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STUDY OF SERUM FERRITIN AND GLYCOSYLATED HEMOGLOBIN LEVELS IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

Introduction: Type 2 Diabetes Mellitus is one of the most common metabolic endocrine disorder characterised by hyperglycemia. It is caused by a complex interaction of genetics and environmental factors. In DM , lipid abnormalities, anaemia, alteration of liver and kidney functional indices have been implicated as major risk factors to the progression of Diabetic complications.

Ferritin is an index of body iron stores & acts as an iron overload marker. The relationship between iron metabolism and type 2 DM is bidirectional. Iron is a potent pro-oxidant that increases cell oxidative stress causing decreased insulin internalization and actions resulting in hyperinsulinemia and insulin resistance. Serum Ferritin, an acute phase reactant is a marker of iron stores in the body. Increased serum ferritin, reflecting body iron overload, is often associated with measures of insulin resistance, such as elevated blood glucose and insulin levels.

Aims and Objectives

a) To measure the level of Serum Ferritin and glycosylated hemoglobin in patient with Type-2 Diabetes mellitus

b) To measure the level of Serum Ferritin and glycosylated hemoglobin in controls.

Materials and Methodology: This is a case control study .The study duration is 2 years. The study was carried out on 75 cases of clinically diagnosed type 2 diabetes mellitus in the age group 40-60 years , attending department of medicine , KIMS ,Koppal. Seventy five age and sex matched healthy subjects were taken as controls . Ethical clearance was obtained from institutional ethical clearance committee.Venous sample was collected and serum biochemical parameters(FBS, PPBS, HbA1C, Ferritin) were measured.

Statistical Test: Data is expressed in terms of mean ± SD. Chi- square test was applied to estimate the difference between the two groups of population. Unpaired 't'-test was used to study the changes in serum ferritin levels between the study groups. p value <0.05 was considered statistically significant.

Results: The study showed statistically significant increase($p<0.05$) in serum ferritin levels in cases compared to controls . Our study showed a positive correlation between ferritin and blood sugar levels.

Conclusion: Type 2 Diabetes mellitus is associated with increased ferritin levels .Reliable and sensitive methods need to be developed to precisely measure catalytic iron that participates in oxidative injury.

Keywords: Type 2 DM(Diabetes Mellitus) , Ferritin , glycosylated haemoglobin , FBS, PPBS

INTRODUCTION

Type 2 Diabetes mellitus (DM) is a group of common metabolic disorders that share the phenotype of hyperglycemia. Type 2 diabetes mellitus (T2DM) is a predominant public health concern worldwide, accounting for 90% of the cases of diabetes globally[1,2,3].

It is caused by a complex interaction of genetics and environmental factors. In DM , lipid abnormalities, anaemia, alteration of liver and kidney functional indices have been implicated as major risk factors to the progression of Diabetic complications[4].The pathogenesis of type 2 diabetes mellitus (T2DM) is complex and involves the interaction of genetic and environmental factors[5]. Individuals with type 2 DM show both insulin

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resistance and beta cell defects [6]. Increased serum ferritin, reflecting body iron overload, is often associated with measures of insulin resistance[7].
Serum Ferritin, an acute phase reactant is a marker of iron stores in the body. Ferritin is an index of body iron stores & acts as an iron overload marker. Iron is a transition metal & a potential catalyst in cellular reaction that produces reactive oxygen species.. Recent studies indicate that increased body iron stores has been associated with the development of glucose intolerance, type 2 diabetes, metabolic syndrome and possibly the development of diabetic retinopathy, nephropathy and vascular dysfunction. The metabolic syndrome is closely linked to insulin resistance and numerous studies indicate a link to iron overload.

Increased serum ferritin, reflecting body iron overload, is often associated with measures of insulin resistance, such as elevated blood glucose and insulin levels. Although the exact mechanism of iron-induced diabetes is uncertain, it is likely to be mediated by three key mechanisms:

- insulin deficiency,
- insulin resistance, and
- hepatic dysfunction.

Several studies have shown that there is increased oxidative stress in Diabetic patients with Iron overload[8] and also positive associations of serum ferritin concentrations with cardiovascular risk factors[9] ,risk of insulin resistance syndrome, and risk of type 2 diabetes[10-12]. More recently the results from prospective studies from Caucasian populations suggested that Iron overload could predict the development of abnormal glucose metabolism[13]. The aim of this study is to find the influence of body iron stores on type II diabetes mellitus and its correlation with HbA1c. We hypothesize that serum ferritin may be acting as a marker of oxidative stress in DM rather than just as a marker of increased iron overload

Although several epidemiological studies have reported a strong association between elevated serum ferritin and increased risk for type 2 diabetes; more so, a link between serum ferritin concentration and insulin resistance or type 2 diabetes has been established. However, it appears that little work on the relationship between iron status and type 2 diabetes mellitus has been done in our locality , hence, the need for this study.

AIMS AND OBJECTIVES

a) To measure the level of Serum Ferritin in patient with Type-2 Diabetes mellitus
b) To measure the level of Serum Ferritin in controls.
c) To compare the levels of serum ferritin between cases and controls

MATERIALS AND METHODS:

This is a case control study .The study duration is 2 years. The study was carried out on 75 cases of clinically diagnosed type 2 diabetes mellitus in the age group 40-60 years , attending out patient department (OPD) of department of medicine , Koppal Institute of Medical Sciences (KIMS) ,Koppal. Seventy five age and sex matched healthy subjects were taken as controls . Ethical clearance was obtained from Institute's ethical clearance committee. Informed consent was taken from both cases and controls after explaining the procedure. Diabetes Mellitus was diagnosed as per the WHO diagnostic criteria[14].

Exclusion criteria:

- The patients with type 1 diabetes mellitus
- Patient with secondary diabetic complications—micro and macrovascular
- Patients with hemolytic anemia
- Patients with multiple blood transfusions
- Hepatic diseases (chronic liver diseases),hepatitis, chronic kidney diseases
- Acute infectious disorders
- Those on corticosteroid therapy
- Pregnant and lactating mothers

Biochemical Analysis: A sample of 3 ml venous blood was collected in both fasting and post prandial state under aseptic precautions. It was allowed to clot and serum was separated by centrifugation.

The following parameters were studied.

- FBS and PPBS –Glucose oxidase peroxidase method[15,16] .(kits supplied by Erba Diagnostics) . The parameters were read using semi auto analyser (STAT FAX 3300).
- HbA1c was estimated by Nycocard reader II[17].

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- Serum ferritin was estimated by chemiluminiscence immuno assay (CLIA) method using Maglumi Snibe 1000 hormone analyser.

Statistical Analysis: Data was expressed in terms of mean ± SD. Chi- square test was applied to estimate the difference between the two groups of population. Unpaired 't'-test was used to study the changes in serum magnesium and zinc in between cases and controls. Pearson correlation was performed to establish the relationship between study variables. p value <0.05 was considered statistically significant.

Results: This was a comparative case control study conducted on 75 cases of type 2 DM (n=75) and 75 age and sex matched healthy controls(n=75). Serum ferritin was estimated, analyzed and correlated with HbA1c, FBS and PPBS. The results were expressed as mean ± standard deviation.

The mean age (in years) of cases was 49.5±11.7 years and that of controls was 46 ±10.3 years and was not significant. **Table 1** shows comparision of serum ferritin , FBS, PPBS and HbA1c levels in both groups and was statistically significant(p<0.05). The mean serum ferritin levels (ng/dL) in cases was 336.9±46.3, and in controls was 127.2±40.9 and was highly significant (p <0.0001)**.**

Serum ferritin and FBS : There was significant positive correlation between serum ferritin and fasting blood sugar (r=+0.47 , p=0001) **(Table 1 ,Figure 1).**

Table 1- Comparision of FBS, PPBS and HbA1c levels in both groups

Characteristics	Groups	Mean ±SD	T	P
FBS (mg/dL)	Cases	204.5±54.4	11.1	0.001*
	Controls	90.1±12.3		
PPBS(mg/dL)	Cases	310.3±62.6	17.2	0.001*
	Controls	110.9±8.6		
HbA1c(%)	Cases	7.9±0.6	15.8	0.001*
	Controls	5.4±0.5		
Serum Ferritin(ngldl)	Cases	336.9±46.3	18.5	0.001
	Controls	127.2±40.9		

*statistically highly significant , FBS- Fasting blood sugar,PPBS-Post prandial blood sugar,HbA1c – Glycosylated Hemoglobin

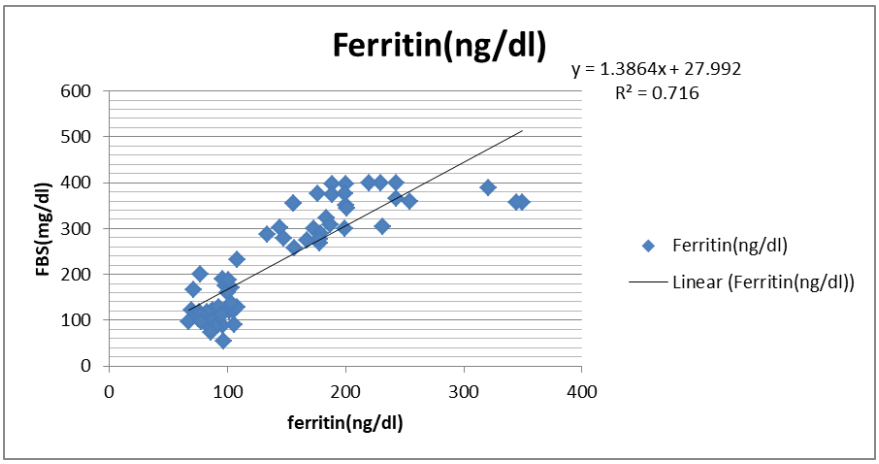

Figure 1-Correlation between Ferritin and FBS

Serum ferritin and HbA1c: There was positive correlation between serum ferritin and HbA1c , r = +0.75, p < 0.001 and was highly significant. **(Table 2,Figure 2).**

Table 2- correlation between study variables

Correlation between	Pearson's Correlation Coefficient(r)	Significance	
FBS and Ferritin	+ 0.47	p < 0.001	Highly significant positive correlation

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PPBS and Ferritin	+0.60	p < 0.001	Highly significant positive correlation
HbA1c and Ferritin	+0.75	p<0.001	Highly significant positive correlation

FBS-fasting blood sugar , PPBS-post prandial blood sugar , HbA1c-glycosylated haemoglobin

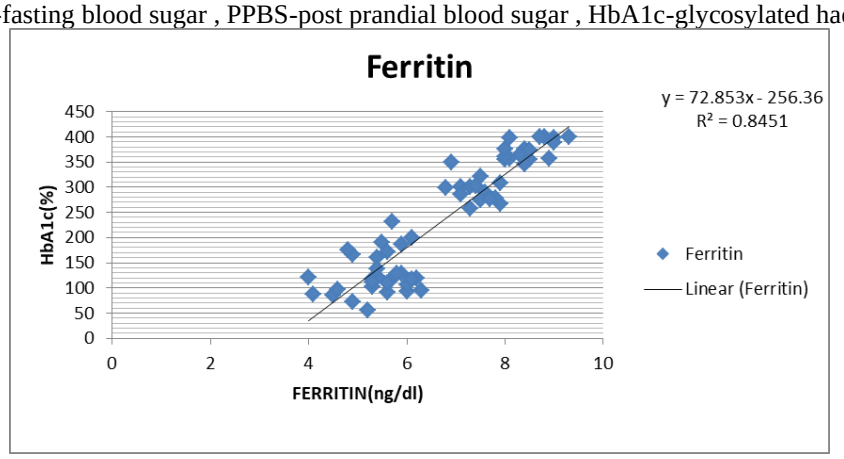

Figure 2-Correlation between Ferritin and HbA1c

DISCUSSION:

Serum ferritin, a reflector of body iron stores was significantly higher in diabetic patients when compared to controls and this significantly increased as the duration of diabetes increased. This possibly reflects the subclinical hemochromatosis developing in a long standing diabetic patient. Fernandez et al in their studies concluded that increased body iron stores are possibly associated with occurrence of glucose intolerance, type-2 DM.

Serum Ferritin had a positive correlation with FBS,PPBS and HbA1c. This reflected the relation between serum ferritin and glycaemic control, both short term and long term. Cantur KZ et al confirmed in their studies that poorly controlled diabetes patients had hyperferritinemia. Excess iron impairs pancreatic β cell function and causes β cell apoptosis[18]. Iron serves as a potent pro-oxidant in human body and participates in the generation of reactive oxygen species (ROS) such as hydroxyl radical[19]. The susceptibility of β-cells to iron-induced oxidative stress and the iron deposition in β-cells usually leads to apoptosis, and consequently, to insulin deficiency . Iron deposition also induces insulin resistance by inhibiting glucose uptake in fat and muscle tissues, and reducing the capacity of liver to extract insulin, which results in an abnormal increase in hepatic glucose production[20].

CONCLUSION:

To conclude, the major issue arises whether to estimate serum ferritin routinely in all type 2 diabetes patients and whether to set a cut off value of serum ferritin for good glycemic control. Though our study is a pointer in this direction, we would recommend further studies in this path for setting up specific guidelines. In summary, there is suggestive evidence that iron plays a pathogenic role in diabetes and its complications such as microangiopathy and atherosclerosis. Reliable and sensitive methods need to be developed to precisely measure the free/ catalytic iron that participates in oxidative injury.

Iron chelation therapy may present a novel way to interrupt the cycle of catalytic iron–induced oxidative stress and tissue injury and consequent release of catalytic iron in diabetes and to prevent diabetes-related complications.

Future study: Further studies on these parameters on large scale is required to establish diagnosic and prognostic role of these parameters in Diabetes mellitus.

Limitations of the study: Small number of the sample

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