Fasting Plasma Lactate and Type 2 Diabetes Mellitus
A Cross-Sectional Study

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ABSTRACT

Introduction: Plasma lactate, a clinical marker of ischemic status, have been related to insulin resistance, type 2 diabetes mellitus and obesity. Elevated fasting plasma lactate levels could be an independent risk factor for type 2 Diabetes mellitus.

Aims and Objectives:
1) To assess the plasma lactate levels in type 2 diabetic patients and healthy controls.
2) To evaluate the correlation of plasma lactate with fasting blood glucose and HbA1c.
3) To evaluate the correlation between plasma lactate and lipid parameters

Materials and Methods: It is a cross- sectional study, conducted in 60 subjects, divided into 2 groups. Group A-30 normal healthy controls. Group B-30 diabetic patients. Plasma lactate, FBS, HbA1c and lipid parameters were assessed in all 3 groups. All the above parameters were compared between the groups using independent student ‘t’ test and Pearson's correlations were obtained between lactate and other parameters, using SPSS 23 software.

Results: Fasting plasma lactate levels were significantly elevated in type 2 diabetes mellitus patients when compared to controls (p=0.000) and had a positive association with fasting blood glucose & HbA1c levels in type 2 Diabetes mellitus patients.

Conclusion: The elevated lactate levels is related to the occurrence of diabetes mellitus and reduced oxidative capacity could be the linking factor between hyperlactatemia and insulin resistance. If hyperlactatemia is an early change in altered glucose homeostasis, it could be a good predictor of future occurrence of type 2 diabetes mellitus.

Key words: Plasma lactate, oxidative capacity, hyperlactatemia, insulin resistance.

INTRODUCTION:

Lactate is the end product of anaerobic carbohydrate metabolism and is being produced by skeletal muscles, brain and erythrocytes and metabolised by liver. It is a measure of the gap between energy expenditure and oxidative capacity. Serum Lactate is used clinically to indicate energy imbalance associated with vigorous exercise, hypoxia and ischemia¹.

Type 2 Diabetes Mellitus (DM) is a chronic disorder with increased blood glucose levels, leading to many complications. Various regulatory hormones and growth factors have been implicated in the pathogenesis of type 2 DM and one such novel molecule is lactate, an intermediate in carbohydrate metabolism. Patients with diabetes mellitus show severe alterations in the intracellular metabolism of glucose such as impaired glucose oxidative metabolism, as a result of which non-oxidative glycolysis is enhanced and lactate production increased²,³.

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Plasma lactates have been found to be associated with type 2 Diabetes Mellitus in older adults. Many studies have shown elevated plasma lactate levels among obese, insulin-resistant subjects. There are various other diseases associated with increased plasma lactate levels. In critically ill patients lactate can also be used as a marker, to predict disease mortality.

India is the world's diabetic capital but there are not much study conducted in Indian population regarding the association between type 2 Diabetes mellitus and increased lactate levels. So the present study was aimed to assess the relationship between hyperlactatemia and type 2 Diabetes Mellitus which could be an independent risk factor in the development of type 2 Diabetes Mellitus.

**MATERIAL AND METHODS:**

**Study Design and setting:**
Our study had been conducted in Vinayaka Missions's Kirupananda Varipayar Medical college Hospital, Salem. It was a cross-sectional study conducted in 60 subjects during the period of March 2017 – September 2017. They were divided into 2 groups. Group A: 30 normal healthy controls. Group B: 30 patients with Type 2 Diabetes Mellitus who attended Diabetic clinic. The study protocol and all the study materials were approved by the Institutional ethical committee. Informed consent from each participant was obtained after explaining the nature of the study. During selection of study participants, the inclusion and exclusion criteria were taken care of. Patients with heart disease, renal diseases of any cause (acute or chronic), any other endocrine disorders, malignancy, pregnancy and other terminal illnesses were excluded from the study.

**Biochemical analysis:**
5ml of venous blood sample were collected from all the subjects after 8 hrs of fasting and were analyzed for plasma glucose, HbA1c, plasma lactate, Total cholesterol (TC), High density lipoprotein-Cholesterol (HDL-C) and Triglycerides (TG) were estimated directly using a semi-auto analyser (photometer 5010), while Low density lipoprotein-Cholesterol (LDL-C) was calculated using the Friedewald's formula. Biochemical parameters such as plasma glucose, plasma lactate, total cholesterol, triglycerides and HDL were measured by Enzymatic method in semi automated analyzer Photometer 5010. HbA1c levels were measured by High performance liquid chromatography method (D-10 Hemoglobin A1c Programme – BIORAD). Body mass index (BMI) was calculated by dividing the body weight (in kilograms) by the square of height (in meters) [Quetelet's index].

\[ \text{BMI} = \frac{\text{Body weight in kg}}{(\text{Height in m})^2} \]

**Statistical analysis:**
Statistical analysis was done using the software SPSS version 23 and data expressed as mean ± SD. All the above parameters were compared between the two groups using independent student's t test and Pearson's correlations were obtained between lactate and other parameters.

**RESULTS:**

Table 1 depicts the Mean and standard deviation of biochemical variables in healthy controls (group 1) and patients with type 2 Diabetes Mellitus (group 2).

Table 2 depicts the Mean and standard deviation of Lipid parameters in healthy controls (group 1) and patients with type 2 Diabetes Mellitus (group 2).

Table 3 depicts the Correlation of plasma lactate with other variables in patients with type 2 Diabetes Mellitus.
There is significant increase in (p = 0.000) in plasma lactate levels in type 2 DM patients of group B (23.47±5.43 mg/dl) when compared to controls in group A (8.51 ± 2.26 mg/dl). A positive correlation were obtained between plasma lactate and fasting glucose (r=0.30 p=0.001) and HbA1c levels (r=0.51, p=0.000) (table 2). On comparing the lipid parameters triglycerides, TGL/HDL ratio were significantly elevated(p = 0.000) in group 2 than group 1. Figure 1 shows the comparison of mean levels of FBS, HbA1c, lactate, BMI, TGL/HDL ratio among controls and Diabetic subjects

### Table 1. Mean and standard deviation of biochemical variables in healthy controls (group 1) and patients with type 2 Diabetes Mellitus (group 2)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group 1 Controls</th>
<th>Group 2 Type 2 Diabetes Mellitus</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS (mg/dl)</td>
<td>92.25 ± 8.86</td>
<td>147.25 ± 54.17</td>
<td>0.001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>4.69 ± 0.56</td>
<td>8.36 ± 1.63</td>
<td>0.000</td>
</tr>
<tr>
<td>Lactate (mg/dl)</td>
<td>8.51 ± 2.26</td>
<td>23.47 ± 5.43</td>
<td>0.000</td>
</tr>
</tbody>
</table>

*P value <0.01 is considered significant.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group 1 Controls</th>
<th>Group 2 Type 2 Diabetes Mellitus</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-Cholesterol (mg/dl)</td>
<td>170 ± 16.40</td>
<td>188.20 ± 33.21</td>
<td>0.121</td>
</tr>
<tr>
<td>TGL (mg/dl)</td>
<td>101.80 ± 35.77</td>
<td>202.67 ± 99.31</td>
<td>0.000</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>49.37 ± 3.10</td>
<td>47.53 ± 3.25</td>
<td>0.129</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>98.55 ± 17.10</td>
<td>99.07 ± 33.60</td>
<td>0.996</td>
</tr>
<tr>
<td>TGL/HDL</td>
<td>2.2 ± 0.8</td>
<td>4 ± 2.14</td>
<td>0.000</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.4 ± 2.9</td>
<td>24.52 ± 3.4</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*P value <0.05 is considered significant.

**Table 2. Mean and standard deviation of Lipid parameters in healthy controls (group 1) and patients with type 2 Diabetes Mellitus (group 2)**

**Table 3. Correlation of plasma lactate with other variables in patients with type 2 Diabetes Mellitus**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Correlation Coefficient</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c</td>
<td>0.507</td>
<td>0.000</td>
</tr>
<tr>
<td>FBS</td>
<td>0.308</td>
<td>0.001</td>
</tr>
<tr>
<td>TC</td>
<td>0.03</td>
<td>0.77</td>
</tr>
<tr>
<td>TGL</td>
<td>0.19</td>
<td>0.04</td>
</tr>
<tr>
<td>HDL</td>
<td>0.144</td>
<td>0.12</td>
</tr>
<tr>
<td>LDL</td>
<td>0.04</td>
<td>0.66</td>
</tr>
<tr>
<td>TGL/HDL</td>
<td>0.44</td>
<td>0.000</td>
</tr>
<tr>
<td>BMI</td>
<td>0.412</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*<0.05 is considered significant.*

**DISCUSSION:**

The study results show a significant increase in plasma lactate levels (23.47 ± 5.43 mg/dl, p=0.000) in patients with type 2 Diabetes mellitus when compared with healthy controls (8.51± 2.26mg/dl). There is no significant correlation of lactate with FBS but it has a fairly good correlation with HbA1c levels(r = 0.507, p = 0.000), which indicates the
Lactate may not be a specific marker of adiposity but could indicate the activity of adipose tissue, or its degree of hypoxia and decreased oxidative capacity, which is not captured by BMI and other measures of adiposity.

Oxidative capacity is also decreased in insulin resistant skeletal muscle and in patients with type 2 Diabetes mellitus, there is evidence of increased glycolysis, decreased mitochondrial size and density, decreased oxidative gene expression, decreased oxidative phosphorylation and decreased aerobic capacity.

So when compared with healthy controls, non-oxidative glycolysis rate remains higher in type 2 DM patients. Insulin resistance results in increased insulin levels which promote glycolysis by activating two rate limiting enzymes, namely, phosphofructokinase and pyruvate dehydrogenase, resulting in enhanced production of lactate. There are various studies done in insulin resistance subjects which have shown increased fasting plasma lactate level in patients with type 2 DM when compared to non-diabetics.

The study conducted by Barnett et al. proposed that hyperlactatemia might be an early change in the development of type 2 diabetes mellitus. Similar study conducted by Beharane et al also reported that the lactate levels were elevated during the early stages of diabetes, prediabetes, and the hyperinsulinemia condition.

So the association of plasma lactate with type 2 diabetes mellitus may result from a decrease in oxidative capacity which leads to altered lactate metabolism and increased lactate release from adipose tissue.
CONCLUSION:

We have found high plasma lactate levels in patients with type 2 Diabetes mellitus, which could be due to insulin resistance, with altered glycolysis and decreased oxidative capacity. Lactate could have an important role as a marker of hypoxia/decreased oxidative capacity and related to the etiology of Diabetes Mellitus type 2. Further studies conducted in larger populations would help in arriving at valid conclusions to the extent of its association with insulin resistance and its implications in the prognosis and management of type 2 Diabetes mellitus.

REFERENCES:


