the first few hours of hospitalization. It is a major cause of death and disability worldwide. MI may be the first manifestation of coronary artery disease (CAD) or it may occur, repeatedly, in patients with established disease. MI is defined in pathology as myocardial cell death due to prolonged myocardial ischemia [2]. The clearest separation between UA and NSTEMI is the absence or presence, respectively, of abnormal concentrations of biomarkers indicative of myocardial necrosis, either the troponins (which are structural proteins) or creatine kinase-MB (which is a cardiac enzyme) [3].

Angiographic, Intravascular Ultrasound (IVUS), and angioscopic studies indicate that UA/NSTEMI usually results from the disruption of an atherosclerotic plaque with a subsequent platelet-rich thrombus that obstructs microvascular blood flow and transiently or partially obstruct epicardial blood flow.

Atherosclerosis is a chronic, lipid-driven inflammatory disease of the arterial wall leading to multifocal plaque development [4]. As a consequence of different technical measures in developed countries, in–hospital mortality from AMI in the general population declined by half, from 15% to about 7.5% and it is now as low as 3.5% [5]. The case fatality rates for cardiovascular events in low–income countries, represented largely by India, was 17%; this is much higher than in higher income countries, which had a case fatality rate of 6.5% [6].

In Bangladesh, data regarding case fatality rate of AMI are based on discrete and small scale studies. The exact proportion of ACS patients receiving early reperfusion therapy (Thrombolysis, Stenting or CABG) is also unknown. Thus, the result would be more alarming in Bangladesh if nationwide study could be conducted.

Acute myocardial infarctions have a substantially increased risk of death after hospitalization, when shock, left ventricular failure (LVF) or arrhythmias occur during their hospital stay. So cardiogenic shock, LVF and arrhythmias should be treated properly. Knowledge of potential complications will help in proper management of acute MI with good outcome [7]. In a French study, conducted from 1995 to 2015, it was shown that in patients with STEMI, mortality has continued to decrease since 2010, to reach an all–time low in 2015. In patients with NSTEMI, despite recent changes in antithrombotic medications at the acute stage, mortality has remained similar in 2015 in comparison with 2010 [8].

The better understanding of the pathophysiology of acute ischemic syndromes is associated with new therapeutic perspectives, which go beyond simple obstruction of coronary artery flow. The continuous development and use of platelet glycoprotein IIb/IIIa inhibitors, stent implantation, and the perfect knowledge of dynamic phenomena, such as thrombosis, genetics, inflammation, and possibly infectious agents and plaque stabilizers, will be the central focus of this old, but always renewed discussion.

Elevated Serum Uric Acid (SUA) level has been recently recognized as a risk factor for the development of the arterial hypertension, subclinical atherosclerosis, stroke and heart failure [9]. Hyperuricaemia is believed to cause endothelial dysfunction, vasoconstriction, platelet aggregation and act as a potent pro–inflammatory agent in the pathogenesis of atherothrombosis. Higher SUA determined on admission (within 48 hours since the symptom onset) in a cohort of patients from Croatia was independently associated with higher short–term mortality and poorer long–term survival after AMI [10].

The baseline levels of SUA strongly and independently predict adverse outcomes, in particular all–cause and cardiovascular (CV) mortality, and regardless of whether patients were on diuretics or not. SUA as a low–cost and widely available biomarker might improve clinical risk stratification of patients with left ventricular systolic dysfunction and/or heart failure following acute MI [11].

In a recent study done in Bangladesh it has been concluded that on admission serum uric acid estimation is a predictor of in–hospital poor outcome in patients with acute myocardial infarction. As it is a cheap and noninvasive procedure, it can be routinely practiced in cardiac emergency department for risk stratification of patients [9].

There have been enormous studies in multiple domains of ACS pathophysiology to detect unknown or less understood etiological and/or associated factors of ACS in the hope of a better understanding of the grave pathological condition so that newer approaches could be invented to combat the ominous impact of atherosclerotic cardiovascular disease on mankind.

Numerous studies on prognostic importance of raised SUA on mortality and complications of AMI patients have been conducted in many countries. Many studies found significant association of raised SUA with increased complications including in–hospital deaths in AMI patients. But there are also several studies that either found no association or inconclusive association between raised SUA and complications in AMI patients [9].

More prospective randomized trials on lowering SUA are needed in order to clarify the role of the uric acid in the development and progression of cardiovascular disease and to establish if reducing SUA level will translate into a better cardiovascular outcome. Hyperuricaemia will become then a meaningful target for the prevention and treatment of cardiovascular disease [9].

Atherosclerosis is an innate inflammatory disease, inflammatory activity is not confined to just a few atherosclerotic lesions but is present, more or less, in all such lesions throughout the body [12]. As a systemic disease atherosclerosis demands for a systemic approach, focusing on cardiovascular risk factors and the overall burden of disease to ensure appropriate identification and treatment of those who are at highest risk, the so called vulnerable patients.
This study was done to observe and record the in–hospital outcome including mortality and other complications in NSTEMI patients with raised serum uric acid level and compare the outcome with that of NSTEMI patients with normal serum uric acid level.

Methods and materials

This was a cross–sectional observational study that was conducted in the Department of Cardiology, MAG Osmani Medical College Hospital, Sylhet, during the period from July 2017 to June 2019. Purposive consecutive sampling of 50 cases of NSTEMI with raised SUA level and 50 cases of NSTEMI with normal SUA level who were admitted in CCU included in this study. Inclusion criteria include Patients with NSTEMI, admitted within 24 hours of symptom onset, 30–75 years of age and both males and females. Exclusion criteria are NSTEMI patients admitted after 24 hours of symptom onset, NSTEMI patients treated outside before admission in CCU, NSTEMI patients with CKD, Liver disease, Malignancy, Myeloproliferative disease, Past history of myocardial infarction, Past history of revascularization (Stenting, CABG), Cardiomyopathy, valvular heart disease, patients on Hydrochlorothiazide, those who refused to enroll in this study. Both quantitative and qualitative data were collected by using pre designed questionnaire. Informed written consent was taken from the patients and/or attendant after detailed explanation of the purpose of the study. Data were collected by the investigator through face to face interview, ECG, physical examination, laboratory investigations and imaging. All patients were followed up hourly in CCU and 3 times in 24 hours (8.00am, 2.00pm and 8:00pm) in post–CCU up to discharge from hospital. During follow up, a 12 lead ECG was recorded daily till discharge. Development of new chest pain (post MI angina), any arrhythmia, heart failure, cardiogenic shock and in–hospital mortality were observed and recorded. All relevant data were recorded in a pre–designed questionnaire that were processed and analyzed manually and using SPSS (Statistical Package for Social Sciences) Version 22.0. The patients were given an explanation on purpose and importance of the study along with the risks and benefits of the study. Written informed consent was taken from each participant with approval of the study protocol from the Institutional Ethical Committee before commencement of the study Tables 1–10.

Discussion

Clinical and epidemiological studies have proved that serum uric acid (SUA) is significantly correlated with cardiovascular occurrence and mortality of coronary artery disease [13]. But few studies have investigated serum uric acid levels in patients with acute myocardial infarction. Several theories have been discussed, such as high serum uric acid has an impact on

| Table 1: Distribution of the patients according to age. |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Age | Group A (n=50) | Group B (n=50) | Total (n=100) | p-value |
| 31-40 years | 3 | 10 | 17 | *p=0.001 |
| 41-50 years | 4 | 19 | 23 |  |
| 51-60 years | 18 | 15 | 33 |  |
| 61-70 years | 18 | 4 | 22 |  |
| 71-80 years | 7 | 2 | 9 |  |
| Mean | 60.8 (SD 9.6) | 49.9 (SD 10.4) | 55.4 (SD 11.4) | *p=0.001 |

SD=standard deviation. *Chi-Square (χ²) test and 'unpaired t-test were done to analyze the data.

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Fisher's exact test was done to analyze the data.

Table 10: Distribution of the patients by In-hospital Complications.

<table>
<thead>
<tr>
<th>In-hospital complications</th>
<th>Study Group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A (n=50)</td>
<td>Group B (n=50)</td>
</tr>
<tr>
<td>Acute left ventricular failure</td>
<td>27</td>
<td>19</td>
</tr>
<tr>
<td>Post MI angina</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Re-infarction</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Atrial Flutter</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Sinus Bradycardia</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Sinus Tachycardia</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Right Bundle block</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Premature Atrial Contraction</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

*Chi-Square (χ^2)* test and *Fisher's Exact test were done to analyze the data.

This study showed that males were predominant in both groups (84.0% and 80.0% respectively). No significant difference of gender was seen between two groups (p=0.603). Male preponderance of NSTMI was reported in several other studies like Belle, et al. (2017) [18].

This study showed that 37.0% of total NSTEMI patients were diabetic with 52.0% of patients of hyperuricemia was diabetic and 22.0% of patients of normal uric acid level were diabetic. The patients of hyperuricemia were more frequently diabetic than that of normal uric acid level (p=0.002). This finding was also supported by Safi, et al. (2004) [19], which showed that hyperuricemia was significantly associated with type 2 diabetes mellitus. However, this finding was in contrast to other study by Das, et al. (2015) [20], in which there was no significant association between serum uric acid level and diabetic status.

This study revealed that 35 (70.0%) patients of group A were smoker and 33 (66.0%) patients of group B were smoker; difference was not statistically significant (p=0.668). Zahid, et al. (2015) [12], in their study reported similar findings.

This study showed that 65.0% of total NSTEMI patients were hypertensive where as 78.0% patients of group A and 52.0% patients of group B were hypertensive separately. In this study, there was no significant association (p=0.241) between raised serum uric acid level on admission and hypertension in NSTEMI patients. This finding is different from that of other studies which showed that hypertensive patients had more hyperuricemia (Bickel et al., 2002) [21].

This study revealed that 30.0% of total NSTEMI had dyslipidaemia with 48.0% patients had dyslipidaemia in group A and 12.0% patients had dyslipidaemia in group B. Patients of group A were more frequently dyslipidaemic than that of group B (p<0.001). In 2012, Omidvar [17], found similar findings of 56.7% patients had dyslipidaemia in group A and 19.2% patients had dyslipidaemia in group B (p=0.862).

This study revealed that 23.0% of total NSTEMI patients had family history of CAD with 20.0% patients in group A and 26.0% patients in group B. Patients of group A had more frequent family history of CAD than that of patients of group B (p=0.476). Belle, et al. (2017) [18], reported that 22.0% of total population of NSTEMI had family history of CAD. Omidvar, et al. (2012) [17], found 26.7% patients were diabetic in group A and 28.3% patients were diabetic in group B (p=0.882).

The present study showed that Killip class I was in 23 (46.0%), Killip class II in 16 (32.0%), Killip class III in 6 (12.0%) and Killip class IV in 5 (10.0%) patients in group A; whereas Killip class I was in 31 (62.0%), Killip class II in 8 (16.0%), Killip class III in 9 (18.0%) and Killip class IV in 2 (4.0%) patients in group B. Killip class did not differ significantly between group A and group B (p=0.127). Biswas, et al. (2016) [23], found that Killip class-I was less frequent in hyperuricemia group compared to normal serum uric acid group; whereas Killip class-IV was more frequent in hyperuricemia group compared to normal serum uric acid group. So, their study found that increasing platelet reactivity [14], mediates inflammation, and stimulation of smooth muscle cell proliferation which probably worsened the acute thrombosis complication. Previous trials suggest that uric acid might be an independent predictor of major adverse cardiovascular events (MACE) in patients with coronary artery disease or only an indirect marker of adverse event due to the association between uric acid and other cardiovascular risk factors [15].

High SUA has been indicated as a risk factor for CAD and as an independent prognostic factor of poorer outcomes (occurrence of AMI, fatal AMI, sudden death, all-cause mortality) in patients with verified CAD [13] Less is known about SUA as a potential prognostic/risk factor for outcomes in patients affected specifically by AMI. A retrospective analysis observed a univariate association between higher SUA on admission (within 48 hours since the symptom onset) and higher thirty-day mortality (fourth versus first quartile SUA values) in AMI patients. It is also reported that an independent association between higher SUA and poorer long-term survival [16]. Having in mind, the potential ethnic/racial specificities and cultural differences (eg, diet, alcohol consumption), we aimed to investigate SUA levels determined on admission as a potential predictor of in-hospital outcome (mortality and complications). This cross-sectional observational study was conducted in the Department of Cardiology, MAG Osmani Medical College Hospital, Sylhet from July 2017 to June 2019 to see the in-hospital outcome of NSTEMI.

This study also showed that the mean age was 60.82 (SD 9.62) years in hyperuricemia group and was 59.90 (SD 10.40) years in normal uric acid group. The mean age of the patients of hyperuricemia was significantly higher than patients of normal uric acid level (p=0.001). Similar result was also observed in the study of Omidvar, et al. (2012) [17].
serum uric acid level is low among patients with lower Killip class and high among higher Killip class. Thus, raised serum uric acid level was associated with increased severity of heart failure and reflected the prognosis in essence with a significant p value (<0.05). This study is discrepant regarding Killip class and raised serum uric acid from that of Biswas et al. This study demonstrated that in-hospital mortality was 7.0% of all NSTEMI with 10.0% patients in group A and 4.0% patients in group B. In-hospital mortality was higher in group A than that of group B but did not reach the level of significance (p=0.05). Hossain, et al. (2016) [12], reported in-hospital mortality of acute MI was 7.3% with 14.3% of patients with raised uric acid level and 3% of patients with normal uric acid level. In-hospital mortality of acute MI was significantly higher in patients with raised uric acid level than normal uric acid level (p=0.020). Lazzeri, et al. (2010) [24], found that in-hospital mortality was higher in “high” SUA patients (9.0% vs. 2.5%), p<0.006 which is a bit different from this study. There were no association between elevated SUA and mortality among these population of this study. However, one of the largest studies, Ndrepepa, et al. (2012) demonstrated the positive association between elevated SUA and 1-year mortality in 5124 patients with ACS [25]. The large study that showed association of mortality with raised uric acid level included all ACS patients (STEM+ NSTEMI+ UA) and in-hospital mortality of STEMI patient is more than double than NSTEMI. In this study there were no STEMI patients and also no UA patients. So discrepancy between that study and this is justified as it is established that NSTEMI patients have comparatively lower in-hospital mortality than STEMI patients.

This study revealed that cardiogenic shock [5 (10.0%) versus 2 (4.0%), p=0.436]; acute left ventricular failure [27 (54.0%) versus 19 (38.0%), p=0.108]; re-infarct [1 (2.0%) versus 0 (0.0%), p=1.000]; sinus tachycardia [1 (2.0%) versus 6 (12.0%), p=0.108]; sinus bradycardia [4 (8.0%) versus 3 (6.0%), p=1.000]; atrial flutter [1 (2.0%) versus 0 (0.0%), p=1.000]; atrial fibrillation [1 (2.0%) versus 0 (0.0%), p=1.000]; right bundle block [0 (0.0%) versus 1 (2.0%), p=1.000], ventricular tachycardia [0 (0.0%) versus 1 (2.0%), p=1.000]; ventricular fibrillation [0 (0.0%) versus 1 (2.0%), p=1.000] did not differ significantly between two groups. But none of the patients of both groups developed mechanical complication. In this regards Hossain et al., (2016) [12], found that cardiogenic shock and acute left ventricular failure were significantly more frequent in hyperuricemia group compared to normal serum uric acid level group (p=0.037 and p=0.004 respectively) whereas arrhythmia and heart block did not differ significantly between two groups (p=0.545 and p=0.629 respectively). The difference may be because of inclusion of all acute Myocardial Infarction cases irrespective of STEMI and NSTEMI in their study but in this study only NSTEMI were included. In-hospital outcome of NSTEMI patients is comparatively better than STEMI patients globally.

**Conclusion**

There is no significant difference between in-hospital outcome (mortality and complications) of NSTEMI patients with raised and normal serum uric acid level.

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**Limitation**

This study was conducted in a single hospital where randomization was not done with minimal sample.

**References**


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