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Correlation between Serum Ferritin and Glycated Hemoglobin Level in Patients of Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: The complications of diabetes mellitus are influenced not only by the duration of the diabetes mellitus but also by the average level of blood glucose along with glycated haemoglobin. Raised serum ferritin may possibly be related to the occurrence of long term complications of diabetes, both microvascular and macrovascular.

Objective: The aim of this study is to establish a correlation between serum ferritin, fasting plasma glucose and glycated hemoglobinin type 2 diabetes mellitus patients.

Materials and Methods: This was a cross-sectional study of 100 cases, visiting medical outpatient department of SGT Medical College and Hospital, Budhera, Gurugram, Haryana. Sample were analysed for the measurement of FPG, HbA1c and Serum Ferritin (by ELISA).

Results: The mean FPG, HbA1c and serum ferritin levels were significantly higher with P<0.01 in diabetic group compared to controls. Serum ferritin was significantly related to the duration of diabetes (P<0.05). As the duration of diabetes increased, serum ferritin levels were also increased. Also there was a positive correlation between serum ferritin and FPG, HbA1c. Serum ferritin is significantly related to FPG (r-0.903, P< 0.01) in diabetic patients. Serum ferritin is also positively related to HbA1c (r-203, P<0.05).

Conclusion: Findings of this study concludes that serum ferritin is elevated in patients with type 2 diabetes mellitus when compared to healthy individuals and it indicates that serum ferritin can be used as a marker for glycemic control in diabetic patients. .

Key Words: Serum Ferritin, Glycated Hemoglobin, Type 2 Diabetes Mellitus

INTRODUCTION

Diabetes is a metabolic disorder characterized by hyperglycemia from defects in insulin secretion, insulin action, or both[1]. People with type 2 diabetes mellitus develop characteristic microvascular complications such as retinopathy, nephropathy and neuropathy. There is also increased risk of macrovascular complications such as cardiovascular, cerebrovascular and peripheral vascular disease[2].

Complications due to diabetes are a major cause of disability, reduced quality of life and death. Approximately 5.1 million people aged between 20 and 79 years died from diabetes accounting for 8.4% of global all cause mortality in this age group[3]. In India 65.1 million in the age group of 20 to 79 have diabetes (8.56%) and expected to rise to 109 million by the year 2035[4].

The pathogenesis of type 2 diabetes mellitus (T2DM) is complex and involves the interaction of genetic and environmental factors. Individuals with (T2DM) show both insulin resistance and beta cell defects[5]. The complications of diabetes mellitus are influenced not only by the duration of the diabetes mellitus but also by the average level of blood glucose along with glycated haemoglobin[2].

Serum ferritin is an acute phase reactant, and is a marker of iron stores in the body[6]. Iron is a transitional metal that can easily become oxidized and thus act as an oxidant[7]. Elevated iron stores may induce diabetes through a variety of mechanisms, including oxidative damage to pancreatic beta cells, impairment of hepatic insulin extraction by liver, and interference with insulin's ability to suppress hepatic glucose production [8].

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Raised serum ferritin may possibly be related to the occurrence of long term complications of diabetes, both microvascular and macrovascular [9,10].

Recent studies have shown that serum ferritin was proportional to serum glucose concentration, diastolic blood pressure, HDL cholesterol, and insulin resistance. In fact, the higher the ferritin levels, the higher the incidence of type 2 diabetes mellitus[11,12]. Amongst the various markers of glycemic control, glycated hemoglobin has now been established as the most reliable. However, ferritin's role as a marker of iron overload in pancreatic damage and peripheral insulin resistance or its role as an inflammatory marker is not clear[13].

Hence this study was carried out to examine the association between serum ferritin and glycated hemoglobin levels in T2DM and to establish a correlation between serum ferritin, Fasting Plasma Glucose (FPG) and Glycated Hemoglobin (HbA1c).

MATERIALS AND METHODS

This was a cross-sectional study of 100 cases, visiting medical outpatient department of SGT Medical College and Hospital, Budhera, Gurugram, Haryana. The study was approved by institutional ethical committee. 50 diabetic patients were compared with 50 age and sex matched normal healthy controls. A written informed consent was also taken from the cases with detailed history.

Inclusion Criteria: Clinically diagnosed type 2 diabetes mellitus patients on treatment in the age group of 35-70 years.

Controls: Healthy controls in the age group of 35-70 years.

Exclusion Criteria:

Chronic Infections

Chronic Liver Disease

Chronic Renal Disease

Overt Thyroid Dysfunction

Patients on Corticosteroids Therapy

Anemia (Hb<10 gm/dL)

5 mL of fasting blood sample was collected and centrifuged for serum/plasma separation. Sample were analysed for the measurement of plasma glucose by glucose oxidase-peroxidase method, whole blood taken in EDTA vial for HbA1c by ion-exchange resin method and serum ferritin was assessed by ELISA method by commercially available kit provided by Calbiotech.

STATISTICAL ANALYSIS

Statistical analysis was done using the SPSS software version 24. The data was represented by counts, percentage and mean± standard deviation. Statistical analysis of the biochemical parameters, FPG, HbA1c and serum ferritin were done by t-test to compare these parameters in cases and controls. Pearson's correlation coefficient was used for comparison of variables. A P –value of <0.05 was considered significant and P-value >0.05 as non-significant.

RESULTS

In this study majority of patients were male (68% vs 32%). The mean age of diabetic patients was 52.37± 7.98 years and that of the controls was 50.85±5.61 years. (Table 1) There was no statistical significant difference of age between the two groups in either gender.

The age of onset of diabetes in 80% of cases was between 40 and 50 years. In majority of patients (64%) the duration of diabetes was between 5-10 years and more than 10 years in 36%. 76% patients were on oral hypoglycaemic drugs and 24% were on insulin therapy.

The mean FPG, HbA1c and serum ferritin levels were significantly higher with P<0.01 in diabetic group compared to controls (Table 2). Serum ferritin was significantly related to the duration of diabetes (P<0.05). As the duration of diabetes increased, serum ferritin levels were also increased.

Also there was a positive correlation between serum ferritin and FPG, HbA1c. Serum ferritin is significantly related to FPG (r-0.903, P< 0.01) in diabetic patients. Serum ferritin is also positively related to HbA1c (r-203, P<0.05)

DISCUSSION

Type 2 diabetes mellitus is a chronic metabolic disorder and its prevalence has been increasing steadily all over the world. People living with type 2 diabetes mellitus are more vulnerable to short and long term complications, which often lead to their premature death[14].

Oxidative stress has been implicated in the pathogenesis of the complications seen in T2DM[15]. Superoxide and hydrogen peroxide appear to be the primary generated species. These species may then play a role in the generation of additional and more reactive oxidants, including the highly reactive hydroxyl radical in which iron salts play a catalytic role in a reaction. This reaction is commonly referred to as the metal catalyzed Haber-Weiss reaction [16].

$Fe^{3+} + O_2 \longrightarrow Fe^{2+} + O_2$

$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+}OH + OH^-$

$O^{2-} + H_2O_2 \longrightarrow OH^{\cdot} + OH^-$

Iron is the most abundant trace element in the body, and almost all iron occurs bound to proteins. Iron is a double-edged sword. In moderate quantities and leashed to proteins, it is an essential element in all cell metabolism and growth, but it is toxic when unleashed[17].

Because of its ability to switch back and forth between ferrous and ferric oxidation states, iron is both a strong biological oxidant and reductant. Although the exact mechanism of iron-induced diabetes uncertain, it is likely, to be mediated by three key mechanisms: Insulin deficiency, insulin resistance and hepatic dysfunction[18].

The central importance of iron in the pathophysiology of disease is derived from the ease with which iron is reversibly oxidized and reduced. This property, while essential for its metabolic functions, makes iron potentially hazardous because of its ability to participate in the generation of powerful oxidant species such as hydroxyl radical[16].

Another endogenous source of catalytic free iron is the iron released when the heme ring is opened by hemeoxygenase[7]. The intracellular generation of apoferritin is a cytoprotective antioxidant stratagem of endothelial cells [19, 20], since serum ferritin is increased in T2DM.

Ferritin is considered a positive acute phase protein and is up regulated intracellularly in many cell types, and extracellularly, in the plasma as a result of an increase in cellular secretion. An important role of ferritin during the acute phase response is to restrict the availability of iron by sequestration into the cavity of the ferritin protein shell [14].

The role of iron in the pathogenesis of diabetes is suggested by an increased incidence of type 2 diabetes in diverse causes of iron overload and reversal or improvement in diabetes (glycemic control) with a reduction in iron load achieved using either phelobotomy or iron chelation therapy [18]. The importance of protein glycation is well known in the pathogenesis of diabetic vascular complications. Transition metals also play a role in protein glycation induced by hyperglycemia. It has been shown that glycated proteins have a substantial affinity for the transition metals, and the bound metal retains redox activity and participates in catalytic oxidation. Thus, should similar glycochelates form in vivo, reactions mediated by the chelates could be involved in the vascular complications of diabetes [21].

Different theories regarding the role of ferritin in T2DM have been suggested. Ferritin has been referred as a marker for insulin resistance possibly due to iron deposition in the liver leading to hepatic insulin resistance and increased hepatic glucose production[11,22]. Others has determined that ferritin just as a marker of pancreatic inflammation, while pancreatic damage due to some degree of subclinical hemochromatosis has been considered in some cases of diabetes [13].

Two large epidemiological studies reported a strong association between elevated serum ferritin concentration and increased risk for diabetes [23, 24]. In present study a statistical significant increase in fasting plasma glucose, glycated hemoglobin and serum ferritin levels were observed in patients of T2DM as compared to healthy controls. This finding is supported by various studies [14, 25, 26, 27, 28, 29]. A prospective case control study conducted by Thilip Kumar G et al reported that patients with T2DM had significantly higher serum ferritin level when compared to healthy controls but there is no correlation between serum ferritin with mean blood glucose and HbA1c [2]. A study by Jose- Manuel Fernandez [22] reported a correlation between serum ferritin with basal plasma glucose and no correlation with HbA1c in diabetics and normal controls. So there is a need for further studies to confirm the implications of serum ferritin as a marker for type 2 diabetes mellitus and its role in pathogenesis of T2DM.

CONCLUSION

Based on this study it is concluded that serum ferritin is elevated in patients with type 2 diabetes mellitus when compared to healthy individuals and it indicates that serum ferritin can be used as a marker for glycemic control in diabetic patients.

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Table 1: Mean age of cases and controls (n=100)

Group	Age Group (yr)	Number of Participants (n)	Mean Age (yr)
Diabetics	35-70	50	52.37± 7.98
Controls	35-70	50	50.85±5.61

Table 2: Comparison of biochemical parameters in control & diabetic groups

Parameters	Controls	Diabetics	P value
FPG (mg/dL)	86.34±11.98	183.89±34.28	<0.01(S)
HbA1c (%)	4.98±0.72	8.15± 1.2	<0.01(S)
Serum Ferritin (ng/mL)	20.71± 8.23	198.37±54.78	<0.01(S)