

A CORRELATIVE STUDY BETWEEN SERUM URIC ACID AND hs-CRP IN PATIENTS WITH ISCHAEMIC HEART DISEASE

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ABSTRACT: INTRODUCTION: Uric acid (UA) contributes to the development of human vascular disease and atherosclerosis through a pro-inflammatory pathway. Highly-sensitive C-reactive protein (hs-CRP) also has emerged as the most exquisitely sensitive systemic marker of inflammation and a powerful predictive marker of future cardiovascular risk. In this study we estimated the levels of serum uric acid and hs-CRP in patients with ischaemic heart disease and association between them. **METHODS:** Study was carried out among fifty (50) newly diagnosed patients of ischaemic heart disease and fifty (50) age and sex matched healthy controls. Serum uric acid, hs-CRP, random glucose, urea, creatinine and cardiac troponin-I were measured.

RESULTS: The mean serum uric acid level in the control group was 4.66 ± 0.97 mg/dl and in case group was 6.86 ± 0.90 mg/dl. Mean hs-CRP level in control group was 0.19 ± 0.09 mg/dl, in case group was 5.14 ± 2.11 mg/dl. There was a positive association between UA and hs-CRP but the correlation was statistically not significant ($p > 0.05$). **CONCLUSION:** Our study indicated that there was a statistically significant association between ischaemic heart disease patients and elevated serum UA and serum hs-CRP and hence a strong role in the pathophysiology of ischaemic heart disease.

KEY WORDS: Ischaemic heart disease, hs-CRP, uric acid.

INTRODUCTION: With urbanization in the developing world, the prevalence of risk factors for Ischemic heart disease (IHD) is increasing rapidly in these regions such that a majority of the global burden of IHD is now occurring in low-income and middle-income countries. Population subgroups that appear to be particularly affected are men in South Asian countries, especially India (1).

The most common cause of IHD is atherosclerosis disease of an epicardial coronary artery (or arteries) sufficient to cause a regional reduction in myocardial blood flow and inadequate perfusion of the myocardium supplied by the involved coronary artery (1). It leads to increased uric acid generation (from adenosine breakdown) and reduced excretion (due to lactate competing with urate transporter in the proximal tubule of kidney) (2).

Hyperuricaemia is most commonly defined by plasma uric acid concentration greater than 7.0 mg/dl in men or greater than 6.0 mg/dl in women (3). The association of hyperuricaemia with cardiovascular disease remains controversial. There has been no test of

hypothesis that a reduction in serum uric acid would prevent cardiovascular disease. Serum uric acid probably reflects and integrates different risk factors and their possible interaction. (4) C-reactive protein is an acute phase reactant initially developed to, evaluate patients with infection. It was originally discovered by Tillet and Francis in 1930 as a substance in the serum of patients with acute inflammation that reacted with the C-polysaccharide of Pneumococcus. A high-sensitivity CRP (hs-CRP) test measures low levels of CRP (5).CRP has been shown to actively participate in both atheromatous lesions formation and plaque disruption (6, 7). CRP increases the expression of endothelial adhesion molecules and monocyte chemoattractant protein-1 (MCP-1), facilitates native LDL uptake into macrophages, promotes monocyte activation and a procoagulant effect by inducing monocytes to synthesize tissue factor (8, 9). CRP can also activate the classic pathway of complement activation and has been demonstrated to co-localize with terminal complement complexes in established coronary plaques (10).

Many recent studies have proved higher serum level of uric acid and high sensitivity C-reactive protein (hs-CRP) associated with ischemic heart disease. But very few comprehensive studies have yet been done to determine the correlation between serum uric acid level and hs-CRP level in ischemic heart disease. This study was therefore undertaken to determine the concentrations of serum uric acid and serum hs-CRP in IHD patients and to evaluate the association and correlation between them if there is any.

MATERIALS AND METHODS: This case-control study was carried out among fifty (50) newly diagnosed patients of ischaemic heart disease ≥ 20 years of age, admitted in Cardiology department of Assam Medical College and Hospital, Dibrugarh. Patients with inflammatory diseases like gout, rheumatoid arthritis, inflammatory bowel disease, renal disease, hypothyroid, diabetes, stroke, malignancy, bacterial infections were excluded from the study. Fifty age and sex matched healthy individuals were taken as control .Blood samples were collected from the subjects and estimation of serum uric acid , hs-CRP, random glucose, urea, creatinine and cardiac troponin-I were measured. Estimation of serum uric acid, random glucose, urea, and creatinine were done in Dimension RxL Max autoanalyzer. Serum UA was estimated by PAP /uricase method. Normal Reference Values with this method were 3.4–7.0 mg/dl for male and 2.5–6.0 mg/dl for female (11).Serum hs-CRP, was analysed in the Dimension RxL Max autoanalyzer using Particle Enhanced Turbidimetric Immunoassay (PETIA) Technique. Normal Reference Value for hs-CRP according to this method was 0.0–0.5 mg/dl (12). Qualitative estimation of cardiac troponin-I was done by using membrane-based immunoassay to confirm the diagnosis of ischaemic heart disease with ready to use Trop I Scan Test Device manufactured by Zydus Pathline.

A database was constructed on Microsoft Excel 2007, and statistical analysis was done using statistical package for social sciences (SPSS) Windows version 14. Student's t-test , and Pearson correlation were done to analyze the data.

RESULTS: The mean levels of serum glucose, urea and creatinine were within reference range in both cases and controls.

The mean serum uric acid level in the control group was 4.66 ± 0.97 mg/dl (in males : 4.98 ± 0.79 mg/dl and in females : 3.53 ± 0.63 mg/dl) and in case group was 6.86 ± 0.90 mg/dl(in males : 7.07 ± 0.86 mg/dl and in females, 6.12 ± 0.58 mg/dl). A highly significant increase in serum uric acid level was found in IHD subjects as compared to that in normal healthy

individuals with $p < 0.001$. Higher values of serum uric acid level was found in the age groups 60–<70 years and 40–<50 years in the control group. The higher values of serum uric acid in the cases were in the age group of 60–<70 yrs and ≥ 80 years. In both the study groups, the mean value of serum uric acid had no relation with age (Table 1).

The mean hs-CRP level in control group was 0.19 ± 0.09 mg/dl (in males: 0.18 ± 0.08 mg/dl and in females : 0.25 ± 0.07 mg/dl) and in case group was 5.14 ± 2.11 mg/dl (in males: 5.06 ± 2.17 mg/dl and in females : 5.44 ± 1.98 mg/dl). A highly significant increase in serum hs-CRP level was found in IHD subjects as compared to that in normal healthy individuals ($p < 0.001$). Mean value of serum hs-CRP level in controls increased with the increase in age. The highest value was in the age group of ≥ 80 years. In the cases, the mean value of hs-CRP level was high in the age groups of 60–<70 years and ≥ 80 years (Table 2).

The correlation coefficient 'r' between serum uric acid and serum hs-CRP was found to be 0.124 with $p\text{-value} > 0.05$ which means that statistically, the correlation is not significant.

DISCUSSION: In the present study, the minimum age of presentation of IHD was found to be thirty-eight (38) years and the maximum was of 85 years. The age-wise distribution revealed the highest percentage of cases in the age group 60–<70 years (26%) followed by 24% in 50–<60 years and 20% in 40–<50 years. Also, there were 2% cases in the age group of < 40 years. Similar findings were also observed by Krisnaswami *et al* (1970) and [Jhatakia KU et al](#) (1967) (13, 14). Yusuf *et al* (2004) reported that mean age of presentation on with new MI was 52 years in South Indians, 9.7% of these cases were younger than 40 years of age (15).

In the present study, there were 39 (78%) males and 11 (12%) females with male to female ratio of 3.5:1. Almost similar finding was found by Singh *et al* (14). They reported a ratio of 3.8:1 between males and females. The lower incidence of IHD in women, especially in premenopausal age, was probably due to high levels of oestrogens and high density lipoprotein, both of which have anti-atherogenic influence.

In our study, the mean serum uric acid level was found to be significantly higher than in ischaemic heart disease patients (6.86 ± 0.90 mg/dl) that in the control group (4.66 ± 0.97 mg/dl). Similar results were also found by Morris London *et al* (1967) and M. Torun *et al* (1998) (16, 17). The role of uric acid as risk factor for myocardial infarction is controversial. The Rotterdam Study concluded that uric acid is a strong risk factor for myocardial infarction and stroke (18). Hong Evy Lim *et al* (2010) has also found that serum uric acid was higher in patients with coronary artery disease as compared to normal healthy individuals (19).

In the present study, the mean serum hs-CRP level in ischaemic heart disease patients (5.14 ± 2.11 mg/dl) was found to be significantly higher than in control group (0.19 ± 0.09 mg/dl). Similar results were found by Arroyo *et al* (2004), N. Yilmaz *et al* (2007) and Suman B Sharma *et al* (2008) (20,21,22). Significantly higher hs-CRP levels were found in angiographically proven CAD patients with acute coronary syndrome as compared to patients with normal coronary angiography; and the levels of hs-CRP correlated well with the angiographic severity of the CAD (23). Also mean hs-CRP level in females (5.44 ± 1.98 mg/dl) is slightly higher as compared with males (5.06 ± 2.17 mg/dl) with IHD. Ross Arena *et al* (2006) also found a significantly higher hs-CRP level in females as compared with males (24).

These findings may indicate that serum uric acid and serum hs-CRP may have some role in the pathophysiology of ischaemic heart disease. The present study is consistent with earlier studies wherein it was concluded that higher levels of serum uric acid and hs-CRP were associated with poor prognosis of the ischaemic heart disease patients.

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In the present study, serum uric acid and serum hs-CRP were found to be positively associated ($r = 0.124$) but the correlation was not found to be significant. This finding is consistent with the study of Zhang Y H et al in 2009 (25). However a statistically significant correlation was found between serum CRP and serum UA in studies done by N. Yilmaz et al (2007) and Christa Meisinger et al (21, 26).

So, for a definitive conclusion regarding the usefulness of these two parameters as markers of cardiovascular risk factors and to know the mechanism by which uric acid and hs-CRP play role in the pathophysiology of ischaemic heart disease, further studies comprising of large number of cases and longer duration of study are required.

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Table 1: Age-wise distribution of serum uric acid

Age group (in years)	Serum uric acid (mg/dl)			
	Range		Mean ± S.D.	
	Controls	Cases	Controls	Cases
< 40	4.3	6.2	4.3	6.2
40-<50	2.6-6.9	5.0-8.2	4.83 ± 1.69	6.63 ± 0.97
50-<60	3.2-5.9	5.2-9.2	4.73 ± 0.77	6.93 ± 1.15
60-<70	3.6-6.2	5.5-8.5	4.85 ± 0.86	7.02 ± 1.00

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70-<80	3.9-5.10	5.9-7.8	4.33 ± 0.39	6.78 ± 0.63
≥ 80	3.9-5.0	6.8-7.3	4.32 ± 0.50	7.00 ± 0.19

Table2: Age-wise distribution of serum hs-CRP

Age group (in years)	Serum hs-CRP (mg/dl)			
	Range		Mean ± S.D.	
	Controls	Cases	Controls	Cases
< 40	0.03	3.81	0.03	3.81
40-<50	0.05-0.25	0.8-7.8	0.15 ± 0.07	3.88 ± 1.98
50-<60	0.10-0.29	1.3-9.2	0.17 ± 0.07	4.30 ± 2.68
60-<70	0.10-0.32	3.27-10.0	0.19 ± 0.08	5.05 ± 2.88
70-<80	0.10-0.40	3.72-8.50	0.24± 0.11	4.99 ± 2.90
≥ 80	0.21-0.35	3.9-8.20	0.28 ± 0.06	5.25 ± 2.28

Table-3: Statistical analysis for serum uric acid in the study groups

Study group	Number of Observation	Serum Uric Acid (Mean±S.D.) (mg/dl)	Degree of Freedom	't' Value	'p' Value
Controls	50	4.66 ± 0.97	98	7.6	< 0.001
Cases	50	6.86 ± 0.90			

Table-4: Statistical analysis for serum hs-CRP in the study groups

Study group	Number of Observation	Serum hs-CRP (Mean±S.D.) (mg/dl)	Degree of Freedom	't' Value	'p' Value
Controls	50	0.19 ± 0.09	98	9.2	< 0.001
Cases	50	5.14 ± 2.11			