Serum Uric Acid Levels in Patients of Ischemic Heart Disease: Estimation & Correlation With Severity

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Abstract:

Hyperuricemia is strongly associated with peripheral, carotid, and coronary artery disease with the development of myocardial infarction & stroke (1).It also is an independent risk factor for hypertension. Many studies have demonstrated that a relation between hyperuricemia and obesity, kidney disease, diabetes & preeclampsia also exists. The present study was performed to estimate the levels of uric acid and study its correlation with severity & complications in patients of coronary artery disease. Total 100 patients of IHD & equal number of age and sex matched controls were studied over a period of two years. It was observed that the levels of uric acid were raised in patients of CAD in statistically significant number. The levels were more in acute myocardial infarction group of IHD& those who were in Killip's class 4 of heart failure. Hence it can be considered as a good marker of severity as well as predictor of mortality.

INTRODUCTION:

Uric acid is the end product of purine metabolism. It is metabolically inert substance without any physiological significance. It is eliminated by body in urine [(1)]. The kidneys excrete two-thirds of uric acid produced in body daily; the remaining is excreted in stools. An overproduction of uric acid occurs when there is excessive cell breakdown &catabolism of nucleic acids as in ischemia, leukaemia or cancer chemotherapy. The excretion of uric acid is affected in renal failure hence leads to hyperuricemia. The normal range of serum uric acid in adult males is 2.0 to7.0 mg/dl and 2.0 to 6.0 in females. The normal range for urinary uric acid is between 250-750 mg over 24-hour period[(2)]. 1 mg/dl rise in serum uric acid level is associated with 26% increase in cardiovascular mortality[(1)].The following conditions are known to lead to **elevated** serum uric acid levels : Gout, Renal failure, Alcoholism, Toxaemia of pregnancy, Leukaemia &lymphoma, Hyperlipidaemia, Starvation, Excessive cell destruction of cells with chemotherapy and radiotherapy [(2)].

Following myocardial infarction, in addition to rise in the levels of CPK-MB, Troponin –T&I, serum uric acid levels also rise. One of the major site for production of uric acid is the vessel wall, particularly endothelium. Adenosine synthesised locally by vascular smooth muscle in cardiac tissue is rapidly degraded by endothelium to uric acid. Xanthine oxidase and Uric acid synthesis are increased under ischemic conditions hence uric acid may act as a marker of cardiac ischemia. This is associated with deleterious effect on endothelial function, oxidative metabolism, platelet adhesiveness, haemorheology & aggregation. [(1)]. Hyperuricemia is associated with rise in circulating ***endothelin*** levels which is a potent vasoconstrictor substance. Also uric acid may have direct role in atherosclerotic process because vessel plaques show more amounts of it. Hyperuricemia via purine metabolism may also promote thrombus formation[(3)].Not only frank hyperuricemia (i.e.> 6mg/dl in women &> 7mg/dl in men) increases the cardiovascular mortality but even higher normal range has significant adverse effects [(4)].There is a well-known association between gout and cardiovascular diseases like hypertension as well as hyperlipidemia & diabetes mellitus [(5)]. The elevated level of uric acid observed in metabolic syndrome has been attributed to hyperinsulinemia, since insulin reduces the renal excretion of uric acid [(6)].

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MATERIAL AND METHODS

The present study was a comparative, hospital based study of estimation of serum uric acid in patients of all 3 categories of ischemic heart disease (IHD) in comparison to controls, carried out at our institute

during November 2007 to October 2009.The study included **100 patients of IHD (**Ischemic Heart Disease**) and 100 controls.** The controls were the healthy persons with age and sex matched and not having hypertension, diabetes, chronic kidney disease or on any drugs like diuretics, ethambutol or pyrizinamide.

The study group contained all adult male & female patients of IHD between the age group of 30-70 yrs .The 3 categories of patients of IHD were grouped as a) **Acute Myocardial Infarction b) Unstable Angina c) Stable Angina.**

The following patients were excluded from the study:

a) Patient with known cause of elevated uric acid level like chronic kidney disease, gout, haematological malignancy, hypothyroidism.

b) Patients taking salicylates (>2gm/day), diuretics, ethambutol, pyrazinamide.

c) Patients of Diabetes and cerebral stroked) chronic alcoholics All patients were studied in terms of clinical history, examination, Routine & specific laboratory tests like ECG, X-ray Chest, 2-D Echo &Doppler studies of heart. Every case was evaluated based on above data. The Serum Uric acid level was measured by **Kinetic method** using Uricase peroxidase & Ascorbate oxidase as reagents. The result was analysed by using 'Z' test [7].

OBSERVATIONS

1) In this study number of male patients (56%) was more than females (44%).

2) The number of both male & female patients was more in age group of 51-70 yrs.

3) Both male & females patients with IHD showed higher mean values of uric acid (6.61+/- 2.09 in males & 6.53+/- 1.75 in females). There was no significant gender difference statistically (The p value was 0.84.)

4) The mean value of serum uric acid of cases was higher than the controls in highly significant amount statistically, as shown in Table- 1.

***Table No.* 1**
Comparison of cases and controls according to mean S. uric acid levels

Serum Uric	Mean	S.D.	Range
Cases (n=100)	**6.57**	**1.93**	**1- 11.2**
Controls (n==100)	**4.41**	**1.17**	**1.6-7.1**
(p value is o.ooo, statistically highly significant)			

5) As shown in the table -2, the distribution of cases indicates that the maximum number of cases which showed significantly elevated levels of serum uric acid were in the category of acute myocardial infarction.

Table No.2
Distribution of cases according to type of IHD & mean s. uric acid levels

Type	No. of Subject	Mean +/- S.D. Uric acid level
1) Acute M.I.	63	6.95+/- 1.76
2) Unstable Angina	06	6.36+/-1.833)
Stable Angina	31	5.84+/2.15

6) There were more number of cases in Killip's class -1 but higher value of s. Uric acid was present in class-4.(table No. 2**)**

Distribution of cases according to Killip's Classification of Heart failure & mean S. Uric Acid levels

***Table No.* 3**

Killip's Class	No. of Subject	Mean +/- S.D. Uric acid level
1) No heart failure	66	6.00+/-1.83
2) Mild to mod. Heart Failure	24	7.17+/-1.68
3) Severe heart failure	08	7.86+/-1.78
4) Cardiogenic shock	02	7.95+/- 0.49

7) Two patients died, one each from group 3 & 4 of heart failure.

DISCUSSION:

The present study was carried out to determine the level of uric acid in patients of IHD & correlate it to various clinical types as well severity of IHD. Uric acid is considered as a marker of cardiac ischemia and predictor of mortality. It is basically released from vascular endothelium in response to ischemia with deleterious effects on vessel resulting in adverse outcome.

In present study 61% patients were in the age group of 51-70 yrs. which correlates with high incidence of IHD in this group .It emphasises uric acid being a risk factor in this population. This was also noted in previous studies by Jeremy G. Wheeler & et al in March 29, 2005 [8] stating that mean age of CHD was 70.2(S.D.= 9.7). The 56% of the patients were male & ratio of male to females was 1.3: 1 in present study. All male patients showed higher levels of uric acid than females. It also is consistent with higher incidence of IHD in males. Oestrogen is said to have protective as well as uricosuric effects in females [9].This finding was also noted by Jeremy G. Wheeler & et al in March 29, 2005, that raised uric acid values were seen in males.

In the present study 100 cases of IHD & equal number of age & sex matched controls were studied. The mean value of serum uric acid was higher in cases, in statistically significant amounts than in controls .Thus it can be concluded that it is an independent risk factor for IHD. This was also concluded by Jing Fang, et al in 2000 & it was found to be associated with increased cardiovascular mortality.[10] Bruce F. Culleton, et al in 2000 reported that uric acid is a marker of poor prognosis in patients of CAD, hypertension & heart failure[11]. Niskanen L., et al in 2006 [12] also reappraised the role of it in cardiovascular disease. Other studies have noted that higher levels predict the development of hypertension, obesity, kidney disease and diabetes [13]. Dehghan A., et al in 2008, using animal models have demonstrated the mechanisms by which uric acid induces the cardiac & renal changes [14]. There have been reports of cardiac and renal benefits of lowering uric acid level [15,16].

The mechanisms which support that hyperuricemia induces the metabolic syndrome are related to the fact that glucose uptake in skeletal muscle depends in part on increase in blood flow mediated by the insulin and the inflammatory & oxidative changes uric acid induces in adipocytes [17].

Dr. Davis wrote, in his presidential address to the American Medical association, that High arterial tension in gout is partly due to uric acid or other toxicsubstances in blood which increase the tonus of renal arterioles [18].

The review summarized by various studies say that although evidence is mounting towards the possible links of hyperuricemia to hypertension, renal disease and cardiovascular disease, it does not support the general treatment of asymptomatic hyperuricemia to reduce cardiovascular risk. However there is need to warrant clinical trials to determine whether lowering uric acid levels would be of clinical benefit in prevention or treatment of cardiovascular and renal disease [19]. Although the improvement of endothelial dysfunction is suggested after lowering uric acid by experimental studies, the improvement of endothelial function observed in patients with hyperuricemia and heart failure or diabetes occurred among patients who received allopurinol but not among those receiving other drugs designed to lower uric acid levels [20].

High insulin can also stimulate the kidney to produce angiotensin, a substance which increases blood pressure. Thus hyperuricemia also is associated with Syndrome X. Fructose is unique among sugars in that it rapidly causes depletion of ATP and increases both generation and release of uric acid. Experimental data support a link between fructose intake, hyperuricemia and increase in blood pressure [21].

In present study 3 categories of IHD were studied i.e. acute myocardial infarction, unstable angina &Stable angina. It was seen that 63% patients belonged to the first group and also the mean serum uric acid level was highest in this group. This suggests its association with severity of IHD. In studies done by M.Y. Nadkar, V. I. Jain in 2008 (1), reported that statistically higher levels of uric acid are found in patients of myocardial infarction on day of admission compared to controls.

The present study also studied the patients in reference to Killip's Classification of heart failure. 66% patients belonged to class 1, and only 2% were in class 4. The mean serum uric acid level was highest in class 4. Thus it can be concluded that uric acid levels correlate with severity and also serves as predictor of mortality. This is also supported by study done by M. Y. Nadkar & V.I. Jain in2008 (1), which said that on all days of MI, uric acid levels were more (>7 mg/dl) in higher class of Killip & those who died after 3 days had levels above 7mg/dl. As the present study had only 2 patients in class-4, this conclusion cannot be postulated strongly and needs more studies for confirmation.

CONCLUSION:

The present study concludes that the serum uric acid

levels are significantly more in patients of IHD, in the age group of 51- 70 yrs. The levels are more in acute myocardial infarction group of IHD in comparison to unstable angina & stable angina. The values are also higher in patients with Killip's class 4 of heart failure. Thus it may be concluded that the serum uric acid is an important independent marker of IHD, as well as predictor of severity &mortality.

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