SERUM URIC ACID IN ISCHEMIC HEART DISEASE

Pages with reference to book, From 203 To 206

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Abstract
Serum Uric Acid was done in 150 male patients suffering from ischaemic heart disease (angina pectoris 67 and myocardial infarction 83) and 30 controls. Serum Uric Acid was significantly raised (P <0.001) in patients as compared to controls.
It is suggested that in assessing the susceptibility of a person to ischaemic heart disease (IHD) serum uric acid Values should be considered as a predictor amongst other risk factors (JPMA 36: 203,1986).

INTRODUCTION
The increasing morbidity and mortality from ischemic heart disease (IHD) particularly in young and middle aged men in spite of the best therapeutic efforts has created a great concern in most of the countries of world including Pakistan. Reduction in the prevalence and impact of coronary heart disease cannot be achieved by mere treatment but it also demands substantial efforts for its primary prevention i.e., measures before clinical illness.
Atherosclerosis a slowly progressive process is frequently associated with certain biochemical and physiological factors and life styles, called as coronary risk factors. Some of these factors have been convincingly demonstrated while others are still under investigation as is elevated serum uric acid levels.
Hyperuricemia was recognised even in nineteenth century as an etiologicat agent because of the high incidence of atherosclerosis in gouty patients. In the last few decades many prospective follow up studies of healthy subjects have shown a high incidence of ischemic heart disease among the individuals having high serum uric acid levels than in those with normal serum uric acid levels. While few other workers also found significantly raised serum uric acid levels in established cases of ischemic heart disease as compared to normal healthy subjects further strengthening its etiological association.
The present study was undertaken to study, the possible significance of raised serum uric acid levels in various clinical entities of the ischemic heart disease and to establish the incidence of hyperuricemia among them which would be important since effective therapy is available to correct it as compared to some other Identifiable risk factors. Serum creatinine level was determined to exclude the azotemic renal disease.

MATERIAL AND METHODS
A total of 150 adult males, clinically diagnosed to be suffering from IHD were studied. They were between 39-64 years of age and were selected from indoor or outdoor patients of Mayo and Services Hospitals, Lahore. Patients on thiazide diuretics, established hypertension, gouty manifestations or diabetes mellitus were excluded from the study. The patients were divided into two main groups according to the extent of ischemia indicated by clinical manifestations and electrocardiographic changes.
Group A: (67)-Ischemic group without infarction.
Group B: (83) Infarction group with previous or present infarction.
The control group comprised of 30 healthy age matched subjects, selected either from the hospital staff or from those admitted in the hospital for elective surgery as hernia etc. In each case a detailed personal, present, past and family history was obtained. A thorough physical examination was done to exclude any other accompanying disease which could possibly cause hyperuricemia. About 7 ml of venous blood was withdrawn from the anticubital vein of each patient as soon as possible after the attack in cases of myocardial infarction preferably in the first 24 hours, while in case of ischemic group without infarction blood was collected irrespective of the last attack. Serum was analysed for uric acid and creatinine. Serum uric acid was estimated by phosphotungstic acid reduction method\textsuperscript{12} while serum creatinine was measured by Jaffe’s reaction.\textsuperscript{13}

\textbf{RESULTS}

The mean values of serum uric acid in patient of ischemic heart disease without infarction (group A) and with myocardial infarction (group B) were 6.07 ± 0.16 and 6.37± 0.16 mg/dl respectively, which were significantly higher (P <0.001, P <0.001 respectively), than the mean value of the control group (4.93 ± 0.18 mg/dl), (Table 1). While the mean values of serum creatinine in group A and B were not significantly different from that of controls (Table 1).

\begin{table}
\centering
\begin{tabular}{ | l | c | c | c |}
\hline
 & \textbf{Uric acid mg/dl} & \textbf{Creatinine mg/dl} \\
& \textbf{Mean} & \textbf{S.E.M} & \textbf{Mean} & \textbf{S.E.M} \\
\hline
Control (30) & 4.93 & ±0.18 & 0.93 & ±0.030 \\
\hline
Group A (67) & 6.07 & ±0.16 & 0.97 & ±0.26 \\
\hline
Comparison of group & & & & \\
A with control & P** &  & N.S. & \\
\hline
Group B (83) & 6.37 & ±0.16 & 1.02 & ±0.27 \\
\hline
Comparison of group & & & & \\
B with control & P** &  & N.S. & \\
Comparison of group & & & & \\
A & B &  & N.S. & \\
\hline
\end{tabular}
\caption{Serum Uric Acid in Controls and Patients of Ischemic Heart Disease.}
\end{table}

The number of subjects is indicated in parenthesis. The difference is statistically significant as P** <0.001; N.S. – Non-significant.

Uric Acid in most of the groups A and B case ranged between 6-7 mg/dl as compared to 5-6 mg/dl in
controls (Table II).

Patients of both diseased groups had about 8 times higher incidence of hyperuricemia than the controls (Table III).

<table>
<thead>
<tr>
<th>Uric acid (mg/dl)</th>
<th>CONTROL</th>
<th>GROUP A</th>
<th>GROUP B</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-3</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>3-4</td>
<td>5</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>4-5</td>
<td>7</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>5-6</td>
<td>11</td>
<td>14</td>
<td>18</td>
</tr>
<tr>
<td>6-7</td>
<td>5</td>
<td>21</td>
<td>30</td>
</tr>
<tr>
<td>7-8</td>
<td>1</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>8-9</td>
<td>-</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>9+</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
</tbody>
</table>
Thus statistically, raised serum uric acid levels appear to be associated with ischemic heart disease.

**DISCUSSION**

In accordance with few earlier reports\(^9,11\) the present study also reveals significantly higher serum uric acid levels in patients of ischemic heart disease as compared to healthy subjects suggesting its association to the disease, irrespec. tive of its clinical entity. However, absence of significant difference in mean serum creatinine levels excludes possible underlying azotemic renal disease. This relationship is further strengthened because of the difference in frequency distribution of patients as compared to controls, based on serum uric acid levels (Table II). For a better understanding that whether hyperuricemia is a cause or an effect of the disease, various prospective follow up studies of healthy subjects have revealed a high incidence of ischemic heart disease among those having elevated serum uric acid levels suggesting its etiological association.\(^7,8\)

Despite all these evidences regarding elevated uric acid levels as a risk factor, its exact pathogenesis is still under debate. It is claimed to act either independently or through other risk factors.\(^15\) Some workers proposed that uric acid being a cationic surface agent, attaches itself to larger cholesterol molecules facilitating its contact with intimal surface of vessels, thus accelerating plaque formation.\(^4\) While others reported the deposition of uric acid crystals in the vessel wall initiating the atherogenic events.\(^16\)

Certain workers have more clearly demonstrated its role in occlusive arterial disease due to its effect on the platelets.\(^17-20\) Elevated serum uric acid levels stabilized the platelet aggregation by producing specific sticky forms of platelets “spread forms” as well as by inhibiting the degradation of ADP in circulation thus facilitating arterial thrombosis and hence atherosclerosis. Furthermore the release of certain constituents from platelets by interaction of monosodium urate crystals with platelets stimulates smooth cell proliferation in the vessel wall accelerating atherosclerotic plaque formation.\(^21\)

The importance of raised serum uric acid level as a risk factor for all the entities of IHD cannot be

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**TABLE - III**

Hyperuricemia in Patients and Controls.

<table>
<thead>
<tr>
<th>Group</th>
<th>No of subjects with Hyperuricemia*</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1</td>
<td>3.33</td>
</tr>
<tr>
<td>Group A</td>
<td>18</td>
<td>26.87</td>
</tr>
<tr>
<td>Group B</td>
<td>83</td>
<td>26.53</td>
</tr>
</tbody>
</table>

*Hyperuricemia has been defined statistically as mean value in controls ± S.D. (Klinenberg,\(^14\) 1977). So calculated hyperuricemic level is \((4.93 \pm 2.04) = 6.97\) mg/dl – Aprox – 7 mg/dl.
denied, it is therefore recommended that raised serum uric level may be included in the list of coronary risk factors. The usefulness of uricosuric drugs may also prove to be of special importance in the preventive efforts.\textsuperscript{14,22}

REFERENCES

12. Tietz, N. Fundamentals of Clinical Chemistry