Association of serum ferritin and hba1c level with diabetes complications in diabetes type-2 mellitus in Rajshahi medical college hospital,Rajshahi, Bangladesh.

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Abstract

Introduction: Diabetes is a metabolic disorder characterized by hyperglycaemia and raised HbA1c. Serum Ferritin is an acute phase protein and it is a marker of iron stores in the body. Excess iron damages β-cells of pancreas due to oxidative stress contributing to pathogenesis of diabetes mellitus. 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 longterm complications of diabetes, both microvascular and macrovascular.

Objective: The aim of this study is to establish a correlation between serum ferritin and glycated haemoglobin levels in type 2 diabetes mellitus patients.

Materials and Methods: This study was done in the department of Medicine, Rajshahi Medical College, and Rajshahi, Bangladesh done from July-2018 to Jun-2019. The study comprised of total 100 subjects. Blood samples were analysed for Ferritin, HBA1C and fasting plasma glucose. Domain OCT was performed using CIRRUS HD OCT after pupillary dilatation. Signal strength of 6 or higher was considered acceptable.

Results: Serum ferritin was significantly higher in diabetic patients when compared with control group ($p<0.001$). Serum ferritin is positively correlated with HbA1c and also serum ferritin had a positive correlation with increasing duration of diabetes. Conclusion: Serum ferritin and HBA1C level were 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.

Keywords: Diabetes mellitus, HBA1C, Ferritin.

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Introduction

Diabetes Mellitus is a metabolic disorder characterised by hyperglycemia and associated disturbances in carbohydrate, fat and protein metabolism because of absolute or relative insulin deficiency or from defects in insulin secretion, insulin action, or both [1,2]. These disturbances are known to be associated with significant long-term complications namely, microangiopathies (nephropathy, neuropathy, retinopathy etc.) and macrovascular diseases (coronary artery atherosclerosis, cerebrovascular and peripheral vascular disease. 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 [3]. Serum ferritin is an acute phase reactant, and is a marker of iron stores in the body [4]. Iron is a transitional metal that can easily become oxidized and thus act as an oxidant [5]. Raised iron stores induce diabetes through a various pathways, 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 [6-8]. 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 [9]. High body iron stores that are serum ferritin have been linked to insulin resistance, metabolic syndrome and gestational diabetes [10-15]. In diabetic patient, the HbA1c not only correlates with blood sugar level but also with the iron status if the patient happens to be suffering from iron deficiency anaemia [16]. Serum ferritin level had a relationship with hyperglycemia and its level decreased with lowering of serum blood glucose [17]. Hence, the present study was conducted to study correlation of serum ferritin with diabetes complications in patients of type 2 diabetes mellitus.

Objective

The aim of this study is to establish a correlation between serum ferritin and glycated haemoglobin levels in type 2 diabetes mellitus patients.

Materials and Methods

This study was done in the department of Medicine, Rajshahi Medical College, and Rajshahi, Bangladesh done from July-2018 to Jun-2019. The study consists of total 100 subjects out of which 50 were diabetic patients compared with 50 ages and sex matched normal healthy controls. Blood samples were analysed for Ferritin, HBA1C and fasting plasma glucose. A written informed consent was taken from the subjects.

Inclusion criteria

Cases: Clinically diagnosed type 2 diabetes mellitus patients on treatment in the age group of 35-70 years. For the diagnosis of diabetes mellitus, FPG ≥126 mg/dl or previous history of diabetes mellitus was required. Controls: Healthy controls in the age group of 35-70 years with no history of any medical disorder. They had fasting plasma glucose levels of <110 mg/dl and hemoglobin levels of more than 12 g/dl. They did not have a history of medication use, and were matched with the diabetic group regarding age and sex.

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 Immunoturbidimetric method and serum ferritin was assessed by ELFA method by commercially available kit provided by Roche Cobas Integra. Results were analyzed with SPSS software and student t-test was done for quantitative variables and Pearson's regression for correlation between variables. P-value <0.05 was considered as a significant.

Results

In the present study we recruited total 100 subjects, out of which 50 subjects were in the cases group (29 males and 21 females) and 50 subjects were in the control group (26 males and 24 females). All the subjects belong to the age groups of 35-70 years. The mean age of the case group and the control group were 50.16 ± 7.0 years and 49.58 ± 6.70 years, respectively (Table 1). Both the groups were statistically similar in the age with the p-value of 0.76. There was no statistical significant difference between the mean hemoglobin level in diabetics (13.65 ± 1.3 g/dl) and normal controls (13.5 ± 1.3 g/dl). The mean BMI in diabetics was 27.5 ± 4.2 kg/m2 and for control group was 23.4 ± 2.8 kg/m2 (p<0.001) (Figure 1).

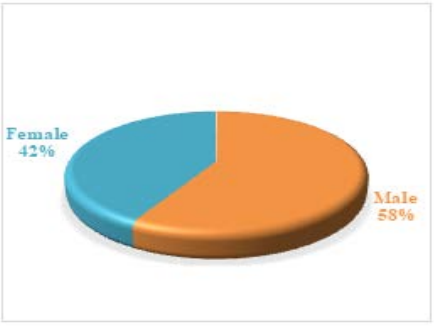

Figure-1: *Sex distribution of patients.*

S.No.	Parameters	Controls	Cases
1	No. of Individuals	50	50
2	Age (Years)	49.58 ± 6.70	50.16 ± 7.0
3	BMI (Kg/m2)	23.4 ± 2.8	27.5 ± 4.2
4	Hemoglobin (g/dL)	13.5 ± 1.3	13.65 ± 1.3

Table 1: *Baseline characteristics of cases and control.*

S. No.	Variables	Controls	Cases	p-Value
1	Serum Ferritin (ng/mL)	64.12 ± 30.38	155.58 ± 48.12	<0.001
2	Fasting Plasma Glucose (mg/dL)	94.08 ± 10.2	164.5 ± 30.02	<0.001
3	HBA1C (%)	5.13 ± 0.82	7.98 ± 1.13	<0.001

Table-2: *Mean values of different variables among controls and cases.*

The mean FPG, HbA1c and serum ferritin levels were significantly higher with P<0.001 in diabetic group compared to controls (Table 2). In addition, there was a positive correlation between serum ferritin and FPG, HbA1c. Serum ferritin is significantly correlated with FPG (r-0.20, P<0.05) in diabetic patients. Serum ferritin is also positively related to HbA1c (r-0.9, P<0.01).

Discussion

Type 2 diabetes mellitus is a chronic metabolic disorder resulting from insufficient or ineffective insulin to control blood glucose concentration [18]. The prevalence of DM-type 2 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 [19]. T2D is primarily attributable to poor lifestyles and excess body weight. Promotion of healthy lifestyles and weight management, unfortunately, has been unsuccessful in curbing the increasing public health burden of T2D. Oxidative stress plays an important role in the pathogenesis of the complications seen in T2DM [20]. Superoxide and hydrogen peroxide appear to be the primary generated species. These reactive oxygen species 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 referred to as the metal catalyzed Haber-Weiss reaction [21]. Another endogenous source of catalytic free iron is the iron released when the heme ring is opened by hemeoxygenase [5]. Ferritin is known as an index of body iron stores and as an inflammatory marker. Ferritin is up regulated intracellularly in many cell types, and extracellularly, in the plasma because of an increase in cellular secretion. 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 phlebotomy or iron chelation therapy [22]. 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 [23]. 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 [24,25]. Pancreatic damage due to some degree of subclinical hemochromatosis has been considered in some cases of diabetes [26-28]. A strong association between elevated serum ferritin concentration and increased risk for diabetes. 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 [3, 29-35] in their studies confirmed that poorly controlled diabetes patients had hyperferritinemia. This showed that serum ferritin was increased in diabetes as long as glycemic control was not achieved. They also found a correlation between ferritin level and diabetic retinopathy. The present study concludes positive correlation between serum ferritin and glycated haemoglobin, which implies the role of ferritin as an indicator of glycemia control and diabetic complications. So serum ferritin can be used as a marker for screening of insulin resistance and type 2 diabetes mellitus. From this study, we recommend that more studies should be performed to confirm the implications of serum ferritin as a marker for type 2 diabetes mellitus and its role in pathogenesis of T2DM.

Conclusion

Serum ferritin and HBA1C level were 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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