

THE ROLE OF HEAVY METALS ON PATIENTS WITH DIABETES MELLITUS IN ERBIL-CITY

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Abstract

Background and Aim: Diabetes mellitus, a chronic metabolic disorder, is a rapidly growing global issue. By 2035, the number of people affected by diabetes is projected to rise by 550 million. obesity has emerged as leading global health concern through recent environmental and societal changes, favoring a positive energy balance and weight gain. Essential metals like copper (Cu) and iron (Fe) are vital for cellular function but can become toxic in excess, particularly in genetic disorders. Imbalances in the homeostasis of these trace elements, due to abnormal metabolism, can contribute to diabetes and its complications. The study aimed to explore the role of diabetes mellitus on heavy metals like copper (Cu), Iron (Fe), in newly diagnosed cases of D.M. before and after treatment.

Method: This study was conducted at Galiawa Diabetes and Endocrinology teaching center in Erbil-Iraq. Over six months from September 25,2024, to March 6, 2025. Thirty- eight of newly diagnosed patients with T2DM. age between (30-65 years) were recruited for this study. Patients were injected insulin therapy 100 IU/ml Solution intravenous use 1 vial of 10 ml 100 IU/ml for three months. Before and after intervention, HbA1c level measurement by whole blood, and serum level of Iron (Fe), Copper (Cu) were measured.

Result: After Insulin injection for three months, there was a statistically significant reduction in HbA1c, Iron (Fe), and Copper (Cu) levels with a p-value < 0.05.

Conclusion: In this prospective cohort study confirmed that the relationship between some heavy metals associated with newly diagnosed T2DM patients. Showed that there is significant relation between heavy metals like Iron, and Copper in newly diagnosed patients with type 2 diabetes mellitus, the present study suggests that Insulin treatment markedly control heavy metals in diabetes mellitus patients.

Keywords: Diabetes mellitus, Heavy metals, Insulin, Iron, Copper

INTRODUCTION

The chronic metabolic disorder diabetes mellitus is a fast-growing global problem with huge social health, and economic consequences (Alam et al., 2014). Obesity is a chronic metabolic disease affecting adults and children worldwide. It has become one of the leading causes of death, as obesity is known to be the main risk factor for a number of non-communicable diseases, in particular type 2 diabetes. This close relationship led to the connotation 'diabesity', highlighting the fact that the majority of individuals with diabetes are overweight or obese (Leitner et al., 2017). Type 2 Diabetes Mellitus is one of the most common metabolic disorders worldwide and its development is primarily caused by a combination of two main factors: defective insulin secretion by pancreatic β -cells and the inability of insulin-sensitive tissues to respond to insulin (Galicia-Garcia et al., 2020). Prediabetes has been linked to early complications such as nephropathy, small fiber neuropathy, retinopathy, and increased risk of macrovascular disease (Bansal, 2015). pancreatic disease has drawn more attention in recent years. However, significant improvements still need to be made in the recognition, diagnosis and treatment of the disorder, and in the knowledge of the pathological mechanisms. The clinical course of DEP is different from type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) (Wei et al., 2020). Brittle diabetes was first used to describe a life "disrupted by episodes of hypoglycemia or hyperglycemia (Hirsch and Gaudiani, 2021). The symptoms of diabetes mellitus are categorized into three main groups, including excessive thirst (polydipsia), frequent urination (polyuria), glucose in urine (glycosuria), extreme hunger (polyphagia), unexplained weight loss, dry skin, fatigue, dizziness, acetone-like breath, nocturia, tachycardia, dehydration, and dry mouth (Adinortey, 2017). Most patients with type 2 diabetes mellitus (T2DM) suffer from insulin resistance and defective insulin secretion. Treatment strategies for T2DM usually include diet control, moderate exercise, and the use of glucose- lowering and lipid-lowering drugs. Despite their therapeutic effects, most drugs cause adverse side effects (Xu et al., 2018). Essential metals like copper (Cu) and iron (Fe) are vital for cellular function but can become toxic in excess, particularly in

genetic disorders. Imbalances in the homeostasis of these trace elements, due to abnormal metabolism, can contribute to diabetes and its complications (Zheng et al., 2008). However, the relationship between diabetes mellitus Heavy metals like Copper (Cu) and iron (Fe) in newly diagnosed diabetic patients are unclear, our hypothesis is to determine the effect of diabetes on both heavy metals before and after treatments that taken by new diagnosed patients with D.M. The study aimed to explore the role of diabetes mellitus on heavy metals like Cu and Iron in newly diagnosed cases of D.M. before and after treatment.

MATERIALS AND METHODS

Study Design, participants and Data Collection

This was a prospective cohort study conducted recruiting 38 individuals (24 Male) patients and (14 Female) patients (Type 2 Diabetic patients). Heavy metal concentrations were assessed from patients with newly diagnosed Diabetes Mellitus (DM), before and after treatment intervention. serum was collected from September 25,2024, to March 6, 2025. The study was carried out from September 2024 to March 2025. Inclusion Criteria for the study is (between 3-6 months) newly diagnosed type 2 diabetes mellitus (T2DM) patients, age between (30-65 years) both gender male and female. The Exclusion Criteria were previously diagnosed patients with T2DM patients (more than 6 months), Type 1 diabetes mellitus (T1DM) patients, and patients were taking treatments to manage D.M.

Phlebotomy procedures for measuring HbA1c, Iron (Fe) and Copper (Cu) level

Blood sample were taken from the vein of the T2DM patients, the blood was put into the specialized EDTA tube for measuring HbA1c level, and blood were put into the HbA1C Machine (Randox RX Imola Chemistry Analyzer). Normal Range of HbA1C less than or equal to 5.6% considered for Normal, and the level above 6.5% is conducted as For Diabetes. Also, some of the blood was collected inside biochemical tubes for coagulation then centrifuged for 15 minutes after that the serum was separated by using micropipette then the level of Iron (Fe) and Copper (Cu) was measured by Spectrophotometer machine (Syntonic S-925 Single Beam UV-VIS Spectrophotometer. Model, S-925. Made in India).

Iron (Fe) measurement in Diabetes mellitus patients

Serum Iron (Fe) level was measured successfully on 38 samples of newly diagnosed T2DM, or patients with HbA1c more than 6.5% before and after treatment. Samples assessed by Spectrophotometer using IRON direct measure ferene kit (BIOLABO S.A.S., LOT 062335A, made in France). Following the manufactures directions, at 580 nm absorbance was measured, standard curve was determined by using a logistic curve fitting technique. Data was represented as ($\mu\text{g}/\text{dl}$).

Copper (Cu) measurement in Diabetes mellitus patients

Serum Copper (Cu) level was measured successfully on all 38 samples of newly diagnosed T2DM, or patients with HbA1c more than 6.5% before and after treatment. Samples assessed by Spectrophotometer using RAME COPPER kit (LTA s.r.i. REF cc02150, made in Italy). Following the manufactures directions, at 580 nm absorbance was measured, standard curve was determined by using a logistic curve fitting technique. Data was represented as ($\mu\text{g}/\text{dl}$).

Treatment Protocol

Overweight patients required to perform lifestyle changes like diet and exercise, Participants were initiated on standard pharmacological treatment for newly diagnosed Type 2 DM. This included: Insulin therapy 100 IU/ml Solution for injection insulin human subcutaneous or intravenous use 1 vial of 10 ml 100 IU/ml.

Statistical analysis

Data were represented as mean values \pm SEM. Statistical evaluations were performed by use of parametrical test (t-test) was performed. p-value < 0.05 was considered significant, and n represents the total number of participants. Statistical analysis was performed by use of SPSS (IBM Corp., Armonk, N.Y., USA).

RESULTS

Distribution of Male and female patients Age (30-65)

A total of 38 patients were included in the study, with an age range between 30 to 65 years old. The gender distribution was as follows, 24 (63.2%) Male Patients. And 14 (36.8%) Female Patients. The pie chart visually represents the proportion of male and female patients. This data provides insight into the gender distribution within the study population, which may be relevant for further statistical.

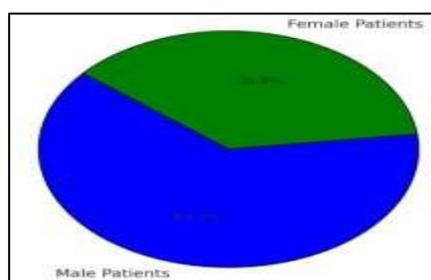


Figure 1: Distribution of male and female patients with the age range between (30-65) years.

HbA1c Levels measurement for Newly Diagnosed Diabetes Mellitus Patients before and after treatment

Evaluating HbA1c levels as an indicator of diabetes mellitus in newly diagnosed patients, the analysis of HbA1c levels before and after treatment in newly diagnosed diabetes mellitus patients revealed a significant reduction in mean HbA1c levels. The mean HbA1c before treatment was 9.69% (± 0.269 SE), whereas the mean HbA1c after treatment was 8.93% (± 0.193 SE). with a p-value < 0.05 This indicates a highly statistically significant reduction in HbA1c levels after treatment as shown in Table 1.

Table 1: HbA1c level before and after treatment for newly diagnosed patients with D.M

	Before treatment	After treatment	P-Value
Mean value of HbA1c	9.69	8.93	< 0.05
SEM	± 0.269	± 0.193	

Serum iron (Fe) levels in male patients with D.M before and after treatment

Iron (Fe) levels before and after treatment in male patients revealed a significant reduction in iron levels following treatment. The mean iron level before treatment was 173.74 Mg/dl (± 1.86 SE), while the mean iron level after treatment was 95.70 Mg/dl (± 4.21 SE). The (P-value < 0.05), indicating a highly significant decrease in iron levels after treatment. As shown in the (Figure 2) below.

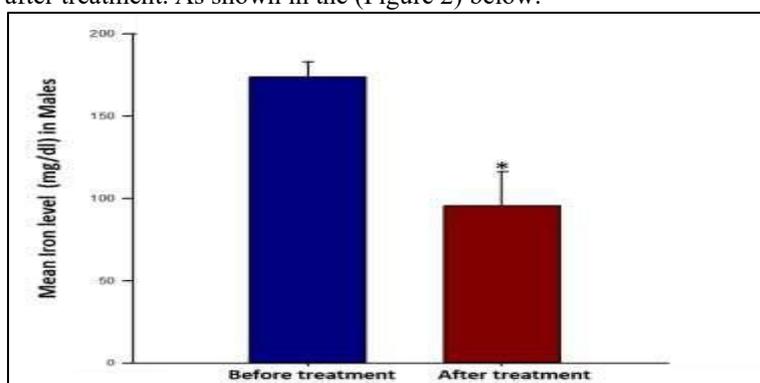


Figure 2: Serum iron level (mg/dl) in newly diagnosed male patients with D.M before and after treatment, (p-value < 0.05), n= 24.

Serum iron (Fe) levels in female patients with D.M before and after treatment

Iron (Fe) levels before and after treatment in female patients revealed a significant reduction in iron levels following treatment. The mean iron level before treatment was 174.39 Mg/dl (± 2.15 SE), while the mean iron level after treatment was 96.04 Mg/dl (± 5.87 SE). The (p-value < 0.05), indicating a highly significant decrease in iron levels after treatment. As shown in the (Figure 3) below.

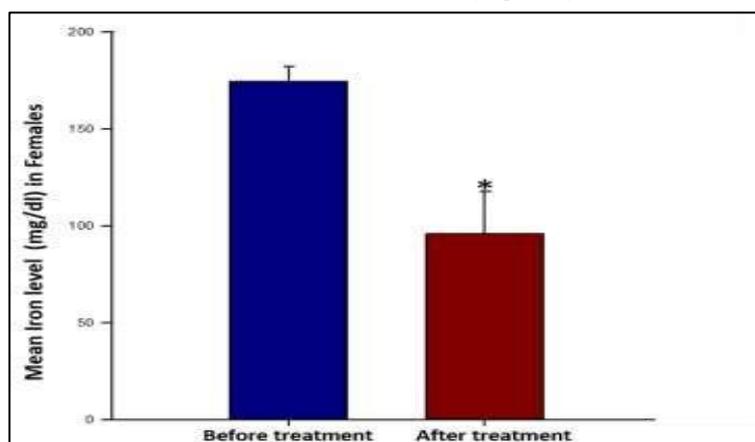


Figure 3: Serum iron level (mg/dl) in newly diagnosed female patients with D.M before and after treatment, (p-value < 0.05), n= 14.

Serum copper (Cu) levels in male patients with D.M before and after treatment

Estimation of serum copper (Cu) levels before and after treatment in male patients showed a significant reduction in copper levels following treatment. The mean copper level before treatment was 185.77 Mg/dl (± 1.63 SE), while the mean copper level after treatment was 106.15 Mg/dl (± 4.12 SE). These findings suggest that the treatment effectively lowered copper levels in male patients, with a very strong statistical significance (p < 0.05). As shown in the (Figure 4) below.

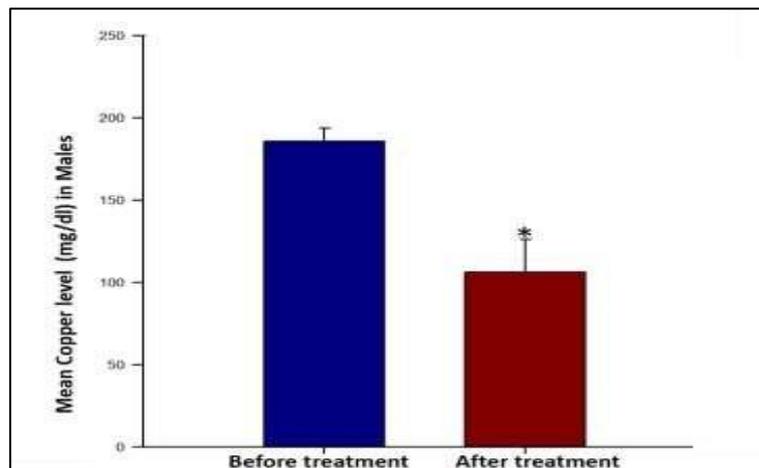


Figure 4: Serum copper (Cu) level (mg/dl) in newly diagnosed male patients with D.M before and after treatment, (p-value < 0.05), n= 24.

Serum copper (Cu) levels in female patients with D.M before and after treatment

Estimation of serum copper (Cu) levels before and after treatment in female patients showed a significant reduction in copper levels following treatment. The mean copper level in female patients before treatment was 186.81 Mg/dl (± 2.01 SE), which significantly decreased to 104.50 Mg/dl (± 5.73 SE) after treatment. These findings suggest that the treatment effectively lowered copper levels in female patients, with a very strong statistical significance ($p < 0.001$). As shown in the (Figure 5) below.

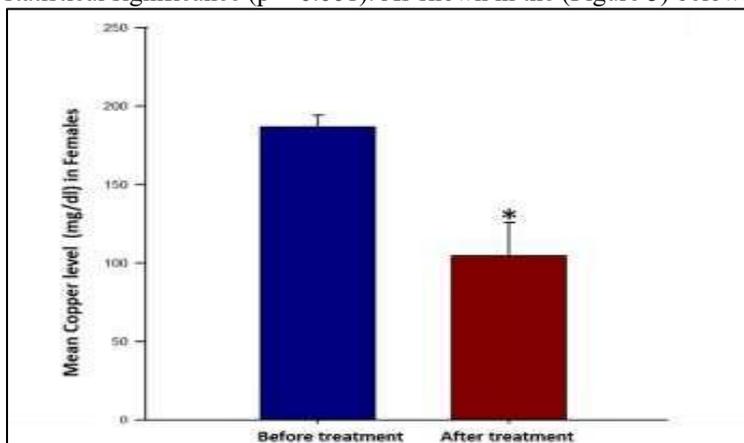


Figure 5: Serum copper (Cu) level (mg/dl) in newly diagnosed female patients with D.M before and after treatment, (p-value < 0.05), n= 14.

DISCUSSION

The major findings in the present study enable us to identify the importance of the relationship between heavy metals like: iron (Fe) and Copper (Cu) measurements in patients with newly diagnosed of type 2 diabetes mellitus. Serum HbA1c level which is one of the indicators for diagnosing D.M. was significantly higher in the newly diagnosed diabetes mellitus patients, before and after metformin treatment in both genders' male and Female. These results along with other researches (Rosenlund et al., 2015),(Vigersky et al., 2018). Indicating that insulin injection can reduce the HbA1c level in diabetes patients. The present study involved T2DM patients they were on insulin injection therapy only and not taking any other agents. To our knowledge, no research has been conducted on the effects of insulin injection on heavy metals like Fe, and Cu in newly diagnosed T2DM patients. injected Patients with insulin therapy for three months led to a substantial significant decrease in Hba1c, Iron and Copper levels in T2D.M (Dahlqvist et al., 2018). Interestingly in the present study the serum level of Iron was Increased to the response of Hyperglycemia in both genders' male, and female with a P-value <0.05, and after specific dose of metformin the level was significantly decreased. Jiang et al. observed elevated ferritin levels in diabetic individuals compared to non- diabetic subjects. A recent study also reported a positive association between serum ferritin levels and iron accumulation in tissues, which increased progressively with the duration of diabetes (Raj and Rajan, 2013). Multiple studies have demonstrated a connection between hemochromatosis and type 2 diabetes (T2D) (Adams et al., 2005), (Acton et al., 2006) , (Worwood, 2002). Increased iron levels can oxidize biomolecules, including nucleic acids, proteins, and lipids, potentially contributing to the development of type 2 diabetes by reducing insulin secretion from pancreatic beta cells while simultaneously increasing insulin resistance (Jiang et al., 2004), (Jehn et al., 2004), (Fernández-Real et al., 2002), (Papanikolaou and Pantopoulos, 2005),(Lee et al., 2006). Previous studies (Sharifi et al., 2008) and (Kim et al., 2011) have demonstrated a strong association

between serum ferritin levels and insulin resistance during the preclinical stage, before the onset of full-blown diabetes mellitus. In this context, research also suggests that, alongside elevated glucose levels, serum ferritin could serve as a potential surrogate marker for predicting diabetes onset (Forouhi et al., 2007), (Rajpathak et al., 2009). However, none of the previous studies have tried to investigate the effect of heavy metals levels in newly diagnosed cases with T2DM before and after treatments as a primary goal. The relationship between heavy metals and cardiovascular diseases has been demonstrated in several studies (Yang et al., 2020), (Houston, 2007). Although there are some researches about the relationship between copper and gestational diabetes (Li et al., 2019). Heavy metals and diabetes mellitus complications (Walter Jr et al., 1991). But none of the previous researches explained the effect of insulin therapy on copper in newly diagnosed patients with T2DM. The available studies' findings regarding the impact of insulin injection on heavy metals and diabetes mellitus are uncertain. In the present study, the participants showed a significant reduce in copper after managing blood glucose level by insulin treatment. Both copper and zinc contribute to protecting body tissues from oxidative damage (John et al., 2010), (Zheng et al., 2006). Recent research from Mosul by Hend Y. revealed the effect of zinc with metformin treatment and lipid profile, uric acid with T2DM (Younis et al., 2021). Recent reports indicate that disruptions in copper levels across various biofluids and tissues are linked to metabolic abnormalities associated with diabetes and its complications (Kazi et al., 2008), (Rajpathak et al., 2006).

CONCLUSION

In this prospective cohort study confirmed that the relationship between some heavy metals associated with newly diagnosed T2DM patients. Showed that there is significant relation between heavy metals like Iron, and Copper in newly diagnosed patients with type 2 diabetes mellitus, the present study suggests that metformin markedly control heavy metals in diabetes mellitus patients.

Recommendations

The present study showed by managing blood glucose level with metformin, the levels of heavy metals are also controlled during diabetes mellitus recommendation for the future studies are below:

1. Future studies may focus on other heavy metals like mercury, and zinc to elucidate the role of other heavy metals on diabetes mellitus.
2. Future studies focus more on the relationship between heavy metals and T1DM.

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