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Correlation between the Glucose, BMI and metalions in Type II Diabetes Mellitus

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Abstract:

Type 2 Diabetes Mellitus (T2DM) is a common metabolic condition caused by inadequate insulin release by pancreatic β-cells and the inability of insulin-sensitive tissues to respond. Obesity is the leading risk factor for T2DM and is linked to metabolic abnormalities that cause Insulin Resistance. Traditional risk factors, such as inheritance and poor dietary habits, cannot fully explain the etiology and high prevalence of diabetes mellitus. Metal exposure is a new and emerging risk factor that is gaining attention. Heavy metals can disrupt mitochondrial processes and increase free radical generation, resulting in oxidative stress and inflammation, both of which may have a role in metabolic disorders such as diabetes mellitus or obesity. In the present study, we aim to check whether there is any correlation between metal ions, glucose, Body mass index (BMI) in patients with T2DM. 50 healthy normal control, diabetic patients with controlled Blood Sugar Level - 50 Subjects and diabetic with Uncontrolled Blood Sugar Level - 50 Subjects were included in the study. A significantly elevated level of blood sugar and BMI was observed in the Type 2DM group. A significantly elevated level of copper and lead was observed in the Type2 DM and a slightly decreased (significant) level of zinc was observed in the Type2 DM case. A low-carbohydrate ketogenic diet can reduce hyperglycemia, hyperinsulinemia, insulin resistance, and type 2 diabetes.

Keywords: Type 2 Diabetes Mellitus (T2DM), Heavy metals, Body mass index

Introduction

Diabetes Mellitus (DM), also referred to as diabetes, is a metabolic disease or syndrome characterized by persistent hyperglycemia (the presence of elevated blood sugar) caused by errors in insulin action, insulin secretion, or both. It is currently ubiquitous over the world, with numerous consequences (1,2). Diabetes can cause a variety of physiological and mental health issues, including sexual disorders (3). Severe vision loss, acute renal disorders requiring dialysis or kidney transplantation, myocardial infarction (also known as heart attack), and cerebrovascular diseases such as stroke, and hypertension are also common. Because of the severity of the negative impacts of diabetes, it is critical to identify the factors and address the issue to contribute to improving the country's health status (4-8).

Type 2 Diabetes Mellitus (T2DM) is a common metabolic condition caused by inadequate insulin release by pancreatic β-cells and the inability of insulin-sensitive tissues to respond (9). Insulin release and action must perfectly match metabolic demand; thus, the molecular mechanisms involved in insulin synthesis and release, as well as the insulin response in tissues, must be strictly controlled. As a result, errors in any of the systems involved might cause a metabolic imbalance, which leads to T2DM pathogenesis.

Obesity (BMI ≥30 kg/m2) is the leading risk factor for T2DM (10) and is linked to metabolic abnormalities that cause Insulin Resistance (IR) (11). There is an inverse linear relationship that exists between BMI and age at diagnosis of T2DM. The specific processes by which obesity causes T2DM and IR are unknown; nevertheless, multiple components have been identified as playing a substantial role in the development of this disease process, which includes both cell-autonomous mechanisms and inter-organ communication (12).

Traditional risk factors, such as inheritance and poor dietary habits, cannot fully explain the etiology and high prevalence of diabetes mellitus. Metal exposure is a new and emerging risk factor that is gaining attention. Heavy metals can disrupt mitochondrial processes and increase free radical generation, resulting in oxidative stress and inflammation, both of which may have a role in metabolic disorders such as diabetes mellitus or obesity. However, the effects of metal exposure, particularly combined exposure to several metals, on diabetes mellitus development have not been thoroughly explored (13,14).

Recent research on the association between multi-metal exposure and diabetes mellitus risk has provided contradictory results. Several population-based epidemiological surveys from various regions revealed that magnesium (Mg), calcium (Ca), iron (Fe), zinc (Zn), arsenic (As), cadmium (Cd), copper (Cu), and lead (Pb) relate to Fasting blood glucose (FBG) or diabetes mellitus prevalence (14-17) while other research found no association (18-20). Furthermore, metal interactions pose a hurdle to correlation exploration. More research is needed to understand how multi-metal exposure affects the incidence and progression of diabetes mellitus.

In the present study, we aim to check whether there is any correlation between metal ions, glucose, Body mass index (BMI) in patients with T2DM.

Methodology:

1. Ethical statement:

This study was approved by the Ethics committee of K.S Hegde Medical Academy, Nitte (Deemed to be University). Informed consent was taken from the patients before collecting the sample.

2. Sample collections:

5ml of blood samples were collected from the controls and diabetic patients visiting the K. S. Hegde Hospital, Mangalore. samples were centrifuged at 1500g for 10 min to separate plasma for estimation of zinc and copper. The concentration of zinc and copper is assessed by an atomic absorption spectrophotometer. Glucose concentration was determined spectrophotometrically using the Glucose oxidase peroxidase (GOD-POD) method.

Inclusion Criteria

- 30-65 years 50 diabetic subjects who were clinically diagnosed with diabetes at least 6 months before this study
- Patient on insulin or oral hypoglycemic drug

Exclusion criteria

- Age above 65 years
- Patients with end-stage renal disease or other systemic diseases unrelated to diabetes

3. Estimation of Glucose:

$$\text{Glucose} + 02 + H_2O \xrightarrow[\text{Glucose Oxidase (GOD)}]{} \text{Gluconic acid} + H_2O_2$$

$$H_2O_2 \xrightarrow[\text{Peroxidase (POD)}]{} H_2O + [O]$$

$$[O] + \text{4-amino-antipyrine} + \text{phenol} \longrightarrow \text{Quinoneimine} + H_2O$$

	Blank	Standard	Test
Distilled Water	10 µl	----	----
Glucose Standard	----	10 µl	----
Plasma	----	----	10 µl
GOD-POD Reagent	1 ml	1 ml	1 ml

Three test tubes were taken and labeled each as Blank, Standard, and Test . Added 10 µl of distilled water to a blank test tube. 10 µl of glucose standard (control) to a standard test tube.

10 µl of the plasma being analyzed in a test tube. 1 ml of glucose reagent added to each test tube. Incubated for 15min and absorbance was read at 500nm.

4. Estimation of Metal ions by Atomic Absorption Spectrophotometer (AAS):

At first sample solution is aspirated into the spray chamber through capillary tube. The liquid sample is aerolized and mixed with combustible gases such as acetylene and air or acetylene and nitrous oxide(mentioned in the diagram as fuel gas and oxidant, Fig. 1) in the spray chamber and burned in a flame and the individual atoms of the sample are released to form a cloud inside the flame. The atoms of the element get free. To bring it from ground state into an excited state by passing UV light is required through hollow cathode lamp. On absorbing UV light at specific wavelengths the ground state metal atoms get transitioned to higher electronic state. The region of the spectrum to be measured is selected by a monochromator. The isolated spectral line falls on the photomultiplier, the detector and the output is amplified and sent to a readout device meter, digital or analogue or through a computer data processing system. The data is processed through the software. Absorption of a selected wavelength is measured by the change in light intensity striking the photomultiplier detector and is directly related to the amount of elements in the sample. Waste is drained out through drain pipe [21].

5. Statistical analysis:

All statistical analysis were carried out using the statistical package for social science (SPSS 16.). Values were expressed as mean ± standard deviation. Correlation between Blood Sugar level, Copper Zinc and Lead levels was analyzed using Spearman correlation**.** $P < 0.05$ is considered as significant.

Results:

In the present study, we aimed to check whether there exists any correlation between metal ions, glucose and BMI in patients with T2DM. The study subjects were divided into 3 groups. Group I - Healthy Controls - 50 Subjects, Group II – Type II Diabetes with controlled Blood Sugar Level - 50 Subjects, Group III- Type II Diabetes with Uncontrolled Blood Sugar Level - 50 Subjects. Mean Blood sugar, BMI, Copper, Zinc and Lead levels in Type II Diabetes Mellitus are shown in **Table 1.**

Table 1: Blood Sugar level, BMI ,Copper, Zinc and Lead levels in Type II Diabetes Mellitus

Parameters	Group I	Group II	Group III	Reference values
Blood Glucose Level (FBS)	85.23 ± 24.6	195 ± 15.3	225.6 ±24.6	70-110mg/dl

BMI (Body Mass Index)	22.3±3.4	27.1 ± 2.1	32.3 ± 1.5	18-24 kg/m²
Copper	99.8 ±12.3	146.3 ± 5.5	198.3 ±25.6	75-160 µg/dl
Zinc	104.3 ± 3.5	81.9± 9.4	68.3± 13.5	70-120 µg/dl
Lead	25.54 ±3.38	33.69 ± 4.4	53.49 ±5.04	20-40 µg/dl

Group I - Healthy Controls - 50 Subjects

Group II - Diabetic with controlled Blood Sugar Level - 50 Subjects

Group III- Diabetic with Uncontrolled Blood Sugar Level - 50 Subjects

A significantly elevated level of blood sugar and BMI was observed in the Type II DM group**.** Obesity (BMI ≥30 kg/m2) is the leading risk factor for T2DM and is linked to metabolic abnormalities that cause IR. There is an inverse linear relationship that exists between BMI and age at diagnosis of T2DM **[Table 2].** We found a statistically significant positive correlation between BMI and cooper, lead and a negative correlation between BMI and Zinc.

Table 2: Correlation between Blood Sugar level, Copper Zinc and Lead levels in Type II Diabetes Mellitus

Parameters	Group I	Group II	Group III	P value
Blood Glucose Level (FBS)	85.23 ± 24.6	195 ± 15.3	225.6 ±24.6	<0.0001****
Copper	99.8 ±12.3	146.3 ± 5.5	198.3 ±25.6	<0.0001****
Zinc	104.3 ± 3.5	81.9± 9.4	68.3± 13.5	<0.0001****
Lead	25.54 ±3.38	33.69 ± 4.4	53.49 ±5.04	<0.0001****

p<0.0001****- statistically significant

A significantly elevated level of copper and lead was observed in the Type II DM and a slightly decreased (significant) level of zinc was observed in the Type II DM case. We found a statistically significant positive correlation between BMI and cooper, lead and a negative correlation between BMI and Zinc. **[Table 3].**

Table 3: Correlation between BMI, Copper Zinc and Lead levels in Type II Diabetes Mellitus

Parameters	Group I	Group II	Group III	P value

BMI (Body Mass Index)	22.3±3.4	27.1 ± 2.1	32.3 ± 1.5	<0.001**
Copper	99.8 ±12.3	146.3 ± 5.5	198.3 ±25.6	<0.001**
Zinc	104.3 ± 3.5	81.9± 9.4	68.3± 13.5	<0.001**
Lead	25.54 ±3.38	33.69 ± 4.4	53.49 ±5.04	<0.001**

p<0.0001****- statistically significant

Discussion:

T2DM is defined by persistently increased blood glucose or an increase in blood glucose following a carbohydrate-containing meal (22). Unlike Type 1 Diabetes, which is characterized by a lack of insulin, most people with T2DM have high insulin levels (fasting and/or post-glucose consumption), unless there has been beta cell loss. Many endogenous factors contribute to an increase in blood glucose levels. At least three hormones boost glucose levels: glucagon, epinephrine, and cortisol. These hormones raise glucose levels by promoting glycogenolysis and gluconeogenesis (23). Without consuming carbohydrates, the normal human body can produce sufficient glucose through the mechanisms of glucagon secretion, gluconeogenesis, glycogen storage, and glycogenolysis. In the present study, we aimed to check whether there is any correlation between metal ions, glucose, Body mass index (BMI) in patients with T2DM. The study subjects were divided into 3 groups. Group I - Healthy Controls - 50 Subjects, Group II – Type II Diabetes with controlled Blood Sugar Level - 50 Subjects, Group III- Type II Diabetes with Uncontrolled Blood Sugar Level - 50 Subjects.

A significantly elevated level of blood sugar and BMI was observed in the Type II DM group**.** Obesity (BMI ≥30 kg/m2) is the leading risk factor for T2DM (10) and is linked to metabolic abnormalities that cause IR (11). There is an inverse linear relationship that exists between BMI and age at diagnosis of T2DM**.** We found statistically significant positive correlation between BMI and cooper, lead and negative correlation between BMI and Zinc.

A significantly elevated level of copper and lead was observed in the Type II DM and a slightly decreased (significant) level of zinc was observed in the Type II DM case. We found statistically significant positive correlation between BMI and cooper, lead and a negative correlation between BMI and Zinc.

It is concluded from the study (24) that the normal levels of metals like Fe, Ca, Mg and P are disturbed in patients with DM. It was observed that Fe levels were raised, and Ca, Mg and P were depleted in patients suffering from DM. The difference in levels of Fe, Ca and P in diabetic and non-diabetic groups was statistically significant; however, Mg was not significant. Altered levels of trace elements Zn and Cu are found to be an important predisposing factor for diabetic patients to develop complications (25). Lead-induced toxicity is irreversible and can harm most human organs due to increased oxidative stress. This toxin typically affects reproductive, renal, central nervous system, and blood-cell components. Diabetic patients with high blood lead levels may experience brain hyperintensities, potentially leading to cognitive, behavioural, and Alzheimer's disease complications (26).

Conclusion:

Diabetes is widely recognized as a rising epidemic, with a cumulative impact on practically every country, age group, and economy in the world. A low-carbohydrate ketogenic diet can reduce hyperglycemia, hyperinsulinemia, insulin resistance, and type 2 diabetes. Although lifestyle changes can prevent or treat insulin resistance and T2DM, they can be challenging to adopt. Future research should focus on enhancing adherence to all beneficial lifestyle or pharmacological interventions.

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Conflict of Interest:
No

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