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Evaluation the Levels of Serum Ferritin in Development Type 2 Diabetes Mellitus

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Abstract:

Insulin resistance and relative insulin insufficiency lead to hyperglycemia in the common chronic metabolic condition known as type 2 diabetes mellitus (T2DM). It is important to be aware of its intricate origins, pathophysiology and approaches to its management due to its growing prevalence in the entire world.

The objectives of the study are: In the context of the Iraqi population, we were also interested in finding out whether blood ferritin levels were found to be correlated with the risk of type 2 diabetes mellitus.

Procedures: Patients with type 2 diabetes mellitus and a control group whose relatives provided blood samples were part of a case-control study that took place at the Imam Al Hussein Medical City Diabetic center in Karbala and the Medical Laboratory Technology Department of the College of Medical & Healthy Technologies at Ahl Al Bayt University. Fifty patients from the Karbala province diabetes center were a part of this trial, which ran from November 2023 to February 2024. The other half of those who participated in this study are healthy-looking people who are not diagnosed to have any diseases. The data collected included surveys and measurements, laboratory testing of such factors as ferritin, hemoglobin A1C, and fat-free mass.

Findings: Type 2 diabetes group had statistically significant increases in serum ferritin, ferritin-binding serum and hemoglobin A1C compared to the control group, but there were no differences in age or sex.

Conclusion: The findings indicate that diabetics have higher levels of ferritin than healthy controls do. therefore, ferritin seems to have a potential role in the etiology of type 2 diabetes. We suggested further studies are required on the role of ferritin in type 2 diabetes, poor glucose tolerance, insulin resistance and pre-diabetes.

Key words: Development Type 2 Diabetes Mellitus, Serum, Ferritin

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INTRODUCTION

Diabetes mellitus is a metabolic disease, which may be caused by many factors. It is characterized by chronic elevated levels of blood sugar and the inability of the body to metabolize carbohydrates, fats and proteins properly as a result of insulin deficiency or insulin resistance (or both) [1]. There are two primary forms of the metabolic disease diabetes, with type 2 accounting for 90%-95% of cases and type 1 for about 5%. In the United States, diabetes, and more specifically type 2 diabetes is drastically on the rise, and is being accompanied by numerous risk factors including the ageing population, the minority population, which is at risk, and the epidemic of obesity. The number of cases of diabetes per year and the risk factors associated with it might have plateaued in the US, yet it is a worldwide epidemic [2]. Long-term effects of diabetes mellitus include damage, malfunction, and ultimate organ failure. It might require a period of time to be diagnosed when hyperglycemia that is severe enough to cause pathological and functional abnormalities lasts a long time. There is a possibility that diabetic issues will get worse with time due to the long-term effect of the disease. Several pathogenesis processes accompany the occurrence of diabetes. The destruction of pancreatic beta cells, as well as the insulin insufficiency and insulin resistance are the consequences of these processes. Insulin insensitivity or insulin deficiency is the having of insulin which fails to act on the target tissues resulting in the problems in the metabolism of glucose, lipid and protein [3]. Diabetes and Mellitus are similar in their pronunciation (Greek). Diabetes: translates to a passer through; a siphon and Mellitus translates to sweet. Greeks might have named it so due to the attraction of flies and bees to the huge amounts of urine in diabetics. Ancient Chinese medicine depended on the attractiveness of ants to urine of a patient as a diagnostic tool of diabetes mellitus. Occasionally described in Gothic ideas, medieval European doctors would taste patients' urine to check for diabetes [4]. The chronic autoimmune condition known as type 1 diabetes mellitus (T1DM) causes hyperglycemia, or high blood glucose levels, as a result of insulin insufficiency, which happens when the pancreatic islet β-cells die out [5]. Type 1 diabetes is one of the most common metabolic and endocrine diseases among children. The loss of β-cells is observed in a large proportion of patients (70-90%) with type 1 diabetes mellitus (also called autoimmune T1DM), which occurs together with the production of autoantibodies of T1DM. There is a substantial hereditary component to idiopathic type 1 diabetes mellitus, when the source of βcell loss is unknown and no immune responses or autoantibodies are discovered in a smaller fraction of individuals [6]. Type 2 diabetes is a metabolic disease that is normally followed by obesity and insulin resistance. In other people, the pancreas produces insulin initially but this is not well used in the body. Finally, how much insulin the body actually requires varies with the individual since the organ, pancreas in this case, cannot synthesize sufficient insulin. The reason is that insulin produced by the body is inadequate and the physiological compensating processes do not work in time. Type 2 diabetes is the most common type of the disease with a prevalence of 8595% in the industrialized world and even higher in the underdeveloped world1. It is possible that type 2 diabetes may not occur at all, or only after several decades or even years. It typically precedes prediabetes, a condition that involves higher blood glucose levels, but not quite high enough to qualify as official diabetes. Many individuals with prediabetes are however able to delay or prevent the onset of type 2 diabetes through weight reduction (through exercise and diet modifications) as demonstrated in the Diabetes Prevention Program and other studies. Type 2 diabetes has been referred to by many names such as adult-onset and non-insulin-dependent diabetes (NIDDM). Due to the ability of the disease to target youngsters, and the fact that some of the patients require insulin therapy, these phrases have become inapplicable. [7] There is more than one cause of type 2 diabetes. Studies indicate that anxiety, stress, physical inactivity, and the desire to eat unhealthy foods in the older adults cause 55 per cent of the cases of type 2 diabetes and internal fat build up. [8]. Transient metabolic failure during pregnancy can happen to any woman who has never had diabetes and is typically experienced in the middle of the second or third trimester. Other risk factors of diabetes are hormonal changes, overweight, and a personal or family history of diabetes. Around 135,000 women are diagnosed of gestational diabetes annually, or 4% of all pregnancies [8]. Although gestational diabetes does completely disappear after a baby is born, it nevertheless necessitates a close follow up by a physician throughout the entire pregnancy. Approximately one out of every five women with this condition develops Type 2 diabetes, and in up to 50 instances [9, 10].

Polyurea

The increased or increased frequency of the urge to urinate is the most common symptom of diabetes. Urine may have a sweet flavor due to an excess of sugar. Since the body reabsorbs glucose as it builds up in the process of urine formation, the glucose is excreted in the body through the kidneys. In cases whereby the level of sugar in the blood increases as a result of diabetes, the kidneys might not be able to reabsorb the surplus. The end result is an increase in the amount of fluid lost from the body by urine [11].

Polydipsia

The individual feels very thirsty with a dry mouth due to the large amount of water lost when urinating. Although they are so much in need of water, they never have enough of it [12].

Polyphagia

This is related to the hunger that one often experiences when he/she is a diabetic. Extreme urine leads to a lack of glucose and, consequently, cellular famine, and, therefore, an increased appetite. Patients can have a feeling of wanting to eat more than usual, which increases the level of blood glucose and may result in weight gain. Moreover, insulin regulates the breakdown of carbs into glucose that supplies energy to the cells, when we eat. The lack of insulin production or being resistant to insulin in cells does not allow glucose to get into the cells, which causes a lack of energy. This can manifest itself as greater fatigue and hunger than normal [13]. Distorted vision Fluid changes in the body may lead to enlarging of the eye lenses and this distorts their shape hence decreasing their ability to focus [14].

Diagnosis of Diabetes

Assay for Fasting Plasma Glucose

To diagnose diabetes or pre-diabetes among individuals who might have it, there are three blood tests, which can be used. One of these tests is [11]. In conjunction with diabetes symptoms and a blood glucose level of 11.1 mmol/L (200 mg/dl) or greater, this test will positively determine the diagnosis of diabetes. Diabetes is diagnosed when the level of fasting blood glucose is 7.0 mmol/L (126 mg/dL) or higher in two tests. A range of 100-125 mg/dL is suggestive of pre-diabetes. A normal fasting blood glucose level is less than 100 mg/dL [15].

An Oral Glucose Tolerance Test

In the application of this test to diagnose diabetes, the normal level of blood glucose in two hours is 200mg/dl and above. The range of 140 to 199 mg/dl of the two-hour blood glucose level is pre-diabetes [16].

Post-Meal Blood Glucose

The postprandial blood sugar level is commonly measured two hours post eating. In case of uncertainty about potential diabetes when fasting glucose tests are taken, or when people display signs of increased blood sugar concentration, it is normally advisable to check the postprandial blood glucose levels. Diabetes is established in case of 200 mg/dl or more levels of blood glucose [17].

HbA1C

Diagnosis of type 2 diabetes and monitoring the effectiveness of people with diabetes in maintaining the level of glucose in their blood are performed by using the hemoglobin A1c test. It involves the examination of the levels of the so-called glycated hemoglobin, or hemoglobin bound to glucose. The level of blood glucose correlates with the level of HbA1c produced. When the hemoglobin A1c level is 6.5% or greater (48 mmol/mol), it is usually considered a diagnosis of diabetes. Confirmation of the initial discovery could sometimes require confirmatory tests [18].

Type 2 diabetes—a result

Acute consequences are unexpected and can come at any time, but chronic ones build up over time and are much more problematic [19].

Problems with the eyes (retinopathy):

Diabetic retinopathy is a condition that may impact the vision of some diabetics. Timely treatment and prevention of vision loss can be made possible by early diagnosis of retinopathy, possible by means of regular eye exams [20].

Foot Issues

This is a very dangerous condition as untreated complications of diabetes may result in amputation. High blood sugar levels prevent circulation, accelerating healing of wounds and cuts and nerve damage may cause loss of foot sensation. So, in case you observe any changes in the appearance or sensation of your feet, you need to check with your primary care doctor as soon as possible [20].

Heart and brain attacks

The elevated blood sugar levels that are capable of damaging blood arteries leading to heart attacks and strokes in diabetics may last long periods of time [21].

Chronic kidney disease (nephropathy)

Kidney damage in the long run may occur in diabetes when the body has difficulty in getting rid of the excess fluid and waste. High blood sugar and blood pressure cause this medical disease that is occasionally referred to as diabetic nephropathy or kidney disease [22].

Injury to the nerves (neuropathy)

Some diabetics may suffer damage to the nerves due to high blood sugar. This could lead to impaired vision, hearing, feeling, and mobility as a result of inefficient signal transmission from the brain to other areas of the body [23].

Acute complications

These can occur and may cause chronic, that is, long-lasting complications at any age [24]. Hypers– when your blood sugars are too low Hypers– when your blood sugars are too high Hyperosmolar Hyperglycaemic State (HHS)– a life-threatening emergency that only happens in people with type 2 diabetes. It's brought on by severe dehydration and very high blood sugars.

Once the ketones are built up because of the high level of sugar in the blood and resistance to insulin, a condition called the diabetic ketoacidosis (DKA) emerges.

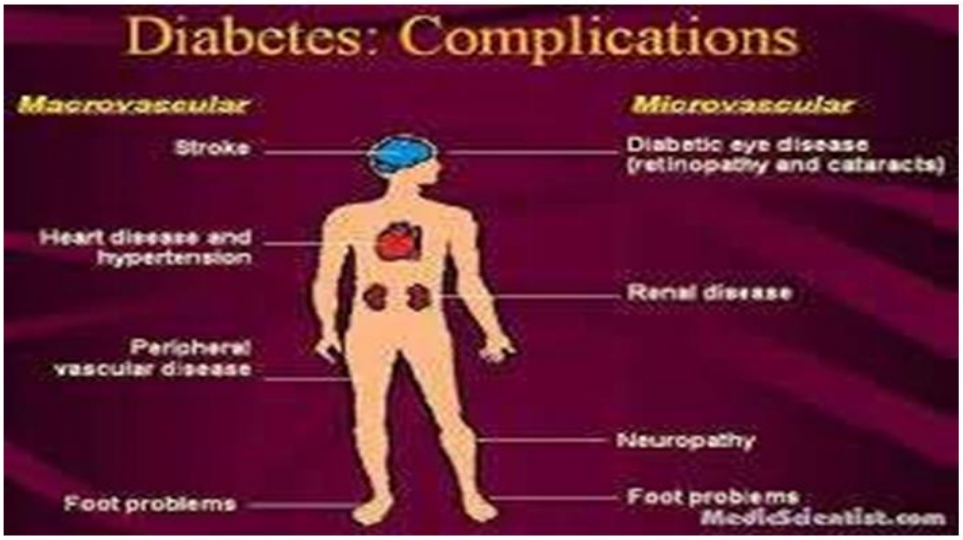

Figure 1. The major complication of type 2 diabetes mellitus [25].

Serum ferritin

Ferritin is one protein that assists cells to store and sequester iron and to ensure that it is not harmful. Ferritin is found in practically every cell of the human organism and is necessary to store iron in order to be able to make heme proteins such as hemoglobin easily. Among the numerous variables that have a strong effect on the production of ferritin are iron, hormones, and cytokines, and oxidative stress, to name but a few [26]. A positive acute-phase reactant in a number of inflammatory disorders, serum ferritin concentrations roughly reflect the body's iron content. Iron overload and hyper ferritinemia are not synonymous: an increase in serum ferritin level is a symptom of a wide variety of diseases, but does not necessarily imply that the iron stores in the body are overloaded. Previous studies have attributed high levels of ferritin to numerous health issues, such as infections, hyperthyroidism, liver and kidney failure, metabolic syndrome, inflammatory diseases, cancer, rheumatoid arthritis, and continuous alcohol use [27]. Increasingly there is research on the relationship between iron metabolism, metabolic syndrome, and type 2 diabetes. It was found that metabolic syndrome and the diseases that are associated with it were strongly related to iron surplus [28]. The association between high levels of iron in the body and the development of glucose intolerance, gestational diabetes, type-2 diabetes, and insulin resistance syndrome has only recently been realized [29]. The resulting net effect of iron depletion through frequent blood donation is a heightened sensitivity of insulin, and a reduction in postprandial hyperinsulinemia [30]. All in all, research, especially Indian one that shows direct evidence that iron overload renders it hard to control diabetes in the patients, is lacking [31]. This is even though somewhat indirect data is available in the western region of the world that indicates that effects of iron overload have a negative effect on DM. Our aim was to ascertain the association between serum ferritin concentrations and the risk of type 2 diabetes mellitus development in a group of Iraqi adults.

Materials and Methods

Subjects

This study was conducted at the Diabetes Center of Karbala's Imam Al Hussein Medical City as well as the Medical Laboratory Technology Department of Ahl Al Bayt University's College of Medical and Healthy Technologies. People with a Type 2 Diabetes Mellitus (T2DM) diagnosis and a control group of center employees had their blood samples taken.

Study groups

Around fifty individuals participated in this study in November 2023-February 2024 who had attended a diabetic center in the province of Karbala. The fifty people were selected as a second set of controls out of the pool of their relatives who apparently were in good health and had no history of illness. Data was collected by questionnaires and measurements and laboratory tests, such as FBS, HBA1C, and serum ferritin levels.

Materials

Instruments and Glassware's

Collecting Blood Samples

Three milliliters of venous blood are taken in the antecubital vein of each person. This is a typical location on the arm where blood is collected.

Instruments and Glassware's.

No.	Apparatus	Manufacturer
1.	Spectrophotometer	Optima japan
2.	Automatic pipettes 1, 0.5, 0.1, 0.02 ml	Slamed Germany
3.	Mix roller	China
4.	Deep freeze	Hetachi japan
5.	Centrifuge tube	Hitachi japan
6.	Centrifuge Eppendorf	Hitachi japan
7.	Refrigerator	Concord Italy
8.	Water bath	Hitachi japan
9.	Distillers	Human Germany
10.	Gel serum tube	Afco Jordan
11.	EDTA tube	Afco Jordan
12.	Stopwatch	Germany
13.	Syring	Midico /UAE
14.	TIPS (YELLOW &BLUE)	LEBANON
15.	Eppendorf tube 0.2,0.5 &1.5 ml	Bio-basic Canada
16.	Fine care	China

Specimen Division: Gel activator tubes are filled with around 2 milliliters of blood. These tubes have the active coagulant that helps in coagulating blood. A milliliter of the remaining blood is moved to an EDTA tube. Ethylenediaminetetraacetic acid (EDTA) is an anticoagulant that prevents blood clots. There are specific tests measurements that require blood without any coagulation, and this tube will be used in these situations.

Centrifugation: The next step is to spin the gel activator tubes at 5,000 rpm for 5 minutes to separate them. Centrifugation is used to separate the mixture using rotational force using the relative densities of the liquid components. Storage: After centrifugation, the clot is discarded and the serum, or the liquid part of the blood that remains after centrifugation is moved to a separate Eppendorf tube. Eppendorf tubes are the choice when it comes to containing small quantities of liquids in a lab.

Freezing: Before testing, serum is isolated, iced in an Eppendorf tube and frozen at -20C. The serum can be frozen and stored to be tested later. Certain blood tests such as biochemical tests are run on serum as opposed to hematological tests which are run on whole blood and this is done so that both types of tests can be run on the same blood sample. In order to come up with dependable test results, different tubes and additives have to be used in order to preserve the blood sample.

Results and Discussion

Characterization features of the different parameters

To analyze the descriptive data of all the participants in this study using SPSS version 22, we discovered such things as the mean, standard deviation, standard error and the P value. As Table 1 and the findings of the current research (p-value = 0.901) show, the age of the patient and the control group did not differ significantly.

Table 1. Explain the age distribution between healthy and control group

Sample	N	Mean± SD	P. Value
Age-patient	50	55.52±9.8	0.901
Age control	50	55.72±5.74	

Table 2. Explain the FBS differences between comparison groups

Sample	N	Mean± SD	P. Value
FBS-Patient	50	155.18±7.04	0.00
FBS-control	50	88.10±5.58	

Table 3. Explain the HbA1C finding of all participants in study.

Sample	N	Mean± SD	P. Value
HBA1C-Patient	50	7.588±1.244	0.00
HBA1C-Control	50	5.144±0.279	

Table 4. Serum ferritin differences between healthy and patients' group

Sample	N	Mean± SD	P. Value
Ferritin-Patient	50	150.30±6.86	0.00
ferritin-Control	50	101.10±9.82	

FBS

The current study revealed that the level of FBS in the patients and the control groups was significantly different (p-value = 0.00) as indicated in Table 2.

HbA1C

Table 3 shows the results of the current study, which showed that the patients' and the control groups' HbA1C levels were significantly different (p-value = 0.00).

Ferritin

The results of the current study showed that, as shown in Table 4, there were statistically significant variations in ferritin levels between the patient and control groups (p-value = 0.00).

Discussion

In a case-control study of a general population in Karbala province, this research looked at the relationships of serum liver ferritin with the occurrence of type 2 diabetes. We found a positive correlation between serum ferritin and a high risk of type 2 diabetes in males and females. Ferritin is also used as a measure of iron deposits in the body in addition to its use as an inflammatory marker. In a number of epidemiological studies, serum ferritin was found to be ranked

third among serum insulin, only preceded by age and body mass index, and second, in regression models, by blood glucose [32]. The function of ferritin in type 2 diabetes is a topic of debate. Cases of diabetes have also given rise to the subclinical hemochromatosis as a possible cause of pancreatic damage [33]. Many researchers have found ferritin to be a marker of insulin resistance, whereas others have concentrated on its importance as a marker of pancreatic inflammation. The authors Fernandez et al. examined the effect of reducing the levels of ferritin by letting blood on the insulin sensitivity and hemoglobin A1c levels of diabetics [34]. The positive impact of the reduction of ferritin on blood glucose regulation was taken as a validation that ferritin is likely to have a role in the pathogenesis of diabetes mellitus. Nonetheless, blood letting can also influence the level of total hemoglobin and the level of HbA1c and hence HbA1c has not been the most suitable level of blood glucose control. In a big representative sample, Wrede et al. [35] have discovered a statistically significant relationship between SF and insulin resistance criteria, which is in line with our findings. Insulin resistance is early onset and is well correlated to total units of blood transfused and serum ferritin in persistently transfused patients of thalassemia major as indicated in similar indirect data by Suvarna et al. [36] in India. Fernandez et al. [37] found out that high levels of iron stores can be associated with the occurrence of glucose intolerance, type 2 diabetes, and gestational diabetes in a population-based study. After phlebotomy, Facchini [38] found out that there was a significant increase in insulin sensitivity and a significant reduction in serum insulin level. Excess iron, as Jiang et al. argue [38], kills cells and leads to insulin resistance by the formation of hydroxyl radicals. Evidence that the antioxidant chelating drug deferroxamine improves fasting blood glucose in thalassemia major patients who undergo chronic transfusions lend credence to this theory.

Conclusion

The amount of ferritin in diabetic individuals increases over that of non-diabetics.it seems that ferritin may play a role in the pathogenesis of type 2 diabetes mellitus. We suggest that additional research into ferritin's function in gestational diabetes mellitus, poor glucose tolerance, insulin resistance, and pre-diabetes is warranted.

Recommendation

- Maximize the power of the study through raising the size of the sample.
- Research needs to include various populations and provinces in Iraq.
- Investigate additional iron, TIBC, and transferrin-related research that is associated with serum ferritin.

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