Research Article

Association of serum free iron and glycemic control among type II diabetes mellitus population in Puducherry – a preliminary study

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Abstract

Background: Iron modify glucose metabolism and glucose metabolism impinges on iron. Glycation of hemoglobin contributes to substantial affinity for transitional metals and the development of complications is linked to the accumulation of glycation.

Objective: This study was undertaken to assess the serum free iron levels in patients with type II diabetes mellitus (DM) and its correlation with good and poor glycemic control.

Materials and Methods: An analytical cross-sectional study was conducted among 100 patients and 50 healthy controls. They are grouped as Group I, 50 normal healthy controls; Group II, 50 type II DM patients with good glycemic control (HbA1C ≤ 7); Group III, 50 type II DM patients with poor glycemic control (HbA1C > 7). Levels of HbA1C I and serum iron were assessed. The data collected were recorded and analyzed using SPSS version 16.0.

Result: The mean serum iron concentration between group I and III ($p < 0.001$) as well as between group II and III ($p < 0.005$) was statistically significant. Difference between group I and II was not statistically significant ($p = 0.205$).

Conclusion: From our study it was concluded that serum free iron concentration was higher in patients with type II DM with poor glycemic control. In addition, there was a positive correlation between serum free iron concentration and glycemic control.

KEY WORDS: Serum free iron, glycated haemoglobin, type-II diabetes mellitus, glycemic control

Introduction

Iron, an abundant transitional metal has a crucial role in the pathophysiology of disease derived from the easiness with which iron is reversibly oxidized and reduced.[1] Type II diabetes mellitus (DM) is a predominant public health concern worldwide, accounts for 90% cases of diabetes globally.[2]

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According to the World Health Organization, 30 million people worldwide had diabetes in 1985. By 2000 there were 171 million diabetes patients and by 2030 it is estimated to be hopping 366 million. The relationship between iron and glucose metabolism is bidirectional, iron affects glucose metabolism and glucose metabolism impinges on iron. Glycation of hemoglobin contributes to substantial affinity for transitional metals and glycation of transferrin decreases ability of transferrin to bind ferrous iron.[3] Also when concentrations of antioxidants are low, the reducing potential and anaerobiosis progressively increases, thereby facilitating a rapid release of iron from ferritin. Additionally, the ferroxidase activity of the heavy chain in apoferritin is also down regulated in this setting resulting in an increase in free iron as prooxidant agent.[4] Potent hydroxyl radicals from iron by Heber–Weiss and Fenton reactions impair mechanism of vasodilatation, disrupt endothelium,[5-7] accelerate development of atherosclerosis,

diabetic nephropathy, and other microvascular complications associated with type II diabetes within 7 years.[8–10] Even moderately elevated iron can cause the above and hence the development of complications are linked to the accumulation of glycation.[11,12] HbA1C is the most reliable and established marker and its value represents the glycemic status of a person over the last 2–3 months.[13] It should be kept less than 6 in normal individuals and less than 7 in diabetic patients.[13] So with these aspects, the study was undertaken to assess the serum iron levels and influence of glycated hemoglobin on iron parameters in well-controlled and poorly controlled type-II diabetic patients. Hence our study was designed to evaluate the correlation between increased serum iron in type-II diabetic patients with good and poor glycemic control.

Materials and Methods

After getting written informed consent from all the patients and Institutional Ethics Committee approval the study was commenced. This analytical cross-sectional study was conducted in Department of Biochemistry at a Tertiary Care Teaching Hospital, Puducherry for a period of 2 months.

Inclusion Criteria

Known type-II diabetic patients for more than 7 years duration with age group between 40 and 60 years, glycated hemoglobin (HbA1C) level more than seven and less than seven. Diabetic patients on lifestyle modifications, oral antidiabetic dugs, insulin or combination of all three, associated with known complications of DM (e.g., diabetic nephropathy, diabetic retinopathy, heart disease, and diabetic neuropathy were included).

Exclusion Criteria

Diabetic for more than 7 years, type-I DM, hemolytic anemia, hemoglobin variants, pregnancy, live and other infectious diseases, etc., were excluded from the study. After meeting the inclusion and exclusion criteria, 150 study participants were included in the study and they were divided into Group I, 50 nondiabetic healthy controls not on any medication and free from any acute or chronic illness selected from general population; Group II, 50 type-II diabetic patients with good glycemic control with HbA1C level less than 7%; Group III, 50 type-II diabetic patients with poor glycemic control with HbA1C level more than 7%. All the groups were assessed for fasting blood sugar, postprandial blood sugar, HbA1C, and serum iron level.

About 5 ml of venous blood was drawn from each patient and separated into two parts. One part was collected in EDTA containing tube for HbA1C measurement and the other part in a non-anticoagulated plain tube for serum iron. After centrifugation, the serum sample was used for the measurement of serum free iron. Serum free iron concentration was carried out by Ferrozine method.[14] Fasting and post prandial (1.5 h) blood sugar (FBS and PPBS) was estimated by Glucose Oxidase-Peroxidase (GOD-POD) enzymatic end point method.[15] Glycated hemoglobin (HbA1C) concentration was measured by immunoturbidimetric method.[16]

Statistical Analysis

The data were collected and analyzed using computer software Statistical Package for Social Science (SPSS) package version 16.0. One way ANOVA followed by Tukey post hoc test was carried out to analyze the significance among the groups. Pearson correlation was applied to correlate between the parameters. A *p*-value of <0.05 was considered statistically significant.

Result

Table1 shows the demographic data, including the mean fasting, post prandial blood sugar and HbA1C levels in group I, II, and III subjects. Table 2 shows the mean ± SD of serum iron concentration among the group I, II, and III subjects. Among the study groups there was statistically significant increase in mean serum iron concentration in group III when compared to group I ($p < 0.001$) and group II ($p < 0.005$). No significant change was noticed with group II compared to group I (*p*-value = 0.205) as illustrated in Table 2. Positive correlation was observed between serum free iron concentration with glycated hemoglobin (HbA1C), fasting, and postprandial blood glucose levels ($p < 0.001$) [Table 3 and Figure 1].

Table 1. Comparison of variables among the study groups

	Group I	Group II	Group III
Number of patients	50	50	50
Mean age (years)	51.8	47.9	51.5
Gender (M/F) %	36/64	50/50	74.5/25.5
Mean height (cms)	156.3	156.3	153.3
Mean weight (kg)	63.9	62.6	64.8
Mean BMI (kg/m^2)	25.7	25.6	25.9
Mean FBS (mg/dL)	80.9	120.9	133.4
Mean PPS (mg/dL)	128.1	161.1	224.3
Mean HbA_1C (%)	5.03	5.3	8.3

Table 2. Serum free iron concentration of Group I, II, and III subjects

Subjects	Number	Mean ± SD
Group I	50	118.16 ± 23.9
Group II	50	129. 2 ± 35.2
Group III	50	149.7 ± 36.1*

Values are expressed as mean ± SD for all three groups.
*$P < 0.001$ as compared with group I.
Comparison was done by one-way ANOVA followed by Post-Hoc Tukey test.

Table 3. Correlation of serum iron with HbA_1C, FBS, and PPS

		HbA_1C (%)	FBS (mg/dL)	PPS (mg/dL)
Serum free Iron concentration (μg/dL)	Correlation value (r)	0.501	0.377	0.540
	P-value (significance)	<0.001	<0.001	<0.001

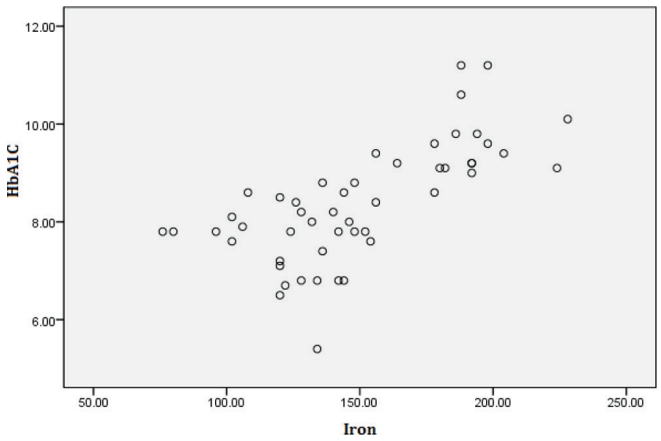

Figure 1. Correlation between serum free iron concentration with glycated hemoglobin (HbA1), fasting blood glucose (FBS), and postprandial blood glucose (PPBS) levels ($p < 0.001$)

Discussion

Our study assessed level of serum free iron concentration in type-II DM patients with good and poor glycemic control and also assessed the correlation between serum free iron concentrations with glycemic control. In this study, statistically significant increase in free iron concentration in group III subjects was observed ($p < 0.001$) than compared to group I and group II. In addition, it was also observed that there was no significant increase in free iron in group II subjects with good glycemic control. Significant positive correlation was associated between free iron concentration and fasting blood sugar, postprandial blood sugar and HbA1C levels, which measures short- and long-term glycemic control in type-II DM patients (p-value < 0.001). Our study report was similar to yet another study conducted by Shetty et al.[17] as evidenced by a positive correlation between serum iron and poor glycemic control. One study had proven that poor glycemic control causes increased glycation of proteins, especially of hemoglobin, which releases the iron in the free state.[18] Free iron catalyzes free radical production, which generates oxidants that can induce lipid oxidation. Thus, increased presence of free iron pool which is a potential catalyst will enhance oxidant generation leading to damage of cellular biomolecules thereby contributing to complications.[19] Moreover, increased serum iron is reported to elaborate hydroxyl radical causing cell damage leading to insulin resistance and earlier complications in DM.[20] One study emphasized the undergoing mechanism in evolution of diabetic complications in a faster manner with high serum iron in diabetes.[21]

Limitations of our study was small sample size, so further studies in large scale populations are needed to establish the relationship between serum free iron and glycated hemoglobin in type-II DM is worth undertaking.

Conclusion

From our study it was concluded that serum free iron concentration was higher in patients with type II DM with poor glycemic control. In addition, there was a positive correlation with serum free iron concentration and glycemic control. These suggest that an important role of iron in metabolic derangement in diabetic patients and its complications. Based on the above study, awareness can be created among people about the early complications in diabetes that will arise due to increased serum iron compared to good controlled diabetes subjects and which can postpone the complications. Further, a large scale study in diabetic population is required to corroborate the role of serum free iron concentration in modifying diabetic state and its complication.

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