International Journal of Medical Science and Education

www.ijmse.com

Original Research Article

pISSN- 2348 4438 | eISSN-2349- 3208

ESTIMATION OF SERUM IRON LEVELS IN TYPE 2 DIABETIC PATIENTS AND ITS RELATION WITH HbA1C LEVEL

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Received: 19/05/2019 ***Revised:20/06/2019*** ***Accepted: 28/06/2019***

ABSTRACT

Background: Excessive iron store is associated with higher risk of metabolic disorders including hypertension, metabolic syndrome and cardiovascular disease. This study determines levels of S. Iron and Total Iron Binding Capacity (TIBC) in type 2 diabetic patients and its correlation with HbA1c. **Methods:** The study was conducted in Department of General Medicine in association with Department of Biochemistry of Mahatma Gandhi Medical College & Hospital, Sitapura, Jaipur. 100 confirmed cases of Type 2 Diabetes Mellitus and 50 age and sex matched healthy subjects were enrolled in study. All were screened for HbA1c, Fasting blood sugar, Post prandial blood sugar, Serum Iron and Total iron binding capacity. **Results:** The fasting blood sugar, post prandial sugar, HbA1c levels were significantly higher in the diabetic subject. S.Iron was significantly lower in diabetic group while S.TIBC did not show any significant variation. S.Iron was highest 62.15±33.96 µg/dl in the HbA1c ≤ 6.0% subgroup and as low as 37.08±14.30 µg/dl for the poor glycemic control group. **Conclusion:** Iron metabolism may participate in etiopathogenesis of type 2 diabetes mellitus. An elevated iron store induces oxidative damage of pancreatic beta cells with impairment of insulin secretion and interferes with hepatic glucose production. Thus leading to development of diabetes.

Keywords: Serum iron, Total iron binding capacity, Type 2 diabetes mellitus, Serum Ferritin.

INTRODUCTION

According to World Health Organization (WHO) 2014, DM, commonly referred to as diabetes, is a group of metabolic diseases comprising of high blood sugar levels over a prolonged period due to defects in insulin secretion, insulin action or both. On the basis of the International Diabetes Federation estimates there were 366 million people suffering from diabetes in 2011, and this is expected to reach 552 million by 2030 **(1).**

Type 2 diabetes is the result of failure to produce sufficient insulin and insulin resistance. Increased blood glucose levels are controlled with decreased food intake, increased physical activity, and through oral medications or insulin **(2).**

According to American diabetes association 2011 hemoglobin A1C (HbA1c) which was primarily used as a test of glycemic control has now been added as a diagnostic test and hence proving its more important

role than earlier. Glycated hemoglobin is synthesised by a ketoamine reaction between glucose and the N-terminal valine of both ß-chains of hemoglobin. The major form of glycated hemoglobin is HbA1c **(3,4).** But in fact, HbA1c levels can be affected by a variety of factors which includes age, ethnicity, smoking, and conditions altering red cell turnover and glucose homeostasis **(5, 6, 7).**

Iron, a transitional metal and micronutrient, is essential for various physiological functions within the body. Also iron is a potent pro-oxidant molecule catalyzing formation of reactive oxygen species **(8)**. Excess iron stores were suggested to be associated with increased risk of metabolic disorders such as hypertension, metabolic syndrome and cardiovascular disease through multiple mechanism including oxidative damage to pancreatic beta cells, impairment of extraction of insulin by the liver and interference in its ability to suppress hepatic glucose production **(9,10,11)**. Also high iron stores have been demonstrated to contribute in development of type 2 diabetes by causing damage to beta cells of pancreas and insulin resistance through increasing the level of oxidative stress **(12).**

Emerging scientific evidence suggest unsuspecting influences among iron metabolism and NIDDM. The relationship being bi-directional as iron influences glucose metabolism, and glucose metabolism in turn alters several iron metabolic pathways. Systemic iron overload leads to abnormal glucose homeostasis by: (i) insulin deficiency due to oxidative stress on the pancreatic beta cells leading to cell death and in turn diminshed secretion of insulin (ii) insulin resistance caused directly by iron overload **(13,14,15).** Thus, recognized that glucose metabolism is influenced by iron stores, even in the absence of marked iron overload.

The catalytic iron converts less reactive free radicals like H2O2 into highly reactive ones like hydroxyl radical and superoxide anion thereby initiating and propagating cascades which lead to oxidative damage **(14,15).** Several studies have shown that there is increased oxidative stress in diabetic patients with iron overload **(13).**

In patients with an earlier stage of damage induced by iron overload the initial and the most common defect is hepatic-mediated insulin resistance **(16).** As per a study hepatic iron overload syndrome comprises of increased prevalence of glucose tolerance and diabetes, with hyperferritinemia and normal transferrin saturation **(17).** Studies have shown that increased iron overload has an adverse effect on the endothelium that contributes to macro vascular complications and accelerates the development of atherosclerosis **(18,19).** The pre-diabetic state of IGT is associated with IR and has an increased risk of development of cardiovascular complications.

In fact a raised level of iron above physiological requirement has no benefit in DM patients. However few indirect evidences from the western countries suggests that iron overload influences DM in a negative way. But overall there is paucity of literature showing direct evidence of poor control of DM among patients having iron overload especially in india. In fact finding out such correlation bears great clinical significance among Indian population as anemia is most prevalent condition in them and continuous efforts are being made at physician, community and Government level to prevent and treat anemia affecting the coexisting diabetic state. Hence, the present study was under taken to compare HbA1c and Iron and find correlation between HbA1c and Serum Iron in type 2 diabetes mellitus (DM) patients.

MATERIALS AND METHODS

The present study was conducted in Department of General Medicine in association with Department of Biochemistry of Mahatma Gandhi Medical College & Hospital, Sitapura, Jaipur.

A study protocol was designed before undertaking this study, which was approved by the Institutional Ethics Committee vide letter No. MGMCH/IEC/JPR/2016/309 dated 22/06/2016 and informed consent was taken before enrolling the patients for the study.

Total 100 patients fulfilling the inclusion criteria were enrolled in clinical group. A control group comprising of 50 healthy non-diabetic subjects of

comparable age and sex distribution were enrolled for comparative study. Detailed history, clinical examination and relevant investigations were conducted to exclude controls suffering from any such disease which is likely to affect serum Iron and serum blood glucose level.

Inclusion criteria: Diagnosed cases of type 2 diabetes mellitus on treatment, Age between 40 to 60 years, either gender, Patients who are willing to participate and sign consent document, Patients willing to comply with the protocol requirements

Exclusion criteria: Overt thyroid dysfunction, Patients with type 1 diabetes mellitus, Patients above 65 yrs age, Chronic kidney disease, On corticosteroid therapy, Patients with acute or chronic liver disease, malignant process or inflammatory disease, Pregnant and lactating females, Patients received recent iron therapy.

Each enrolled patient was subjected to the detailed medical history, general physical examination and blood investigations including S.Iron, Total iron binding capacity, HbA1c and fasting and PP blood glucose. An informed consent was taken before the collection of the sample from cases and controls. The control subjects had the same exclusion criteria as the cases and were not on any drug regimens which could influence the study.

RESULTS

The fasting and post prandial sugar levels were significantly higher in the diabetic subjects (Tables:1). Mean HbA1c in the diabetic group was 8.70±2.88% as compared to 5.37±0.24% for the control group (Table: 1). On comparing the S. Iron and TIBC levels among the groups, it was observed that S. Iron was significantly lower in diabetic group, S.TIBC did not show any significant variation (Table: 1).

The diabetic patients (n=100) were further divided into 3 subgroups based on HbA1c levels

The variables were compared in the 3 groups by applying one way ANOVA test. S. Iron levels in the 3 subgroups were observed to show a negative conclusion with HbA1c levels. S. Iron was highest 62.15±33.96 µg/dl in the HbA1c ≤ 6.0% subgroup and as low as 37.08±14.30 µg/dl for the poor glycemic control group. S.TIBC levels exhibited a fall in the levels with rise of HbA1c (Table: 2 and Table:3).

Table:1 Mean FBS, PPBS, HbA1C, IRON and TIBC of subjects in Control and Diabetic Group

S. NO.	PARAMETERS	CONTROL (50)	DM (100)	t-VALUE	P-VALUE
1.	FBS (mg/dl)	92.33±14.50	136.68±54.00	-5.697	0.000
2.	PPBS (mg/dl)	113.04±10.07	214.50±73.43	-9.709	0.000
3.	HbA1c (%)	5.37±0.24	8.70±2.88	8.148	0.000
4.	Iron (µg/dl)	75.78±51.10	50.46±31.18	3.756	0.000
5.	TIBC (µg/dl)	271.67±92.34	282.10±71.47	0.762	NS

Table:2 Mean distribution of IRON (µg/dl) according to HbA1c Levels.

Group	No. of cases (n)	Iron (µg/dl)	F-value	P-value
HbA1c ≤ 6	13	62.15±33.96		
HbA1c (6.0-8.0)	41	41.59±27.41	-6.80	0.002
HbA1c > 8.0	46	37.08±14.30		

Table 3: Mean distribution of TIBC (µg/dl) according to HbA1c Levels.

Group	No. of Cases (n)	TIBC (µg/dl)	F-value	P-value
HbA1c ≤ 6	13	317.62±76.79	-6.31	0.003
HbA1c (6.0-8.0)	41	299.32±78.62		
HbA1c > 8.0	46	256.72±53.64		

DISCUSSION

DM is one of the most concern seeking health problems both in developing and developed countries. Type 2 DM has a multifactorial etiopathogenesis. The disease gains more attention due to the various complications associated with long standing DM.

Iron metabolism is suggested to participate in etiopathogenesis of type 2DM (20). Increased iron stores may cause oxidative damage of pancreatic beta cells alongwith impairment of insulin extraction by the liver and interference in ablilty of insulin to suppress hepatic glucose production. This together may lead to development of diabetes.

The present study was planned to assess the relation of Serum Iron indices with glycemic index in type 2DM. According to Fernandez-Real JM et al., 2002 increased body iron stores, in general population, might be associated with occurrence of glucose intolerance, type-2 diabetes and gestational diabetes. In a similar study by Arul Senghor et al., 2012 serum TIBC shows no statistical difference between diabetic and non-diabetic group.

Iron is a powerful anti-oxidant. It promotes the production of hydroxyl radicals which attack pancreatic β-cell. This results in impaired insulin synthesis. Moreover, the expression of antioxidant enzymes like catalase, superoxide dismutase, etc is comparatively less. This in turn makes the pancreatic islets more susceptible to oxidative damage (21).

S.Iron levels ranged from 29.5µg/dl to as high as 150.0µg/dl in the group with HbA1c ≤ 6. Thorough research is required to establish the actual correlation of S.Iron with HbA1c levels. However few studies by Hashimoto K. et al in 2008 suggested that a poor glycemic control is favorable for development of Iron Deficiency Anemia.

Also it is proved that association between heme iron intake and risk of T2DM may be distinct from the association between non-heme iron intake and risk of T2DM. (22).

CONCLUSION

S.Iron was significantly lower in diabetic group. Also S.Iron levels in the 3subgroups shows a negative correlation with HbA1c levels. The findings of the present study, therefore confirm that hyperglycemia and a poor glycemic index favours low s. iron levels but elevation of the body iron stores and vice versa.

Also the study recommends further research on the influence of S.Ferritin and other iron indices on Gestational DM and vice versa.

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How to cite this article: Agarwal P, Shah N V, Gupta D, Sinha M, Fiza B. Estimation of serum iron levels in type 2 diabetic patients and it. Int.J.Med.Sci.Educ 2019; 6(2):136-140.