Original Research Article

A comparative study of plasma uric acid, erythrocyte uric acid and urine uric acid levels in type 2 diabetic subjects

Nagendra S.¹, Yogaraje Gowda C. V.² and Kashinath R. T.³*

Abstract

In the recent past, uric acid, the end product of Purine metabolism in humans, has been claimed elevated in type 2 diabetic subjects, with a good correlation to diabetic complications. Uric acid is sparingly soluble in body fluids and information regarding its distribution in body fluids particularly blood and urine as well as in plasma and erythrocytes is scanty. A study was undertaken to assess the distribution of uric acid in type 2 diabetic subjects in plasma, erythrocytes and in urine. The results suggest there is an equal distribution and the urinary excretion is significantly reduced.

Keywords: Erythrocytes, Plasma, Type-2 Diabetes Mellitus, Uric acid, Urine.

INTRODUCTION

Uric acid, the end product of purine catabolism in humans, has been claimed in the recent past, being elevated in type 2 diabetic subjects (Edwards et al., 2002; Guan et al., 2002; Ishihara et al., 1989; Iwaski et al., 1998; Kelly et al., 2001; Lehto et al., 1998; Musceli et al., 1996; Quinone et al., 1995). Though there are few claims that uric acid elevation seems correlating with the diabetic complications (Fukui et al., 2008; Kelly and Palella, 2001; Kumar and Clark, 2002) or with insulin resistance (Bo et al., 2001; Clausen et al., 1998; Moriwaki et al., 1995) much data are not available regarding the distribution of uric acid in blood between plasma and erythrocytes as well as its excretory pattern in type-2 diabetic subjects. Hence a study was undertaken to establish the distribution of uric acid in plasma and erythrocytes and to assess the urinary excretion of uric acid in type-2 diabetic subjects with an emphasis on the evaluation of sex variation regarding these aspects.

MATERIALS AND METHODS

The type-2 diabetic subjects attending the regular medical OPD of Subbaiah Medical College Hospital and Research Center, Purle, Shimoga, who are in the group of 30-60yrs were randomly selected and a brief history was taken to exclude the patients who were having orthopedic or renal involvement. A fasting blood sample with heparin as an anti-coagulant was collected from these selected diabetic subjects after obtaining a written consent. Similarly normal subjects from the employees of the hospital and medical college in the age group of 30-60 yrs were selected. A fasting blood sample was
Table 1. Showing the levels of plasma glucose, plasma uric acid, erythrocyte uric acid, urine uric acid, PUA/EUA as well as UUA/PUA in normal subjects and in type 2 diabetic subjects.

<table>
<thead>
<tr>
<th></th>
<th>Plasma Glucose mg/dl</th>
<th>Plasma Uric acid mg/dl</th>
<th>Erythrocyte Uric acid mg/dl</th>
<th>Urine Uric acid mg/dl</th>
<th>PUA/EUA</th>
<th>UUA/PUA</th>
</tr>
</thead>
<tbody>
<tr>
<td>NORMAL</td>
<td>94.66</td>
<td>3.87</td>
<td>1.57</td>
<td>57.44</td>
<td>2.06</td>
<td>14.84</td>
</tr>
<tr>
<td></td>
<td>±16.06</td>
<td>±1.61</td>
<td>±0.44</td>
<td>±15.54</td>
<td>±0.32</td>
<td>±2.88</td>
</tr>
<tr>
<td>DIABETIC (99) Group D</td>
<td>289.90</td>
<td>11.05</td>
<td>1.99</td>
<td>98.61</td>
<td>6.56</td>
<td>8.92</td>
</tr>
<tr>
<td></td>
<td>±16.06</td>
<td>±1.61</td>
<td>±0.44</td>
<td>±15.54</td>
<td>±0.32</td>
<td>±2.88</td>
</tr>
</tbody>
</table>

NOTE: 1. The number in parenthesis indicate the number of subjects
2. Values are expressed as their Mean ± SD
3. Statistical evaluation –significance level *p < 0.05 , **p < 0.01, ***p < 0.001

Table 2. Showing the levels of plasma glucose, plasma uric acid, erythrocyte uric acid, urine uric acid, PUA/EUA as well as UUA/PUA in normal male subjects and in type 2 male diabetic subjects

<table>
<thead>
<tr>
<th></th>
<th>Plasma Glucose mg/dl</th>
<th>Plasma Uric acid mg/dl</th>
<th>Erythrocyte Uric acid mg/dl</th>
<th>Urine Uric acid mg/dl</th>
<th>PUA/EUA</th>
<th>UUA/PUA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal male (24)</td>
<td>94.66</td>
<td>3.87</td>
<td>1.57</td>
<td>57.54</td>
<td>2.06</td>
<td>14.86</td>
</tr>
<tr>
<td>(GroupNM)</td>
<td>±16.06</td>
<td>±1.61</td>
<td>±0.44</td>
<td>±15.54</td>
<td>±0.32</td>
<td>±2.88</td>
</tr>
<tr>
<td>Male DM (99) GroupDM</td>
<td>288.80</td>
<td>11.04</td>
<td>1.99</td>
<td>98.61</td>
<td>6.56</td>
<td>8.93</td>
</tr>
<tr>
<td></td>
<td>±66.20</td>
<td>±4.52</td>
<td>±0.88</td>
<td>±1.10</td>
<td>±1.06</td>
<td>±2.28</td>
</tr>
</tbody>
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collected from these normal subjects using heparin as the anticoagulant. An urine sample (spot urine) of about 25-50 ml was also collected from both type-2 diabetic subjects as well as from normal subjects. The blood samples were centrifuged at 3000 rpm for 6 minutes to separate plasma. The plasma samples were decanted into a clean tube and preserved for further use. The erythrocytes sediment were washed 4 times with 5ml aliquot of normal saline. The washed erythrocytes were deproteinised with 10% TCA (1:4). Uric acid was estimated in plasma, deproteinised erythrocyte supernatant and in urine (spot urine) by Caraways method (Caraway, 1967).

RESULTS

The results of the present study with type-2 diabetes subjects are given in table 1 - 3.

Table 1 narrates the plasma, erythrocyte as well as urinary levels of uric acid along with plasma glucose levels in normal subjects and in type 2 diabetic subjects. It is evident from the table that in type 2 diabetic subjects the plasma uric acid levels and urine uric acid levels are significantly elevated (p< 0.001) where as a small rise has been observed in erythrocytic uric acid levels in type-2 diabetic subjects as compared to normal subjects. A significant elevation (p<0.001) seen in the calculated ratio of plasma uric acid levels to erythrocytic uric acid levels (PUA/EUA) in type-2 diabetic subjects as compared to normal subjects, where as significant lowering (p<0.001) seen in the calculated ratio of urine acid and to plasma uric acid (UUA/PUA) in type 2 diabetic subjects as compared to normal subjects.

Table 2 gives the plasma glucose levels and levels of plasma uric acid, erythrocyte uric acid as well as urinary uric acid along with the calculated ratios of PUA/EUA and UUA/PUA in normal male subjects and in male diabetic subjects. It is evident from the table that there is a significant (P<0.001) elevation seen in levels of uric acid in plasma and in urine male diabetic subjects as compared to normal male subjects, where as a significant (P<0.01) decrease in calculated ratio, UUA/PUA, suggesting the renal clearance of uric acid might have been affected in type-2 diabetic male subjects.

Table 3 shows the levels of plasma glucose, plasma uric acid, erythrocyte uric acid, urinary uric acid, as well as the calculated ratios of PUA/EUA and UUA/PUA in
normal female subjects and in diabetic female subjects. It is seen from the table that the plasma glucose levels, plasma uric acid levels and urinary uric acid levels are significantly (P<0.001) elevated in female diabetic subjects as compared to normal female subjects, where as no significant alterations seen in erythrocyte uric acid levels . The ratio PUA/EUA is significantly elevated (P<0.001) where as a significant lowering (P<0.001) , in the ratio UUA/PUA seen in diabetic female subjects in comparison to normal female subjects.

**DISCUSSION**

Uric acid, the end product of purine catabolism, is principally excreted in urine as its salts. There are controversial reports regarding the uric acid distribution in blood between plasma and erythrocytes. The findings of the present study indicates a significant rise in plasma uric acid levels (P<0.001) in diabetic subjects as compared to the normal subjects (ref table-1) is in agreement with the previous reports (Edwards et al., 2002; Guan et al., 2002; Ishihara et al., 1989; Iwaski et al., 1998; Musceli et al., 1996). The raised plasma uric acid levels may be in part due to altered uric acid clearance in these diabetic subjects. It is known that raised insulin levels as seen in insulin resistance (or in insulin administration) may lower the uric acid excretion (Quinone et al., 1995). The raised plasma uric acid levels may be in part due to altered uric acid clearance in these type 2 diabetic subjects.

The present study in type 2 diabetic subjects with respect to plasma, erythrocyte and urine uric acid levels suggest:

i) unequal distribution of uric acid between plasma and erythrocytes

ii) an increased plasma uric acid levels in type 2 diabetic subjects compared to normal subjects either due to raised alpha 2 globulin levels hence more uric acid might be transported into the erythrocytes. This unequal distribution may be due to diabetes induced membrane alteration in type-2 diabetic subjects. Thsi abnormal uric acid distribution in type-2 diabetic subjects is in agreement with the earlier reports (Edwards et al., 2002; Guan et al., 2002; Ishihara et al., 1989; Iwaski et al., 1998; Musceli et al., 1996).

Uric acid, in human beings, is excreted in urine in its salt form and as seen from the present studies in type-2 diabetic subjects, the uric acid excretion is significantly increased in type-2 diabetic subjects( P<0.001) as compared to normal subjects as well as a significant elevation of urine uric acid is seen in type-2 male diabetic subjects(P<0.001) and in type-2 female diabetic subjects(P<0.001) as compared to their normal counterparts( ref table 1, 2 and 3). No significant changes observed in these parameters between male diabetic subjects and female diabetic subjects (Ref Table 2 and Table 3). However the ratio UUA/PUA is significantly lowered in type-2 diabetic subjects suggesting uric acid clearance might have been affected in these diabetic subjects. It is known that raised insulin levels as seen in insulin resistance (or in insulin administration) may lower the uric acid excretion (Quinone et al., 1995). The raised plasma uric acid levels may be in part due to altered uric acid clearance in these type 2 diabetic subjects.

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<th>Erythrocyte Uric acid mg/dl</th>
<th>Urine Uric acid mg/dl</th>
<th>PUA/EUA</th>
<th>UUA/PUA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Female</td>
<td>84.32</td>
<td>3.82</td>
<td>1.46</td>
<td>57.54</td>
<td>3.98</td>
<td>15.06</td>
</tr>
<tr>
<td>(14) (Group NF)</td>
<td>± 13.38</td>
<td>± 0.78</td>
<td>± 0.56</td>
<td>± 15.54</td>
<td>± 0.82</td>
<td>± 3.18</td>
</tr>
<tr>
<td>F-DM</td>
<td>337.41</td>
<td>11.63</td>
<td>2.15</td>
<td>120.51</td>
<td>8.78</td>
<td>10.63</td>
</tr>
<tr>
<td>(34) (Group DF)</td>
<td>± 66.90</td>
<td>± 4.47</td>
<td>± 0.67</td>
<td>± 15.61</td>
<td>± 1.41</td>
<td>± 2.24</td>
</tr>
</tbody>
</table>

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have been held in protein bound form or due to altered clearance of uric acid due to insulin resistance.

CONCLUSION

The present study in type 2 diabetic subjects with respect to plasma, erythrocyte and urine uric acid levels suggest: i) unequal distribution of uric acid between plasma and erythrocytes and ii) an increased plasma uric acid levels in type 2 diabetic subjects compared to normal subjects either due to raised alpha 2 globulin levels hence more uric acid might have been held in protein bound form or due to altered clearance of uric acid due to insulin resistance. However a further study in experimentally induced diabetic rats may throw much light in this aspect.

REFERENCES