Serum Uric Acid Level in Hypertensive Patients with Acute Myocardial Infarction

Lalarukh Burki¹, Javed Akram², Asif Mehmood³, Farzauq Burki⁴

ABSTRACT
OBJECTIVES
To estimate serum uric acid level in hypertensive patients with acute myocardial infarction and hypertensive patients without myocardial infarction.

STUDY DESIGN
Cross-sectional study.

SETTING
Department of Medicine, Mayo Hospital, Lahore.

DURATION OF STUDY WITH DATES
Study was carried over a period of six months from 01-01-2007 to 30-06-2007.

SUBJECTS AND METHODS
Eighty hypertensive patients were included in the study out of which 40 patients with acute myocardial infarction were put in MI group and 40 patients without any history of myocardial infarction were labeled as non-MI group.

RESULTS
Mean age of the patients in MI group and non-MI was found to be 50.0±12.4 and 51.8±10.1 years, respectively. Results of Serum uric acid level in MI group were 6.9±1.0 mg/dl [0.407 ± 0.059 mmol/L ] and in non-MI group were 5.8±1.5 mg/dl [0.342 ± 0.088 mmol/L] (p<0.001). (where 1 mmol/L = 16.78 mg/dl or 1 mg/dl = 0.059 mmol/L).

CONCLUSION
The present study proved that raised serum uric acid level can cause hypertension and further rise can lead to MI.

KEY WORDS
Serum uric acid, Myocardial infarction, Hypertension

INTRODUCTION:
Recent studies show that concentrations of serum uric acid can be a cheap and easy-to-obtain indicator of cardiovascular risk [1,2]. Serum uric acid levels are increased in patients with ischaemic heart disease. Levels also increase with age, obesity, high alcohol consumption, combined hyperlipidemias, diabetes mellitus and hypertension. These cluster of abnormalities in turn significantly increase the risk of atherosclerotic vascular diseases like myocardial infarction (MI) and stroke [3,4]. Patient with arterial hypertension and no definable cause are said to have essential or primary hypertension, which is found to be associated with increased levels of serum uric acid [5]. Recent evidence suggests that uric acid may be an important contributing factor to the progression of atherosclerosis and its complications like renal disease and hypertension thus resulting in
cardiovascular disease. The role of serum uric acid as a risk factor for cardiovascular disease was not clear until the results of Rotterdam study, which showed that high serum uric acid levels were associated with risk of myocardial infarction and stroke [6]. In another study serum uric acid was found to be significantly high (P<0.001) in hypertensive patients with ischaemic heart disease. The mean values were also found to be high in normotensive patients with ischaemic heart disease but the difference was statistically non-significant [7]. In the Chin-Shan Community Cardiovascular Cohort Study subgroup analysis was done which showed that serum uric acid had significant risk only in subgroups with metabolic syndrome and hypertension. The conclusion was that in Taiwan serum uric acid could predict cardiovascular events in the population of relatively low coronary heart disease but high stroke risk [8].

Uric acid level of more than or equal to 5.2mg/dl was found to independently impart a 3.5-fold increased risk for cardiovascular death over a 5 year period [9]. This study is being done to find out whether the value of serum uric acid is increased more in hypertensive patients with acute myocardial infarction than in hypertensive patients without myocardial infarction, if so we can prevent myocardial infarction in hypertensive patients by keeping serum uric acid level low.

MATERIAL AND METHODS:
This study was carried out in the Department of Medicine, Mayo Hospital, Lahore, over a period of six months from 01-01-2007 to 30-06-2007. In this cross-sectional study eighty hypertensive patients were included using non-probability and purposive sampling, out of which 40 patients with acute myocardial infarction were put in MI group and 40 patients without any history of myocardial infarction were labeled as non-MI group. Informed consent was taken from all patients. The study included newly diagnosed cases of myocardial infarction on the basis of history, ECG changes and raised cardiac enzymes. All the patients were more than 25 years and included males and females. Those patients who had chronic renal disease, diabetes mellitus or history of gout were not included.

DATA COLLECTION:
In MI group patients with myocardial infarction coming through emergency department fulfilling inclusion and exclusion criteria were admitted. History was taken and examination was done concentrating on the symptoms and signs of myocardial infarction. ECG was done. Blood for cardiac enzymes, serum uric acid, blood sugar random and fasting lipid profile was taken and sent to pathology laboratory of King Edward Medical University.

In non-MI group hypertensive patients coming through emergency or outdoor department was included. History was taken and examination was done. ECG of all the patients was done. For admitted patients blood for serum uric acid, CKMB, blood sugar random and fasting lipid profile was taken and sent to pathology laboratory and the patients who were not admitted advised to get these tests done and report back to outdoor for review.

The confounding variables like age, sex, blood pressure, blood sugar random were matched. There is no risk benefit ratio. The data of each patient was recorded on proforma designed for the purpose. Data was entered using SPSS 12.0 version and analyzed statistically. Variables include age, sex, blood pressure, random blood sugar, fasting lipid profile and serum uric acid level, were analyzed using simple descriptive statistics. These were presented as Mean±Standard Deviation. Frequency and percentage was calculated for qualitative variables i.e. sex and chest pain features.

The two groups were compared regarding serum uric acid levels. The comparison was made by using independent sample t-test as this variable is quantitative in nature. A p-value of equal to or less than 0.05 was considered as significant.
RESULTS:

During the six months study period from 01-01-2007 to 30-06-2007, eighty cases of hypertension were selected from department of medicine Mayo hospital, Lahore, out of which 40 were included in MI group and 40 were included in non-MI. Throughout the study period there was no drop out.

All the patients included in the study were above 30 years. In the MI group 12 patients were between 41 to 50 years (30%), 11 were between 30 to 40 years (27.5%), 10 were between 51 to 60 years (25%) and 7 patients were above 61 years (17.5%). Mean age of the patients was found to be 50.0±12.4 years. In the non-MI group 15 patients were between 41 to 50 years (37.5%), 12 were between 51 to 60 years (30%), 6 were between 30 to 40 years (15%), and 7 patients were above 61 years (17.5%). Mean age of the patients was found to be 51.8±10.1 years.

In MI group 28 patients were male (70%) and 12 patients were female (30%), whereas in the non-MI group 26 patients were male (65%) and 14 patients were female (35%). P value was found to be 0.633.

The ECG that was done in the MI-group showed ST-elevation in different leads according to which diagnosis was made. In Patients having MI 13 patients had acute inferior wall MI (32.5%), 7 had antero-septal wall MI (17.5%), 10 had anterior wall MI (25.0%), 6 had antero-lateral wall MI (15%), 1 had inferior wall MI with right ventricular infarct (2.5%) and 3 had non-ST elevation MI (7.5%). The ECG done in patients in non-MI group were normal in 25 patients (62.5%), showed bradycardia in 3 patients (7.5%) and strain pattern in lateral leads in 12 patients (30%).

On examining the patients pulse was 80.7±11.0 beats per minute in MI group and 73.8±7.7 beats per minute in non-MI group (p=0.002). The reading of systolic BP noted in the MI group was 137.2±11.3 mmHg while that in the non-MI group was 138.0±13.4 mmHg (p=0.788). Diastolic blood pressure recorded in the MI group was 83.2±18.3 mmHg and in non-MI group it was 83.3±10.0 mmHg (p=0.970) (Table-I).

The investigations that were done after admission include cardiac enzymes (CKMB), blood sugar random, fasting lipid profile and serum uric acid levels.

Value of CKMB in MI group was 68.0±59.4 U/L while in non-MI group it was 9.9±7.0 U/L (p < 0.001). Results of blood sugar random in MI group were 114.7±24.9 mg/dl and in non-MI group were 125.7±24.3 mg/dl (p=0.050). Serum cholesterol level in the MI group was 192.9±21.4 mg/dl and in non-MI group it was 184.3±19.0 mg/dl (p=0.061). Value of Serum triglycerides was 180.1±70.1 mg/dl in MI group and was 171.3±43.7 mg/dl in non-MI group (p=0.502). Serum HDL in MI group was 38.5±4.6 mg/dl and in non-MI group was 36.8±5.6 mg/dl (p=0.144). Serum LDL in MI group was 122.7±19.8 mg/dl and in non-MI group was 113.1±13.9 mg/dl (p=0.014). Results of Serum uric acid level in MI group were 6.9±1.0 mg/dl [0.407±0.059 mmol/L ] and in non-MI group were 5.8±1.5 mg/dl [ 0.342±0.088 mmol/L ] (p<0.001). (Table-I). (where 1 mmol/L = 16.78 mg/dl or 1 mg/dl = 0.059 mmol/L)

### Table I
Comparison of Group-A (With myocardial infarction) with Group-B (non-myocardial infarction) n=80

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group-A with myocardial infarction n=40</th>
<th>Group-B without myocardial infarction n=40</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>137.2±11.3</td>
<td>138.0±13.4</td>
<td>0.788 (NS)</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>83.2±18.3</td>
<td>83.3±10.0</td>
<td>0.970 (NS)</td>
</tr>
<tr>
<td>Cardiac enzymes (CKMB) U/L</td>
<td>68.0±59.4</td>
<td>9.9±7.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Serum uric acid level (mg/dl)</td>
<td>6.9±1.0</td>
<td>5.8±1.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Non-significant (NS)

DISCUSSION:

Elevated Serum uric acid levels are commonly associated with Cardiovascular risk factors such as hypertension [10]. Different cohort studies have shown that serum uric acid level is an important risk factor for cardiovascular disease [11]. In the present study uric acid level in MI group was 6.9 ± 1.0 mg/dl [0.407 ± 0.059 mmol/L ] and in non-MI group were 5.8±1.5 mg/dl [0.342 ± 0.088 mmol/L ] (p<0.001). It shows that uric acid level is higher in hypertensive patients with acute MI than in hypertensive patients without MI and uric acid level is a risk factor for acute MI. Similar results were seen in a study by Ioachimescu et al, in which the data showed significant association between uric acid levels and mortality risk in both sexes [17].

Results of the present study agree with those of a study by Short et al in which Uric acid > or = 5.2 mg/dl [0.306 mmol/L] was found to independently impart a 3.5 fold increased risk for cardiovascular death over a 5-year period [9].

In a study by Fan et al, the mean serum uric acid in countryside male and female hypertensive patients were 0.349 ± 0.080 mmol/L [5.85 ± 1.34 mg/dl] and 0.266 ± 0.072 mmol/L [4.46 ± 1.20 mg/dl] respectively. The overall prevalence of hyperuricemia (defined as serum uric acid levels > or = 0.416 mmol/L [6.98 mg/dl] in men or > 0.360 mmol/L [6.04 mg/dl] in women) was 14.0%. Hypertensive patients with serum uric acid level in the highest quartile (≥0.344mmol/L [5.77 mg/dl] ) had higher incidence of coronary artery disease. After adjusting for age, sex, blood pressure, body mass index, glucose, and treatment history with anti-hypertensive drugs, hyperuricemia was still associated with increased risk of coronary artery disease ( odds ratio [OR] 1.428, 95% confidence interval [CI] 1.113 to 1.832) [14].

Similar results were seen in a large cohort PIUMA, in which serum uric acid level, before treatment, was found to be associated with subsequent cardiovascular events and death. In the upper quartile of serum uric acid (>0.369 mmol/L [6.2 mg/dL] in men; >0.274 mmol/L [4.6 mg/dL] in women), this association was found clinically and was independent of many confounding variables like diabetes, creatinine, age, BMI, sex, total cholesterol, HDL, left ventricular hypertrophy and BP during patient follow-up. Final results show that serum uric acid should not be blamed as a causative factor for cardiovascular disease but is most likely a valuable marker that differentiates other risk factors and their interactions. Also as compared to other markers, serum uric acid was more accurate for the prediction of risk of cardiovascular disease and all-cause mortality [12]. In the present study also age, sex, blood sugar random, BP and fasting lipid profile were treated as confounding variables.

Results of the present study match the results of a study by Alderman et al, which was done on a large multiracial population with essential hypertension. It was found that serum uric acid level and subsequent cardiovascular events are associated. This was more demonstrable in non-whites than in whites. Also cardiovascular disease risk was better predicted by in-treatment than by pretreatment serum uric acid, and this association persisted after adjustment for diuretic therapy, serum creatinine, and race in addition to other risk factors. Because the mean serum uric acid levels for men (0.399 mmol/L or 6.69 mg/dl) and women (0.321 mmol/L or 5.38 mg/dl) were found to be different, subjects were distributed using gender specific quartile cut points. After the adjustment of age and gender cardiovascular risks were found to be positively related to serum uric acid levels, with a relative risk of 1.48 (95% CI, 1.18-1.86) for the highest versus the lowest quartile. Smokers, diabetics, obese patients and those with hyperlipidemia showed less increase in cardiovascular events with increasing SUA than the patients without
those characteristics. Mean treatment SUA increased with increasing diuretic exposure [13]. This is again in accordance with the present study as all patients were non-diabetic and did not have hyperlipidemia.

In the present study in the MI group mean age of the patients was found to be 50.0 years with a standard deviation of 12.4 years while in the non-MI group mean age of the patients was found to be 51.8 years with a standard deviation of 10.1 years. According to a study by Nishtar et al there is difference of mean age in different parts of world. In western communities the mean age is higher than in south Asia [15]. In the GRACE trial it was seen that mean age of patients with myocardial infarction in the developed countries ranges from 65 to 68 years, which is higher than that in the developing countries (55 to 65 years). This difference may be because of different environmental, psychosocial factors and genetic makeup of different communities of the world [16]. Also in the Rotterdam study conducted in the west all the patients were above 55 years [6]. Unlike the studies mentioned, present study shows that the patients are suffering from hypertension and MI at a much younger age. Study conducted by Alderman et al had younger patients like present study and the patients were aged 20 to 85 years [13].

In present study in the MI group 28 patients were male (70%) and 12 patients were female (30%), whereas in the non-MI group 26 patients were male (65%) and 14 patients were female (35%). In the study by Alderman et al [13] out of 7978 patients 4883 were men (61%) and 3095 were females (39%), whereas Rotterdam and PIUMA study used sex as a confounding variable [6,12]. Percentage of male and female patients in both the groups of the present study almost matches that of Alderman et al [13].

In the present study blood pressure has been used as a confounding variable, the readings of systolic and diastolic BP noted in both the non-MI and MI group were within the same range and p-value was statistically not significant.

In the present study blood sugar random was within normal range in all the patients as all were non-diabetics also fasting lipid profile was within normal range. Thus blood sugar and fasting lipid profile were also treated as a confounding variable like in study conducted by Alderman et al [13]. Whether reducing uric acid levels will effect survival is still to be determined. Drugs that reduce uric acid levels have been used for many years to treat the patients with gout. Some studies suggest that reduction of uric acid levels has a favorable effect on markers of atherosclerosis and cardiovascular disease. Allopurinol, an inhibitor of xanthine oxidase, has shown to improve flow-mediated dilatation after 3 months of treatment in patients with hyperuricemia at high risk of cardiovascular events [17]. In the present study we did not assess or compare the effects of drugs on serum uric acid level.

CONCLUSION:

Acute Myocardial infarction is a common cause of mortality and morbidity in developing countries. Different risk factors like smoking, hypertension, diabetes mellitus and ischemic heart disease contribute differently to morbidity and mortality in different populations. This difference is because of different genetic makeup and environmental factors. There should be a strong emphasis on early identification and management of risk factors. There should be proper awareness of the masses regarding preventable risk factors and adaptation of healthy life styles.

The present study proved that raised serum uric acid level can be a risk factor for hypertension and further rise can lead to MI. From this inference can be drawn that while monitoring for hypertension and ischemic heart disease we should get serum uric acid level done, if found to be raised it should be controlled so as to prevent or delay hypertension which can further prevent MI.

We have very little data in Pakistan regarding uric acid and its effects on
hypertension and MI, so more studies at national level need to be done to find out whether by lowering serum uric acid levels can we actually reduce the risk of coronary heart disease. The data in the present study was of limited number of patients because of certain constraints and there is a need to conduct a multi center study on larger number of patients with follow-up to develop the national guidelines for the management of myocardial infarction and its risk factors. These guidelines may help us at national level in reduction of morbidity and mortality due to IHD, in a developing country like Pakistan, whose resources are very limited. We also need to study the effects of uric acid lowering drugs like allopurinol, losartan and atorvastatin on patients with cardiovascular disease, whether these can help in lowering the mortality and morbidity in these patients.

REFERENCES:
13. Alderman MH, Cohen H, Madhavan S, Kivlighn S. Serum uric acid and cardiovascular events...
in successfully treated hypertensive patients. Hypertension 1999;34:144–150.


