Study On Correlation Of Inflammatory Markers On Type-II Diabetes

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Abstract: Type-II Diabetes, a metabolic disease, presenting with hyperglycemia resulting from insulin deficiency or decreased glucose utilization or increased glucose production has been found to have an association with various inflammatory markers. To determine and compare the serum level of C-reactive protein and uric acid and also to observe the association between them. The mean values of C-reactive protein and uric acid obtained from 60 subjects, were analyzed by student 't' test and Pearson's correlation. The mean level of C-reactive protein activity of diabetic patients are significantly (p=0.028) higher as compared to normal subjects and the mean serum uric acid is also apparently higher, however, a significant difference could not be established (p=0.072). C-reactive protein and uric acid showed insignificant association to the Diabetic Mellitus. Also, had an insignificant correlation with each other.

"1.Introduction"

Type II Diabetes Mellitus is a metabolic disorder that is characterized by hyperglycemia with the relative lack of insulin[1]. C-reactive protein (CRP) is a phylogenetically highly conserved plasma protein, that is usually used as inflammatory markers in various inflammatory diseases[2]. Uric acid on another hand, the breakdown product of purine, also has been considered same due to its potent oxidative capacity.

Many studies have claimed a significant association between serum CRP and uric acid level in diabetes[3-5]. The rise or fall of CRP gives a fair idea of the degree of inflammation so it is considered a good indicator of appropriate anti-inflammatory therapy. Various in vivo studies done has shown the increase in CRP level in obese is due to the associated chronic inflammation in excess body fat. Therefore, patients with type II Diabetes who are, usually obese, could potentially have high CRP. In relation, obese individuals with diabetes II tends to have hyperglycemia, which in turn have shown very significant correlation with hyperuricemia. If Uric acid is simply a byproduct of impaired glucose metabolism, it may still be useful as an early marker of type II Diabetes Mellitus risk[6-8]. Recent evidence suggests that Uric acid plays a role in cytokine secretion. Moreover, Uric Acid has been identified as a mediator of endothelial dysfunction and systemic inflammation[9,10]. In recent decades, serum Uric acid has emerged as a potential risk factor for type II Diabetes Mellitus. Hyperinsulinemia has been shown to cause hyperuricemia, supporting the hypothesis that elevated Uric acid is simply a byproduct of insulin resistance and glucose metabolism dysfunction[11]. Although, Uric acid levels may also mediate this syndrome.

Despite the controversies, many studies have shown that CRP and uric acid act as inflammatory markers. However, none have shown how they are associated with each other in relation to hyperglycemia. Hence, an attempt was made in this study to highlight the correlation between serum CRP and Uric acid with each other and Diabetes Mellitus type II.

"2.Method"

"2.1.Study type” A Cross-sectional study
"2.2.Study design”
"2.2.1.Place” This study was conducted in Teerthanker Mahaveer Medical College & Research Center, Moradabad, U.P., India.
"2.2.2.Duration of study” 01/06/2016 to 01/10/2016
"2.2.3.Sample size and Sampling method” In the present study 60 subjects participated, out of which 30 were patients aged 35 to 75 years who were diagnosed as diabetics and confirmed by the estimation of fasting serum glucose (> 126 mg/dl) on two occasions were selected from the Medicine OPD & IPD. 30 Normal healthy subjects, age, and sex matched with the diabetic patients were selected as controls. After overnight fasting for 8 hours, about 5ml of venous blood was drawn with aseptic precaution from the antecubital vein of all the subject and dispensed into following vials for various biochemical tests:
• Fluoride oxalate vial for fasting plasma glucose (FPG) estimation.
• Plain vial for C–reactive protein and Uric acid estimation.
Fasting plasma glucose was estimated by the GOD-POD method: Glucose is oxidized by glucose oxidase (GOD) to produce gluconic acid and hydrogen peroxide. The hydrogen peroxide then reacts with 4-aminooantipyrrine (4AAP) and 4-hydroxy benzoic acid (4HBA) in presence of peroxidase (POD) enzyme to form a pink colored quinonimine dye. The intensity of the pink color is directly proportional to the concentration of glucose present and O.D. is measured at 505 nm[12].

Estimation of serum Uric acid by uricase method: Uric acid is oxidized to allantoin by uricase with the production of hydrogen peroxide. The peroxide then reacts with 4-aminooantipyrrine and TOOS in presence of peroxidase to yield Quinoneimine dye. The absorbance of this dye is at 546 nm which is proportional to uric acid in the sample[13].

Estimation of serum CRP with turbidimetric immunoassay: The test specimen is mixed with activation buffer (R1), TURBILYTE-CRP™ latex reagent (R2) and allowed to react. The presence of CRP in the test specimen result in the formation of an insoluble complex producing a turbidity, which is measured at 546nm wavelength. The increase in turbidity corresponds to the concentration of CRP in the test specimen[14].

**2.2.4.Ethical Approval and Patient consent:**
Ethical approval and appropriate patient consent were obtained prior conduct of the study.

**2.2.5.Inclusion and exclusion criteria**
Individuals diagnosed with Diabetes Mellitus by estimation of Fasting Plasma Glucose (FPG) ≥126mg/dl on two occasions were included. Individuals suffering from other inflammatory diseases like Tuberculosis, Leprosy and pregnancy, Cancer, Skin diseases, Gout, Liver, and Kidney diseases were excluded to rule out any increase in inflammatory markers due to other causes.

**2.2.6.Statistical analysis and software used**
The data obtained were analyzed via IBM SPSS version 21 to determine the student ‘t’ and Pearson’s correlation coefficient.

**3.Result**
In the present study, a total of 60 subjects participated out of which 30 were Diabetes patient and 30 were age and sex matched healthy non-diabetic individuals. The study revealed, out of 30 patients, 17 patients i.e. about 56% had increased level of CRP from the reference range (1-5mg/dl). While 14 patients i.e about 46% had increased level of Serum uric acid from the reference range (4-8 mg/dl) and 7 patients i.e about 23% had increased both serum CRP as well as serum uric acid level.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Diabetic Mean ± S.D.</th>
<th>Non-Diabetic Mean ± S.D.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBG (mg/dl)</td>
<td>199±90.78**</td>
<td>97.71±13</td>
<td>0.00</td>
</tr>
<tr>
<td>Uric Acid (mg/dl)</td>
<td>6.45±0.86</td>
<td>4.8±0.83</td>
<td>0.072</td>
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<tr>
<td>CRP (mg/dl)</td>
<td>5.88±2.66*</td>
<td>3.90±1.2</td>
<td>0.028</td>
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</tbody>
</table>

* Highly significant at p < 0.01
** Significant at p < 0.05
In- significant             at p ˃ 0.05  

r:  pearson’s correlation ; n: number of patient

“4. Discussion”

Diabetes is a metabolic condition with the hyperglycemic state with reduced insulin activity or lowered glucose intolerance giving rise to several clinical conditions like Metabolic syndrome, atherosclerosis, cataract, kidney failure and cardiovascular complications. Previous studies have suggested that serum CRP and Uric acid levels are positively associated with the development of type II Diabetes Mellitus[3,4]. However, our study had a contrast result, with the insignificant negative association of hyperglycemia with C- reactive protein and uric acid. Generally, with hyperglycemia rise in oxidative stress has been observed which have been associated with inflammation with enhanced pro-inflammatory cytokines[13,15]. The slight negative association of this hyperglycemia with uric acid could be explained by the dual nature of uric acid ie acting both antioxidant or oxidant[16]. However, the insignificant slight negative association of uric acid with C-reactive protein questions whether or not uric acid should be seen as an inflammatory marker.

“5. Conclusion”

An attempt to see if uric acid acts as an inflammatory parameter was not sufficed due to its insignificant association to C-reactive protein, which is a potent marker of the inflammatory state. Our study has provided an evident that C-reactive protein might not have a significant role and rise in the diabetic state although this finding could go contradictory due to small sample size and short duration of the study.

“6. Limitation”

Our study has shown a contrast result compared to other findings, possibly due to its short duration and small sample size. It has been unable to provide insights into the actual association of uric acid and c-reactive protein with diabetes II. Hence, with an appropriate study duration with sufficient subjects might produce the better correlation and implication, if uric acid could actually be regarded as inflammatory marker corresponding to CRP in diabetes II cases.

“6. Acknowledgement”

Sincere thanks to Department of Biochemistry and Hospital, Teerthanker Mahaveer Medical College & Research Center, Moradabad, U.P., India.

“7. References”


<table>
<thead>
<tr>
<th>Variable (n= 30)</th>
<th>Uric acid</th>
<th>C-reactive protein</th>
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<tbody>
<tr>
<td>Fasting Blood Sugar</td>
<td>r: -0.082</td>
<td>p: 0.669*</td>
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<tr>
<td>Uric acid</td>
<td>r: -0.291</td>
<td>p: 0.119*</td>
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* Highly significant at p < 0.01  
** Significant at p < 0.05  
* In- significant at p > 0.05  

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