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Research Article

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Correlation of Serum Ferritin and HbA1c in Type 2 Diabetes Patients of Tertiary Healthcare Centre in Northern India

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ABSTRACT

Background: Serum ferritin is a valuable marker of glycemic control in patients with type 2 diabetes. Measuring serum ferritin can be used as an indicator of control of glycaemia in type 2 diabetes mellitus patients. It can also be used as a marker to prevent disease complications. Therefore, the present study aimed to examine the association of HbA1c and serum ferritin in patients with type 2 diabetes.

Methods: 42 patients diagnosed with type 2 diabetes of either sex, aged between 20 and 65, were included. Analysis of serum ferritin and HbA_1c by Vitros autoanalyser was done.

Result: A positive and significant correlation was seen between HbA_1c and serum ferritin. A positive and significant correlation was also observed between HbA_1c and serum ferritin in females. Among males, the correlation was positive but non-significant. Among cases of the age group 25–40 yr positive and significant correlation was seen, and among cases of the age group 40–70 yr positive, non-significant correlation was observed.

Conclusion: Both short- and long-term relationship between serum ferritin and glycaemic control is reflected by our findings. To conclude, there are many significant issues regarding good glycemic control, whether to set a cut-off value for serum ferritin or to estimate serum ferritin routinely in all type 2 diabetes patient. Our study results show a significant relationship between serum ferritin and HbA1c levels, suggesting that serum ferritin levels can be used as a routine screening tool for the early diagnosis and treatment of diabetes.

Key-words: Diabetes mellitus, Ferritin, Glycated haemoglobin, Metabolic disorder, Type 2 Diabetes

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia due to defects in insulin action, secretion, or both [1]. Microvascular complications such as retinopathy, nephropathy, and neuropathy develop in patients with type 2 diabetes.

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The risk of considerable vessel complications such as cerebrovascular, cardiovascular, and peripheral vascular disease is also higher [2]. Approximately 5.1 million deaths occur in people between the ages of 20 and 65 from diabetes, accounting for 8.4% of all global all-cause deaths in this age group [3]. The worldwide prevalence of diabetes in 2002 was 171 million, according to the World Health Organization (WHO), and by 2030, this number will have increased to 366 million or more [4]. The most common chronic endocrine disorder is diabetes, which affects approximately 5-10% of adults worldwide [5,6]. Over the past decades, diabetes has steadily increased [4,7]. Several studies have shown that in predicting

diabetes, acute-phase reagents may be helpful [8,9]. However, several other studies failed to find this conclusion [10]. An acute phase reactant is a particular protein that responds to acute stress such as surgery, trauma, tissue necrosis, and infection. Some reactants in the acute phase are ferritin, haptoglobin, fibrinogen, C-reactive protein (CRP), and alpha acid glycoprotein [11,12]. Ferritin limits iron accessibility by accumulating in the compartment of the protein coat and plays an essential role in the acute phase response [13]. Hypoglycemia results in lower serum ferritin levels and is also associated with hyperglycemia [14]. The clear role of ferritin as a marker of excess iron in pancreatic injury or minor insulin resistance is unclear [15]. Serum ferritin converts to excess iron in the body, often associated with insulin resistance measures, insulin levels, and elevated blood sugar [16]. High glucose concentration leads to the glycation of proteins. Glycated haemoglobin (HbA1c) is of clinical importance and is the primary form of glycation of proteins. Blood sugar alone affects HbA1c. However, several studies have demonstrated that in developing countries such as India, iron deficiency anaemia, a significant public health problem and diabetes coexist with many factors. Elevated iron stores may induce diabetes through various mechanisms, such as interfering with insulin's ability to inhibit hepatic glucose production, oxidative damage to pancreatic beta cells, and impaired ability of the liver to extract insulin. Recent studies have shown that subclinical hemochromatosis and increased iron stores in the body are associated with increased glucose tolerance, metabolic syndrome and the occurrence of diabetic nephropathy, dysfunction vascular disease, retinopathy, and even type 2 diabetes [17,18]. Macrovascular complications may be associated with elevated serum ferritin [19,20]. Integrated glucose values for the previous 6–8 weeks represent HbA1c percentage and help determine glycemic status [21]. Recently, it has been noted that high body iron stores are associated with insulin resistance syndrome, type 2 diabetes, and the development of glucose intolerance [22,23]. Serum ferritin indicates body iron stores and an inflammatory marker [24,25]. The present study examined the association of HbA1c and serum ferritin in patients with type 2 diabetes as a marker of glycemic control.

MATERIALS AND METHODS

The study was conducted at the Department of Biochemistry in collaboration with the Faculty of Medicine at Eras Lucknow Medical College & Hospital, Lucknow. Forty-two patients with known type 2 diabetes aged 20 to 65 years, of both sexes, were included to estimate serum ferritin and HbA1c. Detailed history and consent were taken from the patients. Patients' serum ferritin–and HbA1c were calculated using Vitros 5600 auto-analyser using dry chemistry method. The results were analysed using the following reference range (Tables 1 and 2).

Table 1: Expected values for HbA_1c

A1c (NGSP) (%)	Interpretation
< 6.0	Non-Diabetic Range
6.0 – 7.0	ADA Therapeutic Target
>7.0	Action Suggested

Table 2: Expected values for Serum Ferritin

Ferritin	Normal range /Units = ng/ml
Normal male	17.9 – 464
Normal female<50 years of age	6.24 – 137
Normal female >50 years of age	11.1 – 264

Type 2 diabetes was diagnosed according to the ADA criteria [26].

Inclusion Criteria- All patients with known type 2 diabetes in the age group ranging from 20 to 65 years of age in both sexes were included.

Exclusion Criteria

1. History of illness like malignancy and acute and persistent infections.
2. Patients on iron therapy, steroids or immunosuppressive drugs based on history.
3. Known cases of type 1 diabetes.
4. Patients of kidney or haematological disorders.
5. All patients with newly diagnosed type 2 diabetes.
6. Patient not giving their consent.

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Statistical Analysis- Statistical data analysis was performed using the SPSS statistical analysis software (Statistical Package for Social Sciences) version 17.0. Values are represented as Numbers (%).

Ethical Approval- The Institutional Ethics Committee approved the study, Era's Lucknow Medical College, Lucknow, vide letter no. ELMC/R_Cell/EC/2022/19 dated 30/04/2022.

RESULTS

The mean age of the cases was 45.90±11.46 yr. The cases included had a minimum age 26 yr and a maximum 65 yr. Out of 42 cases, 17 (40.5%) belong to the age group 25–40 yr and 25 (59.5%) belong to the age group 41–70 yr (Fig. 1).

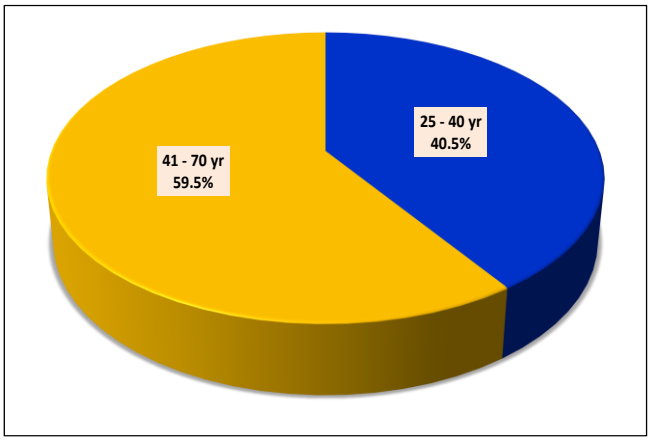

Fig. 1: Case distribution according to age groups

The distribution of cases according to sex is shown in Fig. 2. Out of 42 cases, 24 (57.1%) were females and the rest 18 (42.9%) were males. Hence, female–male proportion was 4: 3.

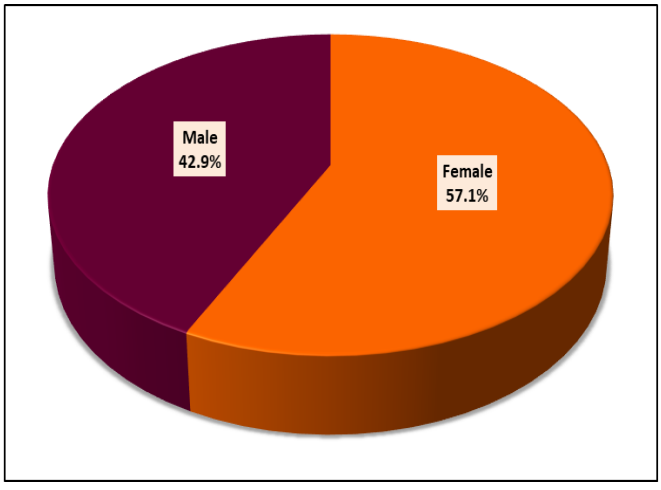

Fig. 2: Case distribution according to sex

The descriptive summary of quantitative variables under study is shown in Table 3. The cases had a mean height of 5.36±0.33 ft (range 4.5–6.0 ft), mean weight was 62.62±8.17 kg (range 50.0–76.0 kg), mean HbA1c was 8.60±1.15% (range 6.10–11.67%) and mean serum ferritin was 165.16±68.19 % (range 61.9–310%).

Table 3: Summary of quantitative variables

Variable	Mean	SD	Min	Max
Height (Feet)	5.36	0.33	4.5	6.0
Weight (Kg)	62.62	8.17	50.0	76.0
HbA1c	8.60	1.15	6.10	11.67
Serum Ferritin	165.16	68.19	61.9	310

The correlation-regression analysis showed the relationship between serum ferritin & HbA1c (Fig. 3). There was a positive and statistically significant correlation between HbA1c and serum ferritin (r=0.425, p=0.005). Further the regression equation for estimating serum ferritin with the help of HbA1c is given by Sr ferritin = 25.20(HbA1c)–51.46.

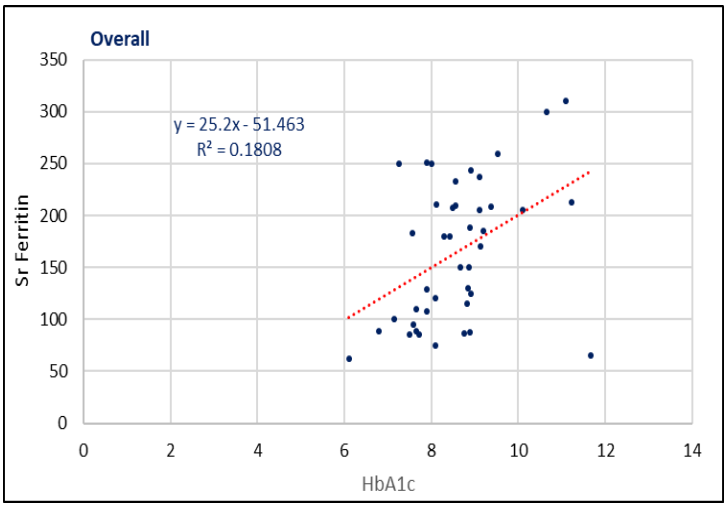

Fig. 3: Correlation-regression analysis showing a relationship between HbA1c & serum ferritin

The correlation-regression analysis showed the relationship between serum ferritin & HbA1c among females (Fig. 4). The correlation between HbA1c and serum ferritin was positive and significant (r=0.633, p=0.001). Furthermore, the regression equation to estimate serum ferritin using HbA1c is given by Serum ferritin = 40.63 (HbA1c) – 175.35.

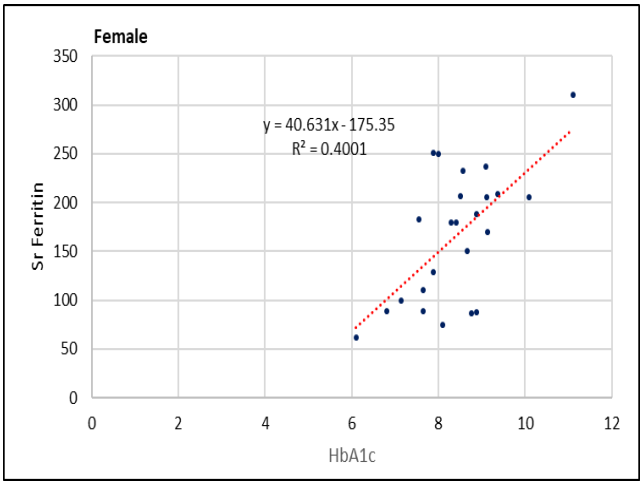

Fig. 4: Correlation-regression analysis showing a relationship between HbA1c & serum ferritin among females

The correlation-regression analysis showed a relationship between serum ferritin & HbA1c among males (Fig. 5). Between HbA1c and serum ferritin, the correlation was positive but not significant (r=0.228, p=0.362). Further, the regression equation for estimating serum ferritin with the help of HbA1c is given by Serum ferritin = 12.92(HbA$_1$c) – 49.52.

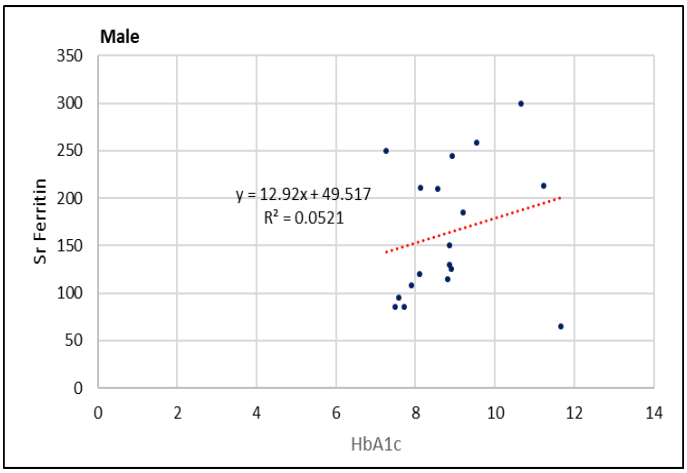

Fig. 5: Correlation-regression analysis showing a relationship between HbA^{1}c & serum ferritin among males

The correlation-regression analysis showed a relationship between serum ferritin & HbA1c among cases of age group 25–40 yr (Fig. 6). The correlation between HbA1c and serum ferritin was positive and significant (r=0.624, p=0.007). Furthermore, the regression equation to estimate serum ferritin using HbA1c is given by Serum ferritin = 36.52(HbA1c) – 123.19.

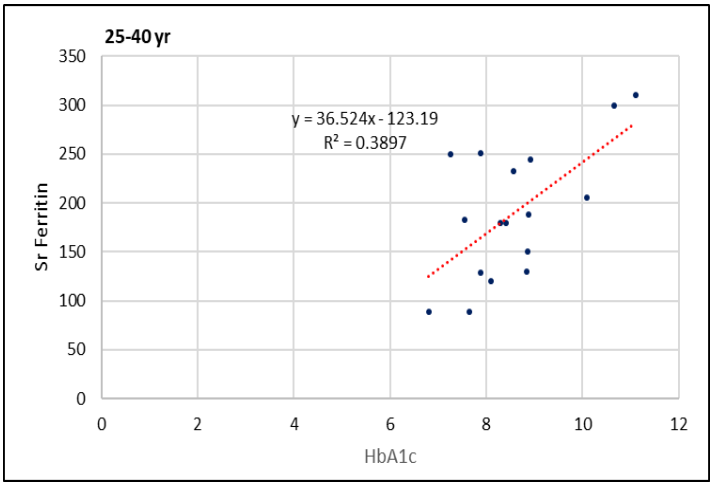

Fig. 6: Correlation-regression analysis showing relationship between serum ferritin & HbA$_1$c among age group 25–40 yr

The correlation-regression analysis showing relationship between serum ferritin & HbA$_1$c among cases of age group 41–70 yr (Fig. 7). Between HbA1c and serum ferritin, the correlation was positive but insignificant (r=0.331, p=0.106). Further, the regression equation for estimating serum ferritin with the help of HbA1c is given by Serum ferritin = 18.25(HbA$_1$c) – 8.92.

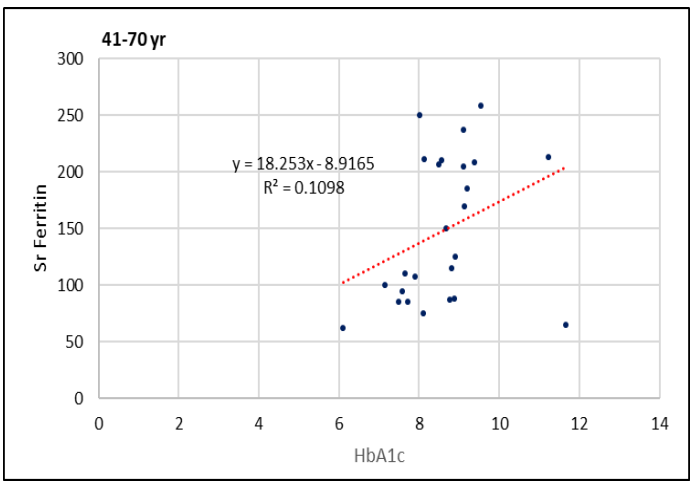

Fig. 7: Correlation-regression analysis showing a relationship between serum ferritin & HbA1c among age group 41-70 yr

DISCUSSION

Worldwide, type 2 diabetes is a common form of diabetes, affecting 85-90% of all people with diabetes. Both genetic and environmental factors predispose to the manifestation of type 2 diabetes. A robust genetic predisposition exists, and the risk is also significantly increased when combined with lifestyle changes such as

less physical activity, high blood pressure, obesity or overweight, and a poor diet. Regular physical activity and a healthy diet can initially control type 2 diabetes. However, most patients with type 2 diabetes require insulin or oral medication.

HbA1c is glycated hemoglobin. It forms when glucose in the blood combines with haemoglobin, a protein in red blood cells that transports oxygen throughout the body. Measuring glycated haemoglobin (HbA1c) gives an overall picture of our average blood sugar over a 6–8-week period, which has been of great help to clinicians. This is important because there is a higher risk of developing diabetes-related complications with higher HbA1c.

In this study, we found that in patients with type 2 diabetes, there was a significant correlation between glycated haemoglobin and serum ferritin. This may suggest that an increase in iron status may contribute to the pathophysiology of diabetes mellitus. Researchers recommend that in diabetic patients, when HbA1c and glucose levels differ, iron deficiency or anaemia should be carefully considered. Elevated haemoglobin levels should be corrected before reintroducing HbA1c for screening if these abnormalities are identified. In iron deficiency anaemia, there is iron deficiency and it affects HbA1c with a false increase in its value. When interpreting HbA1c in type 2 diabetes, the patient's iron status should be considered. In addition, there was a decrease in HbA1c levels in diabetic and non-diabetic patients on iron replacement therapy.

Several studies have not yet recognized a major link between serum ferritin levels and diabetes. Many studies are underway worldwide to assess the association between the risk of developing diabetes and iron stores in the body [27]. Eliman *et al.* [28] conducted a study and found a significant positive correlation between serum ferritin and HbA1c. There was a positive correlation between serum ferritin and fasting blood glucose and HbA1c. These results suggest an association between inflammation and glycemic control in patients with type 2 diabetes. The serum ferritin and HbA1c relationship reflects both short-term and long-term glycemic control. This explains if glycemic control was not achieved, there was an increase in serum ferritin levels in diabetic patients.

Fawaeir *et al.* [29] conducted a study and found that when comparing patients with type 2 diabetes and healthy groups, a strong relationship was observed between HbA1c and high serum ferritin levels. Therefore, sequential observation of ferritin levels may be helpful in diabetic patients.

Moirangthem *et al.* [30] also found a positive correlation between HbA1c and serum ferritin. Several studies have shown that in patients with type 2 diabetes, serum ferritin levels are positively related to fasting blood glucose. However, in female patients, there is a higher positive relationship between serum ferritin levels and fasting blood glucose levels than men. Our study also obtained a positive and significant correlation between HbA1c and serum ferritin in women compared with men.

CONCLUSIONS

Our results reflect a short- and long-term relationship between serum ferritin and glycemic control. The results of our study are like those of many other studies and show a significant relationship between serum ferritin and hyperglycemia. A positive correlation of serum ferritin with HbA1c was observed.

However, in the future, large-scale and long-term prospective studies are needed in different parts of the world to prevent diabetes and better understand the role of serum ferritin. Although our study indicates this, and we suggest further study in this way to establish specific rules.

SUMMARY

In summary, there are major problems with good glycemic control, whether to estimate serum ferritin systematically or to identify threshold values for serum ferritin. Our study results show a significant relationship between serum ferritin concentration and HbA1c, which means that serum ferritin can be used as a routine screening tool for the early diagnosis and treatment of diabetes.

CONTRIBUTION OF AUTHORS

Research concept- Gazala Afrin, Sachin Pal, Vaibhav Shukla
Research design- Gazala Afrin, Sachin Pal
Supervision- Vaibhav Shukla
Materials- Gazala Afrin, Sachin Pal
Data collection- Gazala Afrin, Sachin Pal
Data analysis and Interpretation- Gazala Afrin, Sachin Pal
Literature search- Gazala Afrin, Sachin Pal
Writing article- Gazala Afrin, Sachin Pal

Critical review- Vaibhav Shukla
Article editing- Gazala Afrin, Sachin Pal
Final approval- Vaibhav Shukla

REFERENCES

[1] Valdez R, Liu T, Yoon PW, Khoury MJ. Family history and prevalence of diabetes in the U. S. population. Diabetes Care, 2007; 30: 2517-22.

[2] Thilip Kumar G, Saravanan A, Ramachandran C, Ashok JN. Mean blood glucose level and glycated haemoglobin level in patients of non-insulin dependent diabetes mellitus and its correlation with serum ferritin level. Int J Med Sci., 2011; 4(1&2): 13-17.

[3] Roglic G, Unwin N. Mortality attributable to diabetes: estimates for the year 2010. Diabetes Res Clin Pract., 2010; 87(1): 15-19.

[4] Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care, 2004; 27(5): 1047-53. doi: 10.2337/diacare.27.5.1047.

[5] Alqurashi KA, Aljabri KS, Bokhari SA. Prevalence of Diabetes mellitus in a Saudi community. Ann Saudi Med., 2011; 31: 19–23.

[6] Al-Nozha MM, Al-Maatouq MA, Al-Mazrou YY, Al-Harthi SS, et al. Diabetes Mellitus in Saudi Arabia. Saudi Med J., 2004; 25: 1603–10.

[7] McKinlay J, Marceau L. US public health and the 21st century: Diabetes mellitus. Lancet, 2000; 356: 757–61.

[8] Thorand B, Lowel H, Schneider A, Kolb H, Meisinger C, et al. C-reactive protein as a predictor for incident diabetes mellitus among middle-aged men: Results from the MONICA Augsburg cohort study, 1984-1998. Arch Intern Med., 2003; 163: 93–99.

[9] Hu FB, Meigs JB, Li TY, Rifai N, Manson JE. Inflammatory markers and risk of developing type 2 diabetes in women. Diabetes, 2004; 53: 693–700.

[10] Krakoff J, Funahashi T, Stehouwer CD, Schalkwijk CG, Tanaka S, et al. Inflammatory markers, adiponectin, and risk of type 2 diabetes in the Pima Indian. Diabetes Care, 2003; 26: 1745–51.

[11] Gauldie J, Richards C, Harnish D, Lansdorp P, Baumann H. Interferon beta 2/B-cell stimulatory factor type 2 shares identity with monocyte-derived hepatocyte-stimulating factor and regulates the major acute phase protein response in liver cells. Proc Natl Acad Sci U S A, 1987; 84: 7251–55.

[12] 19. Koorts AM, Viljoen M. Acute phase proteins: Ferritin and ferritin isoforms. University of Petoria, South Africa., 2011; 154-84.

[13] Sheu WH, Chen YT, Lee WJ, Wang CW, Lin LY. A relationship between serum ferritin and the insulin resistance syndrome is present in non-diabetic women but not in non-diabetic men. Clin Endocrinol., 2003; 58: 380–83.

[14] Ali M, Mohammad SB. Serum ferritin has correlation with HbA1c in type 2 diabetic patients. Adv Biomed Res., 2015; 4: 74.

[15] Hramiak IM, Finegood DT, et al. Factors affecting glucose tolerance in hereditary hemochromatosis. Clin Inves Med., 1997; 20(2): 110-18.

[16] Jiang R, Manson JE, Meigs JB J, et al. Body iron stores in relation to risk of type 2 diabetes in apparently healthy women. JAMA., 2004; 291: 711-17.

[17] Ford ES, Cogswell ME. Diabetes andserum ferritin concentration among U.S. adults. Diabetes Care, 1999; 22: 1978-83.

[18] Gallou G, Guilhem I, Poirier JY, Ruelland A, Legras B, et al. Increased serum ferritin in insulin-dependent diabetes mellitus: relation to glycemic control. Clin Chem., 1994; 40: 947-48.

[19] Kim NH. Serum ferritin in healthy subject and type 2 diabetes mellitus. Med Korea, 2000; 41: 387-92.

[20] Eshed I, Elis A, Lishner M. Plasma ferritin and type 2 diabetes mellitus. Endocr Res., 2001; 27: 92-97.

[21] 28. Burtis CA, Ashwood ER, Bruns DE. Teitz textbook of clinical chemistry and molecular diagnostics 4th ed: New Delhi, Saunders Harcourt: 2006; pp. 856-59 & pp. 869-85.

[22] Fernandez-Real JM, Lopez-Bermejo A. Cross talk between iron metabolism and diabetes. Diabetes., 2002; 51: 2348-54.

[23] 31. Wrede CE, Buether R, Bollheimer LC, Scholmerich J, Palitzsch KD, et al. Association between serum ferritin and insulin resistance syndrome in a representative population. Eur J Endocrinol., 2006; 154: 333-40.

[24] Hramiak IM, Finegood DT, Adams PC. Factors affecting glucose tolerance in hereditary hemochromatosis. Clin Invest Med., 1997; 20(2): 110-18.

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[25]Thomas MC, Maclsaae RJ, Tsalamandris C, Jarums G. Elevated iron indices in patients with diabetes. Diabetic Med., 2004; 21: 798-802.

[26]William T. Cefalu (Editor). Classification and Diagnosis of Diabetes. American Diabetes association standards of medical care in diabetes. J Clin Appl Res Edu., 2016; 39: 13-15.

[27]Son NE. Influence of ferritin levels and inflammatory markers on HbA1c in the Type 2 Diabetes mellitus patients. Pak J Med Sci., 2019; 35(4): 1030-35.

[28]Elimam H, Abdulla AM, Taha IM. Inflammatory markers and control of type 2 diabetes mellitus. Diabetes Metab Syndr., 2019; 13(1): 800–04.

[29]AL-Fawaeir S, Daradka HM, Siyam AAA. Study of the association between Serum Ferritin Levels and HbA1c in patient with Type 2 Diabetes Mellitus in Jordanian Population Sample. JPRI, 2021; 33(33B): 1-5.

[30]Moirangthem MM, Rajkumari VD. Study of serum ferritin and HbA1c Levels in Type 2 Diabetes Mellitus. J. Evid. Based Med. Healthc., 2020; 7(27): 1282-85.