

Correlation between Serum Ferritin and Duration of Type 2 Diabetes Mellitus

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Abstract:

Introduction: Hyperinsulinemia in type 2 diabetes mellitus is known to increase ferritin synthesis and iron uptake, increase iron store is associated with glucose intolerance. Iron increases oxidative stress which inhibits internalisation and action of insulin. This study hypothesises that increased body iron store is responsible for the development of insulin resistance and glucose intolerance as well as vascular complications of diabetes.

Objective :

1.To estimate serum ferritin and fasting plasma glucose in diabetes and non-diabetes and to find out the correlation between them.

2.To find out the correlation between serum ferritin and the duration of diabetes mellitus in diabetic group.

Methodology : Study design -a comparative study. 80 clinically diagnosed type 2 diabetes mellitus male and 70 healthy male volunteer were included. Fasting blood sample were taken and plasma glucose and serum ferritin were estimated.

Result : Serum ferritin and fasting plasma glucose level were significantly higher amongst the diabetic subjects and serum ferritin was positively correlated with the duration of diabetes.

Conclusion : Inflammation of low grade exist in type 2 diabetes mellitus and is positively related with hyperglycemia and body iron store.

Keywords: Diabetes mellitus, Insulin resistance, Oxidative stres, Serum ferritin.

I. Introduction

Diabetes mellitus is such a gravest health hazard that it engulfs quality of human life day by day. As it progresses it involves almost all tissue and organ systems. A vicious circle of increased insulin resistance and its resultant complication is created. Several risk factors and causes have been documented for this, increased serum ferritin and body iron store is also one of the risk factor contributing to this. This work hypothesises that progressive increase of body iron store increases insulin resistance and complication of diabetes.

The significance of iron in pathophysiology of diabetes is derived from the ease with which iron is reversibly oxidised and reduced as it plays a critical role in Haber Weis reaction producing reactive oxygen species. Iron is supposed to involve in influencing diabetes by three mechanism ; (a) Insulin deficiency- as pancreatic islet are extremely sensitive to free radical oxidative damage, iron deposited into pancreatic interstitial cells result into collagen deposition and defective microcirculation, (b) insulin resistance and (c) hepatic dysfunction.^[1]

Increased body iron increases the incidence of diabetic complication due to free radical onjury and are positively and independently associated with the prevalence of the metabolic syndrome, increased fasting glucose and dyslipidemia.^{[2],[3]}

A positive association between excess iron store and risk of type 2 diabetes mellitus was found in the work done by Rajpathak et al(2009)and somatra et al(2007). Diabetes frequently develops in the individual with iron overload disease such as Hemochromatosis and recurrent tranfusion in disease like thalassemia.^[4]

A large body of epidemiological evidence suggest that an increase in dietary iron intake such as heme mainly from meat and meat product is associated with increased risk of diabetes.^[5] Hydroxyl radical may attack pancreatic beta cells through oxidative stress and thus results in impaired insulin synthesis and excretion.^[6] Pancreatic islet cells are more susceptible than other tissue due to lower level of antioxidant enzyme such as Superoxide dismutase, Catalase and Glutathione peroxidase.^[7] Plebotomy improves insulin sensitivity.^[8] Serum ferritin is biomarker for iron store and ferritin increases in response to inflammatory stress.^[9]

Purpose of this study is to see whether a relationship exist between increased serum ferritin and duration of diabetes and to consolidate the hypothesis that with continuous intake of red meat the complications of diabetes goes on increasing.

II. Methodology

This comparative study was conducted at the department of Biochemistry of Rajendra Institute of Medical Sciences, Ranchi. Approval for this work was obtained from the ethics committee of the Institute. The period of this work was from december 2014 to november 2015. A total of 150 sample were included and divided into diabetic(n=80) and control (n=70) group. Inclusion criteria consist of uncomplicated type 2 diabetic males of age between 25-70 years with a body mass index between 19-40 kg per meter square. Control group consist of age matched healthy male volunteers having fasting blood glucose level less than 6 mmol/L. Female were not included in this study because menstruation affects serum ferritin level due to blood loss, serum ferritin measured during menstrual phase shows lower values than that measured during luteal and late luteal phase.^[10] Patients having confounding comorbidity like type 1 Diabetes, Hemochromatosis, chronic alcoholics, chronic inflammatory conditions like Systemic lupus erythmatosus, hepatitis, patients with repeated blood transfusion, iron deficiency anaemia, recent history of blood loss, bleeding piles, recent history of major surgery, diabetic foots, hypothyroidism, cardiovascular disorder, diabetic nephropathy, anaemia of any causes, history of malignancy or chemotherapy and those taking anti inflammatory drugs were excluded from the study.

8.0 ml of venous blood were drawn under aseptic condition in fasting state. Fasting plasma glucose was estimated by enzymatic colorimetric method using Hexokinase and Glucose 6 phosphate dehydrogenase (values \leq 6mmol/L were considered normal).^[11] Serum ferritin was estimated by Architect's chemiluminescent microparticle immunoassay methods (values between 21-274.66ng/ml were considered normal). Data was analysed by SPSS version 20. Mean and standard deviation (SD) were used to describe fasting plasma glucose and serum ferritin, these parameters of the two group were compared by Independent sample t test. Pearson correlation coefficient were calculated to check the linear correlation of serum ferritin with fasting plasma glucose and with duration of diabetes.

III. Result

The mean \pm SD value for fasting plasma glucose in diabetic was 162.92 ± 42.9 mg/dl and in control it was 88.96 ± 12.1 mg/dl. P value <0.001 . The mean \pm SD value for serum ferritin in diabetic was 291.38 ± 93.87 ng/ml and in control group it was 83.46 ± 56.01 ng/ml. P value <0.001 .

A significantly positive correlation was found between serum ferritin and fasting plasma glucose with $r=0.810$ and $P <0.001$. A positive correlation was found between serum ferritin and duration of diabetes with $r=0.185$, $P=0.035$.

Table 1: Comparison Between Mean Fasting Plasma Glucose(Fpg)						
	Group	N	Mean	Std. Deviation	Std. Error Mean	P Value
Fpg(Mg/Dl)	1. Diabetic	80	162.91	42.976	4.805	0.000
	2. Control	70	88.96	12.118	1.448	

Table 2: Comparison Between Mean Value Of Serum Ferritin						
	Group	N	Mean	Std. Deviation	Std. Error Mean	P Value
S.Fer(Ng/MI)	1.Diabetic	80	219.3875	93.87596	10.49565	0.000
	2.Control	70	83.4686	56.01362	6.69491	

Table 3: Linear correlation of serum ferritin with FPG and duration of diabetes

	FPG	DURATION OF DIABETES
SERUM FERRITIN	$R=0.810$; $P<0.001$	$R=0.185$; $P=0.035$

IV. Discussion

Metabolism and immunity in a person are interdependent which is beneficial under normal condition, can become deleterious under metabolic stress conditions. The anabolic pathway such as insulin signaling pathway can be suppressed in response to inflammation whereas catabolic pathway are favoured by inflammation.^[12] Thus the process of inflammation can initiate insulin resistance. In this study mean serum ferritin in diabetic and control group support the previous studies which concluded that inflammation plays a

positive role toward insulin resistance and have found that high ferritin level favour a high incidence of type 2 diabetes.^[13] Ferritin has been known as an index for body iron store and also as an inflammatory marker.^{[14],[15]} It releases iron in a controlled fashion and plays a central role in the maintenance of intracellular iron balance. Iron is a potent pro-oxidant that increases cellular oxidative stress and thus decreases insulin internalisation and action, resulting in hyperinsulinemia and insulin resistance.^[16]

Glycation of ferritin decreases its ability to bind iron and increases the pool of free iron which in turn stimulates ferritin synthesis.^[17] With increased duration of diabetes the complex process of advanced glycation end product formation produces reactive oxygen species by metal catalysed reaction. These reactive oxygen species interfere with insulin signaling at various level in the insulin receptor function and inhibits the translocation of glucose transporter GLUT4 in the plasma membrane.^[18] Serum ferritin level has been found to predict the risk of ischemic heart disease.^[19] Hence the investigation of the status of iron overload in diabetes can assess oxidative stress resulting in insulin resistance and the risk of development of diabetic vascular complications ; with increased duration of diabetes, serum ferritin, body iron store, oxidative stress as well as its neural and vascular complications goes on progressing which suggest an interrelationship between these factors.

V. Conclusion

Serum ferritin levels were higher in diabetic group which correlated positively with hyperglycemia and duration of diabetes. Ferritin is the marker of iron overload and has a role in insulin resistance. Thus routine screening for serum ferritin should be carried out in person with impaired glucose tolerance to assess the body iron store and the risk of development of diabetes.

Future studies are needed to explore whether important regulator of iron metabolism are altered in diabetes, namely the transporter DMT1, ferroportin and MTP1 which are critical in intestinal absorption and entry of iron into circulation and Hephaestin which oxidises ferrous ion to ferric ion during this process. Incidence of diabetes in non vegetarian and vegetarian are required to be worked out.

Blood donation or phlebotomy should be conducted to reduce body iron store and oxidative stress. Red meat and meat product in diet should be reduced considerably.

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