



Study of the Association between Serum Ferritin Levels and HbA1c in Patient with Type 2 Diabetes Mellitus in Jordanian Population Sample

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Authors' contributions

This work was carried out in collaboration among all authors. Author SAF designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors HMD and AAAS managed the analyses of the study. Author AAAS managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i33B31791

Editor(s):

(1) Dr. Vasudevan Mani, Qassim University, Saudi Arabia.

Reviewers:

(1) Lucia Stanciakova, Comenius University, Slovakia.

(2) Naveen Kumar B. J., The Oxford medical college, India.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/69542>

Original Research Article

Received 18 April 2021

Accepted 24 June 2021

Published 26 June 2021

ABSTRACT

Background/ aim: The most common endocrine disorder in the world is type 2 DM, affecting 85-90% of all people with diabetes. Several studies have found an association between serum ferritin levels and HbA1c, so the current study was undertaken to examine the association between serum ferritin levels and HbA1c in Jordanian patient's sample with type 2 DM.

Method: 120 patients with type 2 DM were enrolled into the current study, and control group consist of 20 healthy individuals, blood samples were collected after 14 h of fasting, 5 ml of fasting sample for FBS and ferritin, 4 ml whole blood taken in EDTA tube for Hb and HbA1c, sample centrifuged and biochemical tests were done in the same day.

Results: The mean of serum ferritin was significantly higher in patients group (213.87 ± 114.23 ng/ml) than control group (98.34 ± 18.45 ng/ml, $P < 0.05$). There was a positive association between serum ferritin and HbA1c ($P < 0.05$). Also there was a significant correlation between serum ferritin and FBS $P < 0.05$. Among the two groups there was no significant difference regarding demographic features (sex, age and BMI).

Conclusion: collected data showed that there is a significantly association between ferritin and type 2 DM, it was higher in comparison with healthy group, so it can give an indication of glycemic control in diabetic patients.

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Keywords: Type 2 diabetes mellitus; ferritin; HbA1c; association.

1. INTRODUCTION

The most common form of diabetes in the world is type 2 DM, affecting 85-90% of all people with diabetes. Type 2 DM results from a combination of genetic and environmental factors, there is a strong genetic predisposition, the risk greatly increased when associated with lifestyle such as high blood pressure, overweight or obesity, insufficient physical activity and poor diet. Type 2 diabetes can often be initially with healthy diet and regular physical activity [1-4].

Iron deficiency anemia (IDA) is a common type of anemia, a condition in which blood lacks adequate. Red blood cells carry oxygen to the body's tissues. As the name implies, iron deficiency anemia is due to insufficient iron. Without enough iron, your body can't produce enough of in red blood cells that enables them to carry oxygen [5].

The term *HbA1c* refers to glycated haemoglobin, it develops when haemoglobin, a protein within red blood cells that carries oxygen throughout your body, joins with glucose in the blood, becoming 'glycated'. It is used in assessment of glycemic status, as a marker of long term glycemic control and also to monitor a therapeutic target in the prevention. By measuring {HbA1c clinicians are able to get an overall picture of what our average blood sugar levels have been over a period 6 to 8 weeks [6-8].

Ferritin is an iron-storage protein present in all cells and can be measured in serum, plasma, liver, red blood cells, and other specimens, thus it is considered the main biomarker of body iron stores. Low ferritin concentration suggest deficient iron stores, whereas high concentrations suggest iron overload [9].

In recent years several studies have reported a positive association between iron status and development of type 2 DM. [10-12]. The mechanism for the association between serum ferritin and type 2 DM is not clear yet, but iron deposition in the liver may cause insulin resistance by interfering the ability of insulin to suppress hepatic glucose production, and may be by tissue damaging as a result of changing membrane properties by free radicals which are formed by auto-oxidation of Iron, also hyperglycemia through disturbed glucose metabolism as result of oxidative stress [11-13].

Hence this study was carried out to examine the relationship between serum ferritin and type 2 diabetes mellitus and metabolic syndrome and to establish a correlation between S. ferritin and FBS, HbA1c.

2. SUBJECTS AND METHODS

2.1 Study Populations

The subjects were 140 individuals including 120 patients (age 42-68) with type 2 DM and 20 healthy controls (age 45-67), the subjects of this study were selected from non-smoker patients attending to the outpatient specialty clinics in Tohama Medical Center in Zarqa city in Jordan during the period from 18 August 2019 to 22 January 2020. The members of both groups were enrolled in the study voluntarily. After interview for 5 minutes all volunteers completed a written informed agreement for participation in this study, blood samples were collected after 14 h of fasting, 5 ml of fasting sample for FBS and ferritin, 4 ml whole blood taken in EDTA tube for Hb and HbA1c, sample centrifuged and biochemical tests were done in the same day. All tests were done in teryaq alrohh medical Laboratory.

2.2 Exclusion Criteria

Patients with Chronic kidney disease, Chronic liver disease, Overt thyroid dysfunction, individuals on corticosteroid therapy and other states associated with altered serum ferritin like haemochromatosis, bleeding disorder, chronic alcoholics, anemia were excluded from our study. Also the individuals with repeated blood transfusion were not included. Our criteria for the diagnosis of anemia were based on laboratory investigation and a hemoglobin level of less than 13 g/dl, in male and 12 gm/dl in females.

2.3 Methods

Complete blood count (CBC) determination of hemoglobin and hematocrit levels were performed using a multi parameter cell counter Sysmex k 1000 hematology analyzer (Tao electronics, Japan). This analyzer is calibrated and controlled with standard laboratory quality control methods.

Ferritin, FBS and HbA1c concentrations were measured using hormones Auto-analyser Cobas e411 (Roche Diagnostics GmbH, Mannheim, Germany),

2.4 Statistical Analysis

Results are reported as mean \pm standard deviation (SD). All statistical analysis were performed using SPSS for windows 20.0 (SPSS Inc. Headquarters, Chicago, Ill., USA) software program and Microsoft Excel 2010 program. $P < 0.05$ was considered to be statistically significant.

3. RESULTS

The study group consisted of 140 subjects (86 male, 54 female), aged between 42 and 68 years (51.9 ± 12.6 mean \pm SD), the subjects were divided into 120 (86 %) patients with type 2 DM and 20 (14 %) healthy patients (Table 1). The patient group subjects were older than the healthy subjects 51.9 ± 12.6 years versus 47.7 ± 18.7 years as mean \pm standard deviation ($p < 0.05$), males were the predominant in patients subjects (61 %). Mean BMI was 28.1 ± 1.98 Kg/m² in patient group while in healthy group it was 27.4 ± 1.76 Kg/m².

The mean of serum ferritin was significantly higher in patients group (213.87 ± 114.23 ng/ml) than control group (98.34 ± 18.45 ng/ml, $P < 0.05$) (Table 2). There was a positive association between serum ferritin and FBS, HbA1c. a significant relation between serum ferritin and FBS $P < 0.05$, and the same strong significant relation was found between serum ferritin and HbA1c.

4. DISCUSSION

The most common form of diabetes in the world is type 2 DM, affecting 85-90% of all people with diabetes. Type 2 DM results from a combination of genetic and environmental factors, there is a strong genetic predisposition, the risk greatly

increased when associated with lifestyle such as high blood pressure, overweight or obesity, insufficient physical activity and poor diet. Type 2 diabetes can often be initially controlled with healthy diet and regular physical activity. However, over time most patients with type 2 diabetes will also need tablets and many will also need insulin [14].

The HbA1c refers to glycated hemoglobin. It develops when hemoglobin, a protein within red blood cells that carries oxygen throughout your body, joins with glucose in the blood, becoming 'glycated'. By measuring glycated hemoglobin (HbA1c), clinicians are able to get an overall picture of what our average blood sugar levels have been over a period 6 to 8 weeks. this is important as the higher the HbA1c, the greater the risk of developing diabetes-related complications [15].

Recently a systematic study on the influence of anemia and RBC abnormalities on HbA1c analysis was published [16]; the conclusion is that HbA1c is likely to be affected by iron deficiency and IDA with a spurious increase in HbA1c values, but the need for more evidence, especially in identifying the types and degrees of anemia, was stated.

In current study we found that the mean serum ferritin level of the patient group was significantly higher in comparison with that of healthy group ($P < 0.05$), this finding is in agreement with that reported by Khondker et al and also by Raghavani et al [17,18]. Also it was found that there is a strong association between serum concentrations of ferritin and HbA1C levels among both group patients and control, these similar to that which was found in three previous studies in Bangladesh and India [19,20].

Table 1. Demographic features among both groups

Parameter	Patients	Control	P-value
n	120	20	0.44
age	51.9 ± 12.6	47.7 ± 18.7	0.32
male / female	78/42	12/8	0.118
BMI	28.95 ± 2.14	26.88 ± 2.19	0.12

Table 2. Laboratory findings among both groups

Test	Patients	Control	P-value
Hemoglobin (g/dl)	13.9 ± 1.3	14.2 ± 0.95	0.014
HbA1c (%)	8.75 ± 0.92	5.48 ± 1.04	0.007
Serum ferritin (ng/ml)	213.87 ± 114.23	98.34 ± 18.45	0.005
FBS (mg/dl)	245.98 ± 86.94	92.48 ± 8.36	0.004

In patients group it was found that there is a positive and strong association between serum ferritin concentration and HbA1c levels in diabetic patients group ($P < 0.05$), these findings were shown in many studies before [17,18].

In control group there was a strong positive but not significant association between serum ferritin levels and HbA1c, in pervious study in India similar results was found [20].

Among the two groups there was no significant difference regarding demographic features (sex, age and BMI).

5. CONCLUSION

Based on obtained data in the current study, there was a strong association between increasing of serum ferritin levels and HbA1c in patients with type2 DM patients in comparison that of healthy group. So serially monitoring of ferritin levels can be helpful in monitoring DM patients.

CONSENT

Written informed consent was obtained from the patients for publication of this text.

ETHICAL APPROVAL

All procedures performed on the patient were in accordance to the ethical standards of the institution research committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:

The peer review history for this paper can be accessed here:

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