Original Article

Study of Serum Ferritin and Glycemic Status in Type II Diabetic Patients

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Abstract

Introduction: Diabetes mellitus has often found to be associated with iron dysregulation, manifested by increased serum ferritin level. Iron is essential for beta-cell insulin secretion, although, increasing concentration of iron and ferritin induce oxidative damage and dysfunction of pancreatic beta cells, leading to resistance to insulin, thus, consequent in hyperglycemia.

Objective: To observe the association between serum ferritin and HbA1c concentration among type 2 DM patients.

Methods: With an observational study design, the present study has been done among 63 purposively selected type 2 diabetic patients who attended the selected pathology institute during the period of January to June, 2021. Following availing the ethical approval from concerning ethical review committee and informed written consent of the patients, data regarding age, sex, height, weight, body mass index (BMI), diabetic duration, HbA1c concentration and serum ferritin level has been collected and recorded in a semi-structured questionnaire. Data were analyzed using Statistical Package for Social Science (SPSS) 20.

Results: The study recorded that, the mean serum ferritin level was significantly higher among the poor glycemic control group than the good glycemic control group of respondents ($p<0.05$) though no statistically significant difference was observed in terms of age, sex, BMI or diabetic duration among the groups ($p>0.05$).

Conclusion: Higher serum ferritin level among diabetic patients with poor glycemic control may indicate that there is a pathological role of serum ferritin to induce changes in glycemic status, which requires further in depth studies to apprehend about the mechanism.

Key words: Serum ferritin, Diabetes mellitus, HbA1c, Diabetic duration, Body Mass Index (BMI).

Introduction

Diabetes is the 4th most common non-communicable disease and its associated disablements are a growing epidemic[1,2]. In the year of 2015, 7.1 million people were suffering from diabetes, and 129,000 deaths were recorded to be attributed by this disease in our country[3]. A considerable portion of the workforce are being affected by diabetes, thus impacting negatively on the national and personal productivity[4]. Furthermore, the financial expenditure associated with the ailments resulting from uncontrolled hyperglycemia in patients with diabetes mellitus constitute a significant strain on the national economies[5,6]. Reduction in these medical and socioeconomic consequences of diabetes and its complications are of serious concerns for developing countries like ours[4]. Identifying at risk patients to develop the disease and modifying their life style to prevent the onset of the disease can be proven beneficial. Glycated hemoglobin (HbA1c) serves as a suitable option regarding this concern, as it is the standard for monitoring long term glycemic control and estimating complications in diabetes mellitus[4,7,8]. Although, the etiological attributions of the diabetes are not fully established, but, being a metabolic disorder, with heterogeneous causative determinants, recent concerns are growing around body iron overload conditions[9]. On the other hand, HbA1c measurements are also found to be influenced by other various conditions, among whom body iron status is an important one[4,10-15]. Increased hepatic accumulation of iron can affect the synthesis and secretion of insulin in the pancreas and may interfere with the insulin extracting capacity of the liver[16-18]. Iron deposition in muscle also decreases glucose uptake because of damage to the muscle tissue[19]. Concomitantly, insulin stimulates cellular iron uptake through increased externalization of the transfer in receptor[20]. Thus, iron and insulin can reciprocally potentiate each other's effects, ultimately leading to insulin resistance and diabetes. The diagnostic validity of HbA1c is thus required to be ensured regarding its accuracy when there

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is an existent iron overload condition present in an individual. Therefore, the association of body iron status and the HbA1c concentration among diabetic individuals are required to assess in order to exclude any misinterpretation. On this ground, the present study has made an effort to observe the association between the serum ferritin level and HbA1c measurements in patients diagnosed with diabetes.

Materials and Methods

With an observational study design, the present study has been conducted within a period of 6 months from January 2021 to June 2021 among 63 diabetic patients. Data regarding age, sex, height, weight, BMI, diabetic duration, HbA1c concentration and serum ferritin level has been collected and recorded in a semi-structured questionnaire. The standing height of the respondents was measured with a stadiometer in cm and body weight with a weighing scale in kg. Body Mass Index (BMI) was calculated using the formula of weight (kg)/height (m^2). With all aseptic precautions 5ml of morning blood were collected from the median cubital vein of all study subjects by a disposable plastic syringe, labeled well and sent to the lab for the investigation. Assessment of HbA1c has been done by High Performance Liquid Chromatography (HPLC) method by Turbo Variant and ferritin level was measured by electrochemiluminescence method by Cobas 6000. Data were analyzed using SPSS (Statistical Package for Social Science) version 20. Results of the analysis were expressed as frequency distribution and for categorical data as mean±standard deviation for continuous data. Categorical data were analyzed using 'chi-square' test and comparisons between continuous variables were done using Student's t-test. A p value <0.05 was considered statistically significant and p value of <0.001 was considered highly statistically significant. Formal ethical clearance was taken from the concerning ethical review committee. The procedures followed for this study were according to the CIOMS (Council for International Organization of Medical Science) guidelines or Helsinki deceleration[21].

Results

Table-I: Glycemic control status of the respondents in association with patient factors

Characteristics of the patients		Good glycemic control (n_1=26)		Poor glycemic control (n_2=37)		Total (n=63)		p value
Age	40 or below	2	7.7%	2	5.4%	4	6.3%	0.378[a]
	41 to 50	7	26.9%	4	10.8%	11	17.5%	
	51 to 60	8	30.8%	16	43.2%	24	38.1%	
	61 or above	9	34.6%	15	40.5%	24	38.1%	
	Mean ± SD	54.62 ± 12.48		57.78 ± 11.74				0.573[b]
Sex	Male	16	61.5%	26	70.3%	42	66.67%	0.469[a]
	Female	10	38.5%	11	29.7%	21	33.33%	
BMI	Normal	10	38.5%	10	27.0%	20	31.7%	0.538[a]
	Overweight	12	46.2%	18	48.6%	30	47.6%	
	Obese	4	15.4%	9	24.3%	13	20.6%	
	Mean ± SD	26.62 ± 4.33		26.81 ± 3.69				0.76[b]
Duration of Diabetes	5 years or less	12	46.2%	14	37.8%	26	41.3%	0.625[a]
	6 to 10 years	9	34.6%	12	32.4%	21	33.3%	
	more than 10 years	5	19.2%	11	29.7%	16	25.4%	
	Mean ± SD	7.61 ± 6.172		9.56 ± 7.743				0.318[b]
Serum Ferritin Level	Mean ± SD	89.63 ± 8.26		119.83 ± 17.41				0.009[b]

[a]p value reached from chi-square test, [b]p value reached from student's t-test

The age distribution of the respondents showed that, the highest percentage of respondents belong from the age group of 61 years or above in the group of respondents whose glycemic control was good (34.6%). The respondents with poor glycemic control, among them highest percentage of respondents belong from the age group of 51 to 60 years (43.2%). Calculating the age as a continuous variable showed that respondents with poor glycemic control had greater mean (57.78± 11.74) than the respondents with good glycemic control (54.62±12.48). Among the respondents, 61.5% of the male and 38.5% of female had good glycemic control whereas 70.3% of the male and 29.7% of the female had poor glycemic control. The distribution of the respondents according to the BMI classification showed that, 46.2% and 48.6% of the good glycemic control and poor glycemic control group of respondents (respectively) were overweight. And 15.4% and 24.3% of the good glycemic control and poor glycemic control group of respondents (respectively) were obese. The mean of the BMI was 26.62±4.33 and 26.81±3.69 among the good glycemic control and poor glycemic control group of respondents (respectively). Among the good glycemic control group, 46.2% of the respondents gave history of

suffering from diabetes for 5 years or less compared to the poor glycemic control group where 37.8% of the respondents gave history of suffering from diabetes for the same duration. Suffering from diabetes for 6 to 10 years were 34.6% and 32.4% in the good glycemic and poor glycemic control group respectively. Suffering from diabetes for more than 10 years were 19.2% and 29.7% in the good glycemic and poor glycemic control group respectively. The mean of the diabetes duration was 7.61%±6.17 years compared to 9.56%±7.74 years among the good glycemic and poor glycemic control group respectively. In this study the mean of the serum ferritin level was 89.63±8.26ng/mL and 119.83±17.41 ng/mL among the groups of good glycemic and poor glycemic control respectively.

When the respondents were compared for their findings in relation to their glycemic control, it has been found that, the age, sex, BMI or diabetic duration was not statistically different among the good glycemic and poor glycemic control group. But, the mean of the serum ferritin level differed significantly among these groups ($p<0.05$) (Table-I).

Discussion

Impaired insulin secretion and resistance to insulin are the main contributing factors in the development of type 2 diabetes mellitus[22]. Excess iron deposition in the pancreas is known to cause an insulin resistance syndrome which has led to the speculation that higher concentrations of body iron may increase the risk of developing diabetes[23]. In this regard, serum ferritin concentration as an indicator of body iron store has been proposed as a precipitator of impaired glucose tolerance and insulin resistance syndrome[24]. In the present study, among the 63 diabetic respondents, 66.67% of the respondents were male. When the respondents were compared for their findings in relation to their glycemic control, it has been found that, the age, sex, BMI or diabetic duration was not statistically different among the good glycemic and poor glycemic control group. But, the serum ferritin level differed significantly among the groups. The mean age of the respondents was higher in the poor glycemic control group than the respondents with good glycemic control ($p>0.05$). The respondents with poor glycemic control had higher percentage of overweight and obese respondents than the good glycemic control group ($p>0.05$). The mean of the diabetes duration was higher among the poor glycemic control group compared to good glycemic control group ($p>0.05$). This study finds that, the mean of the serum ferritin level was statistically significantly higher among the poor glycemic control group compared to good glycemic control group of respondents ($p<0.05$).

Compared to this study findings, in the study of Raj et al, the mean age of the diabetic respondents were 54.3±9.2 years, where the duration of diabetes was between 5–10 years in 49% cases and more than 10 years in 36% cases. Similar to this findings, they found a significant positive correlation between serum ferritin and HbA1c ($p<0.05$)[24]. In another study, with the mean age of diabetic patients 59.96±11.26 years, mean duration of diabetes 10.69±7.17 years, and the mean BMI of 29.28±6.49kg/m². It has been seen that, the serum ferritin levels of the patient with type 2 DM significantly increased with increasing HbA1c levels ($p<0.01$)[25]. Serum ferritin concentrations increase with the number of features of the metabolic syndrome[26]. According to other study observations, serum ferritin concentrations may indicate more severe hepatic insulin resistance and a higher risk for progression to relevant clinical complications[27]. In another study it has been found that, patients with poorly controlled diabetes mellitus had 1.95 times higher odds of having elevated ferritin levels[28]. Ford et al., also concluded that elevated serum ferritin is a risk factor of DM[23]. Similar results were obtained in another study and they even found that following improvement of diabetes indexes, ferritin level got reduced[23,29]. Khondker et al also found that there was significant positive correlation between serum ferritin and HbA1c in diabetic patients ($p<0.001$)[30]. Another population based study found that increased body iron store was associated with the occurrence of glucose intolerance, type 2 DM and gestational diabetes[31].

Conclusion

In attempt to observe the serum ferritin level and HbA1c status among diabetic patients, this study concludes with the findings that, serum ferritin level was significantly higher among the poor glycemic control group of diabetic patients than the diabetic patients who had fair glycemic control, although, glycemic status or serum ferritin level were not observed to be associated with age, sex, BMI or diabetic duration of the patients. We would recommend further large scale, prospective studies in this track for instituting specific guidelines to avail a better understanding of the role of serum ferritin levels in constituting as well as in the prevention of diabetes.

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