VOLUME-8, ISSUE-4, APRIL-2019 • PRINT ISSN No 2277 - 8160

Original Research Paper

Biochemistry

SERUM IRON PROFILE IN TYPE 2 DIABETES MELLITUS

Pallavi Mahajan*	Assistant Professor, Department of Biochemistry, Acharya Shri Chander College of Medical Sciences, Jammu, J&K *Corresponding Author
Sanjeev Kumar	Assistant Professor, Department of Medicine, Government Medical College, Kathua, J&K
Ashima Badyal	Lecturer, Department of Biochemistry, Government Medical College, Jammu, J&K

ABSTRACT Diabetes Mellitus is a group of metabolic disorders characterized by hyperglycemia due to decreased insulin secretion and glucose utilization and increased glucose production depending on the etiology. The systemic iron overload causes abnormalities in glucose metabolism as a result of oxidative stress on pancreatic beta cells leading to cell death contributing to T2DM. Ferritin is a key protein which regulates iron homeostasis and High levels of circulating ferritin were observed in type 2 diabetes patients. The present study was conducted with the aim to estimate and compare iron profile and glycated hemoglobin in diabetic patients and control group. It was observed that diabetic patients have significantly increased levels of HbA1C, serum ferritin whereas have decreased levels of serum iron and TIBC. Serum ferritin can be used as a sensitive marker of iron status while the biochemical markers like serum iron and TIBC can be monitored at regular intervals.

KEYWORDS : Diabetes mellitus, glycated hemoglobin, ferritin, iron.

INTRODUCTION

Diabetes Mellitus (DM) is a group of metabolic disorders that often share the phenotype of hyperglycemia. The factors that contribute to hyperglycemia include reduced insulin secretion, decreased glucose utilization and increased glucose production depending on the etiology of diabetes mellitus.(1) Its prevalence in South East Asia including India was 82 million in 2017 and will expect to increase up to 51 million in 2045 as per the International Diabetes Federation (IDF).(2) The diabetic patients suffer from various microvascular (that includes neuropathy, nephropathy, and retinopathy), macrovascular (like atherosclerosis) and miscellaneous (like diabetic cardiomyopathy) complications.(3) The presence of complications depends not only on the duration of the diabetes mellitus but also influenced by the average level of blood glucose along with glycated haemoglobin. The estimation of glycated proteins chiefly HbA1c (glycated hemoglobin) is effectual in monitoring long-term glucose control in people with diabetes mellitus.(1) Chronic hyperglycemia leads to increased glycation of proteins including hemoglobin which results in the formation of Advanced Glycated End products (AGE).(4) The various complications of diabetes are due to the presence of reactive oxygen species (ROS) generated by free radicals like free iron leading to oxidative damage. Iron is one of the key micronutrients required for good health and deranged iron metabolism leads to oxidation of lipids and proteins and causes damage to the RBC membrane. In the various research studies, it was shown that the reactive free iron or iron overloads was responsible for diabetes. (5)

Some researchers interpreted that systemic iron overload causes abnormalities in glucose metabolism contributing to T2DM due to insulin deficiency as a consequence of oxidative stress on pancreatic beta cells leading to cell death and diminish insulin secretion or insulin resistance caused straightway by iron overload and hepatic dysfunction. However, few researchers observed that influence on glucose metabolism occurs by serum iron even in absence of considerable iron overload or even in a state of iron deficiency. The excess iron stores have been shown to be associated with increased risk of metabolic disorders including hypertension, cardiovascular disease and metabolic syndrome. (6)

Another key protein which regulates iron homeostasis and widely used as a parameter to evaluate iron homeostasis in the body is ferritin. High levels of circulating ferritin were observed in type 2 diabetes patients complicated with hereditary hemochromatosis. Several clinical studies have investigated the association of increased serum ferritin levels with an increased risk of type 2 diabetes but the results were incoherent between different populations. (7)

Thus, the following study was conducted with the aim to estimate and compare iron profile and glycated hemoglobin in diabetic patients and control group.

MATERIALS AND METHODS

The study was conducted in the Department of Biochemistry, Super Specialty hospital, Government Medical College, Jammu. 50 patients with type 2 diabetes mellitus diagnosed on the basis of raised serum glucose levels and 50 healthy adults in the age group of 20 years and above were selected irrespective of their sex. 5 ml of fasting blood samples were withdrawn from the antecubital vein under aseptic conditions from each individual with his/her consent, duly following the guidelines and norms of the hospital. Blood samples were collected in plain vacutainers, fluoride vacutainers and EDTA vacutainers. The estimation of serum iron, unbinding iron binding capacity (UIBC) and the total iron binding capacity (TIBC) was estimated in fully automated chemistry analyzer in both the groups. Blood glucose levels were estimated by Abott Architect c-Systems by hexokinase method. (8) HbA1c was estimated on Architect c-Systems (9) following the principle consisting of two separate concentrations measurements: glycated Hb and total hemoglobin. Total Hb is oxidized to stable methemoglobin azide by the action of sodium nitrite and sodium azide and the concentration of the hemoglobin is determined by measuring absorbance. The ferritin levels were estimated in abbott architect chemiluminescent microparticle immunoassay.(10) The serum iron and TIBC were performed outside the hospital and the data was collected from the patients.(11)

TIBC= Serum Iron + UIBC

The normal levels of serum iron are 50-170 µg/dl (women) and 65-175 µg/dl (men), UIBC levels 110-370 µg/dl, TIBC 228-428 µg/dl, serum ferritin levels are 30-300 ng/ml for males and 10-160 ng/ml for females.

Inclusion Criteria:

Diagnosed T2DM patients having fasting blood glucose ≥ 126mg/dl or HbA1c ≥ 6.5% and healthy controls.

Exclusion Criteria:

Patients suffering from anemia, thyroid dysfunction, chronic kidney disease chronic liver disease, 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.

RESULT

The study was conducted in 50 healthy controls (comprising of 22 women and 28 men) and 50 type 2 diabetic patients (19 females and 31 males). The mean age of diabetic patients was 48.35±9.44 years and the mean age of control group was 43.54±11.32 years. It was observed that the blood glucose, HbA1C levels and serum ferritin levels were significantly increased in diabetic patients whereas serum iron and TIBC levels were significantly decreased in patients with diabetes.

Table1: Comparison of various parameters in control group and diabetic patients

Parameter	Control	Diabetic patients	p value
Blood Glucose (F) (mg/dl)	81.76 (10.22)	183.37(59.18)	< 0.0001
HbA1C (%)	5.79 (1.28)	7.97(0.97)	<0.0001
Serum Iron (µg/dl)	93.98 (33.79)	65.81 (42.67)	≤0.0004
Serum Ferritin(mg/dl)	89.07 (12.54)	226.09 (34.02)	<0.0001
TIBC (µg/dl)	346.53 (63.69)	254.39 (56.82)	<0.0001
*p value < 0.05 considered significant			

DISCUSSION

In our study, it was observed that diabetic patients have significantly increased levels of blood glucose, HbA1C, serum ferritin whereas have decreased levels of serum iron and TIBC. It was observed in the recent studies that increase in iron stores predicts the risk of developing type 2 diabetes, while decrease in serum iron level is protective. The damage caused by iron also triggers the events of complications in chronic diabetes, in coronary artery disease and endothelial dysfunction. (12) The excess iron in the tissues will enhance the production of free radicals which further amplifies the ladder involved in inflammatory lesion.(13)

Also when body iron stores are normal, absorption of iron is minimal. The absorption of iron present in the heme does not depend on the body iron content. The circulating iron is bound to ferritin and is taken up by specific transferrin receptor from the blood. This transferrin-receptor complex is internalized through endocytosis and is then released into a non-acidic cellular compartment, where it is used for the synthesis of essential cellular components.(14) The rapid uptake of iron by the fat cells is stimulated by insulin, thus redistributing transferrin receptors from an intracellular membrane compartment to the cell surface. In various studies, it has been observed that serum ferritin had significant positive correlation with plasma glucose.(12,15)

There is a close relationship between iron profile and T2DM because deranged glucose metabolism deranges the iron profile and vice versa. The altered iron profile or free iron induces oxidative stress and produces inflammatory cytokines. (16) Hyperglycemia negatively influences numerous metabolic processes including iron metabolism in type 2 DM. (17) It has been observed in various studies that iron overload occurs in type 2 diabetes mellitus. (18) The free iron radicals instigate oxidation of biomolecules leading to production of hydroxyl radical (OH*) via Haber-Weiss and Fenton reactions which further damages cellular membrane protein and nucleic acid. These proceedings lead to insulin resistance and thus type 2 diabetes mellitus.(19) The free OH* radicals causes non-enzymatic glycation of protein followed by a series of reactions that results in the formation of advanced glycation end products (AGEs) which interact with their receptors (RAGE), induce the production of ROS. The free iron and oxidative stress also promote the ferritin synthesis.(5) Iron in a strong pro-oxidant that increases the cell oxidative stress, causes inhibition of insulin internalization and actions, hence leading to hyperinsulinemia and insulin resistance. The oxidative stress increases the release of iron from ferritin and free iron also has a positive feedback on ferritin synthesis. Serum Ferritin is also a marker of insulin resistance. It is an independent determinant of poor metabolic control in diabetic patients. The low serum iron levels in females than the males may be due to the reason that they are generally anemic due to physiological process like menstruation and pregnancy leading to iron deficient state. (20) In our study we observed that serum iron levels do not increase in diabetes mellitus, still iron takes part in the formation of free radicals which are highly toxic and capable of inducing lipid per-oxidation.

CONCLUSION

In our study, it was observed that diabetic patients have significantly increased levels of blood glucose, HbA1C, serum ferritin whereas decreased levels of serum iron and TIBC. Serum ferritin can be used as a sensitive marker of iron status while the biochemical markers like serum iron and TIBC can be monitored at regular intervals in patients with diabetes mellitus so that suitable actions can be taken. Therefore, in conformity with prior studies we propose that serum ferritin should be incorporated in standard screening protocol to identify the risk of developing type 2 DM and also to evaluate the glycemic control in known patients of diabetes mellitus.

REFERENCES:

1. Maheshwari AV, Bhoi BK, Sadariya BR, Javia HN, Gusani JK, Sharma H. Correlation between serum ferritin and glycaemic control in patients of type 2 diabetes mellitus: a case control study. Int J Res Med Sci.2015; 3(9):2327-2330.
2. International Diabetes Federation. IDF Diabetic Atlas 8th Edition 2017. Available from: https://www.idf.org/elibrary/epidemiology-research/diabetes-atlas. [Accessed 20 March 2019].
3. Papatheodorou K, Papanas N, Banach M, Papazoglou D, Edmonds M. Complications of Diabetes 2016. Journal of Diabetes Research. 2016;2016: 6989453.
4. Chandalia HB, Krishnaswamy PR. Glycated hemoglobin. Curr Sci. 2002;83(12):1522-32.
5. Dhakad GS, Sharma AK, Kanwar G, Singh AK, Sharma S. Evaluation of iron profile in type 2 diabetes mellitus patients of tertiary care center of central India. Int J Clin Biochem Res. 2019;6(1):15-19.
6. Albasheer AA, Gaufri NAM. Assessment of Iron Profile in Patients with Diabetes Mellitus Type 2 (DMT2). European Academic Research.2016; 4(4):3369-76.
7. Vaitla P, Sabiullah MD, Vani N. Association between elevated serum ferritin and HbA1C in type 2 diabetes mellitus. IOSR Journal of Pharmacy and Biological Sciences. 2017; 12(3): 57-59.
8. Burtis CA, Ashwood ER, editors. Teitz textbook of clinical biochemistry, 2nd ed. Philadelphia, PA: WB Saunders; 1994:959-60.
9. American Diabetes Association. Position assessment: standards of medical care in diabetes. 2012, In: diabetes care. 2012; 35:11-63.
10. National committee for clinical laboratory standards. Evaluation of precision performance of clinical chemistry devices; tentative guideline-second edition. NCCLS. Document EP5-T2. Villanova, PA: NCCLS;1992.
11. Fairbanks VF. Laboratory testing for iron status. Hosp Prac.1991;26: 19.
12. Kim NH ,Heon Oh J, Choi KM, Kim YH, Baik SH. Serum Ferritin in healthy subjects and type 2 Diabetes patients. Younsei Medical Journal 2000; 41: 387 – 392.
13. Jonathan E Shaw and Donald J Chisholm. Epidemiology and prevention of type 2 diabetes and the metabolic syndrome. J Clin Endocrinol Metab. 2003; 179(7): 379 - 383.
14. James B Meigs, Peter Wilson, Caroline Fox, David M Nathan and Lisa M Sullivan. Body mass index, metabolic syndrome, and risk of Type 2 Diabetes or Cardiovascular Disease. J Clin Endocrinol Metab. 2006; 91:2906-12.
15. Raj S, Rajan GV. Correlation between elevated serum ferritin and HbA1c in type 2 diabetes mellitus. Int J Res Med Sci. 2013;1:12-15.
16. Manikandan A., Ganesh M, Silambanan, S. Study of iron status in type 2 Diabetes Mellitus. Int J Clin Biochem Res. 2015;2:77-82.
17. Arman Y, Ugurlukisi B, Yuruyen G, Akarsu M, Kose M, Cil EO et al. The effect of blood glucose regulation on ironmetabolism and hepcidin in uncontrolled type 2 diabetic patients. Int J Clin Exp Med 2016;9(2):3869-76.
18. Wang H, Li H, Jiang X, Shi W, Shen Z and Li M. Hepcidin is directly regulated by insulin and plays an important role in iron overload in streptozotocin-induced diabetic rats. Diabetes. 2014;63:1506-1518.
19. Misra G, Bhatter SK, Kumar A, Gupta V, Khan MY. Iron Profile and Glycaemic Control in Patients with Type 2 Diabetes Mellitus. Santulli G, ed. Med Sci 2016;4(4):22.
20. Sowjanya Y, Prabodh SV, Desai VS. Role of Iron Metabolic Indices in Type 2 Diabetes Mellitus. IOSR Journal of Dental and Medical Sciences.2017;16(12):1-5.