



## Correlation Between Serum Ferritin And Glycosylated Hemoglobin In Type 2 Diabetes Mellitus

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### Abstract

**Introduction:** Diabetes mellitus (DM) type 2 is an endocrinal that is tormenting the Indian population for decades together. But the etiology is unknown. It is a disease of irregular body metabolic disorder and as far as exact cause which is frequently known is not known and it has been worked out to consider hemochromatosis, which attacks the people in the different countries' worldwide.? Recent studies have stressed that it is either defects lies either release of insulin or stressed-out level of insulin. Iron, leads to irregularity of carbohydrate metabolism.

**Materials and Methods** A study was carried out on 50 patients of diabetes and 50 healthy controls, aging above 30 years, admitted in the Department of Medicine or attending the OPD, GMC, Amritsar. This study was conducted in the Biochemistry department of Govt. Medical College, Medical College, Amritsar; over a period of 12 months. In this case and control study, 50 patients of type 2 diabetes were taken as case, while 50 normal individuals who were either relatives or friends were placed as control group, who were matched to diseased group. Exclusion criteria according to age, sex, BMI and Hb%. Ferritin, hemoglobin, HbA1c and fasting plasma sugar were measured in blood samples

**Aim of this study:** to find a link between serum fasting blood sugar levels HbA1c in type 2 diabetes mellitus and to choose role of serum ferritin upon glycemic status. The participants were categorized into three distinct groups. Estimation of blood glucose, HbA1C, and serum ferritin levels were carried out on all subjects and controls. Three age groups were evolved and categorized as part of the study.

**Results:** Serum ferritin increased significantly in diabetes mellitus patients with high HbA1c or with complications, i.e., up to  $128 \pm 43-01$  ng/ml as compared to healthy controls from  $34.65 \pm 14.23$  ng/ml. Blood Glucose levels were in T2 DM cases was more than 126 mg/dl with mean value of  $176.89 \pm 32.54$  mg/dl while in controls the mean level was  $75 \pm 45$  mg/dl that is the levels were in normal range of 70 -100 mg/dl. Results were kept for statistical Chi-square test, Student's t-test, Pearson correlation coefficient test and Odds ratio. Mean serum ferritin was significantly higher in diabetics than in the control group ( $198 \pm 98$ )  $\mu\text{gm/L}$  vs.  $56.76 \pm 23.64$   $\mu\text{gm/L}$ , p value being highly significant.

**Conclusion;** It was concluded from our study that FBS, HbA1c and serum ferritin levels were associated with T2DM. Excess iron deposition may lead to increased risk of DM as it plays important role in oxidative stress resulting in tissue injury. Elevated ferritin level signifies insulin resistance, hypertension, dyslipidemia, metabolic syndrome and obesity. Elevated iron stores may damage Beta cells of pancreas leading to T2DM. The present study showed positive correlation between increasing serum ferritin amongst Type 2 diabetics with

complications, signaling towards an alarming development of hemochromatosis in a long-standing diabetic patient.

**Keywords:** NIL

## Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by the complete or partial  $\beta$  Cells deficiency in the insulin production by Beta cells of the Pancreas. As a deranged Glucose metabolism leads to increase in body of unmetabolized glucose. It can lead to various disorders like-- neuropathy, nephropathy, retinopathy. CVA and gangrene of extremities. The recent criteria of Diabetes mellitus includes type 1 Diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), gestational diabetes and other types. Type 1 is due to environment and immunological factors that ultimately lead to destruction of pancreatic  $\beta$ -cells. But this phenomenon is not seen in all the cases of DM. In Type 2 DM there is more complexity as there is combination of action of the insulin on liver and muscle together with the impaired pancreatic  $\beta$  cells function leading to the relative insulin deficiency. Risk factor for this DM includes obesity, family history of DM and many more. Onset of complications depends on duration and average blood level of glucose along with glycosylated hemoglobin (HbA<sub>1c</sub>) Latter is investigation of choice in monitoring the treatment of DM. This is most reliable marker to reflect average concentration of glucose for the period of 3 months. This is produced by ketoamine reaction between glucose and N-terminal valine of both the Beta chains of hemoglobin. The level more than 7% indicates an increased chance of progression to diabetic complications mainly microvascular complications. Since erythrocytes have average life span of 120 days, so glycemic level in the preceding month contributes about 50% to the A1c value. Since Ferritin is an acute phase reactant, and is marker of iron stores in the body. This being transitional metal that can be easily become oxidized and thus acts as oxidant. The important role of the ferritin during acute phase response is to restrict the availability of iron by sequestration into cavity of ferritin protein shell. The metabolic syndrome is closely linked to insulin resistance and it indicates a link to iron overloaded. Increased serum ferritin

reflects body iron is overloaded and is often associated with the measures of insulin resistance. Such as elevated blood glucose and insulin levels. In 2020 Study was conducted, observed that serum ferritin level of the diabetic patients was significantly higher than that of controls. There was a positive correlation between HbA<sub>1c</sub> and serum ferritin among diabetic patients. The study conducted in 2015, Observed that the statistically significant increase of FPG (Fasting Plasma Glucose). HbA<sub>1c</sub> and serum ferritin levels was observed in type 2 DM group than controls in both males and females while there was statically significant difference of hemoglobin between diabetic and control group of females and males. There was a high ( $r=0.62-0.66$ ) positive correlation between serum ferritin and HbA<sub>1c</sub> of females and males respectively.

## Review

The term diabetes mellitus is derived from the Greek word Diabetes, means a siphon to pass through and Latin word mellitus meaning sweet. Diabetes mellitus was first reported by Egyptians around 1500 B.C. who defined it as a rare disease where patient urinates excessively and loses their weight. It is a metabolic disorder characterized by chronic hyperglycemia resulting from defects in the insulin secretion, insulin action or both. Metabolic abnormalities in carbohydrates, lipids and proteins results from the role of insulin as an anabolic hormone. Levels of insulin goes down and of the insulin resistance of the target tissue goes down affecting various tissues like skeletal muscle, adipose tissue and to lesser extent, liver, at the level of insulin receptors, spinal transductive system and effect of enzymes or genes are responsible for these metabolic abnormalities. The severity of symptoms is due to type and duration of diabetes. Some patients especially T2DM remain asymptomatic during the early years of disease and others with marked hyperglycemia especially in children with the absolute deficiency may suffer from polydipsia, polyuria, polyphagia, weight loss and blurred vision. Uncontrolled diabetes may lead to stupor, coma and untreated cases will die from

diabetic ketoacidosis. Or from non-kenotic hyperosmolar syndrome. In case the present condition prevails and not much is done, then by the end of 2030, only India will have 79 million cases of diabetes mellitus. Analysis of HbA1c in blood provides gives an average blood glucose level during the previous 2-3 months. This is now recommended as standard of care (SOC) for testing and monitoring the diabetes. In 2009 an International Expert Committee recommended the use of HbA1c as diagnostic alternative to OGGT, leading to strong support as screening modality due to lower cost, lack need for repeated estimations as with blood glucose. It also provides reliable measure of chronic glycemia and correlates with long term complications, so it is used as test of choice for monitoring and chronic management of the diabetes. A false value of HbA1c is seen in high altitude, pregnancy, hemorrhage, blood transfusion, iron supplementation of iron, alcoholics, liver cirrhosis, folic acid deficiency and so many others. Vitamin C supplementation also affects the level of HbA1c. Other major complications are seen are neuropathy, nephropathy and retinopathy. Serum ferritin level measures the condition of iron amount in the body. Iron is transitional metal and that act as an oxidant. An important role of ferritin during the acute phase response is to restrict the availability of iron by sequestration into the cavity of ferritin protein shell. Normally there is little ferritin in the human plasma proportionate to total stores of iron in the body. Plasma ferritin levels are thus considered to be an indicators of body iron stores.

### **Aims and objectives**

The present study was conducted to find a correlation if any between serum ferritin and glycosylated hemoglobin in patients of T2DM. These are as follows:

1. To determine the levels of serum ferritin in T2 diabetes mellitus in comparison to controls.
2. To determine the level of HbA1c in type 2 DM.
3. To find a correlation between levels of serum ferritin and HbA1c in T2 diabetes cases.

### **Materials & Methods**

As per already mentioned the 50 controls and 50 patients of T2DM were taken for study. Parameters taken were standardize as per methodology like:

1. Serum Ferritin was investigated on ELISA by using kit from Bio-Detect Pvt. Ltd.
2. Blood glucose was estimated by glucose oxidase-peroxidase method as described by Trinder P (1969)
3. HbA1c was determined by the method used on ion exchange chromatography as described by Klenk et al, using kits from TransAsia.

### **Observations**

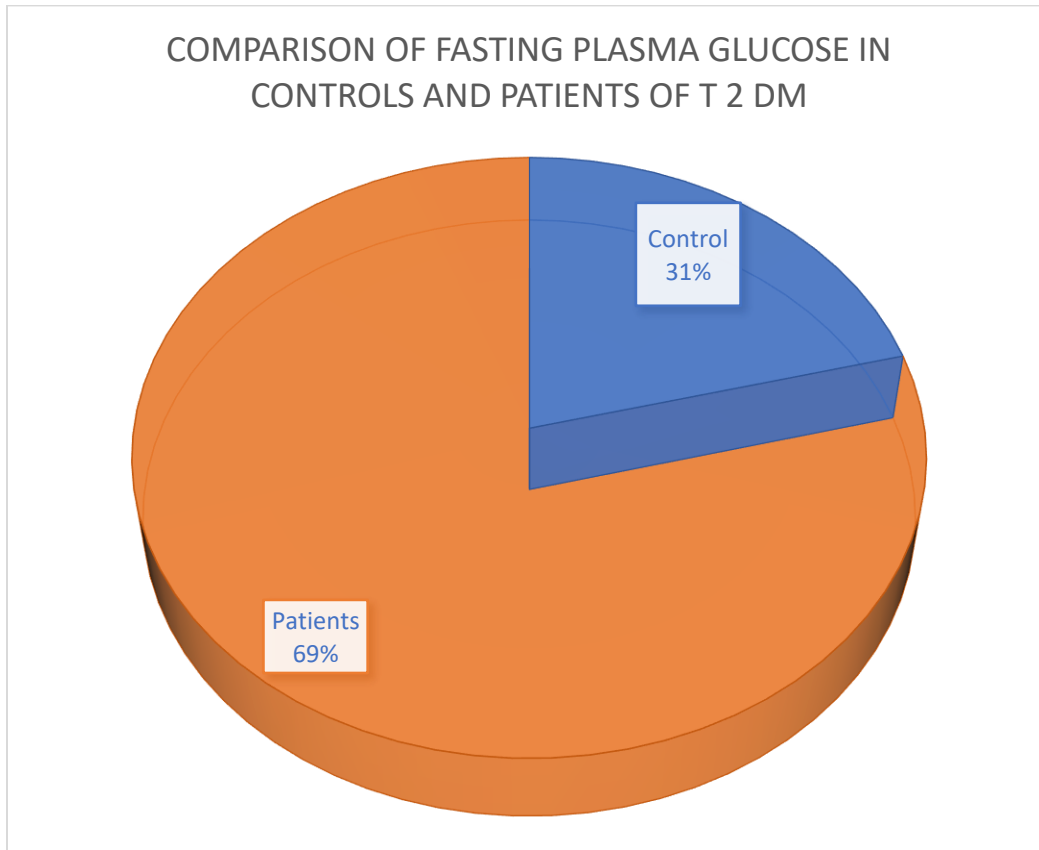
Present study was carried out in Govt. Medical College, Amritsar, Department of Biochemistry in collaboration with Department of Medicine. Both study group and controls had 50 each. The patients included were diagnosed with Type 2 Diabetes Mellitus having age more than 30 years of age belonging to either sex. All the patients and controls were enrolled in the present study were divided into three (3) groups depending on their age:

Group 1 Age 30-45 years

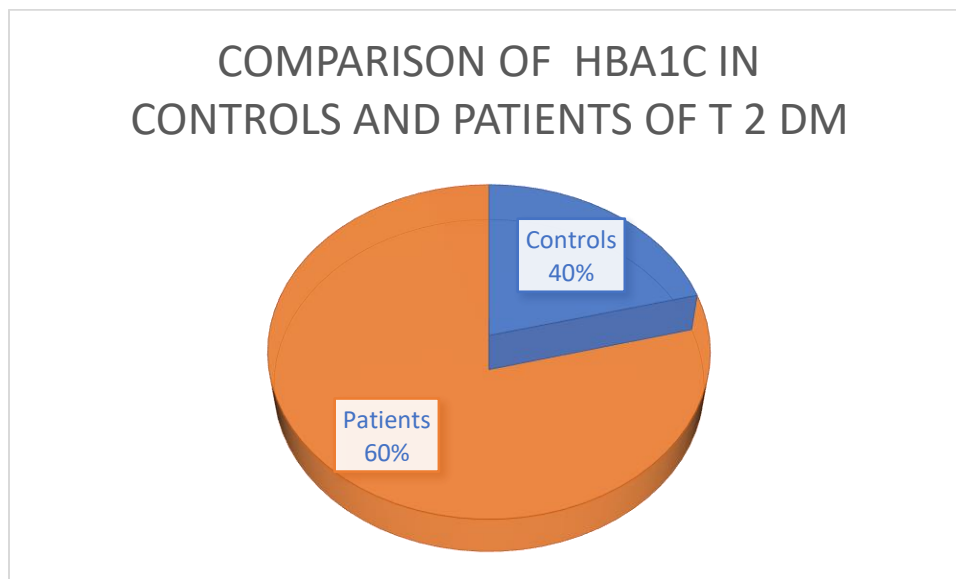
Group 2 Age 45-60 years

Group 3 Age >60 years It was observed that maximum number of patients belonged to age group 2 i.e., 40-60 years. Gender wise, number of females is more as compared to males.

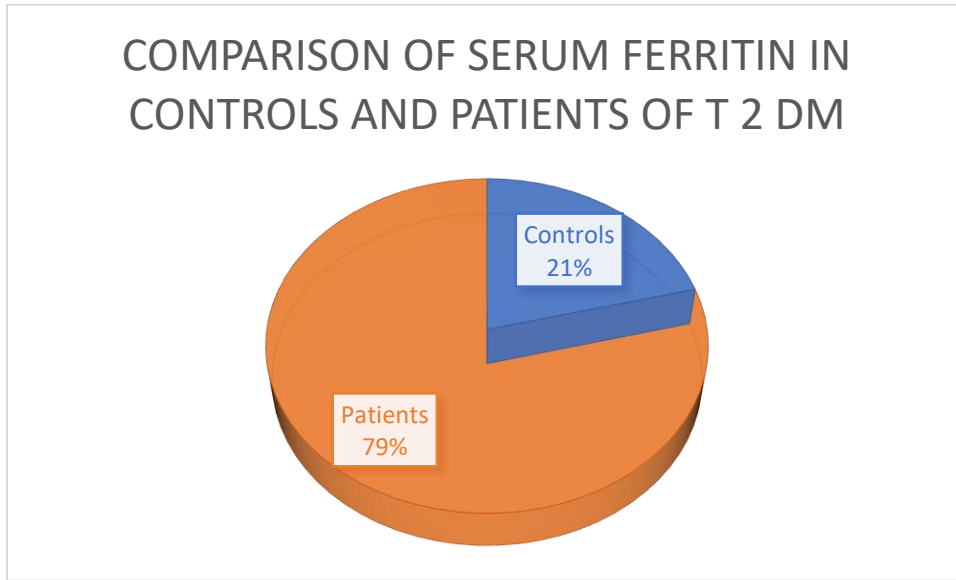
**Fig.1 All the individuals e.g., controls and patients were investigated for Fasting Plasma Glucose, Glycosylated hemoglobin and Serum Ferritin. It was observed that FPG levels increased significantly ( $p < 0.001$ ) in patients of T2 diabetes mellitus.**



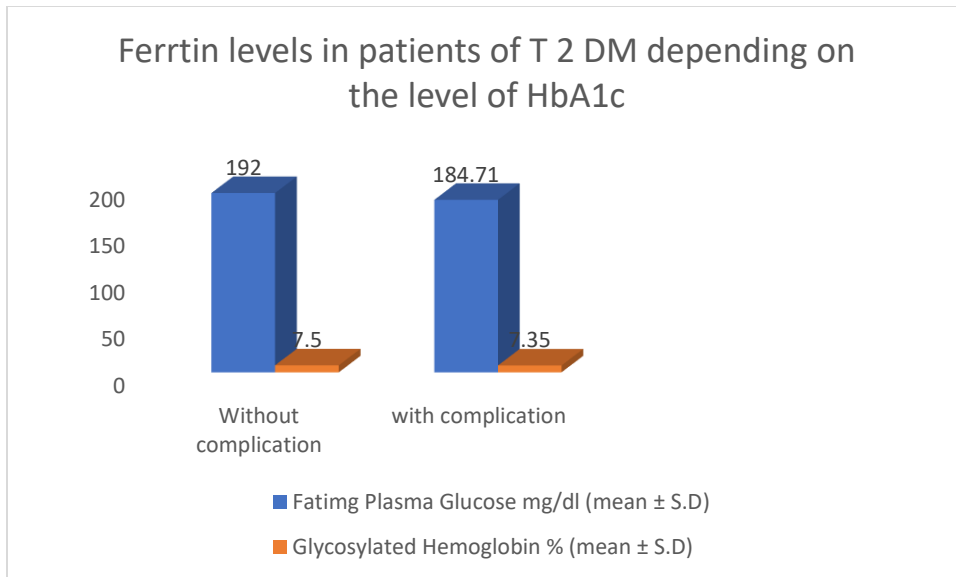
**Fig 2 When the levels of Glycosylated Hemoglobin were compared amongst patients and controls, it was found to be significantly increased ( $P < 0.001$ ) in patients suffering from T2 Diabetes Mellitus.**



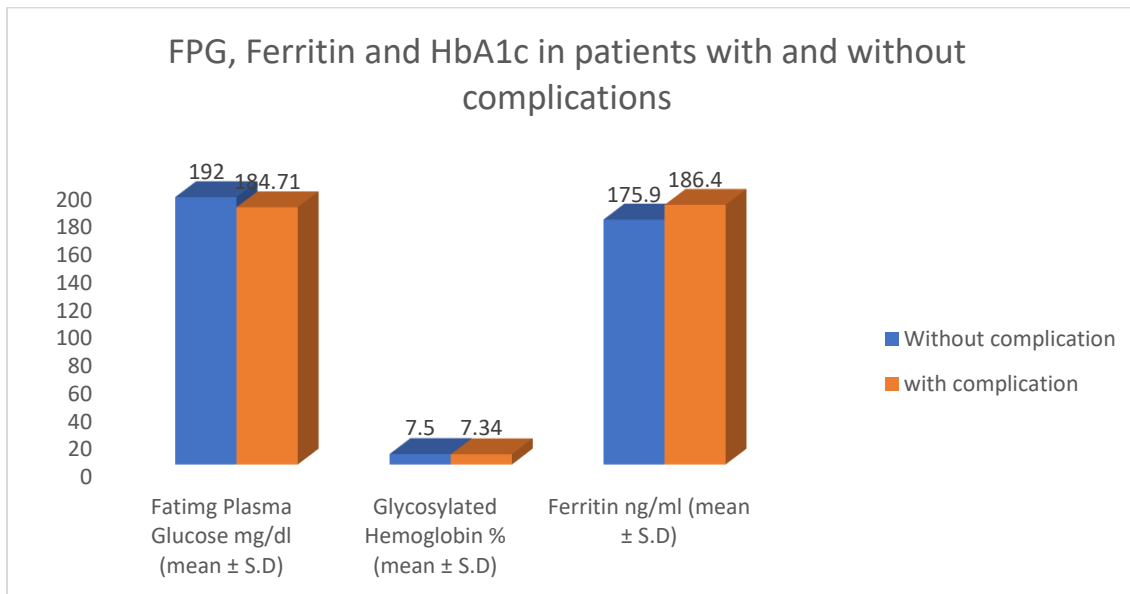
**Fig 3** When the levels of serum ferritin were compared amongst patients and controls was significantly increased ( $p < 0.001$ ) in patients of T2 DM



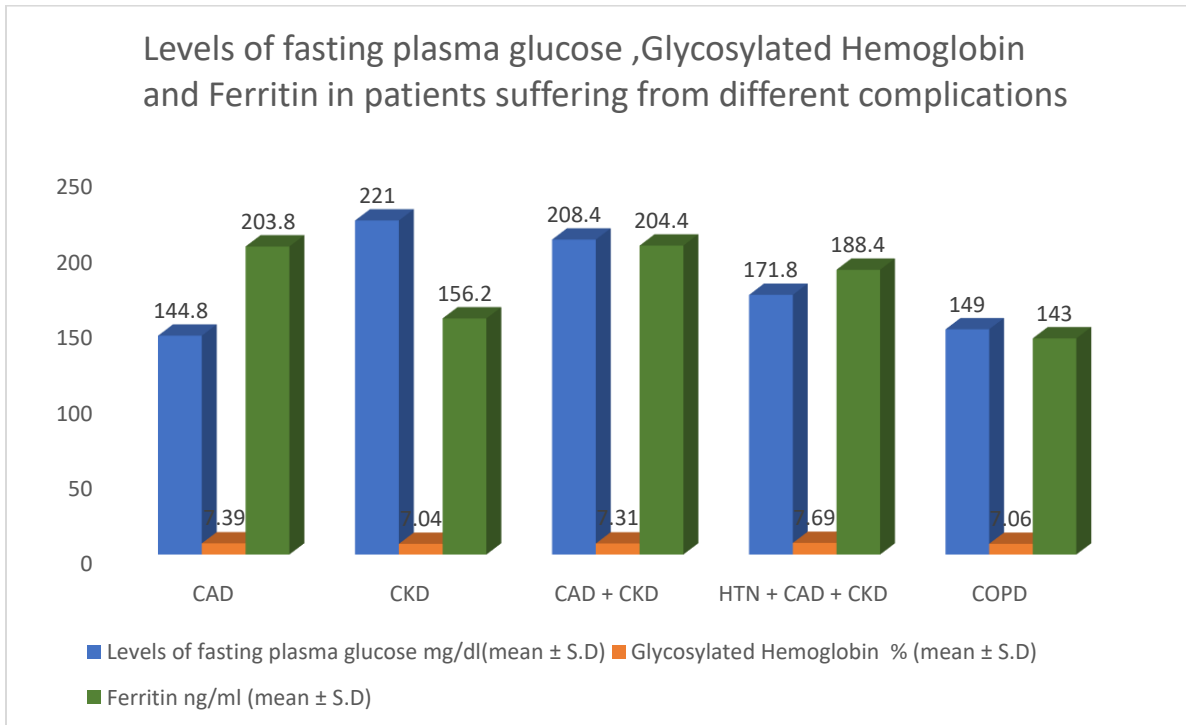
**Fig 4** ( $P < 0.01$ ) seen when glycosylated hemoglobin and serum ferritin in group 1 were compared with Group 2, group 2 versus group 3 and group 3 vs. group 1



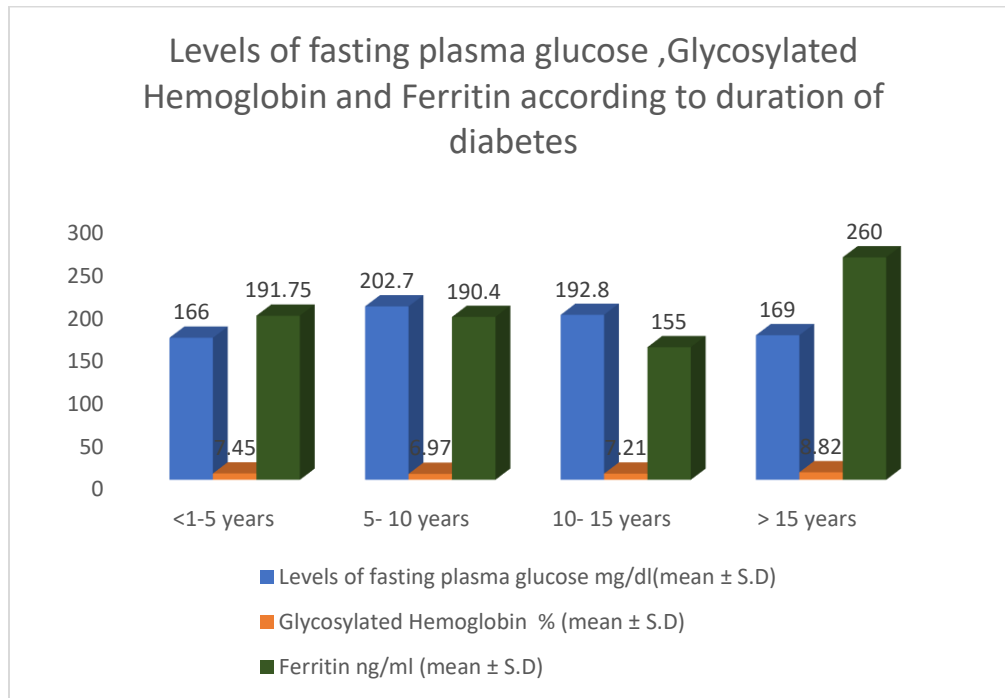
**Fig 5 All the patients of T2 DM were classified into two categories i.e., with and without complications, it was found that complicated cases showed serum ferritin though normal in controls varied significantly ( $p < 0.005$ ) when compared to patients without complications**



**Fig 6 All the patients were subdivided according to different complications that is suffering from CAD, CKD or both, it was observed that equal number of patients suffered from either CAD, CKD or both. Also, in cases of Hypertensions. ( $p < 0.001$ )**



**Fig 7 All the patients suffering from T2 Diabetes Mellitus were divided into various groups depending on duration of diabetes mellitus. It was found that though levels of FPG, HbA1c and ferritin increased when compared to controls but the increase did not show a specific pattern.**



**Summary**

1. It was an observational case control study to estimate and compare the levels of serum ferritin, Fasting Blood Glucose and Glycosylated Hemoglobin in patients of T2 diabetes mellitus and normal healthy individuals.
2. 50 diagnosed cases of with Type 2 diabetes mellitus were selected from the OPD and various wards of Department of Medicine of GMC, Amritsar were selected. Both the sex was included. Maximum number of patients were in the age group of more than 50 years of age.
3. Blood glucose levels in the patients of T2 DM were more than 126 mg/dl with the mean of 189 ±61.76 mg/dl while in controls 85.16±6.2 mg/dl that falls in the normal range.
4. Levels of HbA1c in patients in T2DM cases was 7.5±1.40 % as compared to controls which have levels of 49.52±20.31 ng/dl.
5. Mean levels of serum ferritin have been found to be 181.36±56.08 ng/ml as compared to controls that had levels of 49.52±20.31 ng/ml.
6. All the patients and controls were subdivided depending on age and gender. Fasting blood glucose were more in males of group 1 and

- group 3 as compared to Females as is evident from the case studies
7. Females had a poor control of diabetes as compare to males. It is evident from increasing HbA1c with increasing age.
8. Levels of serum ferritin showed an increasing trend in females and males suffering type 2 diabetes mellitus.
9. Serum ferritin showed a positive significant correlation with HbA1c.
10. Levels of Serum ferritin were significantly increased in patients with complications as compare to without complications. It was further noted that ferritin levels did not have any correlation with HbA1c in patients having different complication. Neither there was any significant variation when levels of ferritin was compared with patient having complication.
11. Dureation of type 2 diabetes did not affect the levels of ferritin as there was no specific pattern increase or decrease in the levels.
12. In patients suffering from various complications with CAD had sedentary life style (100 %). CAD & CKD (60% sedentary & 40 % Exercise) and hypertension along with CKD and CAD had sedentary life style (100%) thus indicating that

complication may be result of uncontrolled diabetes mellitus and sedentary life style.

**Conclusion:** It is concluded from our study that fasting blood glucose, Glycosylated hemoglobin and serum ferritin levels are associated with type 2 diabetes mellitus. Excess iron deposition may lead to increased risk of diabetes it as plays an important role in oxidative stress resulting in tissue injury. Ferritin is also associated with insulin resistance, hypertension, dyslipidemia, obesity and metabolic syndrome. Elevated iron stores may damage pancreatic beta cells leading to type 2 diabetes mellitus. In the present studies, it was observed that the ferritin levels were increased in diabetes patients as compare to control group. Increased ferritin levels also pre disposed the diabetic patients to various complications.

### References

- Jiang R, Manson JE, Meigs JB, Ma J, Rifai N, Hu FB. Body iron stores in relation to risk of type 2 diabetes in apparently healthy women. *JAMA* 2004; 291:711-7.
- Thomas MC, MacIsaac RJ, Tsalamandris C, Jerums G. Elevated iron indices in patients with diabetes. *Diabet Med* 2004; 21:798-802.
- Sharifi F, Sazandeh SH. Serum ferritin in type 2 diabetes and its relationship with HbA1c. *Acta Med Iran* 2004; 42:142-5.
- Ford ES, Cogswell ME. Diabetes and serum ferritin concentration among U.S. adults. *Diabetes Care* 1999; 22:1978-83.
- Kaye TB, Guay AT, Simonson DC. Non-insulin-dependent diabetes mellitus and elevated serum ferritin level. *J Diabetes Complications* 1993; 7:246-9.
- Gallou G, Guilhem I, Poirier JY, Ruelland A, Legras B, Cloarec L. Increased serum ferritin in insulin-dependent diabetes mellitus: relation to glycemetic control. *Clin Chem* 1994; 40:9478.
- Kim NH. Serum ferritin in healthy subjects and type 2 diabetes mellitus. *Med Korea* 2000; 41:387-92.
- Eshed I, Elis A, Lishner M. Plasma ferritin and type 2 diabetes mellitus. *Endocr Res* 2001; 27:91-7.
- Moczulski DK, Grzeszczak W, Gawlik B. Role of hemochromatosis C282Y and H63D mutations in HFE gene in development of type 2 diabetes and diabetic nephropathy. *Diabetes Care* 2001; 24:1187-91.
- Fernández-Real JM, Peñarroja G, Castro A, García-Bragado F, López-Bermejo A, Ricart W. Bloodletting in high ferritin type 2 diabetes: effects on vascular reactivity. *Diabetes Care* 2002; 25:2249-55.
- Cantur K Z, Cetinarslay B, Tarkun I, Canturk NZ. Serum ferritin levels in poorly- and well-controlled diabetes mellitus. *Endocr Res* 2003; 29:299-306.
- Eschwege E, Saddi R, Wacjman H, Levy R, Thibult N, Duchateau A. Haemoglobin A1c in patients on venesection therapy for haemochromatosis. *Diabete Metab* 1982; 8:137-40. HbA1C<6HbA1C (6-8) HbA1C>80200400600S.ferritinHbA1C<6HbA1C(6-8)HbA1C>8 Raj S et al. *Int J Res Med Sci*. 2013 Feb;1(1):12-15 International Journal of Research in Medical Sciences | January-March 2013 | Vol 1 | Issue 1 Page 15
- Wrede CE, Buettner R, Bollheimer LC, Scholmerich J, Palitzsch KD, Hellerbrand C. Association between serum ferritin and the insulin resistance syndrome in a representative population. *Eur J Endocrinol* 2006; 154:333-40.