



## A STUDY ON CORRELATION BETWEEN SERUM FERRITIN AND GLYCATED HEMOGLOBIN IN TYPE 2 DIABETES MELLITUS.

### Diabetology

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### ABSTRACT

**Background:** Serum Ferritin, an acute phase reactant is a marker of iron stores in the body. Recent studies indicate that increased body iron stores and subclinical hemochromatosis has been associated with the development of glucose intolerance, type 2 diabetes, metabolic syndrome and possibly the development of diabetic retinopathy, nephropathy and vascular dysfunction. This study was carried out to examine and establish a relationship between Serum Ferritin with Type 2 diabetes mellitus and metabolic syndrome and to examine whether a correlation between S. ferritin and FBS, HbA1c exists.

**Methods:** 173 Subjects satisfying the inclusion and exclusion criteria were selected. S. ferritin, Hb, ESR, FBS, PPBS, HbA1c were measured.

**Results:** Serum ferritin was significantly higher in diabetic patients when compared to controls and serum ferritin had a positive correlation with increasing duration of diabetes.

**Conclusions:** Serum Ferritin was higher among cases than in controls group. Positive correlation was observed between HbA1c and Serum Ferritin among cases. Hence glycemic status is significantly related to serum ferritin levels among diabetics.

### KEYWORDS

Ferritin, Diabetes, FBS

### INTRODUCTION

The explosive increase of Diabetic population worldwide is a major public health concern both in developing and developed countries. Metabolic syndrome is also on an increasing trend. The metabolic syndrome is closely linked to insulin resistance and numerous studies indicate a link to iron overload. Increased serum ferritin, reflecting body iron overload, is often associated with measures of insulin resistance, such as elevated blood glucose and insulin levels.<sup>1</sup> In addition, two prospective studies have identified an independent association between baseline elevations in iron stores and the incidence of diabetes.<sup>2,3</sup>

Elevated iron stores may induce diabetes through a variety of mechanisms, including oxidative damage to pancreatic beta cells, impairment of hepatic insulin extraction by the liver, and interference with insulin's ability to suppress hepatic glucose production.<sup>3-6</sup>

Raised Serum Ferritin may possibly be related to the occurrence of long term complications of diabetes, both micro vascular and macro vascular.<sup>7,8</sup>

Hence, the present study was carried out to establish relationship between serum ferritin and type 2 diabetes mellitus.

### MATERIALS AND METHODS

The study was designed as a case-control study of diabetic patients visiting medicine outpatient department of RL Jalappa hospital, Tamaka, Kolar, Karnataka. A total of 173 subjects were selected in the study.

### INCLUSION CRITERIA

#### CASE GROUP:

Age > 35 years  
Type 2 diabetes mellitus with or without vascular complications  
Hb > 10g/dl

#### CONTROL GROUP:

Non-diabetic coming to hospital as patient's attendant and also from medical or paramedical staff, persons attending OPD for routine check up.

### EXCLUSION CRITERIA

Type 1 diabetes mellitus

Chronic alcoholics

Hepatitis

Iron deficiency anemia

Hypothyroidism

Pregnant and breast feeding women.

History of repeated blood transfusions.

Chronic inflammatory conditions like SLE/rheumatoid arthritis

Chronic Kidney Disease

### DATA COLLECTION

A detailed proforma was filled up for each patient which included age, sex, past history of coronary artery disease, cerebrovascular accident, history of hypertension. The age of onset and duration of diabetes was recorded, also whether the patient was treated with oral hypoglycemic agents or insulin or whether the patient was on diet control alone.

Laboratory parameters including Serum ferritin, Hemoglobin, ESR, fasting and postprandial blood sugar, glycosylated hemoglobin were estimated.

Proforma including age, sex, medical history, onset, duration and complications of Diabetes was filled. Physical examination was done measuring height, weight, waist circumference and blood pressure.

A fasting plasma glucose  $\geq 126$  mg/dl or previous history of diabetes mellitus was required for the diagnosis of diabetes.

Blood was collected from patients after an overnight (8 hr) fasting and 2 hr postprandial (after a breakfast meal).

### RESULTS

**TABLE 1:**

	Groups				P value
	Cases		Controls		
	Mean	SD	Mean	SD	
Age	49.0	7.6	47.5	6.2	0.051
Hb	11.5	1.5	11.9	1.4	0.003*
Fasting Plasma Glucose	241.4	53.6	90.4	14.3	<0.001*
Serum Ferritin	372.1	49.4	255.9	60.7	<0.001*
HbA1c	11.8	2.6	5.4	0.5	<0.001*

Among cases Mean age was  $49 \pm 7.6$  years, mean Hb was  $11.5 \pm 1.5$  gm%, mean fasting plasma glucose was  $241.4 \pm 53.6$  mg/dl, mean Ferritin was  $372.1 \pm 49.4$  and mean HbA1c was  $11.8 \pm 2.6$ . Among controls mean age was  $47.5 \pm 6.2$  years, mean Hb was  $11.9 \pm 1.4$  gm%, mean fasting plasma glucose was  $90.4 \pm 14.3$  mg/dl, mean Ferritin was  $255.9 \pm 60.7$  and mean HbA1c was  $5.4 \pm 0.5$ . There was significant difference in mean Hb, Fasting Plasma Glucose, Serum Ferritin and HbA1c between cases and controls

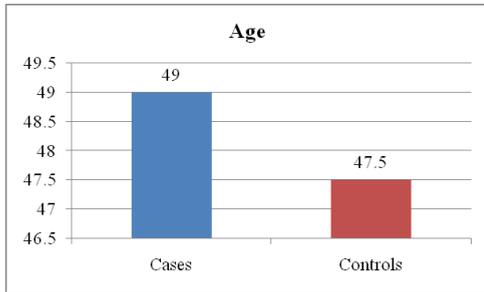


FIGURE 1: Bar diagram showing Mean Age distribution between cases and controls

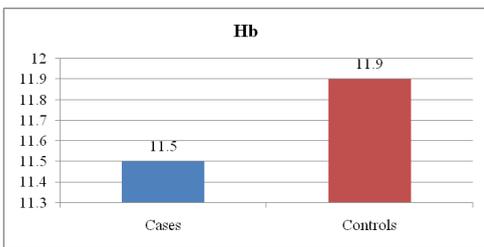


FIGURE 2: Bar diagram showing Mean Hb distribution between cases and controls

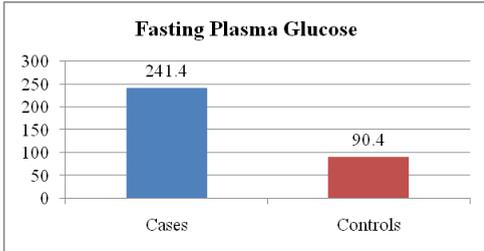


FIGURE 3: Bar diagram showing Mean FPG distribution between cases and controls

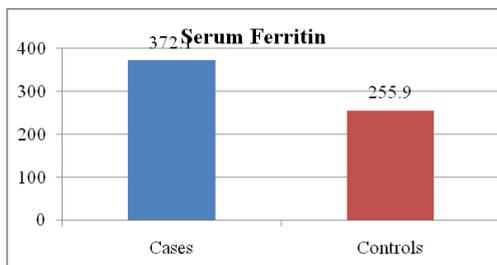


FIGURE 4: Bar diagram showing Mean Serum Ferritin distribution between cases and controls

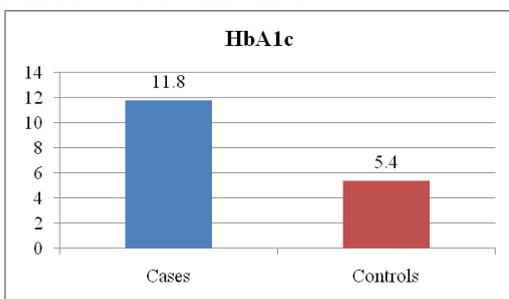


FIGURE 5: Bar diagram showing Mean HbA1c distribution between cases and controls

TABLE 2: Comparison of parameters between females and males among cases

	Cases				P value
	Female		Male		
	Mean	SD	Mean	SD	
Age	49.5	8.0	48.5	7.3	0.388
Hb	11.6	1.6	11.3	1.4	0.291
Fasting Plasma Glucose	237.1	48.6	245.5	57.8	0.303
Serum Ferritin	368.5	39.2	375.4	57.3	0.362
HbA1c	11.9	2.9	11.7	2.2	0.707

In the study there was no significant difference in mean age, Hb, Fasting Plasma Glucose, Serum Ferritin and HbA1c between males and females among cases.

TABLE 3: Comparison of parameters between females and males among controls

	Controls				P value
	Female		Male		
	Mean	SD	Mean	SD	
Age	47.3	6.5	47.7	6.0	0.684
Hb	11.7	1.4	12.1	1.3	0.092
Fasting Plasma Glucose	90.2	8.8	90.6	17.9	0.849
Serum Ferritin	258.8	56.9	253.4	64.1	0.567
HbA1c	5.4	.5	5.4	.4	0.668

In the study there was no significant difference in mean age, Hb, Fasting Plasma Glucose, Serum Ferritin and HbA1c between males and females among controls

TABLE 4: Correlation between HbA1c and Serum Ferritin in Cases

		Correlations		
		HbA1c	Cases	Controls
			Serum Ferritin	Serum Ferritin
HbA1c	Pearson Correlation	1	0.163 <sup>†</sup>	0.124
	P value		0.032*	0.105
	N	173	173	173

In the study there was significant positive correlation between HbA1c and Serum Ferritin among cases i.e. with increase in HbA1c there was increase in Serum Ferritin and vice versa.

In the study there was no significant positive correlation between HbA1c and Serum Ferritin among controls i.e. with increase in HbA1c there was no significant increase in Serum Ferritin and vice versa.

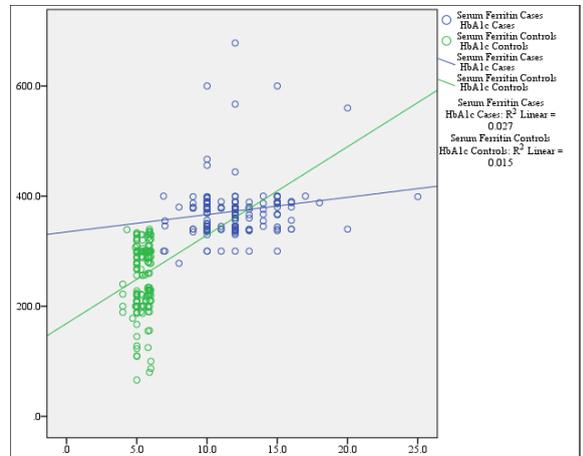


FIGURE 6: Scatter plot showing positive Correlation between HbA1c and Serum Ferritin in Cases and controls

TABLE 5: Correlation between HbA1c and Serum Ferritin among female cases

		Correlations	
		HbA1c	Serum Ferritin
HbA1c	Pearson Correlation	1	0.008
	P value		0.945
	N	83	83

In the study there was no significant positive correlation between HbA1c and Serum Ferritin among female cases i.e. with increase in HbA1c there was no significant increase in Serum Ferritin and vice versa.

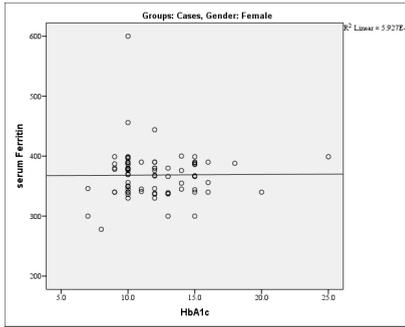


FIGURE 8: Scatter plot showing Correlation between HbA1c and Serum Ferritin among females cases

TABLE 6: Correlation between HbA1c and Serum Ferritin among males cases

Correlations			
		HbA1c	Serum Ferritin
HbA1c	Pearson Correlation	1	0.309*
	P value		0.003*
	N	90	90

In the study there was significant positive correlation between HbA1c and Serum Ferritin among male cases i.e. with increase in HbA1c there was significant increase in Serum Ferritin and vice versa.

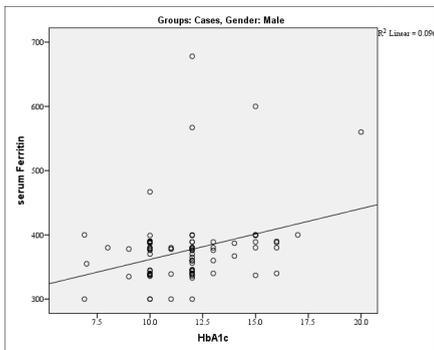


FIGURE 9: Scatter plot showing Correlation between HbA1c and Serum Ferritin among male cases

TABLE 7: Correlation between HbA1c and Serum Ferritin among female controls

Correlations			
		HbA1c	Serum Ferritin
HbA1c	Pearson Correlation	1	-0.015
	P value		0.895
	N	81	81

In the study there was no significant negative correlation between HbA1c and Serum Ferritin among female controls i.e. with increase in HbA1c there was no significant decrease in Serum Ferritin and vice versa.

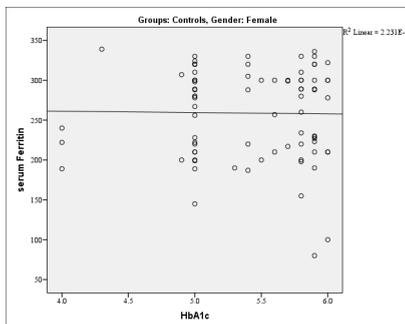


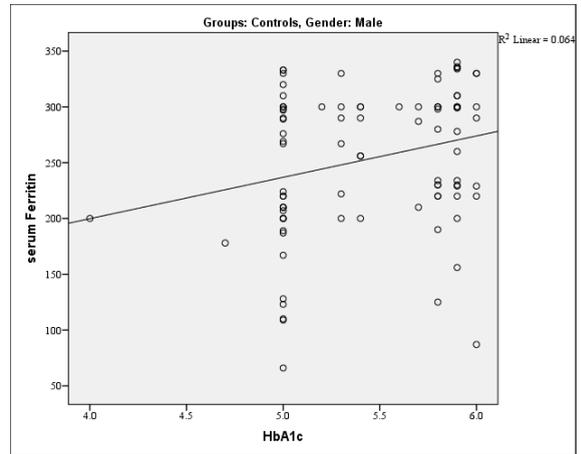
FIGURE 10: Scatter plot showing Correlation between HbA1c and Serum Ferritin among female controls

TABLE 8: Correlation between HbA1c and Serum Ferritin among male controls

Correlations			
		HbA1c	serum Ferritin
HbA1c	Pearson Correlation	1	0.253*
	P value		0.015*
	N	92	92

In the study there was significant positive correlation between HbA1c and Serum Ferritin among male controls i.e. with increase in HbA1c there was significant increase in Serum Ferritin and vice versa.

FIGURE 11: Scatter plot showing Correlation between HbA1c and Serum Ferritin among male controls



DISCUSSION

Serum ferritin, a reflector of body iron stores was significantly higher in diabetic patients when compared to controls and this significantly increased as duration of diabetes increased. This possibly reflects the subclinical hemochromatosis developing in a long standing diabetic patient.<sup>9</sup> Fernandez et al<sup>10</sup> in their studies concluded that increased body iron stores are possibly associated with occurrence of glucose intolerance, type-2 diabetes and gestational diabetes.

Cantur KZ et al<sup>11</sup> confirmed in their studies that poorly controlled diabetes patients had hyperferritinemia. This showed that serum ferritin was increased in diabetes as long as glycemic control was not achieved. They also found a correlation between ferritin level and diabetic retinopathy. In diabetic subjects, a positive correlation between increased serum ferritin and poor glycemic control, reflected by higher HbA1c, has been suggested by Eschwege et al.<sup>12</sup>

The probable correlation between ferritin and DM was considered first in 1993 by Kay et al.<sup>(13)</sup>, after which other studies were focused on this subject. In 1999 a survey by Ford and his colleagues in United States on 9486 diabetic adults determined high levels of ferritin in diabetics<sup>(7)</sup>. Another study by Kwant<sup>(14)</sup> on the prevalence of C282Y mutation of hemochromatosis gene ,determined the higher prevalence of this mutation in type 2 DM, that could be considered as an evidence for some relationship between these two disorders. Fernandez in 1998 studied the relationship between serum ferritin and the results of glucose tolerance test and insulin sensitivity in healthy subjects.

Some studies have determined a higher level of ferritin in people who are high risk for atherosclerosis<sup>(11)</sup>. Since insulin resistance has been considered as the basic factor in the pathogenesis of atherosclerosis<sup>(12)</sup> higher ferritin in atherosclerotic patients can be due to insulin resistance.

CONCLUSION

This study concludes that serum ferritin was higher among cases than in control group. Positive correlation was observed between HbA1c and Serum Ferritin among cases. Hence glycemic status is significantly related to serum ferritin levels among diabetics.

REFERENCES

- Braunwald M, Fauci. Diabetes Mellitus. In: Harrison's principles of internal medicine. 19th Ed. Mc Graw Hill 2001. p. 3341-4.
- Raj S, Rajan GV. Correlation between elevated serum ferritin and HbA1c in type 2

- diabetes mellitus. *Int J Res Med Sci* 2013;1:12-5
3. Carpenter, Giggs. *Diabetes Mellitus. Cecil Essentials of Medicine*. 19th ed. Saunders. 1998. p. 583.
  4. Hramiak IM, Finegood DT, Adams PC. Factors affecting glucose tolerance in hereditary hemochromatosis. *Clin Invest Med* 1997; 20 (2) :110-118. 4. Kim NH. Serum ferritin in healthy subjects and type 2 diabetes mellitus. *Med Korea* 2000; 41(3): 387-392.
  5. Jiang R, Manson JE, Meigs JB, Ma J, Rifai N, Hu FB. Body iron stores in relation to risk of type 2 diabetes in apparently healthy women. *JAMA* 2004;291:711-7.
  6. Thomas MC, MacIsaac RJ, Tsalamandris C, Jerums G. Elevated iron indices in patients with diabetes. *Diabet Med* 2004;21:798-802.
  7. Chang JS, Lin SM, Jane CJ, et al. Serum ferritin and risk of Metabolic Syndrome, a population-based study. *Asia pac J Clin Nutr* 2013; 22: 400-407
  8. Burtis CA, Ashwood ER, Bruns DE. *Teitz textbook of clinical chemistry and molecular diagnostics* 4th ed: New Delhi, Saunders Harcourt. 2006: p.856-859 & p.869-85
  9. Ditzel J, Kajeergaard J. Hemoglobin A1c concentrations after initial insulin treatment for newly discovered diabetes. *Br Med J* 1978; 1: 741-742
  10. Fernandez-Real JM, rICART-eNGEL W, Arrogo E. Serum ferritin as a component of the insulin resistant syndrome. *Diabetes Care* 1998; 21(1): 62-
  11. Cantur K Z, Cetinarslay B, Tarkun I, Canturk NZ. Serum ferritin levels in poorly- and well-controlled diabetes mellitus. *Endocr Res* 2003;29:299-306
  12. Eschevege E, Saddi R, Wacjman H, Levy R, Thibult N, Duchateau A. Haemoglobin A1c in patients on venesection therapy for haemochromatosis. *Diabete Metab* 1982;8:137-40
  13. Kaye TB, Guay AT, Simonson DC. Non-insulindependent diabetes mellitus and elevated serum ferritin level. *J Diabetes Complications* 1993;7:246-9.
  14. Kwant J. Patients with type 2 diabetes have a high frequency of the C282 mutations of hemochromatosis gene. *Clin Invest Med* 1998; 21 (6): 251-257.