# Original Research Article

# Assessment the Levels of Serum Ferritin and Some Biochemical Parameters in Type 2 Diabetic Subjects Attending A Tertiary Hospital in Bangladesh

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*Abstract:* **Background:** Type 2 diabetes (NIDDM) is the commonest form of diabetes constituting nearly 90% of the diabetic population in any country. Iron is an important mineral in normal physiological processes, and ferritin is a specialized iron storage protein, which reflects iron stores in the body. Iron overload is a risk factor for diabetes. The link between iron and diabetes was first recognized in pathologic conditions-hereditary hemochromatosis and thalassemia, but high levels of dietary iron also import diabetes risk. Iron plays a direct and causal role in diabetes pathogenesis mediated both by β-cell failure and insulin resistance. The objective of the study to evaluate serum ferritin level among type 2 diabetes patients. **Method:** A hospital based observational study a total of 240 subjects among them 60 male diabetes patients and 60 female diabetes patients were recruited. Serum ferritin level were checked in all participants. **Results:** The mean age of T2DM was 59 ± 14 years and control group was 50 ± 13 years. The BMI of each group was 27.52 ± 2.6 and 24.80 ± 2.4. Ferritin (ng/dL) level in T2 DM subjects was 231 ± 36 and control subjects was 48 ± 22. Serum ferritin level among the study subjects control vs T2 DM, *t/p* value (8.465/0.0001). **Conclusion:** From this study it was observed that ferritin level is significantly higher among type 2 diabetes patients.

Keywords: Serum ferritin; DM; Iron; HbA1c.

# **1. Introduction**

Diabetes mellitus is a chronic metabolic disorder characterized by rise in blood glucose level called hyperglycemia<sup>[1]</sup>. The worldwide prevalence of diabetes in 2000 was approximately 2.8% and is estimated to grow to 4.4% by 2030. This translates to a projected rise of diabetes from 171 million in 2000 to well over 350 million in 2030<sup>[2]</sup>. Diabetes is of two types, type 1 accounting for 5% prevalence and type 2 for 95% prevalence among diabetics. This calls for improved treatment of hyperglycemia and other risk factors associated with metabolic syndrome. Since it is possible to dramatically lower the risk of both micro and macrovascular complications<sup>[3]</sup>. Persistent elevations in blood sugar increase the risk for the long-term vascular complications of diabetes such as coronary disease, heart attack, stroke, heart failure, kidney failure, blindness, erectile dysfunction, neuropathy (loss of sensation, especially in the feet), gangrene and gastroparesis (slowed emptying of the stomach). Poor blood glucose control also increases the risk of short-term complications of surgery such as poor wound healing<sup>[2]</sup>. Glycated hemoglobin (glycosylated hemoglobin, hemoglobin A1c, HbA1c, A1C, or Hb1c; sometimes also HbA1c) is a form of hemoglobin used primarily to identify the average plasma glucose concentration over prolonged periods of time. The measurement of glycosylated hemoglobin (GHb) is one of the well-established means of monitoring glycemic control in patients with diabetes mellitus<sup>[4]</sup>.

Bangladesh is a developing country where 75% of total population lives in rural area. Subsequently they have poor healthcare access as 26% of rural professionals remain vacant and nearly 40%, absent. In Bangladesh, there are thought to be 10 million diabetics. A more surprising finding from a comparable study is that diabetes affects nearly one in ten persons in Bangladesh. According to the WHO, 83% of people in the 25-65 age group never check for diabetes. A different paper makes a nearly identical claim. 87% of Bangladeshis were non-compliant for an effective control and prevention of diabetes, compared to 71% of Indians and 52% of Europeans. Interesting fact: Over the past 14 years, the state of compliance has not improved. Only 12% of those over 35 who are diabetes or pre-diabetic have their disease under control. Approximately 17% of men and 23% of women were found to have intermediate hyperglycemia, also known as impaired fasting glucose or impaired glucose tolerance<sup>[5]</sup>.

The body needs iron, a transitional metal and micronutrient, for many physiological processes to occur. Reactive oxygen species are known to be catalyzed by iron, a strong pro-oxidant. The risk of metabolic illnesses like hypertension, the metabolic syndrome, and cardiovascular disease has been linked to having excessive iron reserves. Additionally, it has been suggested that having large iron reserves can increase the risk of developing type 2 diabetes by harming the pancreatic beta cells and increasing insulin resistance by raising the degree of oxidative stress<sup>[6]</sup>.

A common indicator used to assess the body's iron homeostasis is ferritin, a crucial protein that controls iron balance. Considering that type 2 diabetes is frequently made worse in people with hereditary hemochromatosis, a condition marked by incredibly high amounts of circulating ferritin. On the above perspective the present study has been undertaken to identify the relationship of ferritin in type 2 diabetic subjects in Bangladesh.

#### 2. Methodology

It was an observational study. The study was conducted in the out patient's department, BIHS General Hospital, Dhaka, Bangladesh. The study was done during the period of August, 2018 to September, 2019. The subjects were selected purposively. Age and sex matched normal healthy controls were selected for the study. A total number of 240 subjects were recruited in the study. Among them 120 were male and 120 were female.

#### 2.1. Inclusion criteria

- Adult subjects with age ranging from 30-70 years both Diabetic and Non Diabetic.
- Both male and female.

#### 2.2. Exclusion criteria

- Patients below 30 years and above 70 years.
- Overt thyroid dysfunction.
- Chronic kidney disease.
- Chronic liver disease.

#### 2.3. Data collection

Before collecting specimen, each patient was interviewed and relevant information was recorded systematically in a pre-designed standard data sheet and then data were checked, edited and processed. Fasting blood samples were collected from all participants. They were allowed to fast overnight (10-12 h). Blood was collected from the antecubital vein after all aseptic precautions. Laboratory parameters including serum ferritin, Hemoglobin, fasting and postprandial blood sugar, glycosylated hemoglobin, serum total cholesterol, serum triglycerides, LDL cholesterol, HDL cholesterol were estimated. A detailed physical examination was done which included measuring height and weight and waist circumference. BMI was calculated.

#### 2.4. Data analysis

Data were analyzed with the help of the software SPSS (statistical package for social sciences) version 23 and Microsoft Excel 2016. The results were expressed as mean  $\pm$  SD (standard deviation). The *p*-value <0.05 was considered as statistically significant.

#### **3. Results**

In this study 240 subjects were included in which 120 diabetic patients and 120 non-diabetic patients. **Table 1** Clinical profile of type-2 DM and control group.

Type-2 DM (n = 120) Control (n = 120)Age (years)  $59 \pm 14$  $50\pm13$ Gender (M/F) 60/60 60/60 BMI  $27.52\pm2.6$  $24.80\pm2.4$ TG (mg/dL)  $210.71 \pm 54.20$  $141 \pm 19.61$ HDL (mg/dL)  $36.34 \pm 4.66$  $33.54 \pm 4.51$ LDL (mg/dL)  $109\pm29.02$  $105.19 \pm 21.29$ FBS (mg/dL)  $133\pm26$ 90 + 13HbA1c  $8.78 \pm 1.3$  $4.68 \pm 0.50$ Ferritin (ng/dL)  $231\pm36$  $48 \pm 22$ Hb (g/dL)  $15.4 \pm 2.3$  $14.2 \pm 2.1$ 

**Table 1** show the clinical characteristics of type diabetes mellitus and control group. The mean age of T2 DM was  $59 \pm 14$  years and control group was  $50 \pm 13$  years. The BMI of each group was  $27.52 \pm 2.6$  and  $24.80 \pm 2.4$ . TG (mg/dL), HDL (mg/dL), LDL (mg/dL), FBS (mg/dL), HbA1c, Ferritin (ng/dL), Hb (g/dL) level in T2 DM subjects was  $210.71 \pm 54.20$ ;  $36.34 \pm 4.66$ ;  $109 \pm 29.02$ ;  $133 \pm 26$ ;  $8.78 \pm 1.3$ ;  $231 \pm 36$ ;  $15.4 \pm 2.3$ . TG (mg/dL), HDL (mg/dL), LDL (mg/dL), FBS (mg/dL), HbA1c, Ferritin (ng/dL), Hb (g/dL) level in control subjects was  $141 \pm 19.61$ ;  $33.54 \pm 4.51$ ;  $105.19 \pm 21.29$ ;  $90 \pm 13$ ;  $4.68 \pm 0.50$ ;  $48 \pm 22$ ;  $14.2 \pm 2.1$ .

Variable	T2 DM ( <i>n</i> = 120)	<b>Control</b> ( <i>n</i> = 120)	<i>t/p</i> value
			Control vs. T2 DM
Age (years)	$59 \pm 14$	$50 \pm 13$	2.885/0.006
Ferritin	$231\pm36$	$48 \pm 22$	8.465/0.0001

**Table 2**Ferritin level among the study subjects.

**Table 2** shows the Ferritin status among the control group and type 2 diabetic subjects. The ferritin (ng/dL) level (mean  $\pm$  sd) in control group was 231  $\pm$  36. The ferritin (ng/dL) level (mean  $\pm$  sd) in type 2 subjects was 48  $\pm$  22.

**Table 3**Ferritin level among male and female of T2 DM subjects.

Variable	Diabetic male $(n = 60)$	Diabetic female $(n = 60)$ –	<i>t/p</i> value
			Control vs. T2 DM
Age (years)	$61 \pm 15$	57 ± 16	0.723/0.475
Ferritin	$248\pm36$	$213\pm17$	0.753/0.458

**Table 3** shows the comparison of ferritin level status (mean  $\pm$  sd) between male and female T2 DM subjects

in a tertiary hospital in Dhaka city. The ferritin (ng/dL) level (mean  $\pm$  sd) in male was 248  $\pm$  136. The ferritin (ng/dL) level (mean  $\pm$  sd) in female was 213  $\pm$  107.

Variable	Control male $(n = 60)$	Control female $(n = 60)$	<i>t/p</i> value
			Control vs. T2 DM
Age (years)	$52 \pm 15$	$48 \pm 11$	1.571/0. 129
Ferritin	$46.79\pm20.82$	$31.15 \pm 11.03$	1.318/0. 203

**Table 4**Ferritin level status among male and female of non-T2 DM subjects.

**Table 4** shows the comparison of ferritin level status (mean  $\pm$  sd) between male and female of non-T2 DM subjects in a tertiary hospital in Dhaka city. The ferritin (ng/dL) level (mean  $\pm$  sd) in male was 46.79  $\pm$  20.82. The ferritin (ng/dL) level (mean  $\pm$  sd) in female was 31.15  $\pm$  11.03.

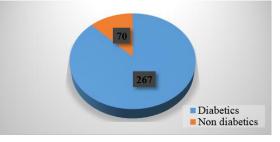


Figure 1 Ferritin level associated with type 2 diabetic mellitus.

The ferritin level was significantly higher in the diabetic subjects compared to non-diabetic subjects.

#### 4. Discussion

It is well recognized that ferritin is a sign of inflammation and that this increases the risk of type 2 diabetes. Increased body iron levels have been linked to the emergence of glucose intolerance, gestational diabetes, type 2 DM, and the insulin resistance syndrome, according to recent investigations<sup>[7,8]</sup>. There are several widely accepted explanations, however it is still unclear exactly how increased serum ferritin is linked to type 2 diabetes mellitus. Insulin resistance is thought to be related to iron excess. Iron buildup in the liver may contribute to insulin resistance by impairing insulin's capacity to reduce hepatic glucose synthesis. At least in certain cases of diabetes, pancreatic damage caused by some degree of subclinical hemochromatosis has been taken into consideration. One study found that, the amounts of insulin, glycosylated hemoglobin, and ferritin were positively and strongly correlated with glucose levels across all subjects. Insulin had the highest correlation and regression coefficient magnitudes were larger for women than for males<sup>[8]</sup>.

T2 DM is becoming more and more common in our region of the world. The emergence of T2 DM has numerous etiologies. One of these is thought to represent a raised serum ferritin level, iron excess, or both<sup>[9]</sup>. Elimam et al. have reported positive correlation between serum ferritin, HbA1c and CRP levels and highlighting the direct association of inflammation and glycemic control in T2 DM patients<sup>[10]</sup>. A study conducted on 9486 participants out of total 16,573 individuals in the United State by Ford et al in 1999 reported that serum ferritin levels were lowest in non-diabetic, higher in pre-diabetic and highest in diabetic patients<sup>[11]</sup>. A study by Andrews et al. conducted on diabetic obese and non-obese patients and healthy controls depicted higher serum ferritin and inflammatory status in obese patients than the control group reflecting a significant positive association of serum ferritin and T2 DM subjects<sup>[12]</sup>.

In the present study, Ferritin level among the study subjects control vs T2 DM, t/p value (8.465/0.0001) which was significant. Ferritin level among male and female of T2 DM subject's t/p value was (0.753/0.458). We found that a serum ferritin concentration was significantly higher in type 2 diabetes subjects compared to

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control subjects. In diabetic patients, our study found no relationship between serum ferritin and BMI. Additionally, there was no association found between S. ferritin and age, sex, HDL, LDL, hemoglobin and serum triglycerides. In our study, we noticed that diabetes patients whose serum ferritin was high had high HbA1c. We need a larger study to confirm this. One study found Serum Ferritin had a positive correlation with FBS and HbA1c<sup>[6]</sup>.

In a cohort study involving 2225 Chinese people, Chen et al. examined the association between serum ferritin levels and the risk of developing T2 DM. In their comparison of the results between diabetic and nondiabetic individuals, the researchers found that T2 DM patients had higher baseline serum ferritin levels, BMI, HOMA, blood pressure, HbA1c, cholesterol, HDL-C, ALT, and TAG values than the non-diabetic group. This study found that serum ferritin levels in Chinese men had a considerably greater incidence of type 2 diabetes (T2 DM), which was correlated with an increase of one standard deviation in serum ferritin levels. It came to the conclusion that serum ferritin levels may be used as a biomarker for predicting the risk of developing type 2 diabetes in men<sup>[13]</sup>.

# 5. Conclusion

In conclusion, there is evidence to show that iron contributes to the pathogenesis of diabetes and associated consequences, including microangiopathy and atherosclerosis. To precisely assess the free/catalytic iron that takes part in oxidative damage, sensitive and trustworthy methodologies must be created. From the above study, it was observed that the ferritin level is significantly higher in type 2 diabetic subjects compared to control group.

## **Author Contributions**

Design and conceptualization: Md. Ashiqur Rahman, Sadia Islam Database searching: Shohanur Rahaman, Md. Rajib Emran Writing, editing, analysis, and interpretation: Md. Ashiqur Rahman, Sadia Islam Drafting and formatting: Md. Ashiqur Rahman, Sadia Islam Data extraction: Sadia Islam, Shohanur Rahaman, Md. Rajib Emran All authors contributed to the reviewing for important intellectual context and approved the manuscript to submit.

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# **Conflict of Interest**

The authors declare no conflict of interest.

# References

- 1. Vinik A, Flemmer M. Diabetes and macrovascular disease. Journal of Diabetes and its Complications 2002; 16(3): 235–245.
- 2. Sultanpur CM, Deepa K, Kumar SV. Comprehensive review on HbA1c in diagnosis of diabetes mellitus. International Journal of Pharmaceutical Sciences Review and Research 2010; 3(2): 119–122.
- 3. Gaede P, Vedel P, Larsen N, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. New England Journal of Medicine 2003; 348(5): 383–393. doi: 10.1056/NEJMoa021778
- 4. The diabetes control and complications trial research group. The effect of intensive treatment of diabetes on the development and progression of long term complications in insulin dependent diabetes mellitus. New England Journal of Medicine 1993; 329: 977–986. doi: 10.1056/NEJM199309303291401
- Mohiuddin A. Diabetes fact: Bangladesh perspective. Community and Public Health Nursing 2019; 4(1): 39.

- Raj S, Rajan GV. Correlation between elevated serum ferritin and HbA1c in type 2 diabetes mellitus. International Journal of Research in Medical Sciences 2013; 1(1): 12–15. doi: 10.5455/2320-6012.ijrms20130203
- Kunutsor SK, Apekey TA, Walley J, Kain K. Ferritin levels and risk of type 2 diabetes mellitus: an updated systematic review and meta - analysis of prospective evidence. Diabetes/metabolism Research and Reviews 2013; 29(4): 308–318. doi: 10.1002/dmrr.2394
- 8. Ford ES, Cogswell ME. Diabetes and serum ferritin concentration among US adults. Diabetes Care 1999; 22(12): 1978–1983. doi: 10.2337/diacare.22.12.1978
- Raj S, Rajan GV. Correlation between elevated serum ferritin and HbA1c in type 2 diabetes mellitus. International Journal of Research in Medical Sciences 2013; 1(1): 12–15. doi: 10.5455/2320-6012.ijrms20130203
- Elimam H, Abdulla AM, Taha IM. Inflammatory markers and control of type 2 diabetes mellitus. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2019; 13(1): 800–804.
- 11. Islam S, Hossen MA, Rahman MA, Lubaba MI, Akram A. Serum uric acid level among type-2 diabetes subjects attending in a tertiary hospital of Bangladesh. World Journal of Biology Pharmacy and Health Sciences. 2022;12(1):081-5.
- 12. Ford ES, Cogswell ME. Diabetes and serum ferritin concentration among US adults. Diabetes Care 1999; 22(12): 1978–1983. doi: 10.2337/diacare.22.12.1978
- 13. Rahman MA, Islam S, Lubaba MS, Akram A. Study of Uric acid and Serum Creatinine in Diabetic and Non-Diabetic patients in a tertiary hospital, Dhaka. Int. j. adv. multidisc. res. stud. 2022; 2(6):226-228.
- Andrews M, Soto N, Arredondo-Olguín M. Association between ferritin and hepcidin levels and inflammatory status in patients with type 2 diabetes mellitus and obesity. Nutrition 2015; 31(1): 51–57. doi: 10.1016/j.nut.2014.04.019
- Chen L, Li Y, Zhang F, et al. Elevated serum ferritin concentration is associated with incident type 2 diabetes mellitus in a Chinese population: A prospective cohort study. Diabetes Research and Clinical Practice 2018; 139: 155–162. doi: 10.1016/j.diabres.2018.03.001
- 16. Amiruzzaman M, Roy MN, Lopa AR, Chanda M, Rahman MA, Akram A. Association of Serum Gamma-Glutamyl Transferase Level with Metabolic Syndrome and Insulin Resistance in Adults.
- 17. Fatema K, Rahman MA, Ahmed ANN, Paul D, Mondal BR, Islam S, Khatun DR, Akram A. Salivary Ferritin is a Diagnostic Marker in Iron Deficiency Anaemia in Children. Int. j. adv. multidisc. res. stud. 2022; 2(6):913-918.