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A study the relationship between trace element (Zinc, magnesium) level and intensity in diabetes mellitus type 1 and type 2

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Abstract

Certain micronutrients known as trace elements are necessary for the body to function normally. Diabetes mellitus development is influenced by specific trace elements. This study aimed to evaluate the relationship and intensity zinc, magnesium in diabetes type 1 and type 2, and to assess Correlations of Zinc, Magnesium to some parameters in diabetes mellitus. This study included 100 patients with DM and 100 healthy controls. T1D with an age range of 10-23 years while T2D with an age range of 40-70 years. Was controls age same age as patients. Serum concentration of trace elements (zinc, magnesium). It has been identified by flameless atomic absorption spectrophotometry techniques employing an atomic absorption spectrophotometer, zinc was of estimated at wavelength 213.9 nm using a slit width of 0.7 nm and lamp current 8 mA. With a slit width of 0.7 nm and a lamp current of 8 mA, Mg was measured at a wavelength of 285.2 nm. The results showed that the average zinc content was found to be (70.13±30.230) vs (87.25±10.720) mg/l significant decreased ($p = .030$) in patients with type 1 diabetes when compared to the control group while that the average concentration zinc (35.64±20.533) vs. (85.82±10.154) mg/l significant decreased ($p = 0.0001$) in patients with type 2 diabetes when compared to control group. But the large effect of zinc deficiency is on type 2 diabetes $r = 0.783$ (Large effect) and the least effect is on type 1 diabetes. $r = 0.242$ (Small effect) and also observed that the average concentration magnesium (1.6855±.38257) vs (1.8650±.13877) µg/L significant decreased ($p = .014$) in patients with type 1 diabetes when compared to the control group while that the average concentration magnesium (1.3717±.30033) vs. (1.8467±.12550). µg/L significant decreased ($p = 0.0001$) in patients with type 2 diabetes when compared to control group. But the large effect of magnesium deficiency is on type 2 diabetes $r = 0.739$ (Large effect) and the least effect is on type 1 diabetes. $r = 0.276$ (Small effect). In conclusion, according to the current findings, serum levels of vital the trace elements (zinc, Mg) are associated with the presence of diabetes mellitus type 1 and 2 but effect in type 2 more than type 1. These findings support the growing amount of data showing that the zinc, Mg is crucial for proper glucose metabolism. Storage, creation, and release insulin. Aid help in normal insulin action and there are no correlations between zinc, Mg with other parameters in diabetes type 1 and type 2.

Keywords: Zinc, magnesium, diabetes mellitus type 1 and type 2, atomic absorption spectrophotometer

Introduction

High blood sugar is a defining feature of diabetes mellitus, a chronic metabolic disorder. It typically happens when the body uses the insulin it generates inefficiently or when the pancreas produces insufficient amounts of insulin [1]. Statistics show that diabetes is a serious global health concern. 463 million individuals between the ages of 20 and 79, or 9.3% of adults worldwide, suffer with diabetes. This domination is expected to increase in the years to come. By 2045, 700 million people are expected to have diabetes [2]. According to the American Diabetes Association (ADA), there are several types of diabetes, including type 1 diabetes mellitus (T1DM), which is brought on by an autoimmune disease. Insulin-resistant cells that are unable to respond to insulin are the cause of type 2 diabetes mellitus (T2DM). gestational diabetes mellitus (GDM), and other causes of diabetes [3]. A number of factors, including trace elements like magnesium and zinc, can either cause diabetes or make it worse [4]. Trace elements are crucial for hormone function, wound healing, insulin synthesis, storage, and secretion in addition to protein synthesis.

Diabetes mellitus also affects how these elements are metabolized. Deficits in trace elements are associated with insulin resistance [5]. After iron, in nature, zinc is the second most common micronutrient. Zinc is found in both plant-based and animal-based meals. The main food sources of zinc include meat, shellfish, oil seeds, and whole grains [6]. The usual range for zinc consumption is 14-30 mg/kg to help maintain the body's zinc balance [7]. The Zinc plays a key role in insulin signaling and crystallization. Zinc especially encourages the PI3K/Akt pathway to be activated, which is necessary for the metabolism of glucose [8]. Zinc also facilitates the translocation of glucose transporter 4 (GLUT4) and the phosphorylation of the insulin receptor's β-subunit [9]. Importantly, insulin needs to bind with two zinc ions to form a hexameric structure in order to mature inside secreting granules of the pancreatic beta-cells and then be released [10]. Pancreatic beta-cells contain certain zinc carrier proteins that are necessary for the release of insulin. ZnT8 is one such crucial protein that is required to the storage and processing, crystallization, and release of insulin in add to the overall metabolism glucose [11]. Zinc deficiency inhibits ZnT8 expression, which in turn inhibits insulin production [12]. Diabetes mellitus may occur as a result of abnormalities in glucose metabolism brought on by zinc deficiency. On the other hand, hyperglycemia may cause increased excretion of zinc in the urine by interfering with the active transport of zinc into renal tubular cells [13]. It has been discovered that individuals with diabetes mellitus have altered amounts of elevated oxidative stress, especially in pancreatic β-cells, and trace elements, like as zinc. These abnormalities can worsen insulin resistance in peripheral tissues such the liver, adipose tissues, and muscle which can impair glycemic control and result in complications from diabetes [14]. Numerous studies have connected reduced glucose tolerance to zinc (Zn) deficiency. Furthermore, it has been found that providing zinc supplements to diabetics enhances their glycemic control, or glucose profiles. Zinc's effect appears to be linked to increased activity of insulin-independent glucose transporters [15]. Magnesium is a trace element that is necessary for hundreds of enzymes to function. For example, during cell signaling, all kinases transfer phosphate groups using the adenosine triphosphate (ATP)-Mg2+ chelate. Hexokinase, phosphofructokinase, aldolase, and phosphoglycerate kinase are among the glycolysis enzymes that also require both Mg^{2+} and ATP-Mg^{2+} to function [16] is essential for both the movement of glucose into the cell and the metabolism of carbohydrates. It aids in the cellular activity of insulin. Low magnesium intake is one risk factor for diabetes. A magnesium deficit weakens the body's defenses against oxidative damage, which reduces cells' ability to withstand the oxidative stress caused by diabetes and hastens the onset of disease-related issues. Thus, hypomagnesemia may exacerbate type 2 diabetes [17]. The phosphorylation of insulin receptor tyrosine kinase, all other protein kinases involved in cellular insulin signaling, and other enzymes related to ATP and phosphate transfer require a concentration of magnesium. As a result, low magnesium would inhibit the activity of insulin receptor tyrosine kinase [18]. The effect of Mg^{2+} on insulin sensitivity, insulin action, and glucose metabolism may account for the negative association between Mg^{2+} intake and the incidence of type 2 diabetes [19]. This study aimed to evaluate the relationship and intensity between zinc, magnesium in diabetes type 1 and type 2, and to assess Correlations of Zinc, Magnesium to some parameters in diabetes mellitus.

Materials and Methods

Atomic absorption spectrophotometer, Shimadzu, 7000f, Japan for Measurement zinc, magnesium, Zinc was assessed at wavelength 213.9 nm utilizing a slit width of 0.7 nm and lamp current 8 mA. Magnesium was calculated at wavelength 285.2 nm applying a slit width 0.7 nm and lamp current 8 mA. Cobas Roche c111, Germany for measurement the (serum Total cholesterol) and (triglycerides) and (serum low-density lipoprotein-cholesterol) and the (high-density lipoproteins-cholesterol) fasting blood glucose, ALT (alanine aminotransferase), AST (aspartate aminotransferase). Blood urea, creatinine. dedication of glycated the hemoglobin (HBA1C) in human whole blood by BIO RAD D-10 HPLC, United states America.

Subjects

A total 100 diabetes patients. 40 T1D with an age range of 10-23 years (22 men and 18 women) while 60 T2D with an age range of 40-70 years (26 men and 34 women) were enrolled in this study after strict application of exclusion and inclusions criteria The participant were chosen among individuals who came to Al Qurna General Hospital and Al Fayha Teaching Hospital in the Basra governorate between August-2024 and February-2025.Data were collected through direct interviews with the patient. Each patient participating in this study provided written agreement in accordance with international research ethical guidelines while the total number of healthy individuals (control) were 100 subjects with the percentage of females and males of (50%). T1D 40 samples (control) with age (10-25) and T2D 60 samples (control) with age (40-70).

Samples Collection and Separation

Five milliliters (ml) of whole blood were drawn from each participant via vein puncture. While the remaining blood was left to coagulate at room temperature in a gel vacuum tube, two milliliters of collected blood were put in an ethylene diamine-tetra-acetic acid (EDTA) tube for the HbA1c test then separated the serum by centrifuging it for 10 minutes at 3600 g. For further investigation, the collected sera were frozen at-20 degrees Celsius (℃). AST, ALT, magnesium, zinc, lipid profile, and renal function test

Statistical analysis

Any meaningful correlations between the selected variables were examined using the Statistical Package for Social Sciences. The Student t-test was used to analyze parametric quantitative data, the Mann Whitney test was used to analyze non-parametric qualitative variables, and the A significant statistical correlation between qualitative factors was examined using the Chi-Square test. Quantitative correlations between parametric data are examined using Pearson's test, whereas correlations between non-parametric data are examined using Spearman's test. A level of probability value of less than 0.05 was deemed significant for association testing purposes.

Results

Type 1 and type 2 diabetes patients were the subjects of the current study. Several characteristics were analyzed, including the blood samples' zinc and magnesium levels. Yet, table (1) compares the levels of zinc, Mg and other parameters in type 1 diabetics with controls. The zinc, Mg concentration in patients with type 1 diabetes. (70.13±30.230), (1.6855±.38257) when compared to the control group. (87.25±10.720), (1.8650±.13877) showed a-significant decrease (p = .030, p = .014) the results of other parameters were significant decreased in patients with type 1 diabetes, when compared to control group. (HOMA-IR, insulin, C-P,). (P = .000, P = .000, P = .000) while GAD there are significant increase in patients with type 1 diabetes when compared to control group (p = .000).

Table 1: Comparison between zinc, magnesium concentration and some parameters between type 1 diabetes and control.

Variables	Control(N = 40)		DM type1(N = 40)		P-value
	mean ± SD	**Median(min-max)**	**mean ± SD**	**Median(min-max)**	
Zinc	87.25±10.720	85.00(72-115)	70.13±30.230	78.50(16-118)	.030
Magnesium	1.8650±.13877	1.9000(1.70-2.20)	1.6855±.38257	1.8000(.80-2.60)	.014
HOMA-IR	1.6125±.21023	1.6500(1.10-2.00)	1.1763±.90114	1.1000(.20-5.70)	.000
Insulin Ulu/ml	8.3258±1.06844	8.2700(6.00-10.10)	2.2205±1.64781	2.0500(.50-9.30)	.000
C-P ng/dl	1.9698±.63115	1.8250(1.00-3.00)	.4375±.67812	.2950(.10-4.30)	.000
GAD IU/ML	5.6762±3.19785	5.1150(1.30-13.97)	75.9575±77.08800	56.7000(2.36-280.0)	.000

*Mann-Whitney U test

Table (2) shows comparison between zinc, Mg concentration and some parameters between type 2 diabetes and control. The zinc, Mg concentration in patients with type 2 diabetes there are significant decreased (35.64±20.533), (1.3717±.30033). When compared to control group. (85.82±10.154), (1.8467±.12550). (p = 0.0001, p = 0.0001). The results of other parameters in type 2 diabetes (HOMA-IR, insulin, C-P, GAD) were significant increase in patients with type 2 diabetes, when compared to healthy group. (p = 0.0001, p = 0.0001, p = 0.0001, P = 0.038).

Table 2: Comparison between zinc, magnesium concentration and some parameters between type 2 diabetes and control.

Variables	Control(N = 60)		DM type2(N = 60)		P-value
	mean ± SD	**Median (min-max)**	**mean ± SD**	**Median (min-max)**	
ZINC	85.82±10.154	84.00(71-108)	35.64±20.533	30.41(9-114)	0.0001
Magnesium	1.8467±.12550	1.8000(1.70-2.20)	1.3717±.30033	1.4000(.70-2.10)	0.0001
HOMA-IR	1.7283±.15524	1.7000(1.40-2.00)	26.5708±13.40220	23.3000(8.80-72.30)	0.0001
Insulin Ulu/ml	8.9200±.95665	9.0000(7.10-10.60)	39.8670±19.92751	31.5900(23.90-110.80)	0.0001
C-P ng/dl	1.9007±.57299	1.7850(1.10-3.22)	6.4245±2.25430	5.5350(3.49-13.12)	0.0001
GAD IU/ML	5.5190±3.0480	5.1250(1.00-12.98)	6.5202±2.89099	6.3500(1.10-12.30)	0.038

*Mann-Whitney U test

Table (3) Correlations of zinc, to some parameters in diabetes type 1 and 2. The results showed that there are no correlations between zinc and other parameters in type 1 diabetes. (Cr, Mg, HOMA-IR, insulin, C-P, GAD). (P = .517, P = .199, P = .585, P = .874, P = .968, P = .812) and there are no correlations between zinc and other parameters in type 2 diabetes. (Cr, Mg, HOMA-IR, insulin, C-P, GAD). (P = .670, P = .456, P = .816, P = .936, P = .378, P = .460).

Table 3: Correlations of Zinc to some parameters in T1DM and T2DM

Correlations	**Variable (N = 40)**						
Zinc in TIDM	R	Cr	Mg	HOMA-IR	Insulin	C-P	GAD
		0.106	0.207	0.089	0.026	-0.007	0.039
	P-value	0.517	0.199	0.585	0.874	0.968	0.812
Correlations	Variable (N = 60)						
Zinc in T2DM	R	Cr	Mg	HOMA-IR	Insulin	C-P	GAD
		0.056	0.098	-0.031	0.011	0.116	-0.097
	P-value	0.670	0.456	0.816	0.936	0.378	0.460

*Spearman's correlations

Table (4) Correlations of Magnesium, to some parameters in diabetes type 1 and 2. The results showed that there are no correlations between Magnesium and other parameters in type 1 diabetes. (Cr, Zinc, HOMA-IR, insulin, C-P, GAD). (P = .187, P = .199, P = .758, P = .831, P = .113, P = .536) and there are no correlations between Magnesium and other parameters in type 2 diabetes. (Cr, Zinc, HOMA-IR, insulin, C-P, GAD). (P = .771, P = .456, P = .275, P = .809, P = .873 and P = .679).

Table 4: Correlations of magnesium to some parameters in T1DM and T2DM

Correlations	**Variable (N = 40)**						
Magnesium in TIDM	R	Cr	Zinc	HOMA-IR	Insulin	C-P	GAD
		-0.213	0.207	-0.050	-0.035	0.254	0.101
	P-value	0.187	0.199	0.758	0.831	0.113	0.536
Correlations	Variable (N = 60)						

		Cr	Zinc	HOMA-IR	Insulin	C-P	GAD
Magnesium in T2DM	R	0.038	0.098	0.143	-0.032	0.021	-0.055
	P-value	0.771	0.456	0.275	0.809	0.873	0.679

*Spearman's correlations

Discussion

Diabetes mellitus (DM) is a long-term metabolic condition marked by high blood sugar levels brought on by an inability or resistance to insulin [20]. Zinc is a crucial trace metal that the pancreas needs for the synthesis, storage, and release of insulin. Low zinc levels can impact peripheral cells' ability to absorb glucose and the pancreas' ability to create and secrete insulin, which can lead to insulin resistance, a hallmark of diabetes mellitus [21]. The two primary mechanisms causing the zinc depletion observed in individuals with diabetes mellitus are increased urinary excretion of zinc and reduced intestinal absorption of zinc (diabetes-associated gastrointestinal modification and changes in zinc transport mechanisms can lead to decreased of intestinal absorption of this essential micronutrient) [22]. The regulation of inflammation, oxidative stress, and metabolism are all linked to zinc homeostasis. In addition to its antioxidant qualities, it controls the release of glucagon and insulin [23]. The metabolism of lipids, proteins, and carbohydrates all require zinc as a cofactor. It is linked to the control of the signal transduction pathway triggered by insulin receptors and the production of insulin receptors. It supports the actions, secretion, and storage of insulin. Zinc is a necessary cofactor for the enzyme carboxypeptidase-H, which transforms proinsulin into insulin [24]. Zinc has become a high-priority micronutrient that is essential for many physiological functions, such as DNA synthesis, cellular metabolism, and immunological function [25]. Additionally, zinc affects glucose absorption and utilization in peripheral organs through its complex relationship with the regulation of glucose transporter proteins [26]. Insulin resistance and poor glucose tolerance have been linked to the disruption of these mechanisms brought on by low zinc levels and zinc insufficiency [27]. Moreover, zinc supplementation has been shown to enhance glycemic control, or glucose profiles, in diabetics type 2. The increased activity of insulin-independent glucose transporters seems to be connected to zinc's impact [28]. Magnesium is an essential component for enzymatic pathways in several metabolisms. According to earlier research, approximately 30% of diabetes patients have hypomagnesemia. Growing data showed that increased magnesium consumption enhanced insulin sensitivity and release, as well as dyslipidemia [29]. In the human body, magnesium (Mg) is an essential mineral that controls a variety of physiological processes. The synthesis of RNA and DNA, the metabolism of proteins, lipids, and carbohydrates, the stability of cell membranes, the metabolism of bone and calcium (Ca), and the operation of the immunological and neurological systems are all facilitated by this trace element, which also serves as an activator or cofactor in over 300 enzymatic reactions [30]. In cell signaling, all kinases transfer phosphate groups using the adenosine triphosphate (ATP)-Mg^{2+} chelate. Additionally, a number of glycolysis enzymes, including hexokinase, phosphofructokinase, aldolase, and phosphoglycerate kinase, depend on both Mg^{2+} and ATP-Mg^{2+} for their function [31]. Low intake of magnesium is a risk factor for diabetes because it impairs cellular defenses against oxidative damage. It is necessary for the transport of glucose into the cell, for the metabolism of carbohydrates, and for the cellular activity of insulin [32]. The metabolic mechanism of insulin-mediated cellular glucose absorption and the regulation of insulin effects are thought to be significantly influenced by magnesium. In a number of physiological processes, such as insulin sensitivity and glucose metabolism, magnesium is crucial. Magnesium has an impact on insulin secretion in addition to insulin resistance [33]. Maintaining appropriate magnesium levels by food or supplementation may be beneficial for people with diabetes or those at risk of getting the disease. This could enhance glycemic management and lessen insulin resistance. Hypomagnesemia has been connected to a number of diabetes-related issues, such as insulin resistance, glucose intolerance, and dyslipidemia [34]. The findings, however, indicated that the zinc levels in diabetes type 1 patients. (70.13±30.230) significant decrease p-value (.030) when compared to the control group. (87.25±10.720) and also results showed that the levels of zinc in diabetes type 2 patients. (35.64±20.533) significant decrease p-value (0.0001) when compared to the control group. (85.82±10.154). But the large effect of zinc deficiency is on type 2 diabetes r = 0.783 (Large effect) and the least effect is on type 1 diabetes. r = 0.242 (Small effect). Furthermore, ionic zinc (Zn), which is beneficial for both type 1 and type 2 diabetes, has been presented to reduce diabetic complications [35]. The synthesis, storage, and secretion of insulin in pancreatic tissue depend heavily on zinc. Insulin resistance and dyslipidemia may be linked to it, and it affects insulin signaling. Antioxidant enzymes like nicotinamide adenine dinucleotide phosphate (NADPH)-oxidase and superoxide dismutase (SOD) depend on it for proper operation. Some studies have found that beta cells with inadequate zinc levels are more susceptible to oxidative stress and contain fewer insulin granules [36]. My research's findings align with those of other studies. In diabetes, zinc influences the inflammatory response and insulin homeostasis in a number of ways. It is essential for the appropriate release of insulin from pancreatic β cells, aids in the transport of insulin, and helps it attach to other cell receptors. The complete scope of zinc's involvement in the molecular processes that underlie the etiology and pathophysiology of numerous chronic illnesses, such as diabetes. However, a study done by Mamza *et al*. revealed high Zn levels in diabetic patients, And the results showed that the levels of magnesium in diabetes type 1 patients. (1.6855±.38257) significant decrease p-value (.014) when compared to the control group. (1.8650±.13877) and also results showed that the levels of magnesium in diabetes type 2 patients. (1.3717±.30033) significant decrease p-value (0.0001) when compared to the control group. (1.8467±.12550). But the large effect of magnesium deficiency is on type 2 diabetes r = 0.739 (Large effect) and the least effect is on type 1 diabetes. r = 0.276 (Small effect). Numerous biological activities, such as oxidative phosphorylation, energy production, glycolysis, and the creation of proteins and nucleic acids, depend on magnesium. When adenosine triphosphate (ATP) is synthesized in the mitochondria, magnesium contributes to the formation of MgATP. In order to phosphorylate proteins and activate cyclic adenosine monophosphate (cAMP), which is important in several biochemical processes, cell signaling requires magnesium ATP. Magnesium ions help move other ions across cell membranes. My study's findings are consistent with those of other studies. According to epidemiologic research, hypomagnesemia is very common in people with diabetes and with Numerous preclinical and clinical symptoms, such as pancreatic beta-cell malfunction, insulin resistance, and an elevated risk of diabetes, are linked to magnesium shortage. While other study we could not find any association of Serum Magnesium with the diabetic control. According to the results, the effect of zinc and magnesium is greater in type 2 diabetes compared to type 1 diabetes. According to my interpretation, according to the explanation above, this is because the mechanism of type 2 diabetes is insulin resistance by cells, and zinc, magnesium plays a role in improving insulin sensitivity. Zinc, magnesium also enhances the function of beta cells that secrete insulin. Zinc, magnesium deficiency can lead to a weakness in insulin secretion, which increases the risk of type 2 diabetes. As for type 1, the cause of its occurrence is immune, and zinc, magnesium has a limited role in this area. There are no studies with results similar to the results of my research to support my results the results of (HOMA-IR, insulin, C-P,). (P = .000, P = .000, P = .000) were significant decreased in patients with type 1 diabetes, when compared to control group while GAD there are significant increase in patients with type 1 diabetes when compared to control group (p = .000). Table (1). While the results of (HOMA-IR, Insulin, C-P, GAD). (p = .0001, p = .0001, p = .0001, P = .038) were significant increase in patients with type 2 diabetes, when compared to control group. Table (2). The results showed that there are no correlations between zinc and other parameters in type 1 diabetes. (Cr, Mg, HOMA-IR, insulin, C-P, GAD). (P = .517, P = .199, P = .585, P = .874, P = .968, P = .812) and there are no correlations between zinc and other parameters in type 2 diabetes. (Cr, Mg, HOMA-IR, insulin, C-P, GAD). (P = .670, P = .456, P = .816, P = .936, P = .378, P = .460). Table (3). The results showed that there are no correlations between Magnesium and other parameters in type 1 diabetes. (Cr, Zinc, HOMA-IR, insulin, C-P, GAD). (P = .187, P = .199, P = .758, P = .831, P = .113, P = .536) and there are no correlations between Magnesium and other parameters in type 2 diabetes. (Cr, Zinc, HOMA-IR, insulin, C-P, GAD). (P = .771, P = .456, P = .275, P = .809, P = .873, P = .679). Table (4).

Conclusion
According to the results of this study, deficiencies and inefficiencies in a particular essential trace element (zinc, magnesium) may have an impact on diabetes mellitus types 1 and 2, which is in line with previous research. Zinc and magnesium concentrations were inversely correlated with the risk of diabetes mellitus. And Zinc, magnesium more effect on type 2 diabetes than type1 These discoveries add to the increasing body of evidence demonstrating the importance of zinc and magnesium for healthy glucose metabolism, insulin synthesis, storage, and release and normal insulin action. Zinc and magnesium levels in type 1 and type 2 diabetes did not correlate with other parameters.

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Zinc, magnesium more effect on type 2 diabetes than type 1 (zinc in type 1, r = 0.242, zinc in type 2, r = 0.783). (Magnesium in type 1, r = 0.276, magnesium in type 2, r = 0.739).

Conflict of interest
The author exhibited that there is no conflict interest

Authors contributions
Mohammad Odeh Jadoo (single author) drafted and approved the manuscript.

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