Original Research Paper

Volume-7 | Issue-9 | September-2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 79.96

Medicine

"SIGNIFICANCE OF SERUM URIC ACID LEVEL IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION "

Dr.M.Subramani M.D, Assistant Professor Of Medicine, K.A.P.Viswanatham Govt. Medical College, Tiruchirapalli, Tamilnadu

Dr.L.Muthumani M.d Assistant Professor Of Medicine, K.A.P.Viswanatham Govt. Medical College, Tiruchirapalli, Tamilnadu. - Corresponding Author

ABSTRACT Acute Myocardial Infarction is the leading cause of mortality in both developed and developing countries. Factors contributing to death following Acute Myocardial Infarction relate mainly to electrical disturbances in the form of Arrhythmia and mechanical disturbances in the form of pump failure. Many trials have been conducted to identify markers that would be helpful to predict the risk of such adverse cardiac events. Those trials have used serum Magnesium level, C-Reactive Protein levels, Malonyldialdehyde, white blood cell count as a predictor for mortality and morbidity and risk of developing adverse cardiac events like sudden cardiac death and congestive heart failure. This study is one of such kind in that it tries to validate the prognostic role of serum uric acid level following acute myocardial infarction.

KEYWORDS : Myocardial infarction, uric acid, cardiac failure

INTRODUCTION

Acute Myocardial Infarction is the leading cause of mortality in both developed and developing countries (Rogers WJ et.al[1]., Kesteloot H et.al[2].,) Factors contributing to death following Acute Myocardial Infarction are many.

These factors relate mainly to electrical disturbances in the form of Arrhythmia (Carmeliet E[3], Thompson CA[4]) and mechanical disturbances in the form of pump failure (Hochman et. al[5]., Bertrand M et. al[6].).

Most sudden deaths in Acute Myocardial Infarction occur within one hour due to ventricular fibrillation and also due to left ventricular failure when there is an extensive injury. (Lewis EF et. al[7].)

Rest of the deaths following Myocardial Infarction occur within first one week and death cannot be predicted and occurs suddenly. Hence many trials have been conducted to identify markers that would be helpful to predict the risk of such adverse cardiac events.

Many trials have used serum Magnesium level,(Milionis HJ et.al[8].,) C-Reactive Protein levels, (Ridker PM, Morrow DA et.al[9].,) Malonyldialdehyde, (Pol Merkuriusz Lek[10]) white blood cell count (Comparan Nunez. A et. al[10].,) as a predictor for mortality and morbidity following Acute Myocardial Infarction and risk of developing adverse cardiac events like sudden cardiac death and congestive heart failure

THIS STUDY IS ONE OF SUCH KIND IN THAT IT TRIES TO VALIDATE THE PROGNOSTIC ROLE OF SERUM URIC ACID LEVEL FOLLOWING ACUTE MYOCARDIAL INFARCTION.

Free radicals produced in large amounts during myocardial ischemia and reperfusion take part in the degradation of cellular and subcellular membrane structures. The source of oxygen radicals in ischemic myocardium are Neutrophils recruited into the necrotic region as well as metabolic transformation of Hypoxanthine and Xanthine to Uric acid (Domonsky L et. al[10].)

Thus it is evident that elevated Uric acid levels is a good marker of oxidative stress and useful to assess the prognostic events in Acute Myocardial Infarction.

This forms the basis of the study.

AIMS OF THE STUDY

1. To assess the prognostic significance of serum Uric acid level in Acute Myocardial Infarction.
2. To correlate serum Uric acid levels with incidence of cardiac failure
3. To validate the relation between Quantitative serum Uric acid level on admission and Killip's class status on Acute Myocardial Infarction.

MATERIALS AND METHODS

STUDY POPULATION:

This study was conducted in the Department of medicine and Department of cardiology K.A.P.V. Govt medical College, Trichy, Tamil Nadu during the period of August 20016 to june 2017. Total number of patients included in this study were 100. There were 78 males 22 females patients ranging from 23 years to 83 years.

STUDY DESIGN :

This study is a prospective study. This study included 100 patients of Acute Myocardial Infarction of which patient who had a normal Uric acid level were taken as a control and the rest who had elevated Uric acid level were taken up as study population.

INCLUSION CRITERIA :

Patients with a diagnosis of Acute ST Elevation Myocardial Infarction were entered into the study. A definite diagnosis of Acute ST Elevation Myocardial Infarction was made if the patients satisfied the following criteria:

1. A History of typical retrosternal compressive chest pain lasting for more than 30 minutes, not relieved by rest or nitrates.
2. Typical ECG changes of Acute ST Elevation Myocardial Infarction (ST,T changes in two contiguous leads)

EXCLUSION CRITERIA :

1. Patients with elevated renal parameters.
2. Patients with Gout.
3. Patients with History of chronic alcoholism.
4. Patients with previous History of Ischemic Heart Disease and on Aspirin therapy.
5. Patients with Diabetes mellitus.
6. Patients on Diuretic therapy.

Above patients were excluded because the coexisting disease or drug therapy might itself produce a high Uric acid level.

Very late presentations of patients more than 72 hours also excluded since uric acid level tends to fall subsequently

VARIABLES RECORDED DURING THE STUDY:

Routine History, physical examination, Routine laboratory investigations were performed in all subjects.

1. Presenting History :
- Duration of chest discomfort
- Associated symptoms like sweating, palpitations, dyspnoea.
- Time of onset of symptoms.
2. Killip's classification on admission :]
3. Admission Electrocardiogram (ECG) :

a) Site of infarction : Anterior, Inferior, Lateral, Right ventricular, Global.

b) No of leads with Q waves or ST Elevation.

4. Laboratory Investigations :
- Full Blood count
- Blood Sugar, Blood Urea, Serum creatinine, Serum Electrolytes.
- Serum Uric acid level on admission.
- Urine Albumin, Sugar, Deposits.
- Serum cholesterol.

Qualifying patients received thrombolytic therapy with 1.5 million units of Streptokinase followed by Heparin for 5 – 7 days.

Assessment of left ventricular ejection fraction by Echocardiography was performed either on day 4 or 5 of hospitalisation in most patients or earlier if clinically indicated.

URIC ACID ESTIMATION :
Immediately after admission blood sample of 3cc was drawn by venipuncture and transferred to dry plain bottle and taken to biochemistry laboratory. The method used for analysis is Enzymatic method (Uricase method) by using Auto analyser.

In our laboratory, values taken as normal range[11]
For Males :3.4 - 7.0 mg/dl
For Females:2.4 - 6.0 mg/dl

METHODOLOGY:
Methods using URICASE, the enzyme that catalyzes the oxidation of uric acid to allantoin are most specific.[12] The simplest of these methods measures the differential absorption of uric acid and allantoin at 293 nm.[13] The difference in absorbance before and after incubation with URICASE is proportional to the uric acid concentration. This method has been proposed as candidate reference method.[14] This method was done in our study. This is the most specific method.

FOLLOW UP :
All the patients were followed up for a period of 10 days . During follow up any changes in killip's classification, features of Cardiac failure, were noted in both group of patients. Routine daily physical examination was done. ECG's were taken daily and additional investigations carried out if necessary. Patients were discharged at 11th day if they were stable otherwise their hospital stay was prolonged.

Framingham criteria for Heart failure like JVP elevation , Basal Rales, Acute pulmonary edema, S_3 gallop, Tachycardia (>120/mt), Lower extremity edema were used in this study for making a diagnosis of CCF.

RESULTS & OBSERVATIONS
The study population consisted of 100 patients with 78 males and 22 females. All patients belonged to places around Trichy District. All patients were admitted in I.C.C.U initially for 5 days then cared in adjoining intermediate cardiac care ward and discharged after an average period of 10 days provided there were no complications.

The various observations made in this study are depicted below

AGE INCIDENCE
Table : 1

Age in years	21-30	31-40	41-50	51-60	61-70	71-80	81-90
No of cases	2	10	20	37	22	7	2

SEX INCIDENCE
Table : 2

Sex	No of cases	Percentage
Males	78	78
Females	22	22

CONTROL AND STUDY POPULATION
Table : 3

Sex	Control Population (53)	Study population(47)
Male	43 (81%)	35 (74%)
Female	10 (19%)	12 (26%)

DISTRIBUTION OF PATIENTS ACCORDING TO URIC ACID LEVEL & SEX – IN TOTAL POPULATION
Table : 4

Uric acid (mg/dl)	3.0-3.9	4.0-4.9	5.0-5.9	6.0-6.9	7.0-7.9	8.0-8.9	9.0-9.9
Male	4	5	10	23	21	10	5
Female	2	1	5	8	3	2	1

KILLIP CLASS IN HIGH SERUM URIC ACID POPULATION (STUDY GROUP)
Table : 5

Killip Class	I & II	III & IV
No of patients	19	28

Percentage of patients with Killip I & II in high serum uric acid population $= \frac{19 \times 100}{47} = 40\%$

Percentage of patients with High killip class III & IV in High serum uric acid population $= \frac{28 \times 100}{47} = 60\%$

KILLIP CLASS IN NORMAL SERUM URIC ACID POPULATION (CONTROL GROUP)
Table : 6

Killip Class	I & II	III & IV
No of Patients	40	13

Percentage of patients with Killip I & II in normal uric acid population $= \frac{40 \times 100}{53} = 75\%$

Percentage of patients with Killip III & IV in normal uric acid population $= \frac{13 \times 100}{53} = 25\%$

TYPE OF INFARCTION
Table : 7

TYPE	IN HIGH SERUM URIC ACID POPULATION	IN NORMAL SERUM URIC ACID POPULATION
AWMI	19	18
ASMI	5	11
IWMI	5	12
Infero posterior MI	6	7
IWMI + RVMI	4	3
Lateral wall MI	6	1
Global MI	2	1

INCIDENCE OF HEART FAILURE IN TOTAL POPULATION
Table : 8

Total no of patients studied	No of patients who developed Heart failure
100	41

ie. 41 % of patients in the study developed Heart failure.

HEART FAILURE ACCORDING TO SEX
Table : 9

Total no of Heart failure patients	Male (%)	Female (%)
41	33 (80%)	8 (20 %)

PROPORTION OF HEART FAILURE CONTRIBUTED BY PATIENTS WITH NORMAL & HIGH SERUM URIC ACID LEVEL
Table : 10

Total no of patients with Heart failure	No of patients with high serum uric acid	No of patients with normal serum uric acid
41	30	11

Contribution of patients with High Serum uric acid level to Heart failure $= \frac{30 \times 100}{41}$

=73 %

Contribution of patients with
Normal serum uric acid level to = 11 x 100
Heart failure 41
=27 %

It is observed that patients with high uric acid level contributes 73% to the total incidence of Heart failure.

INCIDENCE OF HEART FAILURE IN PATIENTS WITH HIGH SERUM URIC ACID LEVEL (STUDY GROUP)
Table : 11

No of patients with high serum uric acid level	No of patients with Heart failure
47	30

Incidence= 30 x 100
47
=64 %

ie. 64 % of patients with high uric acid level developed Heart failure.

ie. 36 % of patients with high uric acid level didn't develop Heart failure.

INCIDENCE OF HEART FAILURE IN PATIENTS WITH NORMAL SERUM URIC ACID LEVEL (CONTROL GROUP)
Table : 12

No of patients with normal serum uric acid level	No of patients with Heart failure
53	11

Incidence=11 x 100
53
=21 %

ie. 21 % of patients with normal uric acid level developed Heart failure.
Ie. 79 % of patients with normal uric acid level didn't develop Heart failure.

ECHOCARDIOGRAM ANALYSIS (Fig :13)
Table : 13

Echo findings	In high uric acid patients	In normal uric acid patients
Normal LV systolic function	6	36
Mild LV dysfunction	14	9
Moderate LV dysfunction	13	3
Severe LV dysfunction	3	2
Total	36	50

DISCUSSION
Total number of patients included in this study was100, out of which 47 patients had elevated level of uric acid above normal range following Acute Myocardial Infarction.

CONTROL & STUDY POPULATION:
Out of 100 patients studied 53 patients had Normal uric acid level and they were taken up as control. Of which 43 (81%) were males and 10 (19%) were females. The rest 47 patients had elevated uric acid level and they were taken up as study group. Of which 35(74%) were males and 12 (26%) were females. (Table 3). Both were compared with various out comes.

CLINICAL STATUS- KILLIP CLASS & URIC ACID:
In this study 43 patients presented with Killip class I, 16 patients presented with Killip class II, 18 patients presented with Killip class III, 23 patients presented with Killip class IV. Killip class III & IV were taken as high risk category in this study and evaluated whether high uric acid concentration after myocardial infarction correlated with this high risk Killip class.

When clinical status of patients based on killip class I to IV and uric acid were analysed, the following observations were made.

In the control group who had normal serum uric acid level, 75 % belonged to I & II Killip class and only 25% belonged to Killip class III & IV as against the study 40 % Killip class I & II and 60% Killip class III & IV which parallely correlates with the elevated uric acid level and the clinical status (Table 5 & 6.)

Our study correlates with kojima S, Sakamoto et al., (American journal of cardiology, 2005 Aug 15) who also showed patients who had high uric acid level belonged to higher Killip class. Hence uric acid can also be used as an predictor of prognosis, but also a predictor of severity.

TYPE OF INFARCTION & URIC ACID :
In this study 37 patients presented with Anterior Wall Myocardial Infarction (AWMI) of which 19 patients had high uric acid level, 16 patients presented with Antero Septal Myocardial Infarction (ASMI), of which 5 patients had high uric acid level, 17 patients presented with Inferior Wall Myocardial Infarction (IWMI), of which 5 patients had high uric acid level, 13 patients presented with Infero posterior wall Myocardial Infarction, of which 6 patients had high uric acid level , 7 patients presented with inferior and Right Ventricular Myocardial Infarction (RVMI), of which 4 patients had high uric acid level, 7 patients presented with Lateral Wall Myocardial Infarction , of which 6 patients had high uric acid level, 3 patients presented with Global Myocardial Infarction ,of which 2 patients had high uric acid level.

When areas of infarction and uric acid levels were observed, an increased level of uric acid in Anterior wall Myocardial Infarction was noted. This cannot be taken into statistical account, because the overall incidence of Anterior Wall Myocardial Infarction itself was high (Table 7).

HEART FAILURE :
41 out of 100 patients in this study had Heart failure in the post Myocardial Infarction period. So the incidence of heart failure was 41 %. Of which 33(80%) were males, 8 (20%) were females.(Table 8&9)

It was observed that among 41 Heart failure patients, 30 patients had high uric acid level and 11 patients had normal uric acid level. So patients who had high uric acid level and normal uric acid level contributed to 73% and 27 % respectively to Heart failure. (Table 10)

It was also found that 30 patients out of 47 patients with high uric acid level had Heart failure amounting to an incidence of 64 % Heart failure in this group. While only 11 out of 53 patients with normal uric acid level had Heart failure. ie. Only 21% of patients with normal uric acid level had Heart failure. (Table 11&12)

The above figures suggest that the occurrence of Heart failure is high in patients with high uric acid level. Our studies comparable with other studies who showed similar findings and elevated serum uric acid level is an early predictor of short term outcome.

ECHOCARDIOGRAM:
In high uric acid population, 6 patients had normal LV function, 14 patients had mild LV dysfunction, 13 patients had moderate LV dysfunction, 3 patients had severe LV dysfunction.

In normal uric acid level population, 36 patients had normal LV function, 9 patients had mild LV dysfunction, 3 patients had moderate LV dysfunction, 2 patients had severe LV dysfunction. (Table 13).

Patients who had elevated serum uric acid level in the study group showed moderate to severe LV dysfunction (34%) This has correlated with an initial observation of cardiac failure which was 27% in this population.

So serum uric acid level can also be correlated with Echocardiographic cardiac dysfunction later, retrospectively with clinical findings earlier.

So uric acid level can be used as a definite predictor of cardiac failure.

CONCLUSION

1. Measuring serum Uric acid level is one of the predictable prognostic indicator in Acute Myocardial Infarction and one of the early and short term predictor.
2. There is a strong correlation of elevated serum Uric acid and cardiac failure
3. Patients with high Uric acid level belonged to higher Killip class status(III & IV) .
4. Elevated Uric acid level had a objective correlation with Echo

cardiographic evaluation of LV dysfunction.

5. Our study is compatible with other studies done with Uric acid as a predictor.

REFERENCES

1. Roger's WJ, Canto JG et.al., Temporal trends in the treatment of over 1.5 million patients with Myocardial Infarction in the US from 1990 through 1999. The national registry of Myocardial Infarction 1,2&3. J.Am.Coll Cardiol 36 ; 2056;2000.
2. Kesteloot H, Sans S et.al., Evolution of all causes and Cardio vascular mortality in the age group of the 75 to 84 years in Europe during the period 1970-1996: A comparison with world wide changes. Eur. Heart J 23:384,2002.
3. Carmeliet E Cardiac inonic currents and acute ischemia: from channels to arrhythmias Physiol.Rev. 79 ; 917;1999.
4. Thompson CA, Goldberg RT et.al., Changes over time in the incidence & case fatality rates of primary VF complicating Acute Myocardial Infarction Am.Heart J 139;1014;2000.
5. Hochman et al., Cardiogenic shock complicating Acute Myocardial Infarction. Circulation 107;2998;2003.
6. Bertrand M, Mc Fadden E , Cardiogenic shock : Is there light at the end of tunnel ? J.Am College cardiology 42;1387;2003.
7. Lewis EF, Moye LA et.al., Predictors of late development of heart failure in stable survivors of Myocardial Infarction: The CARE study. J.Am. College cardiology 42 ; 1446;2003.
8. Milionis HJ, Alexandrides GE et.al., Hypomagnesemia and concurrent acid base and electrolyte abnormalities in patients with CCF. Eur. J Heart failure. 4 : 167,2002.
9. Ridker PM, Morrow DA et.al., C- Reactive Protein, inflammation and coronary risk. Cardiol clin 21:315,2003.
10. Polmerkuriusz Lek, Comparan Nunez A Domanski, L, et.al., Malonyldialdehyde, Uric acid and white cell count as markers of oxidative stress in acute Myocardial Infarction and acute coronary insufficiency. J Clin Pharm Ther. 1998 Feb ;23(1) : 25-9.
11. Trivedi R.C , Robar L, Berka E ., Strong; clinical chemistry. 24 (1978), 1908.
12. 63.Clinical chemistry principles, procedures, correlation and Analytic methods. Michael L. Bishop 5th edition.P.229.
13. Feichtmeier TV, Wrenn HT. Direct determination of uric acid using uricase. Am J clinic pathol 1955; 25:833.
14. Duncan PH, Cooper et.al., A candidate reference method for uric acid in serum.Optimization & evaluation clin.chem. 1982,28;384