Scholars Journal of Applied Medical Sciences (SJAMS)
Abbreviated Key Title: Sch. J. App. Med. Sci.
ISSN 2320-6691 (Online)
ISSN 2347-954X (Print)

A Unit of Scholars Academic and Scientific Society, India
www.saspublishers.com

Biochemistry

A Correlative Study of Serum Ferritin Concentration and Glycated Hemoglobin in Type II Diabetes Mellitus

Dr. Priyanka Mishra[1], Dr. Biswajit Das[2*], Dr. Geetika Mohan[3], Dr. Saurav Rai[4], Dr. Ujjwal Kumar[5], Dr. Ayaz Khurram Mallick[6]

[1,3-5]Postgraduated students, Dept of Biochemistry, Rohilkhand Medical College and Hospital, Bareiliy, India
[2]Professor and Head, Dept of Biochemistry, Rohilkhand Medical College and Hospital, Bareiliy, India
[6]Associate Professor, Dept of Biochemistry, Rohilkhand Medical College and Hospital, Bareiliy, India

Original Research Article

***Corresponding author**
Dr. Biswajit Das

Article History
Received: 04.02.2018
Accepted: 19.02.2018
Published: 28.02.2018

DOI:
10.36347/sjams.2018.v06i02.040

Abstract: According to the Diabetes Atlas 2006 published by the International Diabetes Federation, the number of people with Diabetes in India currently around 40.9 million is expected to rise to 69.9 million by 2025. The present study has been undertaken to study the association between body iron store and diabetes mellitus by comparing serum ferritin and HbA_{1c} levels. 70 diagnosed patients of Type II Diabetes Mellitus aged between 30 to 80 years were taken as cases and 70 apparently healthy age and gender matched individuals were taken as controls. Fasting and post prandial plasma glucose, serum ferritin and HbA_{1c} levels were estimated by glucose oxidase-peroxidase method, solid phase direct sandwich ELISA method and Particle enhanced immune turbid metric method. Our study shows that the maximum number of cases between age groups of 41-50 years and mean ± SD of blood sugars (FBS and PPBS) serum ferritin and HbA1c were highly significant in study group in comparison to healthy control. Thus routine screening for serum ferritin should be carried out in person with impaired glucose tolerance to assess the body iron store and the risk of development of diabetes. There was a positive correlation between serum ferritin and FBS, PPBS, and HbA1c.

Keywords: FBS, PPBS, ferritin, HbA1c, Type II diabetes mellitus.

INTRODUCTION

Diabetes mellitus is one of the most prevalent endocrine disorders in the world. Although type II D.M. is more common than type I, its pathogenesis is well understood. Kaye and Fedstate have reported the possibility for a link between subclinical hemochromatosis and type II DM [1, 2].

Diabetes mellitus type II is caused by a complex interaction of genetics and environmental factors and it is characterized by impaired insulin secretion, insulin resistance, excessive hepatic glucose production and abnormal fat metabolism. The nature of the association between abnormal iron storage and the development of type II diabetes among individuals without hemochromatosis remains unchanged. Serum ferritin an acute phase reactant is a marker of iron stores in the body. The regulation of blood iron levels is mediated by the protein ferritin. Ferritin can release iron if the blood has a low iron concentration and it can help to store excess iron if the blood and tissues have a high iron concentration [3,4]. Recent studies indicate that increased body iron stores and subclinical hemochromatosis has been associated with the development of glucose intolerance and type 2 DM. Increased serum ferritin reflecting body iron overload is often associated with measures of insulin resistance, such as elevated blood glucose and insulin level[3]. In addition, two prospective studies have identified an independent association between baseline elevation in iron stores and the incidence of diabetes [5, 6]. Glycated hemoglobin (hemoglobin A1C or Hb1c; sometimes also called HbA1c) is a form of hemoglobin used primarily to identify the average plasma glucose concentration over prolonged periods of time. It is formed in a non-enzymatic pathway by hemoglobin's normal exposure to high plasma levels of glucose. The measurement of glycosylated haemoglobin (GHb) is one of the well-established means of monitoring glycemic control in patients with diabetes mellitus [7]. The use of hemoglobinA1c for monitoring the degree of control of glucose metabolism in diabetic patients was first proposed in 1976 [8]. The clinical significance of HbA1c test was cemented by Diabetes Control and Complications Trial (DCCT) in type 1diabetes [8] and the United Kingdom Prospective Diabetes Study (UKPDS) in type 2 diabetes [9]. The studies showed that HbA1c is an important marker in assessing a

patient's risk of microvascular complications and hypoglycemia. Hence, measurement of both HbA1c and blood glucose levels are now used in the routine management of patients with type 1 and type 2 diabetes [10]. Several recent studies found that, high serum ferritin levels in uncontrolled Type 2 D.M. patients and it has been shown that lowering elevated serum ferritin levels correlated well with diabetic control and improved fasting plasma glucose and glycosylated hemoglobin. It has been suggested that serum ferritin could be a marker of Insulin Resistance Syndrome. There is paucity of information regarding association of serum ferritin with glycemic control in type 2 diabetic patients in India.

Hence the present study is thus an attempt to find the relation between body iron store and diabetes by comparing serum ferritin and HbA1c levels.

MATERIALS AND METHODS

Case control study was conducted at the Department of Biochemistry, Rohilkhand Medical College and Hospital (RMCH), Bareilly, Uttar Pradesh after obtaining clearance from institutional ethical committee. Study was done in the year of 2015-16. The study population comprise of two groups, the cases and the controls. 70 diagnosed patients of Type II Diabetes Mellitus aged between 30 to 80 years was taken as cases and 70 apparently healthy age and gender matched individuals was taken as controls. Patients suffering from Type-I diabetes mellitus or other states associated with altered serum ferritin levels like hemochromatosis, chronic alcoholics, hepatitis, patients with repeated blood transfusions, iron deficiency anaemia and hypothyroidism were excluded fron the study.5 ml venous blood samples were collected from antecubital vein after an overnight fasting from all participant's with aseptic precautions. The serum, plasma and whole blood were used for estimation of serum ferritin, FBS, and $HbA_{1\,C}$ respectively. 2 ml post prandial blood collected for PPBS .The estimation of the biochemical parameters were carried out within 4-6 hrs.

The following tests were done in each sample during the study.

- Fasting plasma glucose and post prandial plasma glucose estimation was done by using commercially available kits based on GOD-POD (glucose oxidase-peroxidase method) by Chem 5 semiautoanalyzer
- Serum ferritin levels were estimated by ErbaLisascan II using commercially available Ferritin Elisakit is a solid phase direct sandwich ELISA method.
- HbA_{1c} Levels was estimated by automated analyser ERBA EM360 using commercially available kit Particle enhanced immune turbid metric method.

Statistical Analysis

Data were presented as mean ± SD. Comparison of serum levels of the parameters between cases and control was performed by student's t test and $p < 0.05$ was considered as statistically significant.

RESULTS

Table 1 and Fig 1 shows that maximum number of patients in the e age group of 41-50 years with 37.1%, followed by 51-60 years with 27.1%. Least common age group >70 years with 7.2%.

Table-1: Distribution of patients according to age in type ii diabetic mellitus

AGE GROUP IN YEARS	NUMBER	PERCENTAGE (%)
31-40	10	14.3%
41-50	26	37.1%
51-60	19	27.1%
61-70	10	14.3%
>70	5	7.2%
TOTAL	70	100.0%

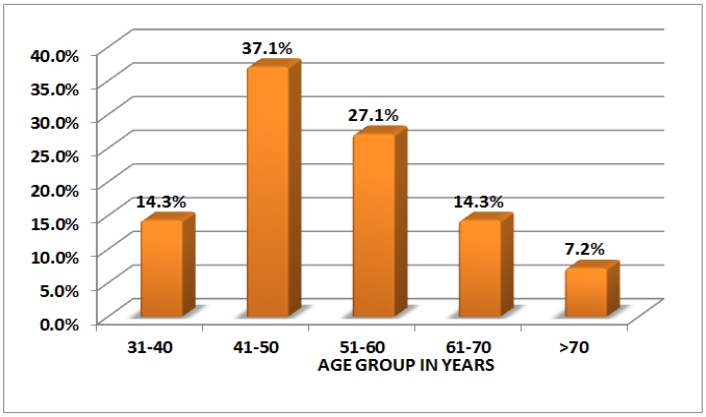

Fig-1: Distribution of patients according toage in type ii diabetic mellitus

Table 2; Fig2 shows the different biochemical parameters of study group and control and found that the plasma fasting and post prandial glucose were significantly higher in cases than control. Ferritin levels were also significantly increased in cases. High significant value of HbA1C also observed in cases in comparison to control.

Table-2: Comparison of mean ± SD of serum ferritin, FBS, PPBS and HbA1c in cases and control group

	MEAN	S.D	t-value	p-value
HbA1c (%)				
CASE	8.56	1.85	15.48	< 0.001**
CONTROL	4.97	0.58		
FBS(mg/dl)				
CASE	127.34	17.76	4.462	< 0.001**
CONTROL	60.59	56.72		
FERRITIN(ng/ml)				
CASE	214.16	220.26	41.52	< 0.001**
CONTROL	96.49	14.97		
PPBS(mg/dl)				
CASE	175.0	18.52	4.460	< 0.001**
CONTROL	95.65	13.72		

** Highly significant

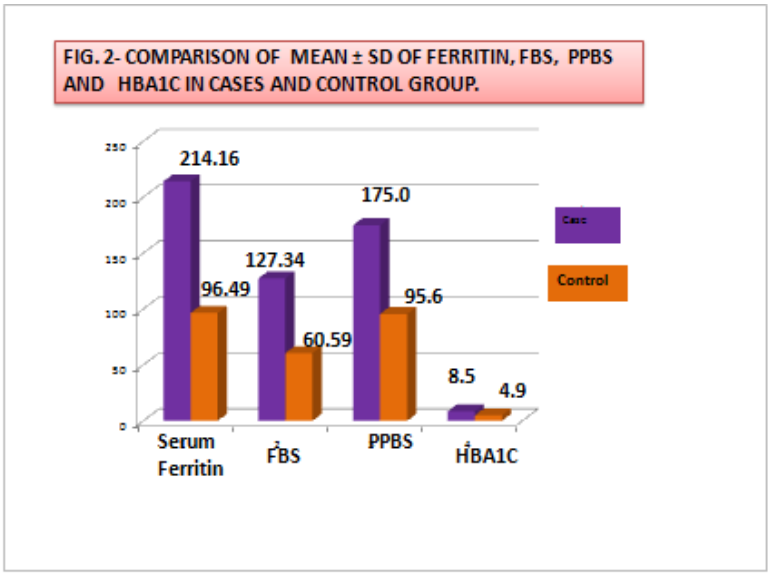

Fig-2: Comparison of mean ± SD of ferritin, FBS, PPBS and HbA1c in cases and control group

Table-3: Shows the correlation of different biochemical parameters in type II diabetic mellitus

Correlations					
		HbA1C	FBS	PPBS	FERRITIN
HbA1c	Pearson Correlation	1	.734**	.726**	.070
	Sig. (2-tailed)		.000	.000	.566
	Sum of Squares and Cross-products	236.93	1666.23	1720.40	1967.06
	Covariance	3.43	24.15	24.93	28.51
	N	70	70	70	70
FBS	Pearson Correlation	.734**	1	.754**	.051
	Sig. (2-tailed)	.000		.000	.677
	Sum of Squares and Cross-products	1666.23	21765.77	17114.00	13686.84
	Covariance	24.15	315.45	248.03	198.36
	N	70	70	70	70
PPBS	Pearson Correlation	.726**	.754**	1	.064
	Sig. (2-tailed)	.000	.000		.600
	Sum of Squares and Cross-products	1720.40	17114.00	23676.00	17954.40
	Covariance	24.93	248.03	343.13	260.21
	N	70	70	70	70
FERRITIN	Pearson Correlation	.070	.051	.064	1
	Sig. (2-tailed)	.566	.677	.600	
	Sum of Squares and Cross-products	1967.06	13686.84	17954.40	3347476.18
	Covariance	28.51	198.36	260.21	48514.15
	N	70	70	70	70
Correlation is significant at the 0.01 level (2-tailed).					

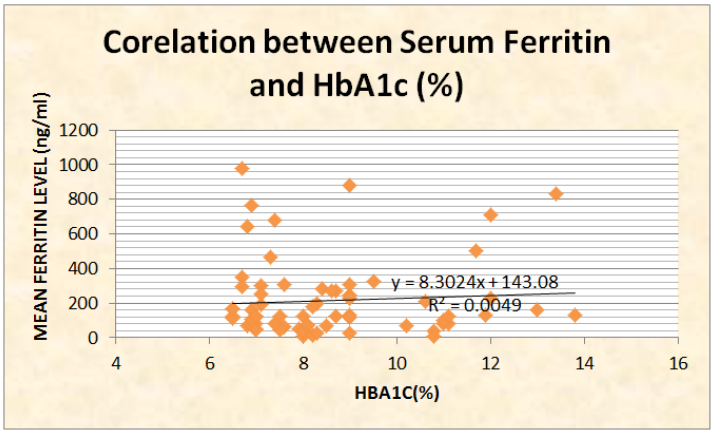

Fig-3: Correlation of ferritin with hba1c in cases

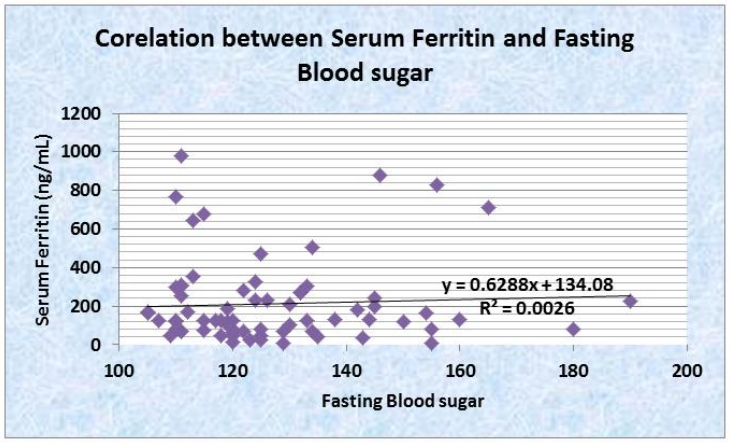

Fig-4: Correlation of ferritin with fbs in cases

Fig 4 shows correlation of serum ferritin with fasting blood sugar in cases. The fasting blood sugar r-value is 0.051 and the p-value is 0.677. Fig 3 shows correlation of serum ferritin with HbA1c in cases. The HbA1c r-value is 0.070 and the p-value is 0.566.

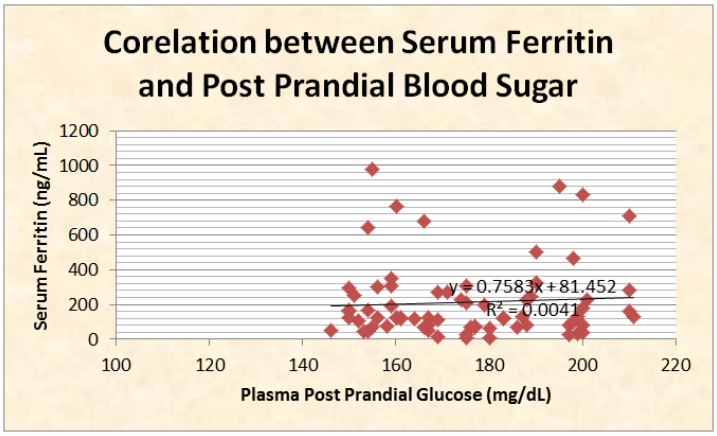

Fig-5: Correlation of ferritin with ppbs in cases

Fig-5: shows correlation of serum ferritin with post prandial blood sugar in cases. The post prandial blood sugar r-value is 0.064 and the p-value is 0.600.

DISCUSSION

The present study was based on true estimation of serum ferritin and HbA1c in 70 diagnosed cases of type II diabetes mellitus and 70 apparently healthy age and sex matched individuals who served as controls. In the present study out of 70 patients of type II D.M., maximum number of patients were in the age group of 41-50 years with(37.1%) , followed by 51-60 years with(27.1%). Least common age group is >70 years with 7.2% as shown in Table -1 and fig-1. This finding was observed by other authors namely Sejong Bae et al [11], Fernandez-Real JM et al [12], Cantur KZ et al [13]. From table 2 and Fig 2; it has been observed that the mean ± SD of serum ferritin (214.16 ± 220.26 vs 96.49 ±14.97), plasma fasting (127.34±17.7vs 60.59 ±65.6) and PPBS(175 ±18.5 vs 95.6 ± 13.7) and also HbA1c (8.56± 1.8 vs 4.97±0.58) values were highly significant in cases in comparison to control ($p < 0.001$). We also observed the correlation of serum ferritin with HbA1c, FBS and PPBS as shown in table 3 and fig 3,4 and 5. Nan Hee Kim *et al*. [14]. at Korea University Hospital reported the similar finding in 2000. Similar finding also observed by Bansal Pankaj et al. in 2011 conducted on 200 Indian male diabetic patients aged between 35-65 years and age/sex matched 200 healthy controls, serum ferritin levels were high in cases (185±3.5ng/ml) compared to controls (113±4.6ng/ml) [15]. In 2008, a study was conducted on 50 type 2 diabetics with poor glycemic control (group I), 53 type 2 diabetics with good glycemic control (group II) and 40 healthy non-diabetic controls, it was found that serum ferritin was increased in group I, though the same correlation did not exist in group II [16]. In 2014, the elevation of serum. Ferritin level in type II Diabetes mellitus also reported by Chandrasekhar H.R *et al*. [17]. Jeevan K. Shetty *et al*. evaluated from the study that ferritin levels were positively correlated with FBS, PPBS and HbA1c. He also reported that diabetics with increased level of serum ferritin had significantly poor glycaemic control reflected by higher levels of HbA1c. [18]. Recent studies indicate that increased body iron stores and subclinical hemochromatosis has been associated with the development of glucose intolerance and type 2 DM. Increased serum ferritin reflecting body iron overload is often associated with measures of insulin resistance, such as elevated blood glucose and insulin level [3]. Some authors believed that elevation of serum ferritin level in type II Diabetes mellitus causes 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 [19-23]. Raised Serum Ferritin may possibly be related to the occurrence of long term complications of diabetes, both micro vascular and macro vascular the level of glycated hemoglobin (HbA1c) reflects the mean blood glucose concentration over the preceding 6–8 weeks [14, 24].

CONCLUSION

In our study it has been observed that type II diabetes mellitus is more prevalent in age group of 41-50 years with 37.1%. Glycosylated hemoglobin assay provides a better discriminate of diabetic from the non-diabetic than a rapidly fluctuating variable like blood sugar. Discrepancy between the results of glycosylated hemoglobin and results of blood sugar level of patients, gives an indication to treating physician to look back into detail history and modify the therapeutic regimen accordingly. Ferritin is the marker of iron overload and has a role in insulin resistance. Thus routine screening for serum ferritin should be carried out in person with impaired glucose tolerance to assess the body iron store and the risk of development of diabetes. There was a

positive correlation between serum ferritin and FBS, PPBS, and HbA1c. The major issue arises whether to estimate serum ferritin routinely in all type II diabetes patients and whether to set a cutoff value of serum ferritin for good glycaemic control. To reduce the pandemic of type II diabetes, it is necessary to have an improved understanding of its etiology, pathogenesis and pathophysiology to focus therapeutic and research efforts appropriately.

REFERENCES

1. Braunwald M, Fauci. Diabetes Mellitus. In: Harrison's principles of internal medicine. 15thEd.McGraw Hill 2001.p. 3341-4.
2. Carpenter, Giggs. Diabetes Mellitus. Cecil Essentials of Medicine. 19thed. Saunders. 1998. P. 583.
3. 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.
4. Casiday R, Frey R. Iron use and storage in the body: ferritin and molecular representations. Can be found under http://www. Chemistry. wustl. edu/~ edudev/LabTutorials/Ferritin/Ferritin. Html. 2000.
5. Thomas MC, MacIsaac RJ, Tsalamandris C, Jerums G. Elevated iron indices in patients with diabetes. Diabet Med 2004; 21:798-802.
6. Sharifi F, Sazandeh SH. Serum ferritin in type 2 diabetes and its relationship with HbA1c. Acta Med Iran 2004; 42:142-5.
7. 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 Sep 30;329(14):977-86.
8. Koenig RJ, Peterson CM, Jones RL, Saudek C, Lehrman M, Cerami A. Correlation of glucose regulation and hemoglobin AIc in diabetes mellitus. New England Journal of Medicine. 1976 Aug 19;295(8):417-20.
9. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). The lancet. 1998 Sep 12;352(9131):837-53.
10. Marathe PH, Gao HX, Close KL. American Diabetes Association standards of medical care in diabetes 2017. Journal of diabetes. 2017 Apr 1;9(4):320-4.
11. Bae S, Le TD, Singh KP, Blair SN, Morro JR. Association between serum ferritin, cardiorespiratory fitness and risk of type 2 diabetes: aerobics center longitudinal study. 18th world IMACS. InMODSIM Congress 2009 (pp. 103-116).
12. Fernández-Real JM, Peñarroja G, Castro A, García-Bragado F, López-Bermejo A, Ricart W. Bloodletting in high ferritin type 2diabetes: effects on vascular reactivity. Diabetes Care 2002; 25(12): 2249-2255
13. 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
14. Kim NH. Serum ferritin in healthy subjects and type 2 diabetes mellitus. *Med Korea* 2000;41:387-92
15. Pankaj B, Puja B, Akshay R, Kansal HM. Is serum ferritin associated with type ii diabetes mellitus: A clinical study in a representative indian population. J Med Sci Res. 2011;2:20-4.
16. Shetty JK, Prakash M, Ibrahim MS. Relationship between free iron and glycated hemoglobin in uncontrolled type 2 diabetes patients associated with complications. Indian Journal of Clinical Biochemistry. 2008 Jan 1;23(1):67.
17. Chandrashekhar HR, Shekar HS, Nagaraju K, Bhagavan BC. Association of serum ferritin levels with glycemic control in type-2 diabetes mellitus. Indian Journal of Pharmacy Practice. 2014;7(1).
18. Shetty JK, Prakash M, Ibrahim MS. Relationship between free iron and glycated hemoglobin in uncontrolled type 2 diabetes patients associated with complications. Indian Journal of Clinical Biochemistry. 2008 Jan 1;23(1):67.
19. Ford ES, Cogswell ME. Diabetes and serum ferritin concentration among U.S. adults. Diabetes Care 1999;22:1978-83.
20. Kaye TB, Guay AT, Simonson DC. Non-insulin-dependent diabetes mellitus and elevated serum ferritin level. Journal of Diabetes and its Complications. 1993 Oct 1;7(4):245-9.
21. Gallou G, Guilhem I, Poirier JY, Ruelland A, Legras B, Cloarec L. Increased serum ferritin in insulin-dependent diabetes mellitus: relation to glycemic control. Clinical chemistry. 1994 Jun 1;40(6):947-8.
22. Fernández-Real JM, Peñarroja G, Castro A, García-Bragado F, López-Bermejo A, Ricart W. Bloodletting in high-ferritin type 2 diabetes: effects on vascular reactivity. Diabetes care. 2002 Dec 1;25(12):2249-55.
23. Moczulski DK, Grzeszczak W, Gawlik B. Role of hemochromatosis C282Y and H63D mutations in HFE gene in development of type 2 diabetes and diabetic nephropathy. Diabetes care. 2001 Jul 1;24(7):1187-91.
24. Eshed I, Elis A, Lishner M. Plasma ferritin and type 2 diabetes mellitus: a critical review. Endocrine research. 2001 Jan 1;27(1-2):91-7.