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# BIOCHEMICAL COMPARATIVE STUDIES FOR SOME TRACE ELEMENTS IN TYPE2 DIABETIC PATIENTS WITH AND WITHOUT METABOLIC SYNDROME

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## ABSTRACT

The aim of this study was to investigate the role of trace elements (copper, iron and zinc) as oxidants and antioxidants in type 2 diabetic patients and metabolic syndrome. Blood samples were obtained from (110) patients with type 2 diabetes with and without metabolic syndrome, as well as (50) healthy subjects as a control group. They divided into three groups as the following: Group A(control ):- Included fifty healthy subjects aged (35-65 years). Group B (Type 2 diabetics):- Included sixty four patients with type 2 diabetes mellitus aged (35-65). Group C (diabetics type 2 with metabolic syndrome):- Included forty six patients with metabolic syndrome aged (35-65). **Results:** The results show a presence of a significant increase in copper and iron in all groups of patients in type 2 diabetes and type 2 diabetes with metabolic syndrome in comparison with control group. But, zinc levels showed a significant decrease in all groups of patients in type 2 diabetes without metabolic syndrome in comparison with control group. Also, Cu, Zn showed a significant increase in all patients groups in type 2 diabetics with metabolic syndrome in comparison with type 2 diabetics group. While, Fe showed a significant increase in all patients groups of patients in type 2 diabetes in comparison with type 2 diabetics with metabolic syndrome group.

**KEYWORD:** The aim of this study antioxidants in type 2 group.

## INTRODUCTION

Diabetes mellitus type 2 is the predominant form of diabetes and accounts for 90% of all cases of diabetes mellitus.[1] DM 2 is heterogenous disorders caused by a group of genetic factors related to insulin resistance, impaired insulin secretion, and environmental factors such as over eating obesity, lack of exercise, and stress as well as aging.[2] It is typically a multifactorial disease involving multiple genes and environmental factors to varying extents.[3] Diabetes type 2 is the common form of idiopathic diabetes and is characterized by a lack of the need for insulin to prevent ketoacidosis . It is not an autoimmune disorder, in most patients the susceptible genes that predispose to DM 2 have not been identified .This could be due to the heterogeneity of the genes responsible for the susceptibility to NIDDM. The pathogenesis of diabetes mellitus type 2under, normal physiological conditions, plasma glucose concentrations are maintained within a narrow range, although wide fluctuations in supply and demand, through a tightly regulated and dynamic interaction between tissue sensitivity to insulin (especially in liver) and insulin secretion.[4] Diabetes mellitus type 2 include some mechanisms which work on broken of regulation between tissue sensitivity to insulin which leads to two major pathological defects are impaired insulin secretion through a dysfunction of the pancreatic β-cell cells and impaired insulin action through insulin resistance.[3] The relation very close between obesity and DM2, both go hand in hand. Abundant of the complications in both diseases are due to underlying primary causes insulin resistance and metabolic syndrome.[5] Metabolic syndrome mean cluster of signs and symptoms occurring in a complex that can increase the risk of cardiovascular disease, Type 2 Diabetes and all-cause mortality. It containing of a cluster of risk factors including elevated Fasting Blood Glucose or Impaired Glucose Tolerance, abdominal obesity, elevated blood pressure, dyslipidemia to mention a few.[6]

### Trace elements

Trace elements are primary nutrients, chemicals with functions of regulatory, immunologic, and antioxidantas they act as essential components or cofactors of some enzymes throughout metabolism.[7]

Copper is the more ample element in the human body.[8] Cu is required for several biological functions. It is required for the catalytic activity of superoxide dismutase (SOD) that participates in the protection of cells from superoxide radicals.[9] It is well known that copper is effective on oxidative stress. Copper is a potent cytotoxic element in its free form due to its redox chemistry. It readily participates in Fenton and Heiber Weiss reactions to produce reactive oxygen species such as hydroxyl radical stress.[10]

Iron (Fe) is an primary transition metal required for thesynthesis of two important functional proteins such as hemoglobin and myoglobin, which are involved in the transport of molecular oxygen during respiration.[11] It is also required in the elastin production along with Zn and ascorbic acid and collagen synthesis.[12]

Zinc (Zn) is a primary mineral that is a component of more than 200 enzymes such as protein kinase C ,carboxy-peptidase A, B, superoxide dismutase and alkaline phosphatases.[13] zinc acts as an antioxidant by protecting the sulfhydryl groups of proteins and enzymes versus free radical damage in the body[14], the antoxidantsynthesis impairs when deficiency of zinc, leading to increased oxidative stress.[15]

**Patients and Method**

**Design of Study**

This study conducted at AL-Hussein Education Hospital and The Special Center of The Endocrine Glands and Diabetes inThi-Qar from Biochemistry Laboratory in College of Science, at the period between 4/11/2015 to 5/5/2016. It included (160) cases, (50) control and (110) patients.

**Table 1: Data of Controls and Patients Groups**

| ***Groups*** | ***N0.*** |
|---|---|
| Controls | 50 |
| Patients | 110 |

There were (160) male and female subjects, control and diabetic of type 2 with trace elements as oxidants or antioxidants aged (35-65) years were included in this study. They divided into three groups as the following:-

***Group A (Control):*** Included fifty (50) healthy subjects aged (35-65).

***Group B (Diabetes type 2):*** Included sixty four (64) patients with diabetes mellitus type 2 aged (35-65).

***Group C (Diabetes Type 2 with Metabolic syndrome)*** Included forty six (46) patients with metabolic syndrome aged (35-65).

**Collection of Blood Samples**

About (10mL) of blood samples from out treated hypertension patients and controls were taken and allowed to clot at room temperature in empty disposable tubes centrifuge to separate it in the centrifuge at 3000 rotor per minute (rpm)for 10 min, the serum samples were separated and stored at (-20ºC) for later measurement of biochemical parameters,
unless used immediately.

**BIOCHEMICAL PARAMETERS**

**Serum Copper**

The cupric ions react with the chromogen Di-BrPAESA forming a blue compound, which intensity is proportional to the concentration present in the sample.[16][17][18]

**Serum Iron**

After dissociation of iron-transferrin bound in acid medium, ascorbic acid reduces $Fe^{3+}$ iron into $Fe^{2+}$ iron . $Fe^{2+}$ iron then form a coloured complex with 3-(2-Pyridyl) -5, -6-difuryl-1, -2, -4-triazine-disulfonate (Ferene). The absorbance thus measured at 600 nm (580-620) is directly proportional to the amount of iron in the specimen.[19]

**Serum Zinc**

Zinc reacts with the chromogen present in the reagent forming a coloured compound which colour intensity is proportional to the zinc concentration present in the sample.[16][20]

**Statistical Analysis**

Statistical analysis was done using the software SPSS version 17.0; the results were expressed as mean ± standard deviation (mean ± SD). One way ANOVA-test was used to compare parameters in different studied groups. P-values ($P \leq 0.05$) were considered statistically significant.

**RESULT AND DISCUSSION**

***Clinical and Characteristic Features of the Studied Groups***

There are 160 study cases included in the present study, with difference between clinical characteristic diabetics type 2 patients Groups and healthy control group in each (Hemoglobin A1c (HbA1c), Trace Elements Copper (Cu), Iron (Fe), Zinc (Zn)) and without difference in each (Age, Sex and BMI). as shown in table 3-1.

**Table: 2 Characteristic data for all studied groups.**

| | | ***Characteristic*** | | | | | | |
|---|---|---|---|---|---|---|---|---|
| ***Groups*** | **N** | **Age years Mean±SD** | **Sex (M/F)** | **SBP (mmHg) Mean ±SD** | **DBP (mmHg) Mean ±SD** | **TG mg/dl Mean±SD** | **FBG mg/dl Mean±SD** | **BMI $Kg/m^2$ Mean±SD** |
| *Control* | 50 | 45.7± 7.53 | 25/25 | 99.9±0.76 | 75.04 ±0.28 | 106.32±19.65 | 87.88±5.96 | 25.46±1.74 |
| *Diabetics Type 2* | 64 | 51.56± 8.11 | 37/27 | 110.06±0.3 | 77.75 3±0.53 | 126.68±28.05 | 201.95±67.83 | 28.93±4.18 |
| *Diabetics Type2 With metabolic syndrome* | 46 | 51.18± 8.44 | 17/29 | 180.93±8.12 | 87± 1.66 | 180.54± 7.83 | 180.75±61.12 | 33.78±4.43 |

**TRACE ELEMENTS**

**Serum Copper Concentration**

Table (2) shows a significant increase in concentrations of serum copper in MS group in comparison with DM 2 group (P≤0.05). Also there is a significant increase in concentrations of serum copper in all patients groups in comparison with control group (P≤0.05).

The present study are matched with the results of study Supriya[10] and Sarkar.[21] The reason for the increase of concentration of copper is due to hyperglycemia that may stimulate glycation[22] which will stimulate release of copper from copper rich compounds such as ceruloplasmin[23] and the impaired synthesis of this transport protein[24] and this accelerate the oxidative stress and can result in the formation of AGEs.[22]

**Serum Iron Concentration**

Table (3) shows a significant increase in concentrations of serum iron in DM2 group in comparison with MS group (P≤0.05) and there is a significant increase in concentrations of serum iron in all patients groups in comparison with control group (P≤0.05). Our results are matched with the results of study of Swaminthan.[25] Evidence shows that the accumulation of body iron is related to the Type 2 diabetes and metabolic syndrome in general populations.[26] Increase iron concentration due to iron is strong pro-oxidant that catalyzed the formation of hydroxyl radicals.[27], this radicals are powerful pro-oxidants that attack cellular membrane lipids DNA and proteins. It has been hypothesized that the formation of hydroxyl radicals catalyzed by iron initially contributes to insulin resistance and subsequently to decreased insulin secretion and then to the development diabetes mellitus type 2.[28]

**Serum Zinc Concentration**

Table (4) showed a significant increase in concentrations of serum zinc in MS group in comparison with control group (P≤0.05). However, there was a significant reduction in the serum concentration of zinc in DM 2 group as compared to control group (P≤0.05). The present study are matched with the results of study Pujar[29] that showed significant decrease in serum zinc levels in type 2 diabetic patients. The present study showed that serum zinc was associated with the components of metabolic syndrome, where the association between zinc and metabolic syndrome in our study are in agreement with the results of other study Arnaud.[30] Zn has a biphasic effect in that it is required for insulin storage and cellular binding, although high concentrations can lead to a reduction in insulin release.[31]

**Table: 3: Serum copper concentrations for studied groups**

| Groups | Cu µmol/L Mean±SD |
|---|---|
| Control | 22.98 ± 9.32[c] |
| DM2 | 25.89± 2.01[b] |
| DM2 with MS | 26.36 ± 1.95[a] |
| LSD | 1.26 |

**Table 4: Serum iron concentrations for studied groups**

| Groups | Fe µmol/L Mean±SD |
|---|---|
| Control | 21.79 ± 7.02[b] |
| DM2 | 23.91± 15.49[a] |
| DM2 with MS | 22.89 ± 15.50[b] |
| LSD | 3.10 |

**Table: 5 Serum zinc concentrations for studied groups**

| Groups | Zn µmol/L Mean±SD |
|---|---|
| Control | 14.44 ± 1.48[b] |
| DM2 | 9.03 ± 1.32[c] |
| DM2 with MS | 30.60 ± 6.98[a] |
| LSD | 0.90 |

**CONCLUSION**

1. There are a disturbances in trace elements that are associated with metabolic syndrome.
2. There is a disorder in trace elements metabolism in patients with diabetes mellitus type 2. The correction for this disorder might have significant value for control of diabetics and prevention of complications.

**REFERENCES**


1. González EL, Johansson S, Wallander MA, Rodríguez LA. Trends in the prevalence and incidence of diabetes in the UK: 1996 – 2005. J. Epidemiol. Community Health, 2009; 63: 332-336
2. Kaku K. Pathophysiology of type 2 diabetes and its treatment policy. JMAJ, 2010; 53(1): 41-46.
3. Holt G. I. Diagnosis, epidemiology and pathogenesis of diabetes mellitus an update for Psychiatrists. Br. J. Psychiatry, 2004; 184: s55- s63.
4. Defronzo R.A., Lily, Ferrannini E., Lecture 1987, the triumvirate: beta cell, muscle, liver. A collusion responsible for NIDDM. Diabetes, 1988; 37: 667–687.
5. Arnold M, Pandeya N, Byrnes G, Renehan AG, Stevens GA, et al. Global burden of cancer attributable to high body-mass index in 2012: a population-based study. Lancet Oncol, 2015; 16(1): 36-46.
6. Okosun I S, Annor F, Dawodu E A, Eriksen M P (2014). Clustering of Cardiometabolic Risk Factors and Risk of Elevated HbA1c in Non-Hispanic White, Non-Hispanic Black and Mexican American Adults with Type 2 Diabetes. Diabetes & Metabolic

Syndrome: Clinical Research & Reviews, 2014; 8: 75–81.
7. Lobo C, Torres P, Fouque D, Mafra D. Zinc deficiency in chronic kidney disease: Is there a relationship with adipose tissue and atherosclerosis, Biol. Trace Elem Res., 2010; 135: 16-21.
8. Chan Y-K. Studies on the roles of transition metals in diabetogenesis: ResearchSpace@ Auckland, 2008.
9. Olivares M, Araya M, Uauy R. Copper homeostasis in infant nutrition: deficit and excess. J Pediatr Gastroenterol Nutr, 2000; 31(2): 102–111.
10. Supriya, Shrabanimohanty, Venkata Bharatkumarpinnelli, Roopamurgod, Raghavendra: Evaluation of Serum Copper, magnesium, and glycatedhaemoglobin in type 2 diabetes mellitus. Asian J Pharm Clin Res., 2013; 6 (2): 188—190.
11. Ganz T, Nemeth E: Iron imports. IV. Hepcidin and regulation of body iron metabolism. Am J PhysiolGastrointest Liver Physiol, 2006; 290(2): G199–203.
12. Stechmiller JK: Understanding the role of nutrition and wound healing. Nutr Clin Pract, 2010; 25(1): 61–68.
13. Bonaventura P, Benedetti G, Albarède F, Miossec P(2015). Zinc and its role in immunity and inflammation. Autoimmune Rev., 14(4): 277-85.
14. Cruz KJ, de Oliveira AR, MarreiroDdo N. Antioxidant role of zinc in diabetes mellitus. World J Diabetes, 2015; 6(2): 333-7.
15. F. Kelly, "Use of antioxidants in the prevention and treatment of disease," Journal of the International Federation of Clinical Chemistry, 1998; 10(1): 21–23.
16. Pasquinelli F., Diagnostica e Tecniche di Laboratorio, (1984; 1103—1104). Rossini Editrice.
17. Ciuti R., Galli A., Giorn. It. Chim. Clin., 1987; 12(2): 91-100.
18. Akita Abe, Sumicoyiamashita, Clin. Chem., 1989; 35(4): 197, 552-554.
19. Douglas, J., Hennesy, Gary R., Reid, Frank E., Smith, and Stephen L. Ferene: a new spectrophotometric reagent for iron. Thompson, Can. J. Chem., 1984; 62: 721-724.
20. Tetsuo Makino. Chimica Clinica Acta, 1991; 197: 209-220.
21. Sarkar A, Dash S, Barik BK, Muttigi MS, Kedage V and Shetty JK: Copper and Ceruloplasmin levels in relation to total thiols and GST in type 2 diabetes mellitus patients. Ind J Clin Biochem, 2010; 25: 74-76.
22. Nicolas W and Jean RR: Trace elements in glucometabolic disorders: an update. Diabetology and metabolic syndrome, 2010. doi: 10.1186/1758-5996-2-70.
23. Mosaad A, Abou-Seif G, Abd-Allah Y. Evaluation of some biochemical changes, in diabetic patients. Clin. Chim. Acta, 2004; 346: 161–70.
24. Quilliot D, Dousset B, Guerci B, Dubois F, Drouin P, Ziegler O. Evidence thatdiabetes mellitus favors impairedmetabolism of zinc, copper and seleniumin chronic pancreatitis. Pancreas, 2001; 22(3): 299-306.
25. Swaminathan S, Fonseca VA, Alam MG, Shah SV: The role of iron in diabetes and its complications. Diabetes Care., 2007; 30: 1926-1933.
26. Bozzini C, Girelli D, Olivieri O, Martinelli N, Bassi A, De Matteis G, et al. Prevalence of body iron excess in the metabolic syndrome. Diabetes Care, 2005; 28(8): 2061-3.
27. Cooksey RC, Jones D, Gabrielsen S: Dietary iron restriction or iron chelation protects from diabetes and loss of beta cell function in the obese mouse. Am J Physiol Endocrinol Metab., 2010; 298: E1236-E1243.
28. Ma, J., Stampfer, M.J., *Clin*. *Chem.*, 2002; 48: 601-603.
29. Pujar S, Pujar BLL, Ganiger A, Hiremath K, Mannangi N, Mahanthesh. Correlation of serum zinc, magnesium and copper with HbA1c in type 2 diabetes mellitus patients among Bagalkot population-A case control Study. Medica Innovatica, 2014; 3(2): 4-9.
30. Arnaud J, de Lorgeril M, Akbaraly T, Salen P, Arnout J, Cappuccio FP, et al. Gender differences in copper, zinc and selenium status in diabeticfree metabolic syndrome European population - the IMMIDIET study. Nutr Metab Cardiovasc Dis., 2012; 22(6): 517-24.
31. D. L. Watts, "Trace elements and glucose disorders," Trace Element Inc Newsletter, 1999; 11: 2.