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**Original Research Article**

# Comparison of Total Iron Binding Capacities between Type 2 Diabetes Mellitus Patients and Healthy Individuals

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## Abstract

***Background:*** Worldwide, diabetes mellitus (DM) is a leading cause of death and disability. Iron overload is increasingly being connected to insulin resistance in patients with type 2 diabetes mellitus (T2DM). Free iron causes the assembly of reactive oxygen species that invariably steer the body's homeostasis toward oxidative stress-mediated diabetic complications. We have very limited research-based data regarding the total iron binding capacities in type 2 diabetes mellitus patients. ***Aim of the study:*** The aim of the study was to compare the total iron binding capacities (TIBC) between type 2 diabetes mellitus patients and healthy individuals. ***Methods:*** This cross-sectional study was conducted in the Department of Biochemistry, Dhaka Medical College (DMC), Dhaka, Bangladesh from July 2015 to June 2016. In total 100 participants were enrolled in 2 groups as the study subjects. In group A, in total 50 diagnosed patients with type 2 diabetes mellitus (T2DM) were included. On the other hand, in group B, 50 age and sex-matched healthy individuals were included. Properly written consent was taken from all the participants before data collection. All the demographic and clinical information of the participants was recorded. All data were processed, analyzed and disseminated by using MS Excel and SPSS version 23.0 program as per necessity. ***Results:*** In this study, the mean serum iron in group A and group B were 112.7 µg/dl and 87.6 µg/dl respectively. The mean serum ferritin concentration in group A and group B were 199.3 µg/dl and 107.0 µg/dl respectively. There was a statistically significant increase in serum iron and serum ferritin concentrations in group A compared to group B. Both serum ferritin and serum iron levels showed strong positive correlations with HbA1C ((r=0.724, p<0.001, r=0.724, p<0.001) and FPG (r=0.724, p<0.001, r= 0.724, p<0.001). The mean TIBC level was found 184 µg/dl in group A and 318.8 µg/dl in group B. In analyzing the total iron binding capacities (TIBC) between the groups we observe that the TIBC (µg/dl) levels in group A and group B were 184.0±79.5 and 318.8 ± 14.0 µg/dl respectively. The TIBC levels were significantly lower in group A than in group B (<0.001). ***Conclusion:*** The total iron binding capacity level is significantly lower in type 2 diabetes mellitus (T2DM) patients than that in healthy individuals. Routine screening for iron status along with glycemic control in diabetic patients might help prevent complications in such patients.

**Keywords*:*** Total Iron Binding Capacity, Type 2 DM, Fasting Plasma Glucose, Serum Ferritin, Iron Status.



## 1. INTRODUCTION

Diabetes mellitus (DM) is a clinical syndrome that is characterized by an increase in plasma glucose [1]. Type 2 diabetes mellitus (T2DM) is a heterogeneous disorder caused by a combination of insulin resistance, genetic factors related to impaired insulin secretion and environmental factors like overeating, obesity, lack of exercise and stress and aging [2]. Typically, it is a multifactorial disease that involves multiple genes as well as environmental factors to varying extents [3]. T2DM is the predominant form of diabetes that accounts for at least 90 % of all cases of diabetes mellitus [4]. Diabetes mellitus comprises a group of metabolic disorders and share a common phenotype of hyperglycemia. Hyperglycemia not only defines DM but is the cause of its most characteristic symptoms and long-

term complications [5]. Increased blood glucose level in diabetes mellitus (DM) stimulates the non-enzymatic glycosylation of several proteins including hemoglobin [6]. Glycation decreases its ability to bind with ferrous iron, hence increasing the free-iron pool that in turn facilitates ferritin synthesis [7]. Under specific circumstances of diabetes mellitus, iron is released from heme and ligated to another moiety, perhaps the distal histidine in the heme pocket this iron termed 'free reactive iron' can be detected by ferrozine reaction [8]. The toxicity of iron in the human body is largely based on its ability to catalyze the generation of radicals, that attack and damages the cellular macromolecules and promote cell death and even tissue injury [9]. Iron is reversibly oxidized and gradually reduced. This property of iron, while essential for its metabolic functions, makes iron grossly hazardous because of its ability of it to participate in the formation of powerful oxidant species like hydroxyl radicals [10]. Iron is a transitional component and also a potential catalyst in cellular reactions that produce oxygen-reactive species like hydroxyl radicals and superoxide anions via Fenton and Haber Weiss reactions that may initiate and propagate a cascade that can lead to oxidative stress that impairs insulin signaling in the skeletal muscle as well as liver and cause β-cell destruction because of an insufficient β-cell deficient antioxidant defense [11]. On the other hand, elevated serum ferritin levels had been found in many chronic inflammation-related diseases [12]. Elevated serum ferritin levels predicted the incidence of T2DM in another study in apparently healthy males and females [13]. From ferritin, iron is usually released by the action of reducing agents that convert $Fe^{3+}$ into $Fe^{2+}$ [14]. The objective of this current study was to compare the total iron binding capacities (TIBC) between type 2 diabetes mellitus patients and healthy individuals.

## 2. METHODOLOGY

This cross-sectional study was conducted in the Department of Biochemistry, Dhaka Medical College (DMC), Dhaka, Bangladesh from July 2015 to June 2016. In total 100 participants were enrolled in this study as the study subjects who were divided into 2 groups. In group A, in total 50 diagnosed patients with type 2 diabetes mellitus were included. On the other hand, in group B, 50 age and sex-matched healthy individuals were included. According to the exclusion criteria of this study, pregnant women and lactating mothers, patients of any chronic inflammatory disease like rheumatoid arthritis and chronic systemic illness (CLD, CKD, COPD), chronic smokers, malignancy, alcoholics, patients using any iron therapy, cases with a recent history of blood transfusions, patients with any hemorrhagic diseases, individuals with known cause of iron overload were excluded. The study was approved by the ethical committee of the mentioned hospital. Properly written consent was taken from all the participants before data collection. All the demographic and clinical information of the participants was recorded. All data were processed, analyzed and disseminated by using MS Excel and SPSS version 23.0 program as per necessity. In statistical analysis, a P value <0.05 was considered as the indicator of significance.

## 3. RESULT

In this current study, we found that serum ferritin levels were higher in group A participant than in group B and the difference was statistically significant (P<0.001). In group A, 46% of patients had serum ferritin levels <150 µg/L and 54% had serum ferritin levels ≥150 µg/L. As per the serum iron level distribution of the study participants, we observed that serum iron levels were higher in group A than in group B and the difference was statistically significant (<0.001). In group A, 44% of patients had serum iron levels <100 µg/dl and 56% had serum iron levels ≥ 150 µg/dl. In this study, in analyzing the total iron binding capacities (TIBC) between the groups we observe that the TIBC (µg/dl) levels in group A and group B were 184.0±79.5 and 318.8±14.0 µg/dl respectively. The TIBC levels were significantly lower in group A than in group B (<0.001). Among the total of our study participants, there were a strong positive correlation between serum ferritin with FPG and serum iron with FPG respectively. A negative correlation between TIBC with FPG was found. There was a strong positive correlation between serum ferritin with HbA1c and serum iron with HbA1c respectively. A negative correlation between TIBC with HbA1c was found.

**Table 1: Distribution of participants as per the serum ferritin levels. (N=100)**

| S. ferritin (µg/L) | Group A (n=50) | | Group B (n=50) | | P value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| <150 | 23 | 46% | 45 | 90% | <0.001 |
| ≥150 | 27 | 54% | 5 | 10% | |

A chi-square test was done to measure the level of significance

**Table I:** showed distribution of study subject according to serum ferritin level in both groups. Serum ferritin levels were higher in Group A than Group B and the difference was statistically significant. In group A, 46% patients had serum ferritin levels <150 µg/L and 54% had serum ferritin levels ≥ 150 µg/L.

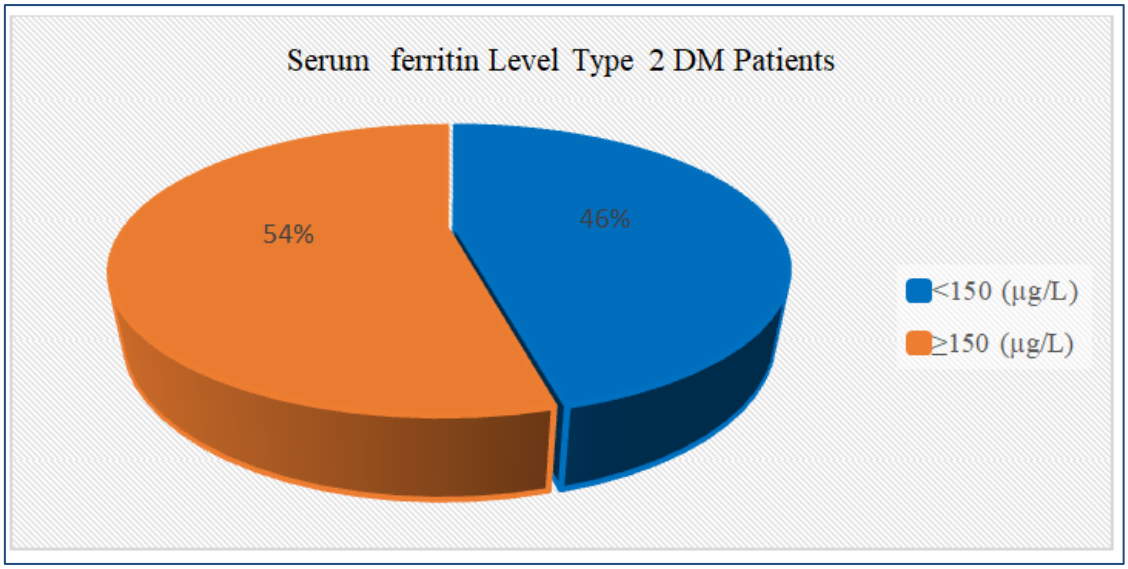


**Figure 1: Pie chart of serum ferritin level distribution in Type 2 DM Patients. (n=50)**

**Table II: Distribution of study subject according to serum iron level in group A and group B. (N=100)**

| Serum iron (µg/dl) | Group | | p value |
|---|---|---|---|
| | Group A n (%) | Group B n (%) | |
| <100 | 22(44.0) | 39(78.0) | <0.001 |
| ≥100 | 28(56.0) | 11(22.0) | |

A chi-square test was done to measure the level of significance

**Table II:** showed distribution of study subjects according to serum iron level in both groups. Serum iron levels were higher in group A than Group B and the difference was statistically significant. In group A, 44% patients had serum iron levels <100 µg/dl and 56% had serum iron levels ≥ 150 µg/dl.

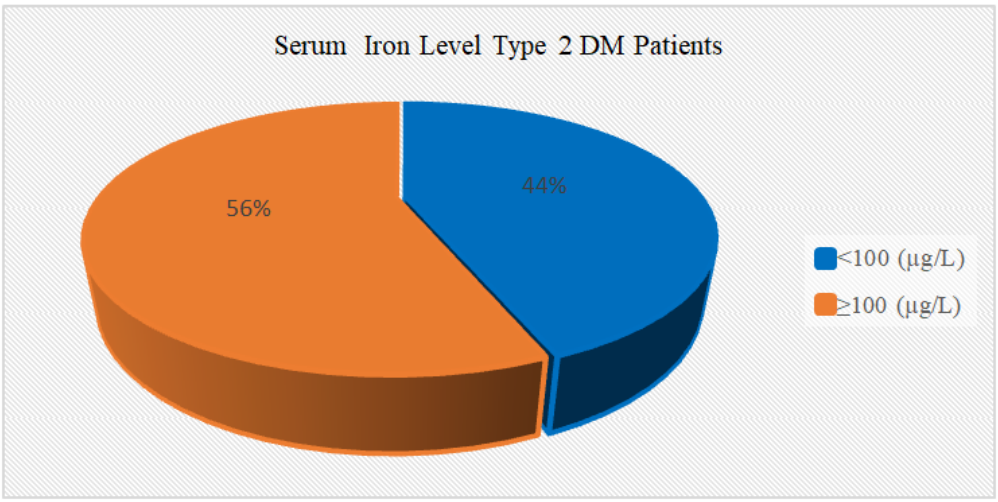


**Figure 2: Pie chart of serum iron level distribution in Type 2 DM Patients. (n=50)**

**Table 3: Distribution of biochemical parameters in Group A and Group B. (N=100)**

| Parameters | Group A (mean ±SD) | Group B (mean ±SD) | P-value |
|---|---|---|---|
| S. Ferritin (µg/L) | 199.3±74.8 | 107.0 ± 30.4 | <0.001 |
| S. Iron (µg/dl) | 112.7±34.1 | 87.6 ± 20.9 | <0.001 |
| TIBC (µg/dl) | 184.0±79.5 | 318.8 ± 14.0 | <0.001 |

An unpaired test was done to measure the level of significance

**Table 4: Correlation of iron status with FPG. (n=50)**

| Biochemical parameters | | r value | | P-value |
|---|---|---|---|---|
| Iron status | FPG | | | |
| Serum Ferritin | | 0.705 | | <0.001 |
| Serum Iron | | 0.92 | | <0.001 |
| TIBC | | -0.747 | | <0.001 |

Pearson's correlation test was done to measure the level of significance

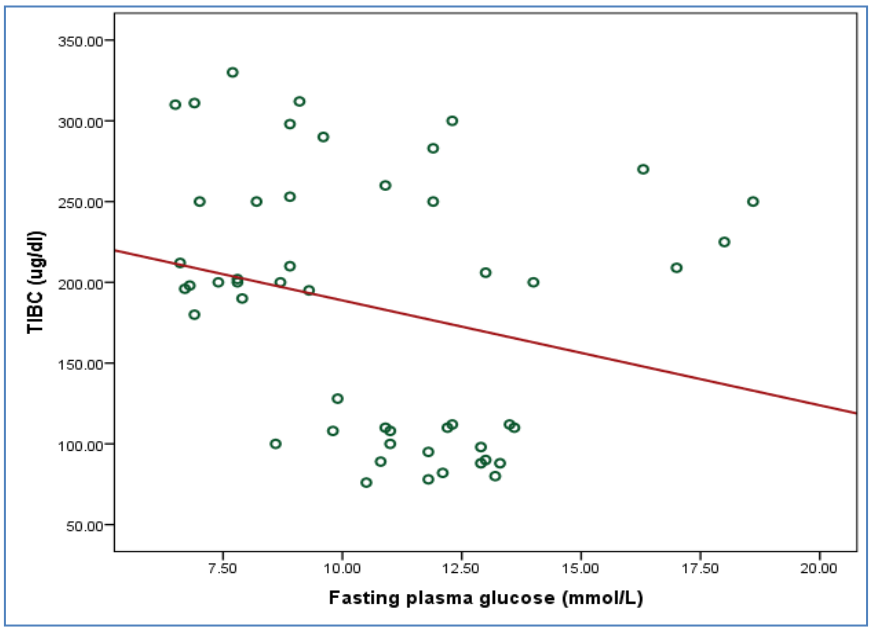


**Figure 3: Correlation of fasting plasma glucose with TIBC in type 2 DM.(n=50)**

**Table 5: Correlation of Iron status with HbA1c (n=50)**

| Biochemical parameters | | r value | P-value |
|---|---|---|---|
| Iron status | HbA1c | | |
| Serum Ferritin | | 0.705 | <0.001 |
| Serum Iron | | 0.92 | <0.001 |
| TIBC | | -0.747 | <0.001 |

Pearson's correlation test was done to measure the level of significance

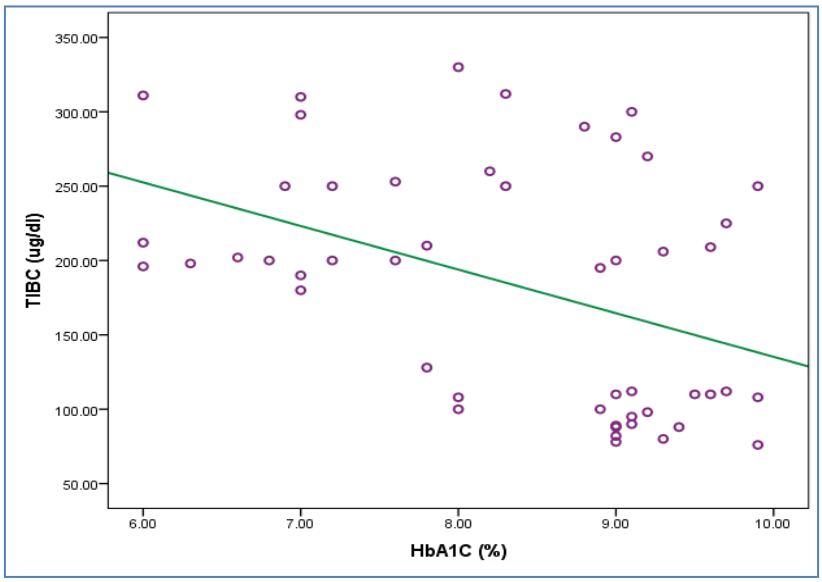


**Figure 4: Correlation of HbA1c with TIBC in type 2 DM. (n=50)**

## 4. DISCUSSION

This study aimed to compare the total iron binding capacities (TIBC) between type 2 diabetes mellitus patients and healthy individuals. In this present study, the mean serum iron concentration in group A and group B were 112.7 and 87.6 respectively and the mean serum ferritin concentration in group A and group B were 199.3 and 107.0 respectively. There was a statistically significant increase in serum iron and serum ferritin concentration in Group A compared to Group B ($p<0.0001$). These results of the study were in agreement with the studies conducted earlier. Studies done by Fernandez *et al.,* [14], *Bozzini et al.,* [15], and Jiang *et al.,* [16] observed an important and highly significant association between serum iron and serum ferritin with type 2 DM. Sudhakar *et al.,* [17] also found high serum iron and serum ferritin concentrations in patients with type 2 diabetes mellitus with poor controls. From this study, the mean value of TIBC was found 184.0±79.5 in group A and 318.8± 14 in group B. TIBC levels were significantly lower in Group A than in Group B. This result was to contrast with the result found by Kapoor and Sharma, [18]. They studied 30 Type 2 DM patients and 30 age, sex-matched healthy controls. According to their result, low TIBC, UIBC and increased transferrin saturation were seen in Type 2 DM patients. In this present study the mean HbA1C was found 8.3± 1.2 in group A and 5.0 ± 0.6 in group B. There was a statistically significant increase of mean value of HbA1c in group A ($p<0.0001$) compare to group B ($p<0.0001$). Fernandez *et al.,* [14] study findings were consistent with the present result. A correlation of serum ferritin and serum iron with HbA1c was found. Both serum ferritin and serum iron levels showed a strong positive correlation with HbA1C. The correlation coefficient was $r = 0.705$ and $p < 0.001$ and $r = 0.920$ and $p< 0.001$ respectively. These results were in harmony with the study done by Wrede *et al.,* [19] who reported a significant correlation between serum ferritin and HbA1c in a large representative population. There was a nationwide epidemiological survey on 1200 populations. Shetty *et al.,* [6] have shown a relationship between free iron and glycated hemoglobin in uncontrolled Type 2 diabetes patients associated with complications. Kar *et al.,* [20] have studied the effect of glycosylation on iron-mediated free radical reactions of hemoglobin and demonstrated that $H_2O_2$-induced iron release is more from HbA1c than that from non-glycosylated hemoglobin (HbA0). There was a strong positive correlation between FPG with serum ferritin ($r=0.705$) and serum iron ($r=0.920$). TIBC showed a negative correlation with FPG. These findings were similar to the findings of Padmaja, Shabanas and Shariq, 2015. They found a statistical increase of FPG, HbA1c and serum ferritin in the Type 2 DM group than the control group. Sudhakar *et al.,* [17] also found a positive correlation between FPG with serum ferritin and serum iron. So, from the above discussion it may be concluded that in comparison with healthy individuals, type 2 DM patients had increased serum ferritin and serum iron level and decreased TIBC. Levels of serum ferritin and serum iron were directly correlated with the glycemic control of diabetic patients (HbA1c). All the findings of this current study may be helpful in further similar studies.

**Limitation of the Study:**

This was a single-centered study with small-sized samples. Moreover, the study was conducted over a very short period. So, the findings of this study may not reflect the exact scenario of the whole country.

## 5. CONCLUSION & RECOMMENDATION

As per the findings of this current study, we can conclude that the total iron binding capacity level is significantly lower in type 2 diabetes mellitus (T2DM) patients than that in healthy individuals. Routine screening for iron status along with glycemic control in diabetic patients might help prevent complications in such patients. For getting more specific results, we would like to recommend conducting similar studies in several places with larger-sized samples.

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**Conflict of Interest:** None declared

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