COMPARISON OF URIC ACID LEVELS IN FIRST DEGREE RELATIVES OF ISCHAEMIC HEART DISEASE PATIENTS AND NORMAL POPULATION

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ABSTRACT
Introduction: Worldwide ischaemic heart disease (IHD) is increasing as a major cause of morbidity and mortality. There is an increasing list of established and evolving risk factors associated with the development of IHD. Uric acid is one of the modifiable risk factors which can be controlled by dietary modification. Better control of uric acid levels can delay the development of IHD in first degree relatives (FDRs) of IHD patients. Aim of this study was to assess serum uric acid levels independent of other established risk factors in FDRs of IHD patients and in normal subjects. It was a cross sectional study conducted in Department of Chemical Pathology, Sheikh Zayed Hospital (SZH), Lahore from January 2008 to January 2009.

Materials and Methods: Seventy five first degree relatives of IHD patients were selected. These were the attendants of the patients coming to the cardiology OPD and patients admitted to Coronary Care Unit (CCU), SZH Lahore. An equal number of subjects were selected as a control group who had no family history of IHD. After a detailed clinical history and physical examination, fasting blood samples were collected. Blood glucose, lipid profile and serum uric acid levels were estimated.

Results and Conclusion: Uric acid levels were found to be higher in FDRs as compared to normal subjects. Further the values were higher in those with an increase in incidence of IHD in the family.

Key Words: Ischaemic heart disease (IHD), First Degree Relatives (FDRs), Coronary Care Unit (CCU), Sheikh Zayed Hospital (SZH).

INTRODUCTION
Arteriosclerosis is a process in which fatty deposits accumulate in the walls of arteries. These fatty deposits build up gradually and irregularly leading to narrowing / hardening of blood vessels. Arteriosclerosis in the coronary arteries leads to their narrowing or occlusion causing ischaemia of heart muscles and can cause angina pectoris or myocardial infarction (MI). From 1990 to 2020, deaths due to cardiovascular diseases (CVD) are expected to rise from 28.4% to 33.4%^1. People of South Asian descent living in United Kingdom were found to have higher risk of cardiovascular disease as compared to Europeans. With changing habits and lifestyle, it is likely that the escalation of global cardiovascular disease epidemic will be most marked in India and Pakistan region.2

A number of risk factors have been described in the aetiology of IHD. These risk factors can be classified into modifiable and non-modifiable factors. It is now certain that reducing the modifiable risk factors, we can both prevent coronary artery disease and delay its progressions and complications after it has become manifest. The main aim of this study was to compare the uric acid levels (modifiable risk factor) in FDRs (non modifiable risk factor) of IHD patients and in normal subjects. Family history of IHD is an independent predictor3 and a positive family history identifies the small subsets of families in the population at highest risk for IHD. These are the people who may benefit most from targeted screening and intensive intervention.4,5

Uric acid, a product of purine metabolism, is degraded in most mammals by hepatic enzyme, Uricase to allantoin. Serum uric acid in the early stages of atherosclerotic process is known to act as antioxidant. It may be one of the strongest determinants of plasma antioxidant capacity.6,7 Thus, it may become prooxidant in atherosclerotic vessels due to certain conditions (timing; acidity and surrounding oxidant milieu) which are different from the normal vessels. Therefore, it is proposed that there is an existence of antioxidant–pro–oxidant redox shuttle in the atherosclerotic micro vascular intima.8 Serum uric acid is a graded marker of risk for the development of cardiovascular disease and stroke compared to patients with normal serum uric acid levels. It is specially observed in those with serum uric acid in the upper half of its normal physiological range.9 Hence, elevation of serum uric acid to more than 4
mg/dl should be considered as “red flag” in those patients at risk of developing IHD. This increase in serum uric acid should alert the clinicians to strive to utilize the global risk reduction programme to reduce the morbidity and mortality associated with IHD.10,11

MATERIALS AND METHODS
This cross sectional study was conducted in Sheikh Zayed-Federal Postgraduate Medical Institute Lahore. Seventy five apparently healthy subjects in age group 20 – 50 years, comprising equal number of males and females, who were first degree relatives of ischaemic heart disease patients, were included in the study. Seventy five healthy people with no history of ischaemic heart disease in family, matching age and gender as in first degree relatives were also studied as a control group.

Subjects came willingly with prior consent to undergo tests and examination. Criterion for inclusion of subjects was that they had one or more first degree relatives who were known cases of IHD. Exclusion criteria were the same for both first degree relatives and controls i.e. who were known diabetics, known hypertensive, smokers, obese and had abnormal lipid profiles. They were called with over-night 12 hours fast for sample collection.

Fasting blood samples (6 ml) were collected from individuals of all groups under study. It was allowed to clot for 20 – 30 minutes, centrifuged at 3000 RPM for 3 minutes and serum separated and estimation for serum uric acid, lipid profile and blood glucose were performed. Dade Behring kit – the urca flex (R) reagent cartridge, Cat No. DF77 was used on Dimension RXL Clinical Chem. System. The data was analysed on SPSS15 (Statistical package for Social Sciences).

Table 1: Serum uric acid levels (mg/dl) in first degree relatives of ischaemic heart disease patients and control group.

<table>
<thead>
<tr>
<th>Serum uric acid levels (mg/dl)</th>
<th>First degree relatives of ischemic heart disease patients</th>
<th>Control Group</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No. of Cases</td>
<td>Percentage</td>
</tr>
<tr>
<td>&lt; 5.2</td>
<td>49</td>
<td>65.3</td>
</tr>
<tr>
<td>&gt; 5.2</td>
<td>26</td>
<td>34.7</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>4.94±1.41</td>
<td>4.72±1.06</td>
</tr>
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RESULTS
Normal range for serum uric acid is from 3.5 – 7.0 mg/dl. The level of serum uric acid was analysed in the first degree relatives and control group as shown in table 1. Serum uric acid levels were divided in the upper and lower halves i.e. greater than 5.2 mg/dl and less than 5.2 mg/dl.9,11-13 There were 49 first degree relatives with the levels less than 5.2 mg/dl whereas 26 had more than 5.2 mg/dl. There were 58 cases in control group with values less than 5.2 mg/dl while 17 cases had more than 5.2 mg/dl. Mean ± SD of serum uric acid was higher in the first degree relatives (4.94 ± 1.41) as compared to controls (4.72 ± 1.06). As there is a strong evidence from a number of studies that with the increasing incidence of ischaemic heart disease (IHD) in a family, the relative risk of developing the IHD increases two to three folds in the first degree relatives.14 Therefore, we analysed the association of serum uric acid with the incidence of ischaemic heart disease in the family (table 2). Serum uric acid when correlated with family history of ischaemic heart disease showed a positive correlation (P < 0.05).

![Graph showing Serum uric acid levels (mg/dl) in first degree relatives of ischaemic heart disease patients and control group.]

Fig. 1: Serum uric acid levels (mg/dl) in first degree relatives of ischaemic heart disease patients and control group.

Table 2: Descriptive analysis of serum uric acid with the incidence of family history of ischaemic heart disease. Pearson’s coefficient of correlation, Mean and S.E.M are given.

<table>
<thead>
<tr>
<th></th>
<th>I Family Member</th>
<th>2 Family Members</th>
<th>&gt;2 Family Members</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Cases</td>
<td>37</td>
<td>32</td>
<td>7</td>
</tr>
<tr>
<td>Serum Uric Acid</td>
<td>4.573 ± 1.003*</td>
<td>5.212 ± 1.436</td>
<td>65.80 ± 2.492</td>
</tr>
</tbody>
</table>

- P = 0.033 significantly low as compared to those with more than two family members affected.
- Pearson’s coefficient of correlation for family history of IHD with serum uric acid = 0.289*
First degree relatives were divided into 3 groups. Group A with history of 1 family member affected from IHD. Group B with history of 2 family members affected and group C with history of more than 2 members in family suffering from IHD. The results showed that as the incidence of family history of IHD increased so did the values of serum uric acid in FDRs of IHD patients.

**DISCUSSION**

Ischaemic heart disease (IHD) is becoming a major health problem worldwide. This disease seems to follow an accelerated course with ischaemic events occurring a decade earlier in Pakistani population as compared to those reported from developed countries.\(^5\) One in four middle aged adults in Pakistan has coronary artery disease and the risk is uniformly increased in young and females.\(^6\) Conventional risk factors do not account for all cases of IHD but still occurs in people with no known risk factor. Amongst the growing list of risk factors for IHD, serum uric acid is a potentially modifiable risk factor. This study was specifically designed to determine the serum uric acid in the high risk group in order to evaluate their future risk of developing ischaemic heart disease. The aim of the present study was to determine the levels of serum uric acid in first degree relatives of IHD patients, as independent predictors to develop IHD, irrespective of known conventional risk factors i.e. (diabetes mellitus, hypertension, hyperlipidaemia and smoking).\(^7\) In the present study, serum uric acid was found to be higher in FDR’s of IHD patients as compared to normal subjects. This association of uric acid with IHD has been observed in a number of studies.\(^8\) Further, it has been observed that association of SUA with IHD is seen not only with frank hyperuricemia but also in subjects with serum uric acid in the normal to high range (\(> 5.2 \text{ mg/dl}\)).\(^9\) Similar results were found in the present study with serum uric acid levels less than \(5.2 \text{ mg/dl}\) in 65% of first degree relatives and 77% of control group, whereas the values were higher than \(5.2 \text{ mg/dl}\) in 35% of first degree relatives and 23% of control group. Mean ± SD of serum uric acid was higher in the first degree relatives (4.94 ± 1.41) as compared to controls (4.72 ± 1.06). According to Bonora et al, this elevation of serum uric acid is also observed in healthy offspring of parents with coronary artery disease, indicating a possible causal relationship.\(^10\) Another objective of this study was to determine correlation between family history of IHD and serum uric acid level. Serum uric acid increased significantly with an increase in incidence of IHD in the family. Pearson’s correlation formula was used that showed a significant positive correlation of serum uric acid with family history.

Main limitation of this study is that these FDR’s should have been followed up as it has been observed that if these people are followed up regularly they are likely to develop IHD earlier than those with normal levels. In a meta – analysis of 15 previous relevant studies — Involving a total of more than 9,000 incident cases and more than 150,000 controls, the overall findings suggest that individuals with baseline serum uric acid values in the top third of the population have about a 10% greater risk of developing IHD over the subsequent decade than those in the bottom third of normal range.\(^11\)

Based on this study it is **recommended** that serum uric acid be analysed on a larger scale. Detailed studies should be carried out to define genetics, mechanism of uric acid pathogenicity in development of atherosclerosis in first degree relatives of IHD in our population. These results suggest a positive association of high uric acid and family history of ischaemic heart disease. It indicates that higher serum uric acid may have a significant impact upon early development of atherosclerosis in FDRs as compared to normal population.

It is **concluded** that uric acid can be reduced by simple dietary modification and healthy eating habits. Based on this study it is recommended that all high risk people should be evaluated for serum uric acid along with other established risk factors.

**REFERENCES**