

## Trace Elements Levels and Oral Manifestations in Type 2 Diabetic Patients

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### ABSTRACT:

#### BACKGROUND:

Diabetes mellitus (DM) has been shown to be associated with oral manifestations and abnormalities in the metabolism of micronutrients, especially copper, zinc, and magnesium.

#### OBJECTIVE:

To study the oral manifestations in type 2 diabetic patients and to estimate trace elements levels such as copper (Cu), zinc (Zn), and magnesium (Mg) in those patients comparing to control group.

#### PATIENTS AND METHODS:

A total of 30 diabetic patients were studied for their oral manifestations and trace elements levels including serum copper, zinc, and magnesium; their age range was (40-55) years and compared with 30 healthy controls.

#### RESULTS:

There was a significant decrease in serum Cu, Zn, and Mg in DM patients as compared with their controls, ( $P < 0.05$ ). Also, several oral complications are seen among diabetics.

#### CONCLUSION:

It can be concluded that several oral complications are seen in diabetic patients. The deficiency of some essential trace metals such as Cu, Zn, and Mg may play a role in the development of diabetes.

**KEY WORDS:** trace elements, diabetes mellitus, oral manifestations.

### INTRODUCTION:

Diabetes mellitus (DM) is a common disease with concomitant oral manifestations that impact dental care <sup>(1)</sup>.

Several soft tissue abnormalities have been reported to be associated with DM in the oral cavity. These complications include periodontal diseases (periodontitis and gingivitis), oral candidiasis, oral mucosal ulcer, and xerostomia <sup>(2)</sup>. Periodontitis is a chronic inflammatory disorder affecting the gingiva and the periodontal tissues initiated by bacteria <sup>(3)</sup>. Oral candidiasis is an opportunistic infection frequently caused by *Candida albicans* species. Many predisposing factors can lead to this infection; these include smoking, xerostomia and endocrine and metabolic diseases <sup>(4)</sup>. Both lichen planus and recurrent aphthous stomatitis have been reported to occur in patients with diabetes <sup>(5)</sup>.

Malnutrition has been suggested as a cause of DM. Numerous studies have found alterations in micronutrient status of patients with diabetes mellitus, and in some studies deficiency of certain minerals or vitamins has been correlated with

presence of diabetic complications. However, the exact pathogenetic role of malnutrition in DM has been disputed <sup>(6)</sup>.

Many trace elements, among which metals, involved as cofactors in myriads of biochemical especially enzymatic reactions. As such they play cardinal roles in many physiological processes, in particular immunity and metabolism <sup>(7)</sup>. Trace elements have been identified for long time as potential candidates for improving metabolic disorders like pre-diabetes [insulin resistance, obesity, metabolic syndrome] or diabetes. In parallel with increasing comprehension of cellular and biochemical mechanisms leading to or aggravating these metabolic disorders, identifying the cellular targets and sites of action of trace elements has reactivated interest in their therapeutic potential <sup>(8)</sup>.

Diabetes mellitus may alter the copper, zinc, and magnesium. Alterations in mineral metabolism are more pronounced in populations with DM with specific complications. It is not known whether differences in trace element status are a consequence of DM or whether they contribute to the expression of the disease <sup>(9)</sup>.

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Zinc has an important role in modulating the immune system and its dysfunction in DM may be related in part to the status of zinc. Copper ions serve as important catalytic cofactors in redox chemistry for biological functions of the patient that are required for growth and development<sup>(10)</sup>. Copper requiring proteins are involved in a variety of biological processes and deficiency of specific enzymes or alterations of their activities often cause disease states or pathophysiological conditions. Changes in the enzymatic activities of several metabolic pathways are seen in DM as a result of relative magnesium deficiency<sup>(11)</sup>.

#### AIM OF STUDY:

The aim of the present study was to clarify the role of trace elements such as copper, zinc, and magnesium and to compare the level of these elements in serum of type 2 diabetic patients and healthy individuals.

#### PATIENTS AND METHODS:

The patients in this study were admitted to Medical City in Baghdad. About 5 milliliters of venous blood was obtained from 30 diabetic patients and 30 healthy individuals as control group. Their age range was (40-55) years. Blood samples were transferred into plain tube, allowed to stand for 15 minutes at room temperature, centrifuged at 3500 rpm for 10 minutes.

#### Measurements:

##### 1-Determination of Fasting Blood Glucose:

Glucose was determined, by using the enzymatic colorimetric method (GOD-POD)<sup>(12)</sup>

##### 2-Determination of Glycated Hemoglobin (HbA1c):

The Bio-Rad VARIANT Hemoglobin A1C Program utilized principles of ion-exchange high-

performance liquid chromatography (HPLC) for the automatic and accurate separation of HbA1c<sup>(13)</sup>.

##### 3-Determination of Serum Trace Elements:

Trace elements Cu, Zn, and Mg under examination were determined using air-acetylene atomic absorption spectrophotometer (AAS). The principle of AAS measurement is as follow: the sample for analysis is dispersed in a beam of energy from a hallow-cathode lamp and atoms in the ground state absorb the incident energy of certain wave length. The absorption causes a decrease in emerging energy and with suitable instrumentation the decrease could be measured and the metal ions concentration was determined<sup>(14)</sup>.

Statistical analysis system-SAS 2004 was performed to analyze of data. The least significant difference (LSD) test compare between the means in this study and correlation coefficient for the variables was done. Data were expressed as means ( $\pm$ SE); statistical significance was set at  $P < 0.05$ .

#### RESULTS:

Demographic and clinical characteristics of DM patients and the control group are shown in table (1). Means  $\pm$ SE values for fasting blood glucose, HbA1c, Cu, Zn, and Mg are shown in table (2). Based on analysis of variance, fasting blood glucose and HbA1c were significantly higher in DM than in the control group. While Cu, Zn, and Mg levels were significantly lower in DM patients than in their controls.

Correlation coefficient of the entire population showed that there was a significant positive correlation between Cu, Zn, and Mg, table (3).

**Table 1: Demographic analysis in DM group and controls (means  $\pm$  SE).**

Parameter	DM	Control
Number	30	30
Age (years)	40-55	40-55
Male n. (%)	15 (50%)	15 (50%)
Female n. (%)	15 (50%)	15 (50%)
Periodontal diseases n. (%)	14 (46.66%)	-
Oral candidiasis n. (%)	7 (23.33%)	-
Oral mucosal ulcer n. (%)	6 (20%)	-
Xerostomia n. (%)	3 (10%)	-

**Table 2: Biochemical characteristic of DM group and controls (means  $\pm$  SE).**

Clinical data	DM	Control	LSD value
Fasting Blood Glucose (mg/dl)	160.73 $\pm$ 4.16	85.40 $\pm$ 1.26	16.55*
HbA1c (%)	7.5 $\pm$ 0.15	4.4 $\pm$ 0.05	0.795*
Cu ( $\mu$ g/l)	107.23 $\pm$ 3.47	130.63 $\pm$ 3.46	9.822 *
Zn ( $\mu$ g/l)	86.77 $\pm$ 3.03	140.97 $\pm$ 3.44	9.177 *
Mg ( $\mu$ g/l)	1.04 $\pm$ 0.07	2.20 $\pm$ 0.04	0.168 *

\* P &lt; 0.05

**Table 3: Correlation coefficient between trace elements.**

Parameter	Correlation coefficient (r)
Cu & Zn	0.87**
Cu & Mg	0.81**
Zn & Mg	0.96**

\*\* P &lt; 0.01

**DISCUSSION:**

Diabetes has become an international health-care crisis that requires new approaches for prevention and treatment. Diabetes management should begin with exercise and diet <sup>(15,16)</sup>. In the present study oral manifestation was significantly higher among diabetics as compared to control group. These manifestations were significantly associated with higher fasting blood glucose levels and HbA1c.

Recent revisions confirm that type 2 diabetes can be considered a risk factor for periodontitis. The postulated mechanism for the effect of diabetes on periodontal disease is that diabetes-enhanced inflammation and apoptosis specifically affects periodontal tissues <sup>(17)</sup>. Additional studies also indicate that the existence of severe periodontitis may adversely influence the control of DM <sup>(18, 19)</sup>.

Diabetes has been shown to be associated with abnormalities in the metabolism of Cu, Zn, and Mg. Impairment of Cu, Zn, and Mg status has been reported as aggravating factors in the progression of diabetes <sup>(20)</sup>. Present study reports that there is a significant decrease in serum Cu, Zn, and Mg concentrations in diabetic patients when compared to controls. The loss of these minerals might be attributed to impaired absorption and/or the excess excretion of these metals in urine (glycosuria) in these patients, which may induce a deficiency or marginal state of these minerals in blood of diabetic patients <sup>(21)</sup>.

Abnormal copper metabolism can lead to several chronic pathogenesis, such as diabetes or diabetic complications <sup>(22)</sup>.

Zinc and insulin concentrations in the pancreas change in the same direction in a variety of situations in humans <sup>(23)</sup>. Zinc may improve

glycemia, and a restored zinc status in patients with type 2 diabetes may counteract the deleterious effects of oxidative stress, helping to prevent complications associated with diabetes <sup>(24)</sup>. Magnesium deficiency has been reported in type 2 DM <sup>(25)</sup>. Similarly, the present study found significantly lower serum magnesium concentrations in type 2 diabetics than in healthy control.

**CONCLUSION:**

That several oral complications are seen among diabetics. Fasting blood glucose and HbA1c were significantly higher among diabetics as compared to those of control, while serum Cu, Zn, and Mg concentrations were profoundly altered in diabetic patients than in controls. This is may be related to the degree of glycemic control.

**REFERENCES:**

1. Bajaj S., Prasad S., Gupta A., Singh V.B.: Oral manifestations in type-2 diabetes and related complications. *Indian J Endocr Metab.* 2012;16:777-79.
2. Al-Maskari A.Y., Al-Maskari M.Y., and Al-Sudairy S.: Oral manifestations and complications of diabetes mellitus. *Sultan Qaboos Univ Med J.* 2011;11:179-86.
3. Kuo L., Polson A.M., Kang T.: Associations between periodontal diseases and systemic diseases: A review of the inter-relationships and interactions with diabetes, respiratory diseases, cardiovascular diseases and osteoporosis. *Public Health.* 2008;122:417-33.
4. McIntyre G.: Oral candidosis. *Dent Update.* 2001;28:132-39.

5. Torrente-Castells E., Figueiredo R., Berini-Aytés L., Gay-Escoda C.: Clinical features of oral lichen planus - A retrospective study of 65 cases. *Med Oral Patol Oral Cir Bucal*. 2010;15:685-90. Thomas B., Kumari S., Ramitha K., Ashwini Kumari M.B.: Comparative evaluation of micronutrient status in the serum of diabetes mellitus patients and healthy individuals with periodontitis. *Indian Society of Periodontology*. 2010;14:46-49.
6. Wiernsperger N. and Rapin J.: Trace elements in glucometabolic disorders-an update. *Diabetology & Metabolic Syndrome*. 2010;2:1-9.
7. Abdul-Ghani M.A. and DeFronzo R.A. (2010): Pathogenesis of insulin resistance in skeletal muscle. *J Biomed Biotechnology*. 2010;47:62-79.
8. Olin K.L., Walter R.M., Keen C.L.: Copper deficiency affects selenogluthathione peroxidase and selenodeiodinase activities and antioxidant defense in weanling rats. *Am J Clin Nutr*. 1994;59:654-58.
9. Ito S., Fujita H., Narita T., Yaginuma T., Kawarada Y., Kawagoe M. et al.: Urinary copper excretion in type 2 diabetic patients with nephropathy. *Nephron*, 2001;88:307-12.
10. Kholoussi R., Fawzy: Malondialdehyde and trace element levels in patients with type 2 diabetes mellitus. *Archives of Hellenic medicine*. 2011;28:83-88.
11. Salem S., Kholoussi N., Massod M.F. (1976): *Am.J.Med.Tech*. 43:243.
12. Hoelzel W., Weykamp C., Jeppsson J. O., Miedema K., and Barr J. R.: IFCC working group on HbA1c standardization. IFCC reference system for measurement of hemoglobin A1C in human blood and the national standardization schemes in the United States, Japan, and Sweden: A method-comparison study. *Clin. Chem*. 2004;50:166-74.
13. Ward F.N., Nakagawa M.M., Harms T.F., and Vansickle G.H.: Atomic absorption methods of analysis useful in geochemical exploration *U.S.Geol surv bull*. 1969:45-47.
14. Akhmemokhan K.I., Eregie A., Fasanmade O.A.: Trace mineral status and glycaemic control in Nigerians with type 2 diabetes. *African J Diab Med*. 2012;4:169-73.
15. Manjunatha G.B.K., Bhavna N., Sarsina D.O., Sathisha T.G., Sweta S., Devaki R.N.: Relation of calculated HbA1c with fasting plasma glucose and duration of diabetes. *Intr J Appl Biol Pharma Tech*. 2011;2:58-61.
16. Pathak A.K., Shakya V.K., Chandra A., Goel K.: Association between diabetes mellitus and periodontal status in north Indian adults. *European Journal of General Dentistry*. 2013;2:58-61.
17. Shrimali L., Astekar M., Sowmya G.V.: Correlation of oral manifestations in diabetes mellitus. *Int J Oral Max Pathol*. 2011;2:24-27.
18. Maik P.V. and Gupta S.: Periodontal management of diabetic patients. *Indian J Dent Sci*. 2011;2:16-19.
19. Farid S.M.: The association between serum glucose and serum lead and selected trace elements in type 2 diabetes mellitus patients in Jeddah, Saudi Arabia. *Medical Journal of Islamic World Academy of Sciences* 2012;20:130-39.
20. Brown I.R., McBain A.M., Chalmers J., Campbell I.W., Brown E.R., Lewis M.J.: Sex difference in the relationship of calcium and magnesium excretion to glycaemic control in type-1 diabetes mellitus. *Clin Chim Acta*. 1999;283:119-28.
21. Zheng Y., Li X.K., Wang Y., Cai L.: The role of zinc, copper and iron in pathogenesis of diabetes and diabetic complications: therapeutic effects by chelators. *Hemoglobin*. 2008;32:135-45.
22. Retnam V.J. and Bhandarkar S.D.: Trace elements in diabetes mellitus. *J Postgrad Med*. 1981;27:129-32.
23. Marjani A.: Plasma lipid peroxidation, zinc and erythrocyte Cu-Zn superoxide dismutase enzyme activity in patients with type 2 diabetes mellitus in Gorgan City (south east of the Caspian Sea). *Internet J Endocrinol*. 2005;2:1540-2606.
24. Schnack C., Bauer I., Pregant P., Hopmeier P., Scherthner G.: Hypomagnesaemia in type 2 (non-insulin-dependent) diabetes mellitus is not corrected by improvement of long-term metabolic control. *Diabetologia*. 1992;35:77-79.

