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Open Access Research Article

Correlation of Serum levels of Chromium, Copper, and Manganese with the Glucose levels in Type 2 Diabetes Mellitus in Iraq

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Abstract:

Background: The metabolism of many trace elements, such as chromium, copper, and manganese were reported to be altered in type 2 diabetes militates. This element may have specific roles in the pathogenesis and progress of this disease.

Objectives: To evaluate the serum levels of copper, chromium and manganese in type 2 diabetic patients in Iraq.

Methods: This case-control study included 100 type 2 diabetic patients, 35-60 years old, with high BMI as the cases and 100 non-diabetic subjects as controls who were healthy volunteers not suffering from type 2 diabetes (staff and students). The data was collected from October 2022 until January 2023. The cases were seen in the Diabetes Consultation Unit / Baghdad Teaching Hospital / Medical City. Serum chromium, copper, and manganese were measured using atomic absorption. ELISA was used to test for insulin. spectrophotometry to measure glucose, and HPLC was used to measure whole-blood HbA1c. Insulin resistance was calculated using the semi-empirical formula: HOMA-IR = glucose * insulin / 405 (glucose in mg/dl). To test for the difference between means of numerical data across several parameters, ANOVA test were utilized. Pearson's. Correlation was used to test the correlation between variables.

Results: Diabetics had higher HbA1c, serum copper and blood glucose than healthy controls. Compared to controls, diabetics had lower serum chromium and manganese. In diabetics, chromium and manganese are highly negatively correlated with insulin resistance. Copper levels increase with increasing insulin resistance. Insulin levels were greater in type 2 diabetics (18.6 ± 4.1mlU/L) than in the control (6.2 ± 1.3). **Conclusions:** Serum copper was high while serum chromium and manganese were low in type 2 diabetics. which indicates that these elements may have a role in the occurrence and development of type 2 diabetes.

Keywords: BMI; Chromium; Copper; Insulin; Insulin resistance; Manganese; Type 2 diabetes.

Introduction

Diabetes is a chronic metabolic disorder that affects the metabolism of carbohydrate, fat and protein, due to a deficiency in insulin secretion or a defect in insulin action, or both. Several trace elements have been implicated in the pathogenesis and development of type 2 diabetes. Alteration of specific trace elements may disturb normal glucose metabolism and insulin action, or could cause increased oxidative stress that may contribute to insulin resistance and the development of type 2 diabetes mellitus (1). Essential micronutrients known as trace elements are found in the body in extremely small amounts (2). Chromium was discovered in 1957 and has an effect on insulin and its control, so chromium supplements have an effect on controlling diabetes (3).

It is an essential component that facilitates the elimination of excess glucose from the body. Nicotinic acid, glycine, glutamic acid, cysteine, glutathione, and chromium as an active component) All living things contain copper. It contributes to the make up the glucose tolerance factor, also known as GTF. It affects insulin receptors, increases their sensitivity, and strengthens intracellular signaling, which improves the peripheral action of insulin (4). creation of suitable protein conformations and serves as an enzyme cofactor. Because it can result in the generation of free radicals or the disruption of protein structures Too much copper inside the cells is detrimental. Lipid peroxidation, which is intimately connected with diabetes, may be induced by Copper-Superoxide Dismutase (SOD) and hydrogen peroxide (H2O2) system (5). Diabetes causes a rise in urine excretion and a fall in serum manganese level. Lack of manganese increases oxidative stress in diabetic individuals, which promotes the emergence of diabetes complications (6). Numerous trace elements function as activators or inhibitors in a variety of biological processes, and as a result, they are crucial to many biological processes, including the permeability of cell membranes, by interfering with enzymatic activities, by vying with other substances and proteins for binding sites, or by other means (7). The objective of this study is to explore the role of serum levels of chromium, copper, and manganese in the pathology and development of type 2 diabetes.

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Patients and Methods

A case control study on 200 individuals with an age range of 35 to 60 years and a BMI classification of overweight to obese. They were seen in the Baghdad Teaching Hospital / Medical City Department from October 2022 until January 2023. They were100 diabetic patients and 100 controls. The diabetics were those with Type 2 diabetes mellitus for a period of no longer than ten years. The exclusion criteria were the following: Type 1 diabetes mellitus, those who take dietary supplements, and patients who have type 2 diabetes complications such as nephropathy, retinopathy, or neuropathy. The assessments of the following biochemical parameters were done using serum samples: HPLC technology to measure whole blood HbA1c, the atomic absorption approach to measure trace elements (chromium, copper and manganese), ELISA to quantify insulin hormone, spectrophotometry to measure glucose, and the semi-empirical formula for calculating insulin resistance HOMA-IR (homeostatic model assessment for insulin resistance) = Glucose * insulin / 405 (glucose in mg/dl). The t-test was used to test the difference between the means of numerical data across many variables.

Results

The means ± SD of the trace elements, insulin and insulin resistance in the diabetics and their controls. The differences between these mean values appear to be statistically significant (P<0.01), with lower serum chromium and manganese in the cases than in the controls. The other three parameters were higher in the cases than in the controls, as shown in Table 1. Table 2 shows the correlation between HOMA-IR and the trace elements in type 2 diabetic patients. The correlation was negative for chromium and manganese and positive for copper. All correlations were statistically significant.

In the figure 1, the correlation of serum chromium and HbA1C show negative correlation, in Figure 2, the correlation of serum copper and HbA1C show positive correlation, and in Figure 3, the correlation of serum manganese and HbA1C show negative correlation.

Table (1): The means for trace elements and insulin variables for the two study groups

Parameter	Type 2 D.M Mean ± SD	Control Mean ± SD	*p*-value
Serum Cr^{3+}	0.1 ± 0.01	0.3 ± 0.04	<0.01
Serum Mn^{+2}	6.8 ± 1.9	11.3 ± 3.2	<0.01
Serum Cu^{2+}	160.6 ± 6.4	100.5 ± 5.05	<0.01
Insulin	18.6 ± 4.1	6.2 ± 1.3	<0.01
HOMA-IR	6.5 ± 1.5	1.4 ± 0.35	<0.01
HbA1c	7.8 ± 1.1	5.03 ± 0.74	<0.001

Table 2: The correlation between the levels of trace elements and insulin resistance within two groups

Parameter	Mean ± SD	*p-value*	
Serum Cr^{+3}	0.12±0.01		Significant Negative correlation
HOMA-IR	6.25 ±1.5	<0.01	
Serum Mn^{+2}	6.8±1.9		Significant Negative correlation
HOMA-IR	6.25 ±1.5	<0.01	
Serum Cu^{+2}	146.3 ± 14.9		Significant Positive correlation
HOMA-IR	6.25 ±1.5	<0.01	

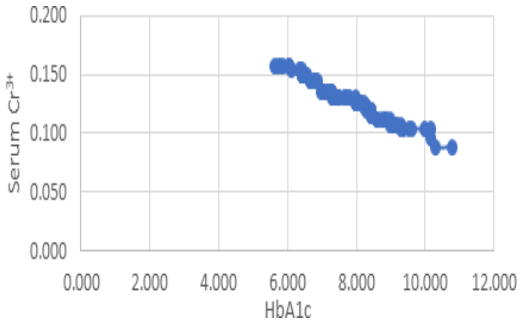

Figure (1): The correlation of serum chromium and HbA1C

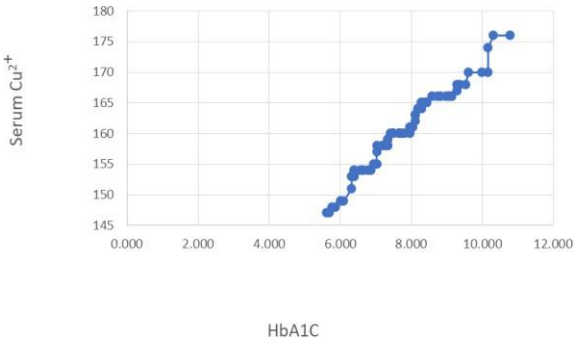

Figure (2): The correlation of serum copper and HbA1C

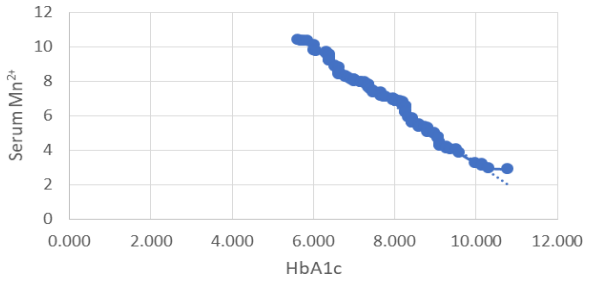

Figure (3): The correlation of serum manganese and HbA1C

Discussion

Diabetes mellites is intricate and multifaceted. Diabetes-related metabolic dysregulations lead to secondary pathophysiologic alterations in a number of organ systems, which place a significant load on morbidity and death from macrovascular and microvascular consequences (8). The significant decrease in the level of chromium in diabetics in comparison to that of normal subjects was observed in other research (9). One possible explanation for these findings of the trivalent chromium properties

are by overcoming insulin resistance, delaying the onset of diabetes mellitus, inhibiting the production of free radicals, because low chromium appeared insulin resistance and hyper glycemic state (10). The important functions of Cr^{3+} are to bind to the insulin receptor beta subunit, which has already been activated by the hormone. This causes the receptor tyrosine kinase to become active and amplifies the insulin signal. As a result, the glucose transporter protein GLUT4(glucose transporter 4) is co-localized to the cell membrane upon activation of the intracellular insulin signal transduction pathway. The primary glucose transporter, GLUT4, mediates glucose transfer across the cell membrane (11). The rise in serum Cu2+ that was seen is consistent with type 2 DM results made earlier (12). An important trace element, Cu2+, is needed for many biological processes. It was an essential component of many metalloenzymes and is necessary to the redox process. (13). Epidemiology studies also shown an association between blood copper levels and the prevalence of type 2 diabetes. This might be the case because copper could regularly create an active site and increase oxidative stress, which supports in the development of diabetes (14). A significant and high negative correlation in serum manganese for patients with type 2 diabetes. Low manganese can lead to impaired glucose metabolism (15). Furthermore, manganese is necessary for producing and secreting insulin normally; a change in its metabolism has been linked to the development of diabetes (16). This study agrees with the study, and compared to their control subject, type 2 diabetic individuals had lower levels of manganese (15).

Conclusion

The current study shows lower serum levels of chromium and manganese and a higher serum level of copper in type 2 diabetics than in controls. Serum chromium and manganese levels were negatively correlated with HOMA-IR, while serum copper level was positively related to HOMA-IR.

Authors' Declarations:

The authors have signed an ethical considerations approval. The project was approved by the local ethical committee of the Iraqi Ministry of Health, the Medical City Consultative Unit / Baghdad Teaching Hospital, Code number (ISU.47237.9.11.22).

Authors' Contributions:

Study conception & design: (Hedef Dh. Al-Yassin). Literature search: (Ahmed Z. Khamees). Data acquisition: (Hedef Dh. Al-Yassin). Data analysis & interpretation: (Ahmed Z. Khamees & Hedef Dh. Al-Yassin). Manuscript preparation: (Ahmed Z. Khamees). Manuscript editing & review: (Ahmed Z. Khamees & Hedef Dh. Al-Yassin).

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دراسة المتغيرات من العناصر الندرة المختارة في عينة من المرضى العراقيين المصابين بداء السكري من النوع الثاني

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الخلاصة :
الخلفية: التغيير في التمثيل الغذائي للعديد من العناصر النزرة مثل الكروم والنحاس والمنغنيز في مرض السكري من النوع 2. قد يكون لهذا العنصر أدوار محددة في التسبب في هذا المرض وتطوره.
الهدف: لتقييم مستويات النحاس والكروم والمنغنيز في الدم لدى مرضى السكري من النوع الثاني في العراق.
المنهجية: تضمنت دراسة الحالة والشواهد 100 مريض بالسكري من النوع 2، تتراوح أعمارهم بين 35-60 عامًا، مع مؤشر كتلة جسم مرتفع و 100 شخص غير مصاب بمرض السكري كعناصر تحكم، تم اختيارهم عشوائيًا من أكتوبر 2022 حتى يناير 2023 في وحدة استشارة خبراء مرض السكري في مستشفى بغداد التعليمي / مدينة الطب. تم قياس مصل الكروم والنحاس والمنغنيز باستخدام الامتصاص الذري. تم استخدام إليسا إليسا لتحليل اختبار الأنسولين. مقياس الطيف الضوئي لقياس الجلوكوز. و HPLC تم استخدامه لقياس نسبة HbA1cفي الدم الكامل. تم حساب مقاومة الأنسولين باستخدام الصيغة شبه التجريبية = HOMA-IR :الجلوكوز * الأنسولين / 405 (الجلوكوز في مجم / ديسيلتر). لتحليل اختبار الفرق بين وسائل البيانات الرقمية عبر العديد من المعلمات ، تم استخدام دراسة الحالة والشواهد واختبار .ANOVA تم استخدام ارتباط بيرسون المترابط لاختبار الارتباط بين المتغيرات.
النتائج: كان لدى مرضى السكر نسبة سكر تراكمي ومصل النحاس عالي (الأحتمالية اقل من 0.01) مقارنة بالضوابط الصحية وكان لدى مرضى السكر انخفاض في قيمة الكروم والمنغنيز (الأحتمالية اقل من 0,01). رتبط الكروم والمنغنيز بشكل سلبي للغاية بمقاومة الأنسولين. تزداد مستويات النحاس مع زيادة مقاومة الأنسولين. كانت مستويات الأنسولين أكبر في مرضى السكري (18.6 ± 4.1 ملل / لتر) من مجموعة التحكم(6.2 ± 1,3) .الأحتمالية أقل من 0,01).
الإستنتاجات: كان لمستويات الكروم والمنغنيز في المصل في الدراسة الحالية علاقة سلبية مع الجلوكوز في مرضى السكر. في مرضى السكر، كانت هناك علاقة إيجابية بين النحاس والجلوكوز في الدم. قد تكون هذه أحد الأشياء التي تقلل من حساسية الأنسولين. ومع ذلك، هناك حاجة إلى مزيد من البحث للتأكد من الوظيفة الجزيئية للكروم المنغنيز والنحاس في ظهور مشاكل السكري.
الكلمات المفتاحية: داء السكرالنوع الثاني، الأنسولين، مقاومة الانسولين، النحاس، الكروم، المنغنيز، مؤشر كتلة الجسم