ORIGINAL RESEARCH

The State of Ferritin in Patients With Diabetes Mellitus Type II/Iraq

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ABSTRACT

This study aims to examine the effects of anemia on patients with diabetes mellitus type II (DM). The cross-sectional study included 75 patients with (DM). They were divided into two groups according to the presence of anemia. The first group includes 50 diabetic patients suffering from anemia, while the second group contains only 25 patients with diabetes only. There was no specification in gender; the patients included both sexes and their ages were above 20 years. A blood sample was collected from each patient to measure (fasting blood glucose, hemoglobin, glycosylated hemoglobin, and ferritin). The results revealed an increase in anemia in females with diabetes mellitus more than males while the levels of HbA1c was on the contrary; it increased in males and decreased in females. A significant negative correlation is confirmed between ferritin and HbA1c in anemic diabetic women. Diabetic patients suffering from anemia recorded a sharp decrease in the levels of ferritin compared with patients with diabetes only. In conclusion, the incidence of anemia increase in diabetic patients with increased levels of HbA1c.

Keywords: Anemia, Diabetes mellitus, Ferritin, Glycosylated hemoglobin.

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INTRODUCTION

Diabetes mellitus (DM) is a common metabolic disease which results in hyperglycemia due to reduced tissue response to insulin, absolute insulin deficiency or both. It is a non-infectious disease that also has a high prevalence worldwide.[1] Diabetes mellitus (DM) leads to various events, including micro and macrovascular complications. It accounts for a high incidence of morbidity.[2]

"Diabetes is a highly disabling disease, which can cause blindness, amputations, kidney disease, anemia, cardiovascular, brain complications and impairing the functional capacity and autonomy and individual quality of life."[3] The evaluation and management of patients with diabetes mellitus w conducted by measuring glycosylated hemoglobin (HbA1c). HbA1c assesses long-term glycemic control and predictsere micro-vascular complications in diabetes.[4] The level of HbA1c in the blood sample provides a glycemic history of the average erythrocyte lifespan.[5]

Anemia means a deficiency of hemoglobin in the blood, which can be caused by either reduced hemoglobin in the cells or a few erythrocyte numbers or both.[6] Anemia represents an emerging global health problem that negatively impacts the quality of life and requires an ever-greater allocation of healthcare resources.[7] Anemia has a significant adverse effect on the quality of life in diabetic persons and is related to disease progression and the comorbidities development.[8] Several studies indicate that anemia in diabetics is twice as common compared with non-diabetics.[9] However, anemia in 25% of diabetic patients is unrecognized.[10] Hyperglycemia has a direct relationship with the development of an inflammatory condition shown by the increased expression of proinflammatory cytokines such as IL-6, TNF-α, and NFαB.[11]

It should be highlighted that from diabetic patients themselves, anemia is an unknown complication of their disease." In a pan-European study, the patient's level of awareness and understanding of anemia and other complications of diabetes mellitus were assessed. Only 32% of responders had been given information about anemia, although 83% had heard about anemia, and only 14% attributed anemia to diabetes.[12]

MATERIAL AND METHODS

Patients and conditions of study

This study included data from 75 diabetic patients with type II diabetes mellitus in the center of Diabetes and Endocrines in Al- Sadr Medical City for the period from 1 May to 10 October 2017. The patients were of both sexes older than 20 years. Type II diabetes mellitus was diagnosed when the fasting glucose

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value was >125 mg/dL or random blood glucose >200 mg/dL. This diagnosis of diabetes was based on the "Definition and description of diabetes mellitus" from the American Diabetes Association 2010.[13] Fifty patients of the 75 diabetic patients were considered anemic as per the World Health Organization's gender-specific criteria, (Hb<13 g/dL in men and Hb<12 g/dL in women),[14] the remaining patients (n = 25) were not anemic.

The study excluded pregnant patients with a family history of hereditary anemia, liver and renal diseases, or any other chronic illness or malignancy and patients who have received treatment for anemia.

About 5 mL blood sample was collected from each diabetic patient who were fasting for an overnight. Two milliliters of the blood were put into ethylenediaminetetraacetate (EDTA) tube to measure HbA1c level, fasting blood sugar (FBS), and hemoglobin Hb. At the same time, 3 mL was placed in a plain tube and left for clotting. Then the serum was separated by centrifuge and kept in very low temperatures (-20C°) to measure ferritin.

Laboratory measurements

The levels of HbA1c was measured by quantitative colorimetric (Stanbio-Glycohemoglobin Kit, USA). The hematology autoanalyzer, Ruby estimated hemoglobin. Ferritin estimation was performed by minividus using monobind kit, USA. Plasma glucose was measured by spectrophotometers.

Statistical analysis

The statistical analysis is performed by using SPSS version 20 for obtaining mean, standard deviation, and ANOVA one way. Correlation between ferritin and HbA1c is obtained by Pearson's coefficient. The significance of the results was $P \leq 0.05$.

RESULTS

Figure 1 shows that females in the diabetic, anemic group recorded a high percentage (40%) compared to females in the diabetic non-anemic group, which recorded only (17%). Regarding males also diabetic, the anemic group recorded higher percent (27%) than a diabetic non-anemic group with only (16%).

The figure also illustrates that the incidence of anemia in patients with diabetes mellitus was more significant in females with (40%) than males with (27%).

The level of HbA1c of males in the diabetic, anemic group was higher (8.2) compared with females in the same group (7.8), as explained in figure (2). Males in both groups (diabetic anemic and diabetic non-anemic) have higher levels of HbA1c (8.2, 7.6), respectively, compared with females (7.8, 7.2), respectively.

Figure 3 illustrates a negative correlation between levels of glycosylated hemoglobin and ferritin in female patients, and the relation was statistically significant. This means when female diabetic patient has increased in the HbA1c will have a decrease in the levels of ferritin, leading to developing anemia.

Figure 4 shows the negative correlation between levels of glycosylated hemoglobin and ferritin in male patients, and the relation was statistically not significant.

Table 1 clarifies that the levels of hemoglobin and ferritin significantly decreased in a diabetic-anemic group (7.35, 8.07), respectively, compared with their levels in a diabetic non-anemic group (13.75, 67.51) respectively. Meanwhile, the levels of HbA1c increased significantly in diabetic, anemic patients (7.97 ± 1.11) compared to diabetic non-anemic patients who recorded (7.46 ± 0.96). Fasting blood sugar increased in a diabetic non-anemic group (138.32) and decreased in a diabetic, anemic group (136.76).

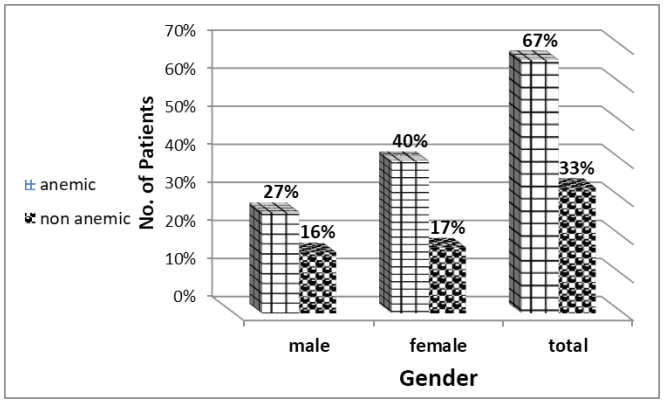

Figure 1: Distribution of diabetic patients according to gender

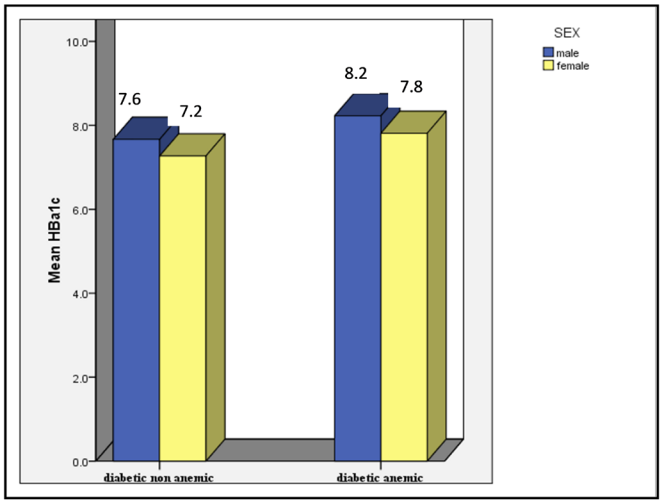

Figure 2: levels of HbA1c in diabetic anemic and non-anemic patients according to gender

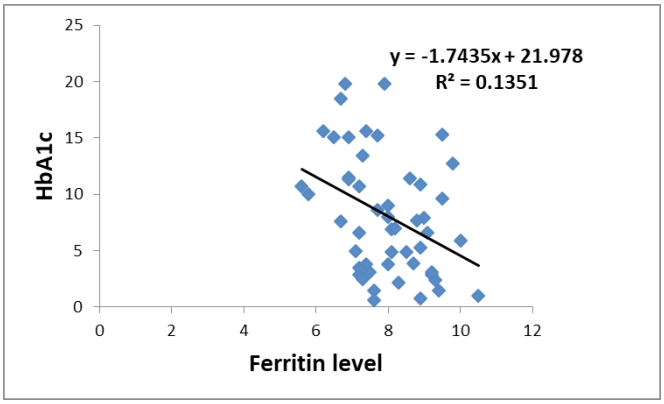

Figure 3: Correlation between the levels of HbA1c and ferritin in female diabetic anemic

Table 1: Levels of FBS, HbA1c, Hemoglobin, and Ferritin in diabetic non-anemic and diabetic, anemic patients

Studied groups	*No.*	*FBS (mg/dL)* ± *SD* *Mean*	*HbA1c (%)* ± *SD* *Mean*	*Hemoglobin (g/dL)* ± *SD* *Mean*	*Ferritin (ng/mL)* ± *SD* *Mean*
Diabetic non-anemic	25	138.32 ± 36.30	7.46 ± 0.96	13.75 ± 1.19	67.51 ± 42.07
Diabetic anemic	50	136.76 ± 41.66	7.97 ± 1.11*	7.35 ± 1.98*	8.07 ± 5.30*
Total	75	137.28 ± 39.72	7.80 ± 1.09	9.48 ± 3.50	27.88 ± 20.26

* significant difference $p < 0.05$

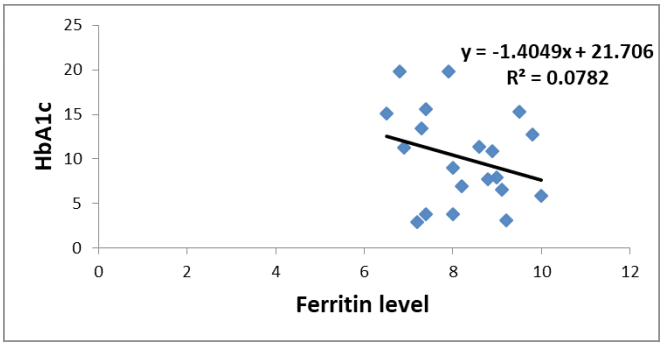

Figure 4: Correlation between the levels of HbA1c and ferritin in male diabetic anemic

DISCUSSION

The study indicates that the incidence of anemia among diabetic patients recorded an increase of 40% in females compared to 27% in males, as shown in Figure 1. This result is consistent with Merlin C. *et al*.,[15] who suggested the prevalence of anemia in patients with diabetes mellitus (DM) was 15% in females versus 13% in males. In a recent study in Kuwait,[16] the results were nearly close to those in figure (1) where diabetic anemic females were accounted for 38.5% versus 21.6% for males. The explanation for this is the lack of health care and malnutrition because of the low empowerment. This can be amended by educational interventions, especially in the rural areas by health awareness programs, provision of food rich with iron, prescription of supplements with vitamins and iron, and knowledge on the complications of diabetes.[17]

There was a rise in the glycosylated hemoglobin level (8.2%) in anemic diabetic males in comparison with the level of it in females (7.8%) as in Figure 2, and this result comes in line with a Chinese study by researcher Ma Quigling[18] in 2016 who revealed a significant difference $P \leq 0.0001$ in HbA1c level between males and females, where it is elevated in males compared with females. This increase in HbA1c levels in males in the age of (30-59) years is attributed to various factors like percentage of fat and blood pressure whose control is difficult as they increase with age "compared to women where the extent of the impact of these factors is less because of the menstrual cycle".[19]

The diabetic patients in this study suffer from a decrease in the level of ferritin, which represents one of the most important storage of iron in the body and reflects the real state of it. Hence the study looked for an assessment of the relationship between the ferritin and HbA1c in patients with diabetes mellitus (DM) type II. The results confirm a negative correlation between ferritin and HbA1c in Figures 3 and 4, showing that HbA1c will increase the likelihood incidence of anemia in diabetic patients (as the levels of ferritin decrease) especially after measuring the level of hemoglobin which recorded very low levels. These results were contrary to the study previously conducted,[20] where there was no relationship between ferritin and HbA1c. There are several theories that explain the role of ferritin in diabetes mellitus, including the marker for insulin resistance is ferritin, and that could be because of the deposition of iron in the liver leading to elevated production of hepatic glucose and insulin resistance.[21]

There was a sharp drop in hemoglobin and ferritin levels in diabetic patients who were diagnosed with diabetes based on the "Definition and description of diabetes mellitus" from American Diabetes Association 2010 (13) as in Table 1 which indicates increase anemia in patients with diabetes who suffer from the continuous increase in HbA1c. This result is consistent with Samuel *et al*., who demonstrated in their study a low level of hemoglobin in males and females accompanied by the decline of the ferritin. In a previous study in 2015, Jassica *et al*. found that patients with diabetes have a reduction in hemoglobin level.[23]

Diabetic anemic patients in this study had an increase in the glycemic hemoglobin level compared with diabetic patients who do not suffer from anemia as in Table 1, and this is identical with what Lavanya R *et al*. found proposing an elevated level of HbA1c in anemic diabetic patients versus patients with diabetes mellitus only. "The interpretation of this increase is that anemia is associated with variations in the quadratic form of the hemoglobin molecule by increasing the ability of the globin chain to receive the sugar molecules and the transformation of hemoglobin into the glycated hemoglobin."25 Some studies have suggested that the glycation of hemoglobin is a permanent process and hence the HbA1C levels in red blood cell will increase as the cell's age increases.26

CONCLUSION

This study revealed that one of the complicated increased glycosylated hemoglobin HbA1c in DM patients is developing anemia by recording low levels of hemoglobin and ferritin. Further research is required to explain the type of anemia and if there is any genetic relation.

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