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Original Research Article

Study of Iron Status in type 2 Diabetes mellitus

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Abstract: Type 2 diabetes mellitus is a clinical condition characterized by hyperglycemia due to the absolute or relative deficiency of insulin. It is also followed by pathological abnormalities like impaired insulin secretion, peripheral insulin resistance, and excessive hepatic glucose production. The objective is to study the levels of Serum Ferritin, Total Iron Binding Capacity, Iron and Hemoglobin in Type 2 Diabetes patients. A total of 120 subjects were included in this study (60 with type 2 Diabetes Mellitus, and 60 normal subjects). Fasting plasma glucose tests were done on blood samples collected after overnight fasting and 2-hour post-prandial plasma glucose was also done along with iron, total iron binding capacity (TIBC), Ferritin and hemoglobin. The level of serum Ferritin which is considered a sensitive marker of iron status was significantly higher in diabetic group. The other parameters like Hemoglobin, TIBC and Iron do not show any positive correlation. We can conclude that Serum Ferritin can be considered as sensitive marker of iron status in Diabetic group. Serum Ferritin can be assessed in non-Diabetic first-degree relatives of diabetic people for identifying the risk.
Keywords: Serum Ferritin, TIBC, Serum iron, type 2 Diabetes Mellitus Fasting and Post Prandial plasma glucose

INTRODUCTION:

In India, there were 31.7 million Diabetic patients reported in the year 2000. By 2030 the number is expected to reach 79.4 million. India is expected to have the highest number of people with diabetes by 2030 [1]. Type 2 diabetes is a common and ever-increasing worldwide health problem. Although well described in terms of its hallmarks of insulin resistance and β-cell failure, the proximal cause(s) of type 2 diabetes and the mechanisms underlying its genetic predisposition remain largely unknown [2,3]. Plausible cases have been made for the primacy of abnormalities in insulin signaling, insulin secretion, activation of stress pathways, mitochondrial dysfunction, hepatic fuel homeostasis, and CNS regulation [4]. It is well accepted that the most reliable predictor for the disease is obesity; therefore much attention has also been paid to the contribution of nutrients and nutrient sensing pathways in situations of chronic caloric excess. Most of the interest in the role of nutrients in diabetes is centered on macronutrients, but a micronutrient, iron, is also closely associated with diabetes risk in a number of hereditary syndromes as well as in common forms of type 2 diabetes[5,6].

METHODS AND MATERIALS

The study was conducted over a period of three months. The study was done using oral glucose tolerance test for control, and fasting and post prandial plasma glucose for type 2 diabetes, among subjects attending PDU Medical College and hospital at Rajkot, Gujarat, India for a period of 3 months from July to August. There were 30 females and 30 males with normal glucose tolerance; and 30 females and 30 males who were known diabetic. They were in the age group of 35 to 55 years. Each group was classified as Diabetic and Non Diabetic based on WHO criteria.

Fasting blood samples(8 hr fasting) were collected from all participants in to Flouride & Plain vaccutainer and Uniq ID number was given to each sample. All samples were centrifugated at central

laboratory in REMI centrifuge at 3000 RPM for a period of 10 minutes and plasma sugar was estimated from Flouride container. Serum iron, TIBC & Ferritin was estimated from Plain vaccutainer. Post Prandial blood samples is also taken after 2 hr of lunch and analyzed fro plasma glucose.

Glucose was analyzed in semi automated analyzer by using GOD-POD method. Ferritin was estimated by Automated Chemiluminescence's method using commercially available kit by Beckman Coulter and Iron & TIBC were estimated by colorimetric method in a semi-automated biochemistry analyzer. For adequate quality control, both normal and abnormal reference control serum solutions and calibrators were run before each batch. Other factors influencing the quality, like proper functioning of instrument, temperature, glassware, cuvettes, distilled water were also taken care of.

RESULTS

A total number of 120 samples were selected to study the level of Hb, Iron, TIBC, Ferritin, FPG, and PPPG in Type 2 Diabetes patients and normal individuals. The subjects were divided into 2 groups, Normal Glucose Tolerance (NGT) group and Type 2 Diabetes Mellitus (DM) group. Each group had 60 subjects. Data evaluation was done using SPSS programme. The results were expressed as Mean (standard deviation). The P value was used to compare the different groups. The P value <0.05 was considered significant.

Table 1: Demographic table of 2 groups

Parameters	NGT (n-60)	Diabetes(n-60)
Age	43.5 (5.9)	48.7 (5.7)
Sex M/F	30 / 30	30 / 30

Table 2: Comparison of age between Male and female NGT group and DM group

Parameters	Sex	NGT	DM	P value
Age (yrs)	Male	49.03 (5.9)	44.8 (5.8)	0.008
	Female	48.4 (5.5)	42.2 (5.7)	0.000

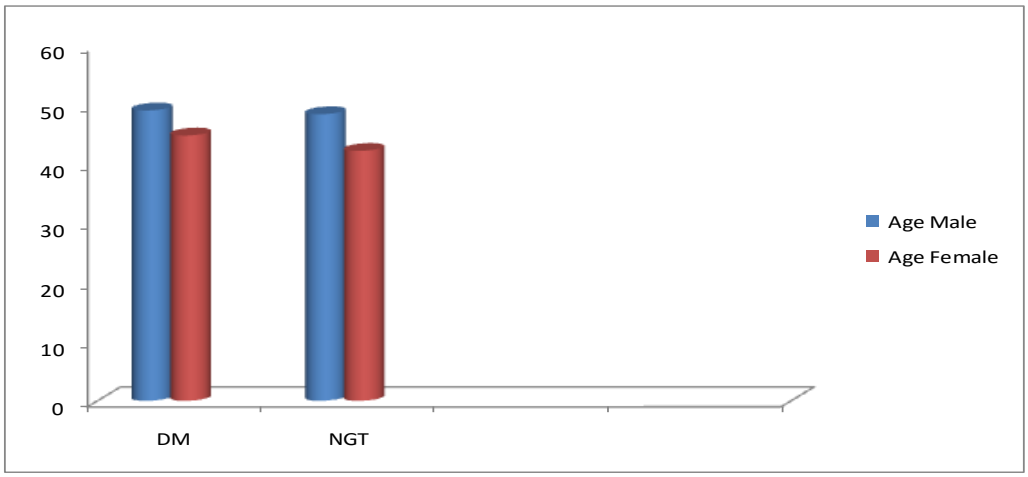

Fig 1: Age for Male and Female DM and NGT group

Table 3: Comparison of BMI between Male and female NGT group and DM group

Parameters	Sex	NGT	DM	P value
BMI	Male	20.9 (1.5)	24.7 (3.6)	0.000
	Female	19.8 (1.7)	23.9 (3.1)	0.000

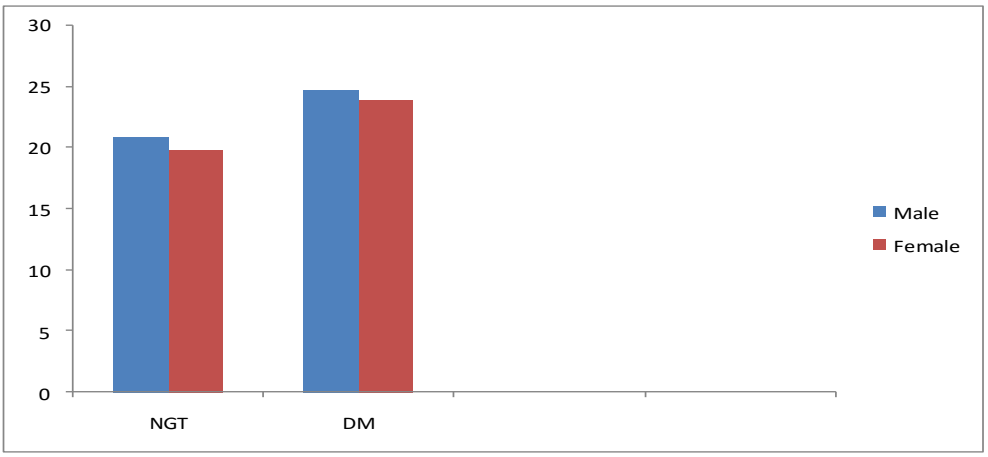

Fig 2: BMI for Male and Female DM and NGT Group

Table 4: Comparison of biochemical parameters for male NGT and DM group

Parameter	Male NGT (n-30)	Male DM (n-30)	P value
FPG (mg/dl)	95.7 (8.1)	156.8 (61.5)	0.000
PPBG (mg/dl)	109.1 (13.5)	234.2 (76.6)	0.000
Ferritin (ng/ml)	73.38 (31.5)	100.75(55.8)	0.002
Hb (gms %)	14.57 (1.5)	14.27 (1.8)	0.502
TIBC (µg/dl)	337.6 (52.2)	324.7 (71.7)	0.429
Iron (µg/dl)	111.3 (42.7)	91.3 (29.0)	0.039

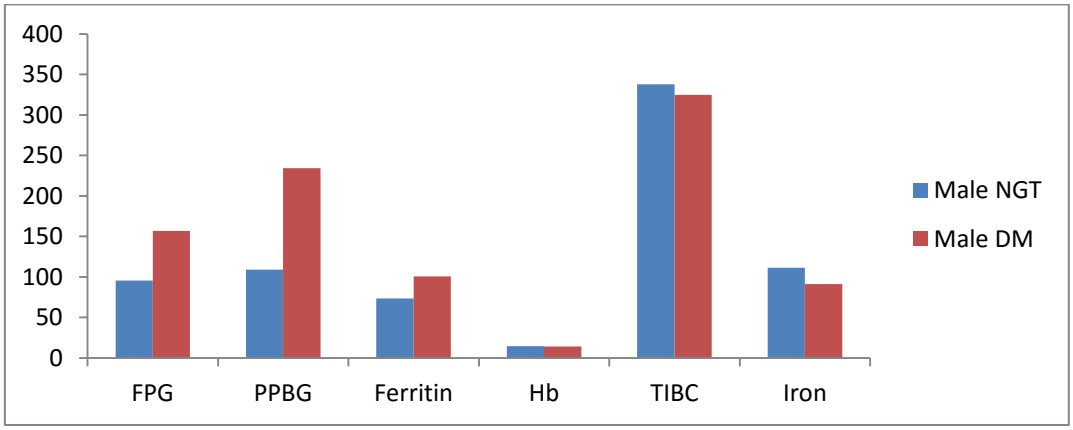

Fig 3: biochemical parameters of male DM AND NGT Group

Table 5: Comparison of biochemical parameters for female NGT and DM group

Parameter	Female NGT (n-30)	Female DM (n-30)	P value
FPG (mg/dl)	91.7 (15.6)	182.0 (84.2)	0.000
PPBG (mg/dl)	107.3 (17.0)	267.7 (121.9)	0.000
Ferritin (ng/ml)	35.14 (16.8)	58.02 (40.8)	0.006
Hb (gms %)	12.26 (1.3)	12.36 (1.1)	0.747
TIBC (µg/dl)	378.4 (72.4)	342.7 (105.0)	0.131
Iron (µg/dl)	76.9 (28.1)	66.2 (43.8)	0.266

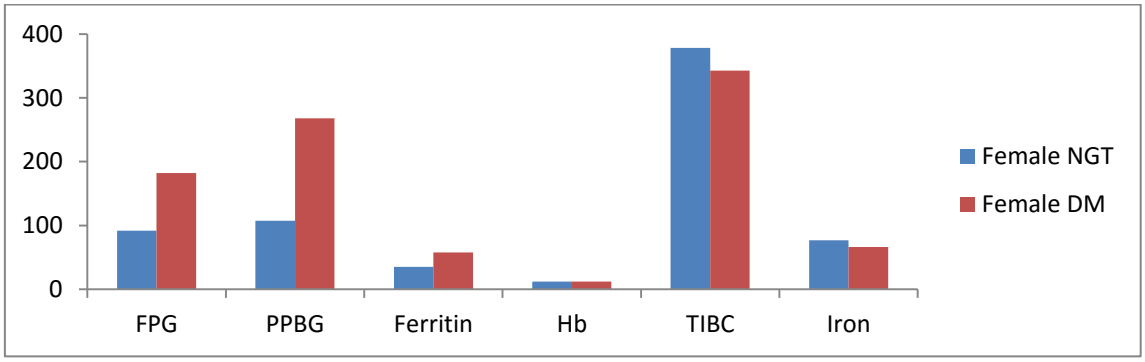

Fig 4: Biochemical parameters of female DM and NGT group

Table 6: Comparison of biochemical parameters for male NGT and female NGT group

Parameter	Male NGT (n-30)	Female NGT (n-30)	P value
FPG (mg/dl)	95.7 (8.1)	91.7 (15.6)	0.217
PPBG (mg/dl)	109.1 (13.5)	107.3 (17.0)	0.553
Ferritin (ng/ml)	54.26 (31.82)	35.14 (16.8)	0.000
Hb (gms %)	14.57 (1.5)	12.26 (1.3)	0.000
TIBC (µg/dl)	337.6 (52.2)	378.4 (72.4)	0.015
Iron (µg/dl)	111.3 (42.7)	76.9 (28.1)	0.001

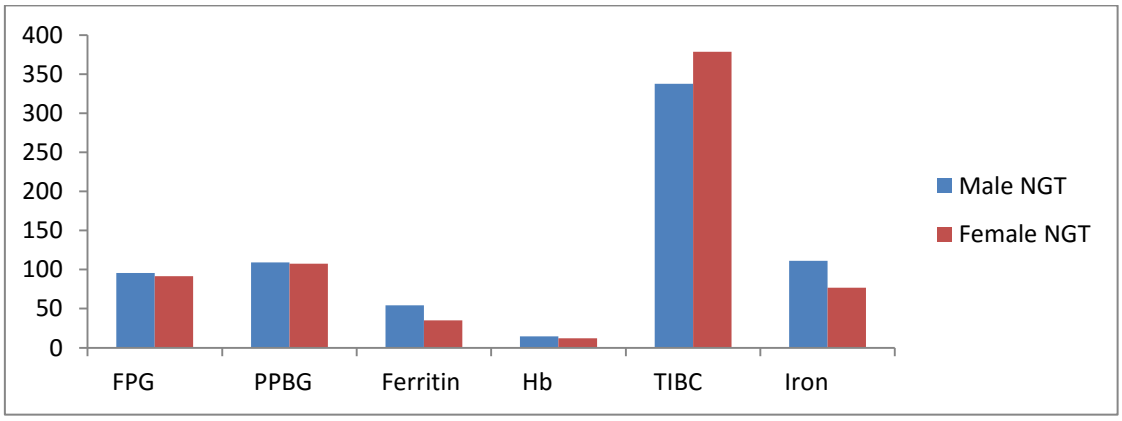

Fig 5: Biochemical parameters Of NGT Group

Table 7: Comparison of biochemical parameters for male DM group and female DM group

Parameter	Male DM (n-30)	Female DM (n-30)	P value
FPG (mg/dl)	156.8 (61.5)	182.0 (84.2)	0.191
PPBG (mg/dl)	234.2 (76.6)	267.7 (121.9)	0.207
Ferritin (ng/ml)	100.75 (55.8)	58.02 (40.8)	0.001
Hb (gms %)	14.27 (1.8)	12.36 (1.1)	0.000
TIBC (µg/dl)	324.7 (71.7)	342.7 (105.0)	0.442
Iron (µg/dl)	91.3 (29.0)	66.2 (43.8)	0.011

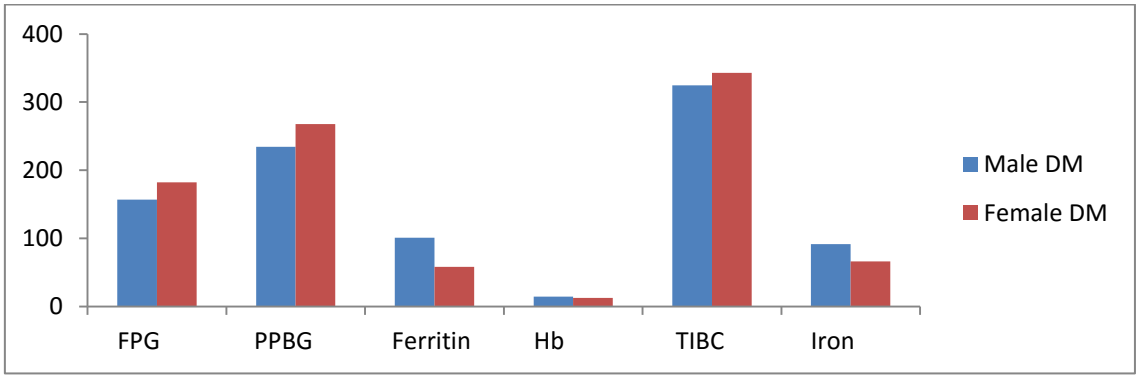

Fig 6: Biochemical Parameters of DM Group

DISCUSSION

The systemic iron homeostasis is achieved by regulating iron absorption and storage and recycling mechanisms. The ferroportin-mediated efflux of Fe2+ from enterocytes and macrophages into the plasma is critical for systemic iron homoeostasis. This process is negatively regulated by hepcidin, a liver-derived peptide hormone that binds to ferroportin and promotes its phosphorylation, internalization and lysosomal degradation. Thus hepcidin acts to decrease the absorption of dietary iron and the release of recycled iron from macrophage stores by diminishing the effective number of iron exporters on the membrane of enterocytes or macrophages. Under conditions of high iron, hepcidin-induced down regulation of ferroportin in duodenal enterocytes prevents dietary iron from entering the circulation. Defects in human hemochromatosis protein (HFE) cause iron overload due to reduced hepatic hepcidin secretion [7, 8].

Recent studies show that increase in iron stores (ferritin) predicts the risk of developing Type 2 Diabetes, while decrease in iron level is protective. Damage caused by iron also triggers the events of chronic diabetes complication, in coronary artery responses and endothelial dysfunction. Tissue iron excess increases the production of free radicals which in turn amplifies the steps involved in inflammatory lesion [9, 10]. Recent epidemiological studies have shown that increased iron stores predicted the development of diabetes. Ferritin is the storage form of iron. Iron converts reactive free radical into highly reactive ones. As the serum Ferritin level increases it affects the insulin synthesis and secretion in pancreas and interferes with the insulin extracting capacity of liver. Deposition in muscles leads to muscle damage and decreases glucose uptake. The initial and the most common defect in patients with an earlier stage of damage induced by iron overload is liver – mediated insulin resistance. Hepatic iron overload is characterized by hyperferritinemia, normal transferrin saturation, and increased prevalence of glucose tolerance and diabetes. Transition metals play an important role in protein glycation induced by hyperglycemia. Plasma glucose levels are strongly associated with serum ferritin levels even in healthy subjects [11].

Hemoglobin, Iron, TIBC when compared in NGT group against DM group it was found that both male and female patients do not show any statistical significance. This is in agreement with those stated in the literature. Ferritin values are found to be positively correlated in the male and female subjects when NGT group is compared against DM group. Serum Ferritin is a marker of insulin resistance. It is an independent determinant of poor metabolic control in diabetic patients. Diabetic microangiopathy is associated with abnormal increased ferritin level in serum. Men with moderately higher ferritin levels had a significantly worse coronary risk profile than men with lower levels. Mean serum ferritin levels are higher in men than in premenopausal women [11]. Ferritin concentration in male NGT is higher than female NGT implies that hyperferritinemia occurs before the elevation of plasma glucose. NGT first degree relatives in the type 2 diabetic pedigrees have higher ferritin concentration than normal control subjects [12].

The low levels of serum iron and higher levels of TIBC in both female groups than the male group may be due to the reason that they are mostly anemic due to physiological process like menstruation and pregnancy leading to iron deficient state. Increase in Serum Iron level contribute to macro vascular disease as iron has an adverse effect on endothelium and accelerates the development of atherosclerosis [13, 14]. During the course of atherosclerotic plaque formation, ferritin gene expression increases. In our study we observed there was no increase in serum iron among those with

diabetes mellitus. Even though there is no increase in serum iron in diabetes, iron participates in the formation of free radicals which are highly toxic and capable of inducing lipid peroxidation. Invariably in iron overload, insulin resistance is reported. Hence periodic monitoring of serum iron may be needed among those with diabetes mellitus. Further long term prospective studies including all the parameters of iron metabolism may throw more information in this field.

CONCLUSION

We can conclude that Serum Ferritin can be considered as sensitive marker of iron status in Diabetic group. Serum Ferritin can be assessed in non-Diabetic first-degree relatives of diabetic people for identifying the risk.

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