

Correlation of the Serum Insulin and the Serum Uric Acid Levels with the Glycated Haemoglobin Levels in the Patients of Type 2 Diabetes Mellitus

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ABSTRACT

Background: Type 2 Diabetes mellitus (DM) is a heterogeneous disease which is characterized by variable degrees of insulin resistance and impaired insulin secretion. Insulin is a hormone that regulates the body's use of glucose. The present study was undertaken to find the correlation of the serum uric acid levels in the patients of Type 2 Diabetes mellitus.

Material and Method: This was a case control study. The subjects who were included in the study were divided into two groups. Group A included 50 normal healthy individuals who were in the age group of 40-65 years, who were of either sex and with no family history of Diabetes mellitus. Group B included 50 newly diagnosed patients of Type 2 Diabetes Mellitus, who were in the age group of 40-65 years, who were of either

sex, from the same population. Fasting blood samples were drawn and they were investigated for the serum insulin, serum uric acid, fasting blood sugar and the HbA1C levels. The values were compared with those of normal healthy subjects.

Results: All the three parameters, HbA1C, serum insulin and serum uric acid were found to be increased in the patients of Type 2 Diabetes Mellitus as compared to their levels in the controls ($p < 0.001$).

Conclusion: In the present study, it was concluded that the serum uric acid levels linearly increased with increasing serum insulin levels, in newly diagnosed diabetic patients. Therefore, uric acid serves as a potential biomarker of the glucose metabolism.

Key words: Glycated Haemoglobin (HbA1C), Fasting Blood Sugar (FBS), Serum Insulin

INTRODUCTION

Diabetes mellitus is a metabolic disorder which is characterized by hyperglycaemia and insufficiency of the secretion or the action of endogenous insulin. Although the aetiology of the disease has not been well defined, viral infections, autoimmune diseases, and environmental factors have been implicated [1]. The prevalence of diabetes has been growing rapidly from 135 million in 1995 to an estimated 380 million in 2025 [2].

Insulin, a hormone that regulates the body's use of glucose (blood sugar), is released by the cells of the pancreas which are called the islets of Langerhans. If the pancreas malfunctions, it may produce an inadequate supply of insulin, or no insulin at all. Type 1 diabetes mellitus then develops [3]. Type 2 diabetes mellitus is a heterogeneous disease which is characterized by variable degrees of insulin resistance, impaired insulin secretion and increased glucose production. Insulin resistance occurs when the cells become less sensitive to the effects of insulin [4].

Uric acid is the end product of the purine metabolism in humans [5]. Although hyperuricaemia and gout are associated with an increased future risk of diabetes, diabetes may reduce the future risk of gout through the uricosuric effect of glucose or the impaired inflammatory response [6]. The recognition of high levels of serum uric acid as a risk factor for diabetes has been a matter of debate for a few decades, since hyperuricaemia has been presumed to be a consequence of the insulin resistance rather than its precursor [7]. The present study was undertaken to find the correlation of the serum uric acid and the serum insulin levels in patients with type 2 Diabetes mellitus.

MATERIAL AND METHODS

The present case control study was undertaken in the Department of Biochemistry, in collaboration with the Department of Medicine. The subjects who were included in this study were divided into 2 groups:

- Group A included 50 normal healthy individuals, who were in the age group 40-65 years, who were of either sex and without any family history of DM.
- Group B included 50 newly diagnosed patients of Type 2 Non Insulin Dependent Diabetes mellitus (NIDDM), who were in the age group 40-65 years, who were of either sex, from the same population.

Informed consents were taken from all the subjects who were included in the study. The patients who suffered from Type 1 Diabetes mellitus, those with the acute complications of Diabetes mellitus, those with a history of acute infections and other ailments like gross congestive heart failure, tuberculosis, gout, rheumatoid arthritis and skeletal muscle injury, those with serum creatinine levels of >1.5 mg/dl and renal failure and those who were on hypoglycaemic drugs and on insulin therapy were excluded from the study.

A detailed history was taken from each patient and a thorough clinical examination was carried out on each patient. Fasting blood samples were drawn and they were investigated for serum insulin, uric acid, blood sugar and HbA1C, and the values were compared with those of normal healthy subjects. Serum insulin was estimated by the ELISA method [8], Serum uric acid was estimated by an Enzymatic colorimetric method [9], Fasting blood

sugar (FBS) was estimated by the GOD-POD Method [10] and HbA1c was estimated by using a Nycocard Reader [11].

STATISTICS

The comparisons were done by using the Student's 't' test on the number of variables for each parameter. The correlations were done by Pearson's correlation analysis. A logistic regression analysis was also done on the variables of each parameter.

RESULTS

The statistical analysis showed no difference between the sexes with regards to their mean age. The sex and the number distribution in these groups were comparable [Table/Fig-1].

The mean FBS level of group A was 75.14 ± 8.43 mg/dl and that of group B was 140.98 ± 42.0 mg/dl, which was significantly higher than that of group A ($p < 0.001$) [Table/Fig-2]. In the present study, it was observed that the HbA1C value of group B was statistically significant higher than that of group A, the value of group A being $4.77 \pm 0.56\%$ and that of group B being $7.78 \pm 1.87\%$ ($p < 0.001$) [Table/Fig-3]. The serum insulin level in group A was 10.16 ± 3.47 μ U/ml and that in group B was 14.4 ± 5.79 μ U/ml. The statistical analysis showed that the value in group B was significantly higher than that in group A ($p < 0.01$) [Table/Fig-4]. Similar findings were observed in the values of the serum uric acid levels, which showed a significantly higher value for group B as compared to that of group A ($p < 0.001$) [Table/Fig-5].

Sex	Control Group	Study Group	Total
Male	26 (52%)	20 (40%)	46 (46%)
Female	24 (48%)	30 (60%)	54 (54%)
Total	50	50	100

[Table/Fig-1]: Showing the comparison of age and sex in control and study groups ($p = 0.229$), not significant

S. No.	Subjects	Number	Fasting Blood Sugar (mg/dl)		
			Range	Mean \pm SD	\pm SE
1.	Group A	50	60-90	75.14 ± 8.43	1.19
2.	Group B	50	80-240	140.98 ± 42.0	5.95

[Table/Fig-2]: Showing FBS levels in control & study group where No is number of cases & SD is standard deviation. $t = 10.849$ ($p < 0.001$), highly-significant

S. No.	Subjects	Number	Glycated Hemoglobin/ HbA1C (%)		
			Range	Mean \pm SD	\pm SE
1.	Group A	50	3.2- 6.0	4.77 ± 0.56	0.080
2.	Group B	50	4.5- 11	7.78 ± 1.87	0.264

[Table/Fig-3]: Showing HbA1C levels in control & study group. $t = 10.905$ ($p < 0.001$), highly-significant

S. No.	Subjects	Number	Serum Insulin (μ U/ml)		
			Range	Mean \pm SD	\pm SE
1.	Group A	50	5- 21	10.16 ± 3.47	0.49
2.	Group B	50	1.8- 24	14.4 ± 5.79	0.81

[Table/Fig-4]: Showing comparison of serum insulin levels in both the groups. $t = 1.335$ ($p < 0.01$), significant

The Pearson's correlation co-efficient for the correlation between serum uric acid and HbA1C showed a positive correlation ($r = 0.092$) [Table/Fig-6]. Similarly, the correlation coefficient for the correlation between serum insulin and HbA1C showed a negative correlation ($r = -0.532$) [Table/Fig-6].

The Pearson's correlation coefficient for the correlation between serum uric acid and serum insulin showed a positive correlation ($r = 0.139$) [Table/Fig-6].

S. No.	Subjects	Number	Serum Uric Acid (mg/dl)		
			Range	Mean \pm SD	\pm SE
1.	Group A	50	2-6.5	4.54 ± 1.19	0.080
2.	Group B	50	4.9-7.8	6.6 ± 0.591	0.264

[Table/Fig-5]: Showing the comparison of serum uric acid in both the groups. $t = 10.884$ ($p < 0.001$), highly-significant

Parameter	HbA1C	Insulin
HbA1C	R	-0.532
	P	0.000
Uric Acid	R	0.139
	P	0.336

[Table/Fig-6]: Showing the correlation between HbA1C, serum insulin and serum uric acid levels

DISCUSSION

Diabetes mellitus is the most common endocrinological disorder which is characterized by metabolic abnormalities and long term complications [12]. The prevalence of diabetes has been growing rapidly from 135 million in 1995 to an estimated 380 million in 2025 [2]. Type 2 Diabetes mellitus or non insulin dependent Diabetes mellitus (NIDDM) typically occurs in old age and in obese people [13]. Type 2 Diabetes mellitus is a heterogeneous disease which is characterized by variable degrees of insulin resistance, impaired insulin secretion and increased glucose production [4].

In the present study, it was observed that the serum insulin level of group B was significantly higher than that of Group A ($p < 0.01$). The reason for this finding could be that the insulin resistance occurs when the cells become less sensitive to the effects of insulin. This results in rising blood sugar levels (hyperglycaemia) and a drop in the energy production. To compensate for the insulin resistance and to keep the blood glucose levels from spiraling out of control the pancreas tries to restore the balance by producing more insulin. If they are left unchecked, the cells become even more resistant to insulin, even as the pancreas secretes ever greater amounts of insulin, in a desperate attempt to bring the system back under control. This results in dangerously high blood levels of insulin (hyperinsulinaemia). If this is not corrected, the pancreas eventually becomes exhausted, resulting in diabetes.

Similar results were reported by G Srinivasa Nageswara Rao et al., [14] and Pagano G et al., [15]. In the present study, it was observed that the serum uric acid level of group B was significantly higher than that of Group A ($p < 0.001$). The serum uric acid levels were increased in the Type 2 diabetic patients and they were associated with the insulin resistance syndrome, impaired glucose tolerance and nephropathy. The clearance of uric acid gets reduced, with an increase in the insulin resistance. The actual mechanism of hyperuricaemia, which was found in these patients, was not known, but it was observed that the compensatory hyperinsulinaemia in the insulin resistant individuals imposed an antihypertensive effect on the kidneys [16]. Similar results were reported by Joseph B. Herman et al., [17], T P Whitehead et al., [18] and Causevic et al., [19].

In the present study, it was also observed that when a comparison was made between the serum insulin and HbA1C, there was a negative correlation ($r = -0.532$) which was statistically significant ($p < 0.01$) and there was a significant ($p < 0.05$) positive correlation ($r = 0.092$) between serum uric acid and HbA1C, which meant that there was an increase in the serum uric acid with an increase in HbA1C. This can be explained on the basis of the mechanisms which suggest an association of hyperinsulinaemia with increased uric acid production. An increased purine biosynthesis which occurs due to an increased activity of the hexose monophosphate pathway shunt [20] can be conceptually linked to the disorders which are characterized by insulin resistance and/or hyperinsulinaemia. The increased flux of glucose-6-phosphate through the hexose monophosphate pathway shunt due to impairment of the glycolytic pathway, has been suggested as an explanation for the increased uric acid in impaired glucose tolerance [17] and this may also include excess carbohydrates and an enhanced lipogenesis in the presence of excess insulin [21]. Similar findings were explained by HK Choi et al., [22].

The Pearson's correlation coefficient for the correlation between serum uric acid and serum insulin showed a positive correlation ($r = 0.139$), which means that whenever there is an increase in the serum insulin levels, there is also an elevation in the serum uric acid levels. The elevation of serum uric acid, which is associated with impaired glucose tolerance and newly found type 2 diabetes, seemed to occur only in the presence of hyperinsulinaemia. Elevated serum uric acid is a feature of hyperinsulinaemia/insulin resistance. However, as hyperinsulinaemia is apparently a cause as well as a consequence of insulin resistance [5]. Similar results were reported by M Modan et al., [23] and HK Choi et al., [22].

In conclusion, our study suggests that there is an increase in the serum uric acid levels with an increase in the HbA1C levels. Furthermore, it was found that there was a decrease in the insulin levels with an increase in the HbA1C levels. The serum uric acid and the serum insulin levels showed a positive relationship in Type 2 Diabetes mellitus.

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