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Comparative assessment of iron profile in diabetes and control patients

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Abstract

Iron is one of the most important micronutrients for good health and disturbed iron metabolism leads to lipid-protein oxidation and also damages RBC membrane. Various research studies found that the reactive free iron or iron overloads was responsible for diabetes. The exact mechanism by which the altered iron metabolism leads to disease like diabetes is remains not understood. Hence the present study was planned to evaluate the iron profile in type 2 diabetes mellitus patients.

The present study was planned in the Department Of Biochemistry, Jawaharlal Nehru Medical College, Bhagalpur, and Bihar. Total 50 patients were enrolled in the present study. The 25 patients were enrolled in the group A as control cases and remaining 25 cases of diabetes were enrolled in group B. All the patients were undergone the biochemical evaluation as per standard protocol.

The findings of this study is in accordance to earlier studies, that there is dyslipidaemia, increased lipid peroxidation, inflammation and oxidative stress in diabetics compared to non-diabetics; and the oxidative stress further increases as diabetes to cardiovascular diseases. The evaluation of iron profile can be a useful outcome of the predictable studies on diabetes and related complications. Elevated iron and ferritin is a risk factor for diabetes and produce many complications. Proper management must be taken to remove the excess iron that can be very harmful to the body.

Keywords: iron profile, diabetes, type 2 diabetes mellitus

Introduction

Diabetes mellitus type 2 (also known as type 2 diabetes) is a long-term metabolic disorder that is characterized by high blood sugar, insulin resistance, and relative lack of insulin. Common symptoms include increased thirst, frequent urination, and unexplained weight loss. Symptoms may also include increased hunger, feeling tired, and sores that do not heal. Often symptoms come on slowly. Long-term complications from high blood sugar include heart disease, strokes, diabetic retinopathy which can result in blindness, kidney failure, and poor blood flow in the limbs which may lead to amputations. The sudden onset of hyperosmolar hyperglycemic state may occur; however, ketoacidosis is uncommon [1].

Type 2 diabetes primarily occurs as a result of obesity and lack of exercise. Some people are more genetically at risk than others. Type 2 diabetes makes up about 90% of cases of diabetes, with the other 10% due primarily to diabetes mellitus type 1 and gestational diabetes. In diabetes mellitus type 1 there is a lower total level of insulin to control blood glucose, due to an autoimmune induced loss of insulin-producing beta cells in the pancreas. Diagnosis of diabetes is by blood tests such as fasting plasma glucose, oral glucose tolerance test, or glycated hemoglobin (A1C) [2].

Type 2 diabetes is partly preventable by staying a normal weight, exercising regularly, and eating properly. Treatment involves exercise and dietary changes. If blood sugar levels are not adequately lowered, the medication metformin is typically recommended. Many people may eventually also require insulin injections. In those on insulin, routinely checking blood sugar levels is advised; however, this may not be needed in those taking pills. Bariatric surgery often improves diabetes in those who are obese [3].

Rates of type 2 diabetes have increased markedly since 1960 in parallel with obesity. As of 2015 there were approximately 392 million people diagnosed with the disease compared to around 30 million in 1985. Typically it begins in middle or older age, although rates of type 2 diabetes are increasing in young people. Type 2 diabetes is associated with a ten-year-shorter life expectancy. Diabetes was one of the first diseases described. The importance of insulin in the disease was determined in the 1920s [4].

The classic symptoms of diabetes are polyuria (frequent urination), polydipsia (increased thirst), polyphagia (increased hunger), and weight loss. Other symptoms that are commonly present at diagnosis include a history of blurred vision, itchiness, peripheral neuropathy, recurrent vaginal infections, and fatigue. Many people, however, have no symptoms during the first few years and are diagnosed on routine testing. A small number of people with type 2 diabetes mellitus can develop a hyperosmolar hyperglycemic state (a condition of very high blood sugar associated with a decreased level of consciousness and low blood pressure) [5].

Type 2 diabetes is typically a chronic disease associated with a ten-year-shorter life expectancy. This is partly due to a number of complications with which it is associated, including: two to four times the risk of cardiovascular disease, including ischemic heart disease and stroke; a 20-fold increase in lower limb amputations, and increased rates of hospitalizations. In the developed world, and increasingly elsewhere, type 2 diabetes is the largest cause of nontraumatic blindness and kidney failure. It has also been associated with an increased risk of cognitive dysfunction and dementia through disease processes such as Alzheimer's

disease and vascular dementia. Other complications include acanthosis nigricans, sexual dysfunction, and frequent infections [6].

The development of type 2 diabetes is caused by a combination of lifestyle and genetic factors [24, 26]. While some of these factors are under personal control, such as diet and obesity, other factors are not, such as increasing age, female gender, and genetics. Obesity is more common in women than men in many parts of Africa. A lack of sleep has been linked to type 2 diabetes. This is believed to act through its effect on metabolism. The nutritional status of a mother during fetal development may also play a role, with one proposed mechanism being that of DNA methylation. The intestinal bacteria Prevotella copri and Bacteroides vulgatus have been connected with type 2 diabetes [7].

Type 2 diabetes is due to insufficient insulin production from beta cells in the setting of insulin resistance. Insulin resistance, which is the inability of cells to respond adequately to normal levels of insulin, occurs primarily within the muscles, liver, and fat tissue. In the liver, insulin normally suppresses glucose release. However, in the setting of insulin resistance, the liver inappropriately releases glucose into the blood. The proportion of insulin resistance versus beta cell dysfunction differs among individuals, with some having primarily insulin resistance and only a minor defect in insulin secretion and others with slight insulin resistance and primarily a lack of insulin secretion [5].

Other potentially important mechanisms associated with type 2 diabetes and insulin resistance include: increased breakdown of lipids within fat cells, resistance to and lack of incretin, high glucagon levels in the blood, increased retention of salt and water by the kidneys, and inappropriate regulation of metabolism by the central nervous system [10]. However, not all people with insulin resistance develop diabetes, since an impairment of insulin secretion by pancreatic beta cells is also required [5].

Diabetic patients have various microvascular (like neuropathy, nephropathy, and retinopathy), macrovascular (like atherosclerosis) and miscellaneous (like diabetic cardiomyopathy) complications. The various complications are produced by reactive oxygen species leads to oxidative damage which is generated by free radicals like free iron. Iron is one of the most important micronutrients for good health and disturbed iron metabolism leads to lipid-protein oxidation and also damages RBC membrane. Various research studies found that the reactive free iron or iron overloads was responsible for diabetes. The exact mechanism by which the altered iron metabolism leads to disease like diabetes is remains not understood. Hence the present study was planned to evaluate the iron profile in type 2 diabetes mellitus patients.

Methodology

The present study was planned in the Department Of Biochemistry, Jawaharlal Nehru Medical College, Bhagalpur, Bihar. Total 50 patients were enrolled in the present study. The 25 patients were enrolled in the group A as control cases and remaining 25 cases of diabetes were enrolled in group B. All the patients were undergone the biochemical evaluation as per standard protocol.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: Diagnosed type 2 Diabetes mellitus patients having fasting blood glucose ≥ 126mg/dl or HbA1c ≥ 6.5%.

Exclusion Criteria: Patients taking drugs which disturbed iron metabolism, patients undergo previous blood transfusion, patients having haemoglobinopathies, genetic mutations which causes iron overload and pregnant women were excluded from the study.

Results & Discussion

Diabetes mellitus is a complex and multifactorial disease, indulging severe insulin dysfunction in conjunction with gross abnormalities in glucose homeostasis, lipid and protein metabolism. It contributes for macrovascular and microvascular complications in diabetes. Of all cardiovascular cases are the leading causes of mortality and morbidity in diabetes mellitus.

Iron is an essential metal for hemoglobin synthesis of erythrocytes, oxidation-reduction reactions, and cellular proliferation, whereas excess iron accumulation causes organ dysfunction through the production of reactive oxygen species. The total amount of body iron is ~3-4 g, two-thirds of which is composed of red blood cell iron and recycled iron by red blood cell destruction, and the remainder is stored in ferritin/hemosiderin, whereas only 1-2 mg of iron is absorbed in the intestinal tract and circulated in the blood. Body iron metabolism is a semiclosed system and is critically regulated by several factors, including the newly identified peptide hepcidin. In the circulation, iron is usually bound to transferrin, and most of the transferrin-bound iron is utilized for bone marrow erythropoiesis [8].

Table 1: Comparison of Demographic Details

Group Cases of Control		Group B Diabetes
No. of Cases	25	25
Age	23- 46	25 - 39
Males	19	17
Females	6	8

Table 2: Control with Type 2 Diabetes Mellitus

Parameter	Group A (Mean±SD)	Group B (Mean±SD)
Cases of	Control	Diabetes
Fasting blood glucose (mg/dl)	89.5 ± 4.5	185.9 ± 41.8
Postprandial blood glucose (mg/dl)	130.8 ± 11.2	270.9 ± 68.3
Total Cholesterol (mg/dl)	160.8 ± 4.6	210.4 ± 20.9

Triglycerides (mg/dl)	142.8 ± 9.4	157.6 ± 35.4
HDLC (mg/dl)	42.6 ± 6.8	33.5 ± 5.2
LDLC (mg/dl)	92.3 ± 7.1	129.9 ± 21.8
VLDLC (mg/dl)	26.95 ± 2.50	40.60 ± 15.3
Ceruloplasmin (mg/dl)	30.5 ± 4.3	36.8 ± 7.3
Ferritin (ngm/ml)	65.4 ± 14.2	187.6 ± 43.6
Iron (mcg/ml)	73.5 ± 5.20	81.9 ± 25.3
TIBC (mcg/dl)	311.6 ± 12.6	339.6 ± 16.9
Transferrin (mcg/dl)	214.9 ± 15.6	249.6 ± 12.7

HDLC: High density lipoprotein (HDL) cholesterol
LDLC: Low density lipoprotein (HDL) cholesterol
VLDLC: Very Low density lipoprotein (HDL) cholesterol
TIBC: Total iron binding capacity

Elevated serum iron concentration among the general population is found in cases of haemolytic anaemia, hepatitis, and lead and iron poisoning, whereas low serum iron concentration is a marked feature of anaemia caused by iron deficiency due to the impaired intake or absorption of iron, heavy blood loss, late pregnancy, and cancer. The role of iron in the pathogenesis of T2DM calls for further studies owing to increased incidence of iron overload encountered among diabetics, which can be reversed by achieving targets of good glycaemic control using either phlebotomy or iron chelation therapy [9].

An increase in the levels of serum free iron concentration and serum transferrin saturation levels with poor glycaemic control in our study indicate an important role of free iron in the development of diabetic complications. A study in Iran has pointed out that elevated levels of iron in first-degree relatives of T2DM patients might be a predisposing factor for them towards the development of diabetes in future or vice versa (i.e., as a result of diabetes development) [10].

Evidence that systemic iron overload could contribute to abnormal glucose metabolism was first derived from the observation that the frequency of diabetes is increased in classic hereditary hemochromatosis (HH). However, with the discovery of novel genetic disorders of iron metabolism, it is obvious that iron overload, irrespective of the cause or the gene involved, results in an increased incidence of type 2 diabetes. The role of iron in the pathogenesis of diabetes is suggested by an increased incidence of type 2 diabetes in diverse causes of iron overload and reversal or improvement in diabetes (glycemic control), with a reduction in iron load achieved using either phlebotomy or iron chelation therapy [11].

A link has been established between increased dietary iron intake, particularly eating red meat and increased body iron stores, and the development of diabetes. A causative link with iron overload is suggested by improvement in insulin sensitivity and insulin secretion, with frequent blood donation and decreased iron stores [12].

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There is an increasing concern about the relationship between iron stores and type 2 diabetes with evidence that moderately elevated body iron stores below levels commonly found in genetic hemochromatosis may be associated with adverse health outcomes. Elevated serum ferritin levels were independently predicted incident of type 2 diabetes in prospective studies among apparently healthy men and women [14]. Ferritin is an iron-phosphorus-protein complex that is a biomarker for evaluating body iron contents. Tissue and organ damage occurs when iron concentrations are elevated [15]. Increased accumulation of iron affects insulin synthesis and its secretion from the pancreas and interferes with the insulin-extracting capacity of the liver. Iron deposition in muscle decreases glucose uptake because of muscle damage.

Conversely, insulin stimulates cellular iron uptake through increased transferring receptor externalization. Thus, insulin and iron can mutually potentiate their effects leading after a vicious cycle to insulin resistance and diabetes [16].

In study done by Salonen *et al*, serum ferritin had significant positive correlation with plasma glucose [17]. In a study by Nan Hee Kim *et al*, the serum ferritin had a positive correlation with fasting plasma glucose [18]. Increase in Serum Iron level contribute to macro vascular disease as iron has an adverse effect on endothelium and accelerates the development of atherosclerosis [19]. During the course of atherosclerotic plaque formation, ferritin gene expression increases [20]. 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.

It's evident from the study that ferritin levels were positively correlated with FBS, PP2BS and HbA1c. Similar study conducted by Sumeet Smotra *et al* [21] and Jeevan K. Shetty *et al* [22] found increased levels of Serum Ferritin and also reported that diabetics with increased level of Serum Ferritin had significantly poor glycaemic control reflected by higher levels of HbA1c as compared to diabetes cases under good glycaemic control and healthy controls.

Conclusion

The findings of this study is in accordance to earlier studies, that there is dyslipidaemia, increased lipid peroxidation, inflammation and oxidative stress in diabetics compared to non-diabetics; and the oxidative stress further increases as

diabetes to cardiovascular diseases.

The evaluation of iron profile can be a useful outcome of the predictable studies on diabetes and related complications. Elevated iron and ferritin is a risk factor for diabetes and produce many complications. Proper management must be taken to remove the excess iron that can be very harmful to the body.

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