Original article

Evaluation of serum uric acid and serum lactate dehydrogenase in hypertension.

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Abstract:
Background: Uric acid has been observed to be associated with hypertension in various studies involving different populations but very little information was found on this association in an Indian population. Serum lactate dehydrogenase (LDH) levels are increased in acute myocardial infarction and other disorders like pregnancy induced hypertension, preeclampsia and eclampsia. We did not find any studies for LDH association in essential hypertension.
Aims and objectives: The aim of this study is to correlate serum uric acid and LDH with blood pressure measurements in individuals who are hypertensive and normotensive, and to find out the possibility of existence of an association between uric acid levels and LDH with hypertension.
Material and methods: It is a case control study consisting of 100 cases with hypertension (50 male and 50 female) compared with 100 healthy controls (50 male and 50 female). Systolic and diastolic blood pressures were recorded and serum levels of LDH and uric acid were estimated in both the study groups.
Results: We found statistically significant increased values for serum uric acid and LDH in both male and female cases with hypertension as compared to male and female controls respectively (p value < 0.001). There was positive correlation of serum uric acid with systolic and diastolic blood pressure in both the groups of study cases.
Conclusion: This study concludes that serum uric acid and LDH levels were significantly elevated in patients with hypertension with significant positive correlation of serum uric acid with systolic and diastolic blood pressure.
Key words: Uric acid, lactate dehydrogenase, hypertension, blood pressure, hyperuricemia.

Introduction:
Epidemiological studies have shown that hypertension is present in 33% of urban and 25% of rural populations in India1. According to the 2001 census, the absolute numbers of hypertensive in India were 31.5 million rural and 34 million urban subjects, a total of 65.5 million2. Hypertension is considered to be the third leading killer disease in the world and is responsible for 57% of all stroke deaths and 24% of all coronary heart disease (CHD) deaths in India3. Uric acid is the end product of purine metabolism, 2/3 of which is formed in blood from endogenous purine substances and 1/3 from diet. It is filtrated through the glomeruli and almost totally reabsorbed in the proximal convoluted tubules by both active and passive carrier mediated processes4. Level of uric acid in the body is affected by the balance of its
formation and excretion. Conditions associated with excessive production of uric acid and its reduced renal excretion causes hyperuricemia which can be defined as level of uric acid in the blood that is abnormally high. Ten percent of cases show uric acid overproduction in conditions with high cellular turnover, genetic errors and tumor lysis syndrome. Rest of cases (90%) show impaired uric acid excretions which occur in renal insufficiency of any cause. Generally Male have a greater risk of developing hyperuricemia than female in all age groups, although the gender ratio tends to equalize with increasing age. Hyperuricemia is becoming a modest problem all over the world with a steady progress in its prevalence.

Elevated levels of serum uric acid is strongly associated with development and progression of hypertension and renal diseases, but whether uric acid plays a causal role or whether it simply acts as an indicator in patients at risk for these conditions remains controversial.

Many authorities do not consider an increased uric acid to be a true risk factor for cardiovascular diseases, because patients with hyperuricemia mostly have other well established risk factors for cardiovascular conditions like hypertension, renal disease, obesity, dyslipidemia, and insulin resistance.

Strong evidence based on epidemiological and experimental studies suggests that serum uric acid is independent and significant risk factor for cardiovascular and renal disease particularly in patients with hypertension, heart failure, acute myocardial infarction and diabetes.

In consideration of this controversy we conducted this study to estimate serum uric acid level in both male and female cases of hypertension to see its association with blood pressure and to compare with controls.

Lactate dehydrogenase (LDH) is an intracellular enzyme that is widely distributed in tissues. In glycolysis, LDH converts pyruvate to lactate, when oxygen is not available. LDH is raised in number of pathological conditions like hematological disorders, acute myocardial infarction, liver diseases and several respiratory diseases. Underlying mechanisms for increased serum LDH include tissue injury, inflammation, hypoxia, necrosis, hemolysis or malignancies.

Many studies have shown that there was increased level of serum LDH in pregnancy induced hypertension, preeclampsia and eclampsia. We didn’t find any studies showing association of serum LDH and essential hypertension in Indian population. So it was our attempt to study the levels of serum LDH and serum uric acid in patients with hypertension.

Material and methods:

It was a case control study of 200 subjects divided into two groups consisting of 100 healthy controls and 100 cases of essential hypertension. Each group consists of 50 males and 50 females for the study. The study was conducted in department of Biochemistry, GMERS Medical College and Hospital, Valsad. Newly diagnosed hypertensive subjects were included in the study cases. All the participants gave written informed consent and this study design was approved by the institutional research and ethics committee.

Hypertension was defined as a systolic blood pressure equal to or more than 140 mmHg and or diastolic pressure equal to or more than 90 mmHg. Blood pressure was measured 3 times consecutively in the right arm placed at the heart level using sphygmomanometer after the
subjects had rested for at least 10 minutes in a sitting position. The measurements were taken 1 minute interval and the average systolic and diastolic blood pressures were recorded and used for our analyses. Individuals with diabetes mellitus, gout, history of cardiovascular or kidney disease, pregnant females, Patients already on hypertensive drugs or any other medication which can affect the serum uric acid levels were excluded from the study. 50 healthy males and 50 healthy females with no hypertension and normal blood pressure and of similar age group were selected as controls. Blood samples were taken by venipuncture in plain vaccutainer. Grossly hemolysed and lipemic samples were excluded from the study. All the samples were analysed by Microlab RX 50 diagnostic equipment. Serum uric acid was estimated by uricase-trinderend point method. Serum LDH was estimated by DGKC kinetic method.

Statistical analysis:
The data of the study was analyzed by Graph pad prism software version 7. Students unpaired’t’ test was applied for the comparison of variables between controls and cases. P value <0.05 was considered as statistically significant. Pearson’s Correlation Coefficient was derived to study the relationship of serum uric acid and serum LDH with systolic and diastolic blood pressure among cases.

Results:
We found that family history of hypertension was present in 57% of male cases as compared to 25% in male controls. Same history was found in 58% of female cases as compared to 39% female controls.

Table 1 and table 2 shows that mean age of cases and control groups were statistically non-significant. There were significantly elevated values for systolic and diastolic blood pressure along with significantly increased serum uric acid and serum LDH in male and female cases in comparison to male and female controls respectively.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Male controls</th>
<th>Male cases</th>
<th>‘t’ value</th>
<th>P value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>43.98</td>
<td>2.86</td>
<td>43.16</td>
<td>2.59</td>
<td>1.50</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>122.4</td>
<td>6.07</td>
<td>161.3</td>
<td>7.27</td>
<td>29.02</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>82.28</td>
<td>4.16</td>
<td>98.36</td>
<td>4.74</td>
<td>18.03</td>
</tr>
<tr>
<td>Serum uric acid (mg/dl)</td>
<td>4.50</td>
<td>0.68</td>
<td>5.81</td>
<td>0.79</td>
<td>8.83</td>
</tr>
<tr>
<td>Serum LDH(U/l)</td>
<td>274.5</td>
<td>30.87</td>
<td>351.1</td>
<td>30.05</td>
<td>12.57</td>
</tr>
</tbody>
</table>

Table 1: Comparison of variables of male controls and male cases.
Table 2: Comparison of variables of female controls and female cases

<table>
<thead>
<tr>
<th>Variable</th>
<th>Female controls</th>
<th>Female cases</th>
<th>‘t’ value</th>
<th>P value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.14±2.19</td>
<td>42.42±2.95</td>
<td>1.39</td>
<td>0.169</td>
<td>Non-significant</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>114.2±5.94</td>
<td>154.5±6.24</td>
<td>33.10</td>
<td>&lt;0.001</td>
<td>Significant</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>76.92±4.64</td>
<td>98.08±5.85</td>
<td>20.02</td>
<td>&lt;0.001</td>
<td>Significant</td>
</tr>
<tr>
<td>Serum uric acid (mg/dl)</td>
<td>3.48±0.68</td>
<td>5.03±0.65</td>
<td>11.57</td>
<td>&lt;0.001</td>
<td>Significant</td>
</tr>
<tr>
<td>Serum LDH(U/l)</td>
<td>210±13.60</td>
<td>316±18.4</td>
<td>32.69</td>
<td>&lt;0.001</td>
<td>Significant</td>
</tr>
</tbody>
</table>

Discussion:

We found significantly elevated levels of serum uric acid in both male cases and female cases as compared to their respective control group. Similar findings were observed by Emokpae and Abdu who observed elevated serum uric acid in male cases (9.1±1.2) &in female cases (8.1±1.4)\(^1\). Similar findings were reported in other few studies\(^19,20\).

There are two schools of thought for elevated uric acid, according to one it is elevated secondary to hypertension, and beneficial to body being antioxidant. Recent epidemiological studies have other opinion that uric acid is a major and independent risk factor for the development of cardiovascular disorders and play a significant role in development of hypertension and renal disease\(^10,13\).

Experimental studies have demonstrated that increased uric acid induces systemic hypertension and renal injury via activation of the renin angiotensin system. Uric acid enters directly into both endothelial and vascular smooth muscle cells and causes local inhibition of endothelial nitric oxide levels. It is responsible for stimulation of vascular smooth muscle cell proliferation, and stimulation of vasoactive and inflammatory mediators, resulting in constriction of vessels and hypertension\(^21,22\).

Serum uric acid may be considered as a precursor of hypertension or a reflector of subclinical renal dysfunctions, which may induce both the elevated serum uric acid level and elevated blood pressure\(^23\).

Some studies put forwarded various mechanisms for association of increased uric acid in hypertension. According to this, intra renal ischemia in hypertension may lead to increased generation of uric acid via xanthine oxidase. Sympathetic activity or hyperinsulinemia may produce impairments in renal sodium management, leading to elevated arterial pressure, decreased renal blood flow and decreased uric acid secretion. This increases purine oxidation, which leads to increased reactive oxygen species, subsequent vascular injury, reduced nitric oxide level followed by vasoconstriction and elevated blood pressure\(^24,25\).
Recently therapeutic trial with uric acid lowering drug allopurinol have significantly reduced blood pressure in in newly diagnosed hypertensive patients with hyperuricemia which proves the role of uric acid in hypertension as a causative factor\textsuperscript{26}.

Thus, experimental, epidemiologic, therapeutic trial studies and our study clearly show that increased uric acid is a marked associated factor for hypertension. In the present study, we showed that serum uric acid levels were positively correlated with the severity of both systolic and diastolic blood pressures.

We also found significantly elevated levels of serum LDH in both male cases and female cases. Our study is the first study of its own kind to see the association of serum LDH and essential hypertension. Similar to results of pregnancy induced hypertension\textsuperscript{15-17}, we found significantly increased levels of serum LDH in essential hypertension.

We also found significant rise in serum LDH in one study of idiopathic pulmonary arterial hypertension\textsuperscript{27}. Serum LDH is intra cytoplasmic enzyme present in all the tissues of the body. It is also considered as one of the cardiac marker for acute myocardial infarction and its level is increased in tissue injury, inflammation, hypoxia, ischemia and malignancy\textsuperscript{28}.

It was proposed that hypertension produces renal micro vascular disease and local tissue hypoxia which leads to increased activity of LDH and increased levels of serum lactate. Lactate would be expected to decrease the tubular secretion of uric acid; resulting in increased levels of serum uric acid.

Parallel to cancer, anaerobic glycolysis is a dominant vascular feature in hypertension which leads to the increased activity of LDH and lactate production\textsuperscript{27,29}. Our study showed that the Serum LDH level was significantly elevated in hypertension which suggests that vascular smooth muscle cells and endothelial cells may be the sources of the increased Serum LDH; however, this observation requires further investigation for verification.

**Conclusion:**

We have observed that serum uric acid levels were highly significant and strongly associated with the newly diagnosed hypertension in the study population. In clinical practices, increased serum uric acid in hypertensive patients has been associated with increased risk of coronary artery disease or cerebrovascular diseases. Significant positive correlation of serum uric acid with systolic and diastolic blood pressure can be considered for the treatment of hypertension with uric acid lowering drugs which should be confirmed by large scale clinical therapeutic trial. Serum LDH estimation is a simple, noninvasive, relatively low cost and routinely available procedure. Serum LDH, as a biochemical marker for hypertension should be studied in detail by extensive research.

Conflict of interest: Nil

**Acknowledgement:**

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**References:**
