IOSR Journal of Biotechnology and Biochemistry (IOSR-JBB)
ISSN: 2455-264X, Volume 4, Issue 6 (Nov. – Dec. 2018), PP 53-57
www.iosrjournals.org

Iron and ferritin levels showed positive correlation with glycosylated hemoglobin in type 2 diabetic patients

Viswan Santhosh[1], Amar Nagesh Kumar[2]
[1]*Professor and HOD, Department of Biochemistry, Karpaga Vinayaga Institute of Medical Sciences and Research Centre, Madhurantagam, Tamilnadu*
[2]*Assistant Professor, Department of Biochemistry, Karpaga Vinayaga Institute of Medical Sciences and Research Centre, Madhurantagam, Tamilnadu*
Corresponding Author: Dr G Amar Nagesh Kumar PhD

Abstract: *Type 2 diabetes mellitus is one of the most prevalent diseases worldwide which is characterized by hyperglycemia. Chronic hyperglycemia causes increased glycation of proteins especially hemoglobin. It is well known that measurement of glycosylated hemoglobin (HbA1C) is useful in monitoring of glucose control in diabetic patients. Study consists of 45 type 2 diabetic patients. Out of which 26 patients were males and 19 were females. Fasting and postprandial blood samples were collected and analyzed for serum fasting glucose (FBS), postprandial glucose (PPBS), hemoglobin, iron, unsaturated iron binding capacity (UIBC), ferritin levels along with glycosylated hemoglobin (HbA1C) in all the subjects using commercially available kits in the market. All the results were expressed as mean and standard deviation. Pearson correlation was used to find out the correlation among the parameters. In the present study increased serum iron levels were found. FBS, PPBS and HbA1c levels had shown positive correlation with serum iron and ferritin levels. A 'r' value >0.4 is considered as significant with a p value of <0.05. In early 1990s, iron stores were expressed as serum ferritin concentration. Increased serum iron was observed in subjects with metabolic syndrome. Elevated serum ferritin levels might reflect systemic inflammation leading oxidative stress which can lead to progression of metabolic syndrome to type 2 diabetes (T2DM). Finding of the present study suggests that increased serum iron and ferritin levels has potential role in the development of type 2 diabetes.*

Keywords: *Type 2 diabetes, iron stores, ferritin, glycosylated hemoglobin, metabolic syndrome*

Date of Submission: 14-12-2018 Date of acceptance: 31-12-2018

I. Introduction

Type 2 Diabetes mellitus is one of the most prevalent diseases worldwide. It is characterized by hyperglycemia[1]. Factors responsible for hyperglycemia include diminished insulin secretion, decreased glucose utilization, and increased glucose production. Chronic hyperglycemia causes increased glycation of protein especially hemoglobin[2]. It is well known that estimation of glycosylated hemoglobin (HbA1C) gives the average blood glucose value of three months. Measurement of glycated proteins primarily HbA1c (glycated hemoglobin) is effective in monitoring long term glucose control in people with diabetes mellitus[3].

Several mechanisms have been proposed for the onset and progression of type 2 diabetes mellitus and its complications, one of which is alteration in the mineral status[2-4]. It is well known that iron as an important mineral for human health. Iron is involved in binding and transporting of oxygen and carbon dioxide, regulating cell cycle, required as iron-sulphur proteins in electron transport chain etc[5-7]. In the body iron is stored in the form of ferritin and the transport form of iron is transferrin. So clinically, estimation of serum ferritin concentration gives an idea about the body iron stores. Ferritin is not only an important mineral but also acts an acute-phase reactant. Therefore, it is expected to increase under conditions of low-grade inflammation[4-6].

Attention of researchers has been given on iron and ferritin levels, since the identification of link between insulin resistance and serum ferritin for the first time in 1998. In some studies it is showed that insulin resistant patients had mild abnormalities of iron metabolism[5,6]. Elevated serum ferritin levels may induce diabetes through a variety of mechanisms like oxidative damage to pancreas, impairment of hepatic insulin extraction and interference with insulin's ability to suppress hepatic glucose production[4-6]. It is also observed that serum ferritin levels correlated with serum triglycerides, glucose and other markers of insulin resistance[6-8]. In this context, it is observed that there is lack of sufficient data and less number of research studies on serum iron, ferritin levels in diabetic patients in our population. Hence, the present study is undertaken to find out whether there is any relation between serum iron, total iron binding capacity (TIBC), ferritin levels with glycosylated hemoglobin (HbA1C) level in type 2 diabetic patients.

II. Material And Methods

This study was conducted at Karpaga Vinayaga Institute of Medical Sciences, Madhurantagam, Tamilnadu. The study population consisted of 45 subjects with known type 2 diabetes; out of which 26 patients were males and 19 were females. The subjects selected for the study were in the age group of 34-50 years. Mean age of the study population is 41.8 ± 0.74 years. Patients with type 2 diabetes mellitus without any diabetic related complications such as neuropathy, retinopathy, nephropathy, hypertension were recruited for the study. Diabetic patients with known hypertension, anemia, chronic kidney diseases and other complications were excluded from the study.

5 ml of blood was collected from the anticubital vein in fasting and postprandial state from all the subjects. The blood samples were collected in fluoride tubes, clot activated tubes and EDTA tubes for the estimation of glucose, serum iron, ferritin and hemoglobin and glycosylated hemoglobin (HbA1C) respectively.

Serum glucose is estimated by Glucose Oxidase – Peroxidase method using Biosystems kit. Serum Iron is estimated by Ferrozine method using Biosystems kit. Serum Unsaturated Iron Binding Capacity (UIBC) was estimated by Ferrozine method using Biosystems kit. These parameters were analyzed on fully automated biochemistry analyzer BA 200 (Biosystems, Barcelona, Spain). Total Iron Binding Capacity (TIBC) was calculated by addition of serum Iron and UIBC. Hemoglobin is estimated by rapid kit method, Glycosylated hemoglobin was estimated by using Biosystems kit, turbidimetry method on fully automated biochemistry analyzer BA 200. Estimation of serum ferritin was done by using automated analyzer Biomeriux Minividas by Enzyme Linked Immunofluroscent Assay (ELFA) method. The normal ranges for the parameters are mentioned in table 1.

SPSS 20.0 version was used for statistical analysis. All the results were expressed as mean and standard deviation. Pearson correlation was used to find out the correlation of serum iron, TIBC, ferritin levels with HbA1C. A p value less than 0.05 is considered as significant.

III. Results

Table 2 shows the descriptive statistics of all studied parameters in type 2 diabetic patients. It is evident from the table 1 the mean and standard deviation of FBS values 123.51 ± 13.32 mg/dl, while that of PPBS is 210.24 ± 28.28 mg/dl. The mean value of Hemoglobin is 12.86 ± 0.82 g/dl. The mean and standard value of glycosylated hemoglobin (HbA1C) is 7.70 ± 0.35. The mean value of serum iron is 186.88 ± 20.31 µg/dl, serum unsaturated Iron Binding Capacity (UIBC) 51.88 ± 9.48 µg/dl, serum TIBC is 238.77 ± 27.18 µg/dl. The mean serum ferritin level is 228.06 ± 24.72 ng/ml (Table 2).

Table 3 shows the Pearson correlation of all the parameters and their values. A 'r' value greater than 0.4 is considered as significant with a p value <0.05. FBS and PPBS values showed a positive correlation with HbA1C.A strong positive correlation was observed between HbA1C and serum IRON, TIBC and ferritin levels (Figure 1 and Figure 2). Similarly positive correlation was observed with serum ferritin levels and TIBC (Table 2).

IV. Discussion

In early 1990s, iron stores were expressed as serum ferritin concentration, and increased serum iron in the body was observed in subjects with metabolic syndrome[9,10]. Insulin resistance was also found to be associated with total body iron stores, even in the presence of normal glucose tolerance[10,11]. Serum ferritin concentration in the apparently healthy general population was positively correlated with fasting and postprandial glucose[8-10]. Iron stores have accordingly been associated with increased risk of developing T2DM[4-6]. The first prospective case control study was published by Salonen et al[10] in 1998. They reported that there is positive correlation between the ratio of transferrin to ferritin and risk of type 2 diabetes mellitus (T2DM) [4-6, 10, 14]. Since then only few authors have studied this association, reviewed and updated in several articles[11-15].

The present study was designed to find out the correlation of serum iron, TIBC, ferritin levels with glycosylated hemoglobin (HbA1C) in type 2 diabetic patients. Earlier studies showed evidences about the relationship between iron stores and type 2 diabetes. Increased body iron store is most commonly seen in hemochromatosis which is associated with adverse health outcomes. From the results of the present study, it is evident that increased concentration of serum ferritin in patients with type 2 diabetes is associated with serum glucose and HbA1C level (Figure 1 and Figure 2). It is also evident from the study that an increased body iron store reflected by serum ferritin levels is statistically significant and positively correlated with FBS, PPBS (Table 2). In the present study it is observed that there is positive correlation between serum iron levels and HbA1c (Figure 2) in type 2 diabetic patients indicating that increased iron levels leads to poor glycemic control. These findings are on par with the previous studies[5,7,10-12, 14] . Increased HbA1c indicates, hyperglycemia causing increased glycation of hemoglobin and increased release of free iron from glycated proteins like hemoglobin[15]. This makes a vicious cycle of hyperglycemia, glycation of hemoglobin and increase in levels of free iron and

ferritin. This increased presence of iron pool will enhance oxidant generation leading damage to biomolecules[14-16].

Elevated serum ferritin levels might reflect systemic inflammation in addition to increased body iron stores[16]. It has been observed that inflammation regulates expression of ferritin mRNA & protein levels and its secretion[14-16]. Excessive iron deposits produce hydroxyl radicals which cause lipid peroxidation. This leads to DNA fragmentation and tissue damage. Therefore, one of the mechanisms involved in progression of metabolic syndrome to T2DM is inflammation and oxidative stress mediated through ferritin[15].

V. Conclusion

The present study results suggest that increased serum iron and serum ferritin levels has the potential role in the development of type 2 diabetes. Therefore, it is suggested that estimation of serum iron and serum ferritin levels should be considered to identify patients who are at risk of developing T2DM. More number of multicentric based studies needs to be conducted at all levels to create the data on iron, total iron binding capacity (TIBC) and ferritin levels in Indian Diabetic patients.

Acknowledgements

Our sincere thanks to the Managing Director, Dr Regupathy Annamalai, M.S Ortho., MCh, for giving permission and support in accomplishing this project.

References

[1]. Kumar R, Kumar AN, Ahmed S. Changes in Erythrocyte Membrane in Type-2 Diabetes Mellitus with and without Dyslipidemia. J Diabetes Metab 2011;2:141. doi:10.4172/2155-6156.1000141
[2]. Dongiovanni P, Valenti L, Ludovica Francanzani A, Gatti S, Cairo G, Fargion S. Iron depletion by desferroxamine upregulates glucose uptake and insulin signaling in hepatoma cells and in rat liver. Am J Pathol 2008; 172:738-47.
[3]. Wilson JG, Lindquist JH, Grambow SC, Crook Ed, Maher JF. Potential role of increased iron stores in diabetes. Am J Med Sci. 2003; 325: 332-339.
[4]. Fernandez-Real JM, McClain D, Manco M. Mechanisms Linking Glucose Homeostasis and Iron Metabolism Toward the Onset and Progression of Type 2 Diabetes. Diabetes Care 2015; 38:2169–2176. DOI: 10.2337/dc14-3082
[5]. Sumesh Raj, G. V. Rajan. Correlation between elevated serum ferritin and HbA1c in type 2 diabetes mellitus. Int J Res Med Sci. 2013; 1(1):125.
[6]. Megan Jehn, Jeanne M. Clark, Eliseo Guallar. Serum ferritin and risk of the metabolic syndrome in U.S. adults. Diabetes Care. 2004; 27(10):2422-8.
[7]. Fernandez-Real JM, Ricart-Engel W, Arroyo E, et al. Serum ferritin as a component of the insulin resistance syndrome. Diabetes Care 1998; 21:62–68.
[8]. Fernandez-Real JM, L opez-Bermejo A, Ricart W. Cross-talk between iron metabolism and diabetes. Diabetes 2002; 51:2348–2354.
[9]. Bozzini C, Girelli D, Olivieri O, et al. Prevalence of body iron excess in the metabolic syndrome. Diabetes Care 2005; 28:2061–2063.
[10]. Salonen JT, Tuomainen TP, Nyyss¨onen K, Lakka HM, Punnonen K. Relation between iron stores and non-insulin dependent diabetes in men: case-control study. BMJ 1998; 317:727.
[11]. Swaminathan S, Fonseca VA, Alam MG, Shah SV. The role of iron in diabetes and its complications. Diabetes Care 2007; 30:1926–1933.
[12]. Simcox JA, McClain DA. Iron and diabetes risk. Cell Metab 2013; 17:329–341.
[13]. Fernandez-Real JM, Manco M. Effects of iron overload on chronic metabolic diseases. Lancet Diabetes Endocrinol 2014; 2:513–526
[14]. Rui Jiang, JoAnn E. Manson, James B. Meigs, Jing Ma, Nader Rifai, Frank B. Hu. Body iron stores in relation to risk of type 2. JAMA. 2004; 291(6):7117.
[15]. Liang Sun, Oscar H. Franco, Frank B. Hu, Lu Cai, Zhijie Yu, Huaixing Li, et al. Ferritin Concentrations, metabolic syndrome, and type 2 diabetes in middle-aged and elderly Chinese. J Clin Endocrinol Metab. 2008; 93(12):4690-6.
[16]. Jeevan K. Shetty, Mungli Prakash, Mohammad S. Ibrahim. Relationship between free iron and glycated hemoglobin in uncontrolled type 2 diabetes patients associated with complications. Indian J Clin Biochem. 2008; 23(1):67-70.

Table 1: Shows the normal ranges of all the parameters

S.NO	Parameter	Normal ranges
1	FBS	70 – 110 mg/dl
2	PPBS	80 – 160 mg/dl
3	Hemoglobin	Males: 13 – 17 g/dl Females: 12 – 15 g/dl
4	HbA1C	< 5.7 Non Diabetic 5.8 to 6.4 Prediabetic > 6.5 Diabetic
5	IRON	Males: 65 – 175 µg/dl Females: 50 – 170 µg/dl
6	UIBC	120 – 350 µg/dl
7	TIBC	200-500 µg/dl
8	Ferritin	Males: 68 – 434 ng/ml Females: 9.3 – 159 ng/ml

Table 2: Descriptive statistics of all studied parameters in all type 2 diabetic (T2DM) subjects

S.NO	Parameter	T2DM subjects (n=45)	Range (Min. to Max.)
1	FBS (mg/dl)	123.51 ± 13.32	101-148
2	PPBS (mg/dl)	210.24 ± 28.28	168-250
3	Hemoglobin (g/dl)	12.86 ± 0.82	11-15.2
4	HbA1C (%)	7.70 ± 0.35	7-8.2
5	IRON (µg/dl)	186.88 ± 20.31	135-230
6	UIBC (µg/dl)	51.88 ± 9.48	34-68
7	TIBC (µg/dl)	238.77 ± 27.18	173-295
8	Ferritin (ng/ml)	228.06 ± 24.72	180-278

Table 3: Pearson correlation for all the studied parameters showing 'r' values

Parameter	Age	FBS	PPBS	Hb	HbA1c	IRON	UIBC	TIBC	Ferritin
Age	1	-	-	-	-	-	-	-	-
FBS (mg/dl)	0.38	1	-	-	-	-	-	-	-
PPBS (mg/dl)	0.14	**0.83****	1	-	-	-	-	-	-
Hemoglobin (gm%)	0.17	0.07	0.04	1	-	-	-	-	-
HbA1c (%)	0.07	**0.65****	**0.71****	0.05	1	-	-	-	-
IRON (µg/dl)	0.03	**0.45***	**0.54****	-0.05	**0.85****	1	-	-	-
UIBC (µg/dl)	0.16	**0.47***	**0.48***	0.07	**0.53****	**0.61****	1	-	-
TIBC (µg/dl)	0.08	**0.50***	**0.58****	-0.01	**0.81****	**0.96****	**0.81****	1	-
Ferritin (ng/ml)	-0.04	0.22	0.31	0.13	**0.65****	**0.84****	**0.58****	**0.83***	1

Level of significance *p <0.05; **p<0.01

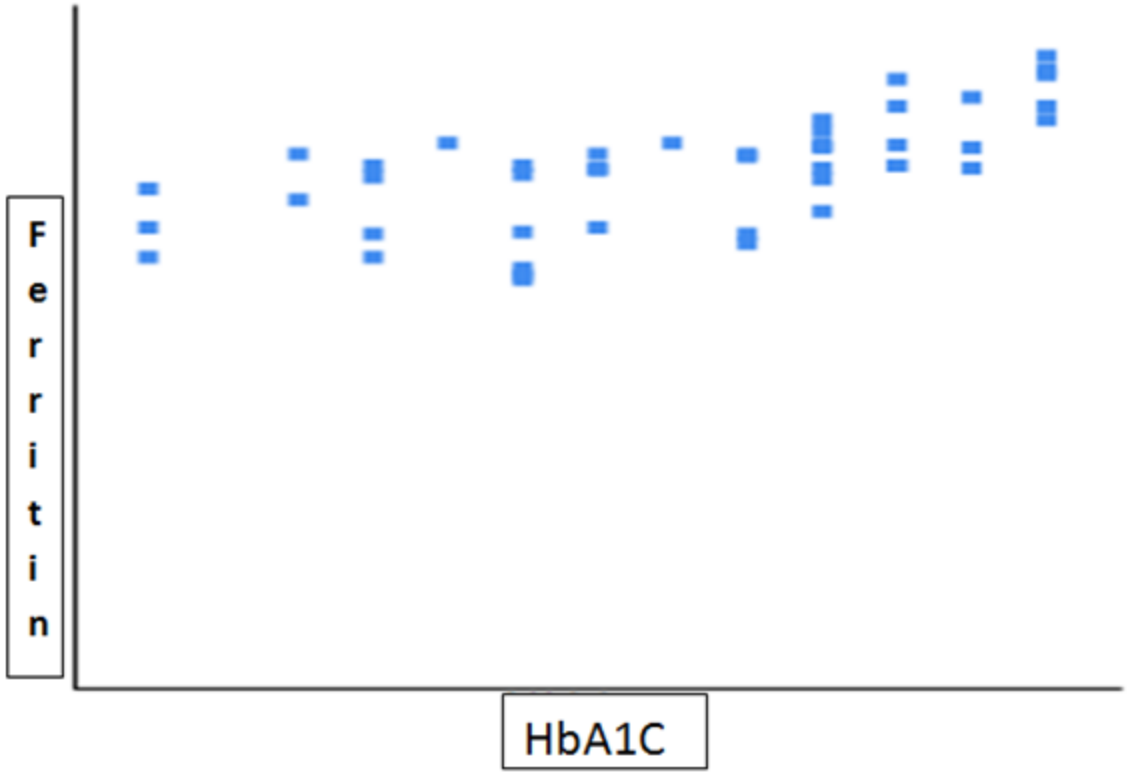

Figure 1: Correlation graph between HbA1C and serum ferritin

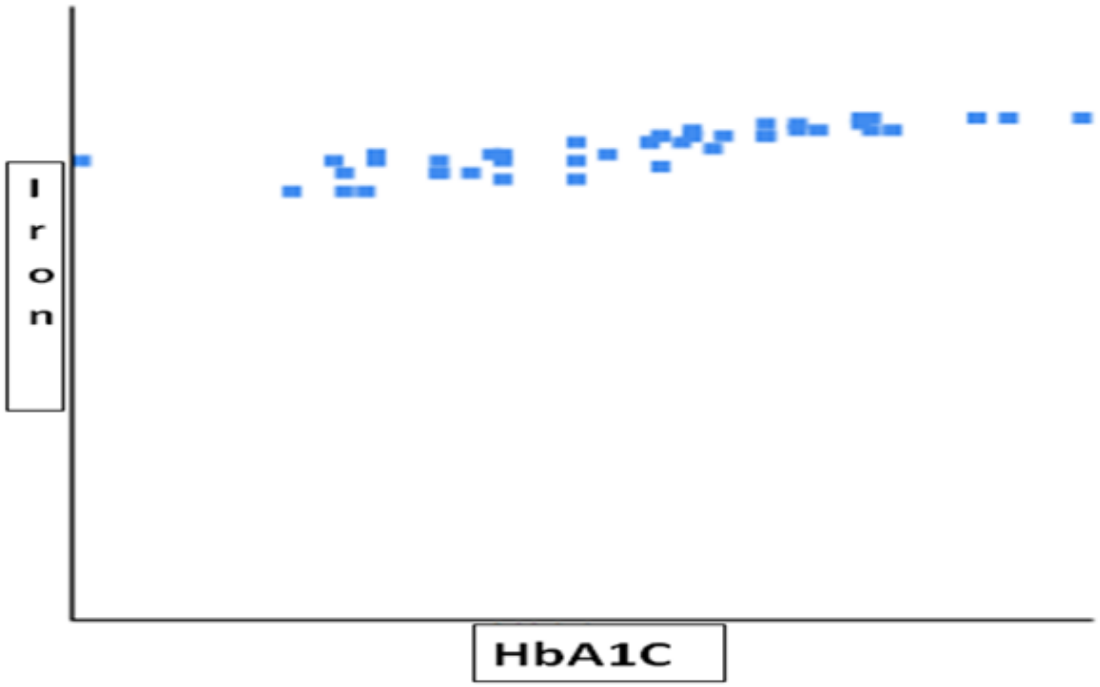

Figure 2: Correlation graph between HbA1C and serum Iron

Dr G Amar Nagesh Kumar PhD.” Iron and ferritin levels showed positive correlation with glycosylated hemoglobin in type 2 diabetic patients." IOSR Journal of Biotechnology and Biochemistry (IOSR-JBB) 4.6 (2018): 53-57.