Impact of serum uric acid level in patients with acute myocardial infarction

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Abstract: Background: Acute myocardial infarction (AMI) continues to be a significant health problem and leading cause of death worldwide. increased serum uric acid level are observed in (AMI) patients and associated with high morbidity & mortality. Studies have shown that there is a close correlation between serum uric acid concentration and Killip classification for heart failure in patients of acute myocardial infarction: as uric acid levels are higher in patients with higher Killips class. **Objectives:** To assess the clinical value of serum uric acid level in early diagnosis & as a Prognostic value regarding complication and mortality during hospital stay. **Material and methods:** The study included 100 patients diagnosed as (AMI) besides 50 subjects as Control group. Serum uric acid level was measured on day 0, day 3 & day 7 of admission. Killip's classification was carried out and correlated with serum uric acid level with estimation of complications and mortality during hospital stay. **Results:** levels of uric acid- in three samples- in day of admission, 3rd day and 7th day were significantly higher in patients with AMI in the three samples with mean $\pm$ SD (10.88 ± 2.45, 8.33 ± 2.01 and 7.37 ± 1.91 mg/dl respectively) in comparison to the control group in which mean $\pm$ SD were (6.13 ± 1.95, 5.11 ± 1.43 and 5.02 ± 1.23 mg/dl respectively), with P value of (p< 0.02, p < 0.02 and p < 0.01) respectively. Patients with khillip class IV had the highest level of serum uric acid in comparison to other classes at (day 0), 3rd day and 7th day. Serum uric acid was significantly higher in those patients with complications than those without complications with P value was 0.04, 0.03 and 0.04 respectively. Also, Serum uric acid was significantly higher in 20 (20%) died patients compared to 80 (80%) survived patients with P value was < 0.01, < 0.02 and < 0.01 respectively. **Conclusion:** Serum uric acid was significantly elevated in patients with myocardial infarction compared to controls, patients with high serum uric levels had higher khillip classes, complications and had higher mortality So serum uric acid can be used as a prognostic marker regarding complication and mortality in patients with acute myocardial infarction.

Introduction

Acute Myocardial Infarction (AMI), overwhelmingly the most important form of CVD considered to be the leading cause of death.

Uric acid may function as the most important antioxidant in the plasma, and there was a relation between hyperuricaemia and acute Myocardial Infarction.

As Adenosine synthesized locally by vascular smooth muscle in cardiac tissue was rapidly degraded by the endothelium to uric acid, which undergoes rapid efflux to the vascular lumen due to low intracellular pH and negative membrane potential, Xanthine oxidase activity and uric acid synthesis are increased in vivo under ischemic conditions, and therefore elevated serum uric acid may act as a marker of underlying tissue ischemia. Hyperuricaemia is associated with deleterious effects on endothelial dysfunction, oxidative metabolism, platelet adhesiveness, and aggregation. **(1).**

Epidemiological studies have shown that elevated serum uric acid may be a risk factor for cardiovascular diseases and considered to be a prognostic marker for mortality in subjects with pre-existing heart failure in AMI patients (2).

Patients with elevated serum uric acid levels belonged to higher Killip's classification and had higher mortality. There was an association between serum uric acid and risk of complications in acute myocardial infarction (3).

Materials and methods
Patients:

The current study was conducted in Internal Medicine department, Assiut University Hospitals, between September 2016 and September 2017. The study included 100 patients **(Patients group)** diagnosed as acute myocardial infarction according to Omidivar et al., 2012 **(4)** besides 50 healthy subjects as **Control group**.

*Inclusion criteria***:**

After the approval from the ethical commitie of Assiut university and a written consent from all the participants. One hundred patients included in the study were selected among those admitted to coronary care unit of Assiut university hospital with AMI on the basis of the following inclusion criteria: Chest pain lasting more than 30 min., Typical ECG changes and Rise of serum cardiac enzymes concentration CK-MB and Troponin I (4)**.**

Exclusion criteria:

The patients who had liver and kidney diseases, younger than 18 years, gout, malignancy, drugs which increase uric acid level as (corticosteroids, cytotoxic drugs, ethambutol, salicylates more than 2g / d, diuretics and pyrazinamide), chronic alcoholism, hypothyroidism and violent exercise were excluded.

Methods:

 All patients were subjected to detailed history taking stressing on risk factors as Age, Sex, Previous Myocardial infarction, Smoking, Hyperlipidemia, Hypertension, Diabetes Mellitus, Obesity, Family history of coronary artery disease and through **clinical examination** with estimation of body mass index & blood pressure measuring.

investigations included: 12-lead ECG, echocardiography, Cardiac enzymes (Troponin I, CK and CK-MB), Serum uric acid levels (mg/dl) were measured to all the studied groups on the day of admission (day 0), **3rd** day and **7th** day.

Hyperuricaemia was defined as uric acid level more than 6 mg/dl in women and more than 7 mg/dl in men, Lipid Profile, Urea and creatinine, Blood Picture, Na & k and Random blood sugar were estimated.

Heart failure was stratified according to Killip classification into:

- Killip class I: no clinical signs of heart failure.

- Killip class II: patients with mild heart failure with roles involving one third or less of posterior lung fields, third heart sound and elevated jagular venous pressure.

- Killip class III: patients with acute pulmonary oedema.

- Killip class IV: cardiogenic shock (systolic blood pressure less than 90 mmhg and evidence of peripheral vasoconstriction (oligouria, cyanosis and diaphoresis).

Statistical analysis:

A detailed statistical analysis was carried out. Levels of serum uric acid on day 0 & day 3 & day 7 were compared using the paired "t" test. serum uric acid & Killip Class was compared with coefficient of correlation.

Data are demonstrated as mean ± SD for normally distributed continuous variables, median (minimum– maximum) for skew-distributed continuous variables and frequencies for categorical variables. Independent sample t-test.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows, version 20 (SPSS Inc., Chicago, IL, USA) and two-tailed p-value less than 0.05 was considered statistically significant.

Results

Baseline Laboratory data in all the studied subjects:

There were statistical significant increase levels of LDL, cholesterol and TGs in the patients group compared to the control group with *P* value of < 0.03, < 0.01 and < 0.01 respectively.

Also there were decreased levels of HDL in patients group compared to control group with *P* value < 0.02. Also random blood sugar and body mass index were significantly higher in patients group compared to control group with *P* value < 0.01 and < 0.03 respectively.

Cardiac enzymes in all the studied groups:

There were statistically significant increased levels of CK, CK-MB and troponin I in the patient group compared to control group with *P* value < 0.05 **(Table 3).**

Table 3: Cardiac enzymes in both study and control groups

Variables mean ± SD	patient group (n= 100)	Control group (n= 50)	*P* value
CK (ng/ml)	997.89 ± 213.45	88.13 ± 19.05	**0.03**
CK-MB (ng/ml)	136.33 ± 30.89	23.01 ± 3.22	**0.04**
Troponin (ng/ml)	6.37 ± 1.98	0.02 ± 0.01	**0.02**

P value was significant if < 0.05. CK, creatine kinase; CK-MB, creatine kinase- MB; n, number

Killip class and complications among patients:

Heart failure class I was detected in 37 (37%), while 25 (25%) of patients had class II, 22 (22%) of patients had class III and 16 (16%) of patients had class IV.

The short term complications occurred during hospital stay among our patients were; arrhythmias in 22 (22%) patients in which (ventricular ectopics occurred in 8 patients, atrial fibrillation in 7 patients, heart block in 5 and ventricular tachycardia in 2 patients), impaired systolic function EF (%) in 90 (90%) of patients, wall motion hypokinesia in 70 (70%) of patients and cardiogenic shock occurred in 8 (8%) of patients.

Level of Uric acid among all the studied groups:

It was noticed that level of uric acid- estimation in thee samples in day (0), 3rd day and 7th day - was significantly increased in patients group compared to control group.

There was significant increased serum level of uric acid at admission in patient group compared to control group, also There was significant increased serum level of uric acid in day (0) compared to 3rd day and 7th day with P value of (p < 0.01 and p < 0.01 respectively).

Table 4: Uric acid level in both patients and control groups

Time of estimation	Serum uric acid (mean ± SD)		P value
	Patient group (n= 100)	Control group (n= 50)	
Baseline (0)	10.88 ± 2.45	6.13 ± 1.95	**0.02**
Third day (3rd)	8.33 ± 2.01	5.11 ± 1.43	**0.02**
Seventh day (7th)	7.37 ± 1.91	5.02 ± 1.23	**0.01**
P1	**0.01**	0.09	
P2	**0.01**	0.77	
P3	0.34	0.66	

P1; between day 0 and day 3, P2; between day 0 and day 7, P3; between day 3 and day 7
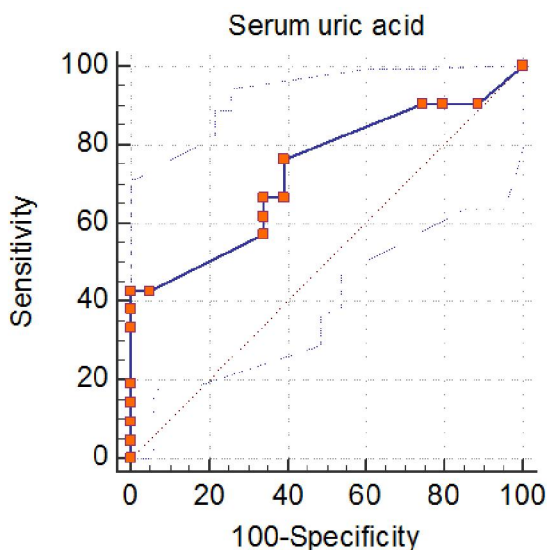

Figure 3 showed that serum uric acid above 8.7 mg/dl had 43% sensitivity and 100% specificity and 93% accuracy for prediction of complications in patients with AMI (AUR= 0.79 and *P*= 0.00).

Serum Uric acid based on Killip class

Killip class IV had significant higher level of uric acid in comparison to other classes at baseline, at the 3rd day and $7^{th.}$

Hospital stay and outcome in the studied patients:

Mean hospital stay was 8.33 ± 1.5 day with range of 7- 12 day. and deaths occurred in 20 (20%) patients.

Serum uric acid was significantly higher in those patients with complications than those without complications with *P* value was 0.04, 0.03 and 0.04 respectively**.**

Serum Uric acid in relation to mortality

Serum uric acid in the three samples was significantly higher in died patients compared to survived patients with *P* value was < 0.01, < 0.02 and < 0.01 respectively.

Prognostic Indices for Uric acid in prediction of complications:

Table 11: Prognostic indices of serum uric acid for prediction of complications

Indices	Value
Cutoff point	> 8.7 mg/dl
Area under the curve	0.79
Sensitivity	43%
Specificity	100%
Positive predictive value	100%
Negative predictive value	86.6%
Accuracy	93%

Discussion

In this study, level of uric acid in three samples, at base line (admission), 3rd day and 7th day, was significantly higher in all patients with AMI in comparison to the control group. This result was in agreement with **Agrawal et al., 2014 (1)** who found the same result.

In the present study we found that Heart failure class I was detected according to Killip classification in 37 (37%) of patients, while 25 (25%) of patients had class II, 22 (22%) of patients had class III and 16 (16%) of patients had class IV This result was in agreement with that reported by **Agrawal et al., in 2014** (1) who found that 60% of their cases were killips class 1, 12 % had class II, 10 % had class III and 18% class IV**.**

Also **Nozari and Geraiely., in 2011 (5)**, showed that according to Kllip Class, (50%) were class I, (34.6%) were class II, (11.7%) were class III, (3.7%) were class IV.

In the present study the mean hospital stay was 8.33 ± 1.5 day This finding was in agreement with **Omidvar et al., 2012** (4) who found that the duration of hospitalization was 7.3 ± 3.5 days.

The results of this study revealed that serum uric acid was significantly higher in those patients with complications than those without complications at baseline, 3rd day and 7th day. These results were in agreement with that of *Storhaug* et al in 2013 (6) and *Eisen et al in* 2013 (7).

Out of 100 patients in our study; death occurred in 20 (20%) patients This finding was in agreement with **Patil et al., in 2015 (3)** who found that Out of 100 patients, 20 died during 7 day follow up.

Also,. Elevated serum uric acid is highly predictive of mortality in patients with heart failure or coronary artery disease. **(Padma, 2017) (8)**.

The results of the current study revealed that serum uric acid at baseline, 3rd day and 7th day were significantly higher in those patients who died than those survived, in accordance with the study done by **Nadkar and Jain in 2008 (9)** who stated that uric acid was a good predictor of mortality in patients with AMI.

Also this result in agreement with that reported by **Agrawal et al in 2014** (1) who concluded that there was a higher & early mortality as uric acid levels increases at day 0, day3 and day7 in their patients.

Conclusion

- Serum uric acid was significantly elevated in patients with myocardial infarction compared to controls, patients with high serum uric levels had higher khillip classes, higher complications and had higher mortality, Hence combination of serum uric acid level and khillip classes can be used as a short prognostic marker for complication and mortality in patients with acute myocardial infarction.

- As regard significant increased level of serum uric acid in day of admission (day 0) in patient with AMI compared to day 3 & 7 and also compared to control group. so serum uric acid can be considered as an inexpensive and widely available biomarker when added to troponin I improve early diagnosis, detection of short term prognosis and complications in acute myocardial infarction patients.

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