Journal of Netrokona Medical College
Frequency: Bi-Annual
Volume-1 | Issue-1 | Jul-Dec 2024
https://nmcj.org/jnmc
eISSN: 2664-738X
RESEARCH ARTICLE

Change in Serum Iron Level in Patients with Type 2 Diabetes Mellitus

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ABSTRACT: ***Background:*** Type 2 diabetes mellitus (T2DM) is a growing global public health concern of new era, with prevalence steadily increasing especially in Bangladesh. Disturbance of serum iron metabolism causes several biochemical reactions those may be related with subsequent disruption in glucose metabolism and glycemic control. ***Methods:*** This cross-sectional analytical type of study was performed from July 2023 to June 2024, in the Biochemistry department of Mymensingh Medical College and samples were collected from the Endocrinology department of Mymensingh Medical College Hospital, Mymensingh. Purposive non-random sampling technique was used to select study subjects according to inclusion and exclusion criteria. Total 132 subjects were included. Among them, 66 subjects were selected as Group-I (case) patients with type 2 diabetes mellitus, diagnosed according to ADA criteria, aged from 30 to 65 years of both male and female. Another 66 subjects were selected as Group-II (control) non diabetic apparently healthy individuals of the same age & sex matched. Informed written consents were obtained. Baseline parameters were recorded in pre-designed data collection sheets. Fasting serum glucose and serum iron were analysed, mean ± SD was used to express all values. ***Results:*** Following comprehensive analysis, it was revealed that highly significant ($P < 0.001$) raised of serum iron level in patient with T2DM (140.27 ± 20.45 µg/dl) case group when compared with non-diabetic apparently healthy individuals (86.61 ± 19.34 µg/dl) control group. Also showed that, highly significant positive correlations of fasting serum glucose with serum iron in patients with T2DM ($r = 0.432$, $P < 0.001$). ***Conclusion:*** This study will provide facility to the clinicians to improve their knowledge to overall management of T2DM. So, it is recommended early evaluation & monitoring of serum iron in T2DM.

Keywords: Type 2 Diabetes Mellitus, Serum Iron, Fasting Serum Glucose.

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How to cite this article:
Hasan TM, Hoque MR, Saadi MM, Hasan MS, Bashar A; Change in Serum Iron Level in Patients with Type 2 Diabetes Mellitus. J Netr. Med Coll. 2024;1(1): 9-14.

Article history:
Received: August 16, 2024
Accepted: November 13, 2024
Published: December 31, 2024

Peer Review Process:
The Journal abides by a double-blind peer review process such that the journal does not disclose the identity of the reviewer(s) to the author(s) and does not disclose the identity of the author(s) to the reviewer(s).

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders of multiple aetiology characterized by hyperglycemia with disturbances of carbohydrate, protein and fat metabolism resulting from defects in insulin secretion, action or both.[1] Type 2 diabetes mellitus (T2DM) precisely involves progressive decline in insulin secretion, results from ineffective use of insulin characterized by insulin resistance (IR) and often accompanied by metabolic syndrome.[2] Globally DM is most prevalent non communicable disease, around 537 million adult population in 2021, that is projected to reach 783 million in 2045.[3] T2DM is the account of 90% to 95% of all diabetes cases, almost 1 in 2 people with this disease, don't aware that they have it. Each year persons with this disease are increasing gradually.[4] The position of Bangladesh was 8th in number in the world, with 13.1 million diabetic people, prevalence 14.2% in 2021. By 2045 this number is projected to 22.3 million with prevalence 15.3% and 7th in position globally.[3] The consequences of this disease & related complications have an extremely undesirable influence on the socio-economies conditions. Prevalent of the disease is spreading progressively, posing major challenges for health policy planners.[5] T2DM is related to many risk factors like high calorie diet, obesity, sedentary life style, genetic predispositions, metabolic and environmental influence. In addition to known risk factors, the role of different micronutrients increase incidence of

T2DM has been proposed.[6] Serum iron is the highly significant micronutrient for human life.

It is related with many metabolic and cellular processes including oxygen transport, mitochondrial respiration and structural component of different proteins. Proper balance within iron intake, metabolism, utilization & loses is needed for homeostasis.[7] Disturbance of serum iron metabolism causes several biochemical reactions those may be related with subsequent disruption in glucose metabolism and glycemic control.[8] In T2DM, because of hyperglycemia blood osmolarity is changed. That may cause more hemolysis due to increase fragility of red blood cells, can interfere with iron metabolism and changes serum iron level.[9] Unregulated iron can lead to oxidative stress by Haber-Weiss & Fenton reactions, may contribute to β-cell dysfunction, insulin resistance and subsequent disruption in glucose metabolism.[10] Highly toxic free iron deposition in the liver may lead to abnormal metabolic processes in the liver and adipose tissue, that causes decrease insulin extraction and increase hepatic gluconeogenesis.[11] Association with some genetic factors, dietary more iron intake, excess parenteral iron therapy, obesity and inflammation may be role in pathogenesis & progression of T2DM.[12] Thus, in T2DM alteration of iron may effects on glucose dysregulations and glucose on iron vice-versa, with bi-directional relationship.[13] Appropriate monitoring & regulation of iron level along with glycemic control of T2DM is useful for homeostasis. The present study was undertaken to evaluate the changes of serum iron in patients with type 2 diabetes mellitus (T2DM) and compared with non-diabetic apparently healthy individuals.

METHODS

This was cross sectional analytical type of study was performed in the Biochemistry department of Mymensingh Medical College & samples were collected from the Endocrinology department of Mymensingh Medical College Hospital, Mymensingh, from July 2023 to June 2024. The study was reviewed and approved by Institutional review board (IRB) of MMC, Memo no: IRB/24/628, Date: 04.12.23. Total 132 subjects were included. Out of them, 66 subjects were selected as Group-I (case) patients with type 2 diabetes mellitus, diagnosed according to ADA criteria serum glucose (fasting) level ≥7.0 mmol/L or ≥126 mg/dl, aged from 30 to 65 years of both male and female. Another 66 subjects were selected as Group-II (control) non diabetic apparently healthy individuals of the same age & sex matched. Exclusion criteria were persons receiving iron supplementation, chelating agents and other drugs those alter test parameter. Known case of iron related disorders, chronic kidney disease, chronic liver disease, patients with prediabetes and other types of DM also excluded. On the base of inclusion and exclusion criteria, study objectives were described to the study subjects and who gave written consent consciously and voluntarily were enrolled. Baseline parameters were recorded in pre-designed data collection sheets. For laboratory investigations, under aseptic precaution 05 ml of fasting venous blood was collected, processed and preserved for estimation of serum iron by photometric colorimetric test for iron with lipid clearing factor (LCF) by chromazurol B (CAB) method 14 and serum glucose by enzymatic colorimetric test for glucose, glucose oxidase - peroxidase with amino phenazone & phenol (GOD-PAP) method 15. By using SPSS (statistical product and service solutions) version 26.0. windows package; statistical analysis was done. Qualitative variables were presented by percentage (%) and compared between groups by Chi-square test. Quantitative continuous variables were presented by Mean ± SD and compared between groups of subjects by using Student's unpaired 't' test. Correlations were done by using Pearson's correlation coefficient test. Level of significance was defined as ($P < 0.05$) at the level of 95 % confidence interval (CI), ($P > 0.05$) was taken as not significant and ($P < 0.001$) was considered as highly significant result.

RESULTS

Total study subjects were 132, In group-I (case) subjects were 66, among them 29 (43.94 %) were female and 37 (56.06 %) were male. And in group-II (control) subjects were 66, among them 31(46.97 %) were female and 35 (53.03 %) were male. The subjects were ranged from 30 to 65 years, Mean ± SD of age was 49.27 ± 8.74 years in group-I (case) and 48.67 ± 8.87 years in group-II (control). The analysis showed that the difference in the demographic characteristics (age and sex) was not significant (NS) ($P > 0.05$) in patients with T2DM compared to that of the control group. Comparison of mean value of demographic characteristics among the study subjects were presented in Table 1.

Table 1: Demographic Characteristics Among the Study Subjects

Variables	Group I (Case) n=66	Group II (Control) n=66	P value
Age (years) Mean ± SD	49.27 ± 8.74	48.67 ± 8.87	0.693 NS [a]
Sex n (%)			
Male	37 (56.06 %)	35 (53.03 %)	
Female	29 (43.94 %)	31 (46.97 %)	0.727 NS [b]

To measure the level of significance in Table 1, a = Student's unpaired 't' test, b = Chi- square test Group- I (case): Patients with T2DM. Group- II (Control): Non diabetic apparently healthy individuals. NS = (P > 0.05) Not significant result, SD = standard deviation.

It also observed that, The Mean ± SD values of serum iron were 140.27 ± 20.45 µg/dl in group-I (case) and 86.61 ± 19.34 µg/dl in group-II (control). The Mean ± SD values of fasting serum glucose were 8.63 ± 1.17 mmol/L in group-I (case) and 4.91 ± 0.40 mmol/L in group-II (control). This study revealed that, serum iron and fasting serum glucose were higher in group-I (case) than that of group-II (control) significantly. The analysis showed that the difference in mean values of serum iron and fasting serum glucose was statistically highly significant (P < 0.001) in patient with T2DM compared to that of the control group. Comparison of mean serum iron & fasting serum glucose levels in the study subjects was presented in Table 2.

Table 2: Comparison of Mean Serum Iron & Fasting Serum Glucose Among the Study Subjects

Variables	Group I (Case) Mean ± SD n=66	Group II (Control) Mean ± SD n=66	P value
Serum iron (µg/dl)	140.27 ± 20.45	86.61 ± 19.34	< 0.001**
Fasting serum glucose (mmol/L)	8.63 ± 1.17	4.91 ± 0.40 mmol/L	< 0.001**

To measure the level of significance in Table 2, Student's unpaired 't' test was done. Group- I: Patients with T2DM. Group- II: Non diabetic apparently healthy individuals. ** = (P < 0.001) considered as highly significant result. SD = standard deviation.

Table 3: Correlations Between Fasting Serum Glucose and Serum Iron in Patients With T2DM

Dependent	Independent		Co-efficient value (r)	P value
Glucose (fasting) (mmol/L)	Serum iron (µg/dl)		0.432	< 0.001**

To measure the level of significance in table-3, Pearson correlation co-efficient test was done. ** Correlation is highly significant when P < 0.001 r = Pearson correlation co-efficient test, which ranges from -1 to +1. Positivity indicates direct or positive relation. Negativity indicates indirect or negative relation.

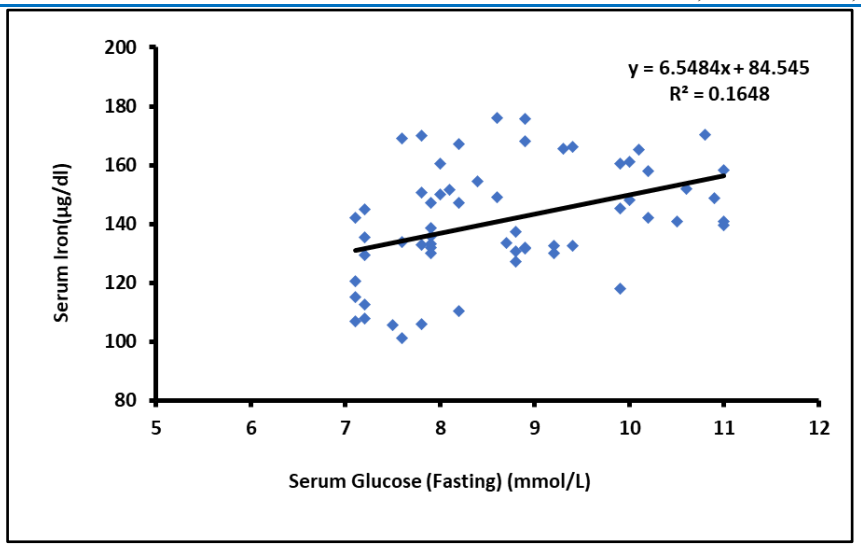

Figure 1: Correlation Between Fasting Serum Glucose and Serum Iron in Patients with T2DM

In this study also showed that, highly significant positive correlations of fasting serum glucose with serum iron in patients with T2DM (r = 0.432, P < 0.001). Pearson correlation coefficient test was done to see the relation & level of significance. That is presented in table-3 and Figure 1.

DISCUSSION

The present study revealed that there was, no statistically significant (P > 0.05) difference in demographic characteristics (age and sex distribution) between the patients with T2DM group and non-diabetic apparently healthy group. The present study revealed that, highly significant (P < 0.001) increase of serum iron in case compared to that of the control group. This finding agreed with the studies of Saha *et al*., Zerin *et al*., Akhter *et al*. and other studies.[7, 9, 11, 13, 16, 17] They observed that, serum iron level was raised in patient with T2DM (case) when compared with non-diabetic apparently healthy individuals (control) group. Disturbance of iron metabolism causes several biochemical reactions those may be related with disruption in glucose metabolism.[8] Thus, in T2DM subsequent alteration of iron level effects on glucose dysregulations and glucose on iron vice-versa, with bi-directional relationship.[13] Because of hyperglycemia blood osmolarity is changed in T2DM.

That may cause more hemolysis due to increase fragility of red blood cells, can interfere with iron metabolism and increase serum iron level.[9] Low level of hepcidin may be linked to insulin resistance, for this increased iron absorption and elevated serum iron level in T2DM.[18] Increased iron levels might be role in pathogenesis in T2DM by oxidative strain, beta cell distraction & impairment of insulin function. That exacerbating insulin resistance and related metabolic syndrome.[19] Association with some genetic factors, dietary more iron intake, excess parenteral iron therapy, obesity and inflammation that is contributing to the development of neurological and vascular complications with T2DM.[12] However, some conflicting studies conducted by Lagisetty *et al.,* and Manikandan *et al*., observed that serum iron was decreased in patients with T2DM.[20, 21] Chronic duration of diabetes, inadequate daily nutritional supply of iron, malnutrition or other associated complications may be related with low level of serum iron in T2DM.[20] Although, in contrast to this result some studies conducted by Kuba et al., and Sowjanya et al., were reported that no significant change of serum iron in T2DM compared to control.[22, 23] For this situation possible reason may be all patients involved in those studies were almost stable diabatic state or under control by proper treatment. Pearson's correlation coefficient test also done between fasting serum glucose and serum iron in patients with T2DM. Highly significant positive correlation of fasting serum glucose with serum iron in patients with T2DM (r = 0.432, P < 0.001) This finding was well correlated and supported by most of the previous studies Zerin *et al*., Akhter et al., Zimiao *et al.* and Dhakad *et al*.[7, 13, 16, 24] However, controversial studies conducted by Saha *et al.*, & Sharifi *et al*., reported that correlation between fasting serum glucose and serum iron was not significant.[11, 25] The observed variations may be attributed to differences in study groups, methodologies or other related factors that influence

iron metabolism in the context of type 2 diabetes mellitus.

CONCLUSION

Accordingly, this study revealed that serum iron level was significantly elevated in type 2 diabetes mellitus and positive correlation with fasting serum glucose. This study sheds light on the bi-directional interplay between iron and glucose dysregulation, emphasizing the importance of these parameters for effective disease management and control of associated complications for homeostasis.

Funding: No funding sources.
Conflict of Interest: The authors declare no conflicts of interest related to this study.

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