

Serum copper levels in Non-Insulin Dependent Diabetes

Mellitus

HAZZIM H. EDAN^o

ABSTRACT

Background: The findings of previous research on the status of trace elements in diabetic patients have been controversial.

A comparative study of serum copper in diabetic patients and healthy Iraqi controls is becoming important, particularly after the dietary shortage, as sequel of 13 years of sanctions.

Objective: To study the difference of serum copper between the diabetic patients and healthy Iraqi people.

Method: This is an outpatient-based study; it was carried out in AL-Rhasid Military Teaching Hospital during a period from March 2002 till February 2003 the study included seventy – four non insulin dependent diabetic patient (NIDDM) aged (40-62) year, forty – four from which have retinopathy and twenty – four have albuminuria (>50 mg/day) other seventy normal healthy control with comparable age (38-65) year. Blood samples were drawing fasting and the blood was left at room temperature for 10 minuets. Centrifuged 3000 rpm for 10 minuets, then serum was separated and stored at -20c^o. The urine sample taken freshly, randomly on early morning and urine albumin was measured quantitatively by Lowry method, data were analyzed and compared with previous study result

Conclusion: The clinical significance of serum copper in diabetes mellitus remain conflicting as well as controversial and many questions still remain unanswered but the decreased serum copper found in NIDDM in our study may merit further investigation of the relationship between copper and non-insulin dependent diabetes.

Key Words: Serum Copper, Diabetes Mellitus

oDepartment of Biochemistry
Collage of Medicine
Al-Mustansriya University
Baghdad, Iraq.

dominant role in divers' proteins such as cytochrom oxidase and cytoplasmic superoxide-dismutase. (9,10)

INTRODUCTION

Copper is an integral component of at least (16) essential metalloprotein within the body predominantly on connective tissue formation, CNS function and haemotopoiesis. (1)

Direct association of trace element in relation to human disease has been observed in many research studies, in many cases, an alteration in the metabolism of these minerals has been demonstrated. (2, 3, 4, 5)

Diabetes mellitus is a neterogenous disease characterized by an absolute or relative deficiency of insulin as well as insulin resistance. (6) Numerous authors have evaluated mineral levels and status in diabetic subjects yet; often inconsistent and contradictory results have been presented. (7) This difference may be due to number of subjects, sex, laboratory processing and life style. (8)Copper act as antioxidant and prevent membrane peroxidadtion. Cereuloplasmin, the major plasma copper – transporting protein, possesses a potent antioxidant property. (9) Also Copper is involved in oxidation – reduction reaction and has a

In this study we evaluated the levels of copper in the serum of Iraqi patients with non-insulin dependent diabetes mellitus (NIDDM) in an effort to evaluate the status of this element in such patients particularly after the dietary shortage as sequel of 13 years of sanctions and to, clarify its role in this disease.

MATERIALS & METHODS

This study was conducted during the period from March 2002-Feb. 2003 in AL-Rashid Military Teaching Hospital, the study included seventy-four NIDDM patients aged (40-62) and other seventy normal healthy control person aged (40-65) years. Within diabetic patients there were forty-four patients had retinopathy and twenty-four had albuminuria (>50mg/day). Blood samples were drawn fasting and the blood was left at room temperature for 10 minutes, centrifuged 3000 RPM for 10 minutes, then serum was separated and stored at -20c⁰.

Urine samples taken randomly freshly on morning and urine albumin were measured quantitatively by Lowery method. (11)

RESULTS

The serum copper were determined by International Head quarter, Randox Laboratories LTD, Diamond Road, Crumlin, CO. Autrim, United Kingdom, when copper at pH 4.7, is released by reducing agent, then reacts with a specific color reagent, to form stable colored chelate, the intensity of color is directly proportional to the amount of copper in the sample (Randox - Cu 2340, Cu2341).⁽¹²⁾

Table (1) show significant decrease in serum copper levels in NIDDM patients (80 ± 20 $\mu\text{g}/\text{dl}$) as compare to normal healthy control (105 ± 34 $\mu\text{g}/\text{dl}$) $P < 0.001$. The NIDDM patient, with positive retinopathy had significantly lower serum copper (69 ± 39 $\mu\text{g}/\text{dl}$) as compare to NIDDM patient with no retinopathy (89 ± 40 $\mu\text{g}/\text{dl}$) as table (2) showed. Table (3) demonstrated the serum copper in NIDDM patient with positive albuminuria (>50 mg/dl) was lower than patient with negative albuminuria (<50 mg/dl).

Table (1): shows the biostatistical calculation and student t-test for serum copper in NIDDM patient as compare to normal healthy control groups

| Cu $\mu\text{g}/\text{dl}$ | NIDDM | Normal control |
|----------------------------|----------|----------------|
| No | 74 | 70 |
| Mean | 80 | 105 |
| SD | 20 | 34 |
| SE | 2.4 | 3.9 |
| t-test | 6.4 | - |
| P-value | <0.001 | - |

Table (2): the biostatistical calculation and student t-test for serum copper in NIDDM patient with retinopathy as compare to non-retinopathic patients.

| Cu $\mu\text{g}/\text{dl}$ | NIDDM <i>Retinopathy</i> | NIDDM <i>No retinopathy</i> |
|----------------------------|--------------------------|-----------------------------|
| No | 44 | 30 |
| Mean | 69 | 89 |
| SD | 39 | 40 |
| SE | 5.9 | 7.4 |
| t-test | 2.2 | - |
| P-value | <0.01 | - |

Table (3): shows the biostatistical Calculation and student t-test for serum copper in NIDDM patient with positive albuminu as compare to negative

| Cu $\mu\text{g}/\text{dl}$ | NIDDM Positive albuminuria | NIDDM Negative albuminuria |
|----------------------------|----------------------------|----------------------------|
| NO | 24 | 50 |
| Mean | 63 | 83 |
| SD | 31 | 42 |
| SE | 6.4 | 6.0 |
| T-test | 2.2 | - |
| P-value | $P < 0.01$ | - |

DISCUSSION

Generally, serum copper level has been found to be a non specific indicator of disease activity in many diseases, ⁽¹³⁾ and abnormalities in copper metabolism have become as a hallmark for diagnosis of many disease states. ⁽¹⁴⁾

Our result from diabetic patients revealed significant lower serum copper in diabetic patient as compared to normal and there was a significant decrease in complicated diabetic patient with retinopathy and albuminuria (nephropathy) as compared to non-complicated cases. This finding consistent with results reported by Ibrahim and Watts 1999 ⁽¹⁵⁾ 2000 ⁽¹⁹⁾.

When deficiency of certain minerals or vitamins has been correlated with presence of diabetic complication, although Zargar AH, *et al* 1998 ⁽⁷⁾ Noto R, *et al* 1983 ⁽¹⁶⁾ reported that serum copper levels were significantly elevated in diabetic patients.

The lowering serum copper in our NIDDM patients particularly with complication could be due to poor dietary intake during sanction and

copper deficiency has long been associated with disturbed carbohydrate metabolism and with oxidative stress. ^(17, 20) Also the disturbances in mineral metabolism are more pronounced in diabetic population with specific complication. ^(18, 21) It is not known whether this change in element status is a consequence of diabetes or alternatively, whether it contributes to the expression of the disease. ⁽¹⁸⁾

CONCLUSION

We concluded that the clinical significance of serum copper in diabetes mellitus remains conflicting as well as controversial and many questions still remain unanswered.

Even though, the data presented in this paper is consistent in some aspects with previous findings of other researchers, the author feel that large number of specimen should be obtained in order to fully elucidate the relation ship between copper, diabetes mellitus and life style.

REFERENCES

1. Aspin N, Sass-Kortsak A. Copper. In: Bronner F, Coburn JW, Eds. Disorders of mineral metabolism, VOL I: Trace minerals .New York: Academic, Press, 1981.
2. Prasad AS, Zinc deficiency in human: a neglected problem. J Am. collage Nutr, 1998, 17: 542-3.
3. Chansmer AB Zinc, Insulin and diabetes J.Am. College Nutr. 1998, 17:109-14.
4. Mertz W. The essential trace elements Science 1981 ;213:1332
5. Nour Mohammed I, Reayzi GH, Ghaemg hai j. serum and urine levels of Cu, Zn, Mg and Ca in Iranian patients exposed to chemical war gases. J Trace Elem. Exp. Med.1989 ,2:88
6. Walter RM, Uriu-Hare JY, Olin KL. Copper, Zinc, manganese, magnesium status and complication of diabetes mellitus. Diabetes Care .1991 14: 1050-6.
7. Zargar AH, Shah NA, Massodi SR: copper, Zinc and magnesium levels in non - insulin dependent diabetes mellitus Postgrad Med. J. 1998; 74:665 - 8.
8. EL -Yazigi A; Hanna N, Raine, DA. Urinary excretion of chromium, copper and manganese in diabetes mellitus and associated disorders. Diabetes Res. 1991; 18:129-34.
9. Bond JS, Failla MI Unger DF. Elevated manganese concentration and arginase activity in livers of streptiozotocin-include diabetic rats. J. Biol chem. 1983, 258: 8004-9.
10. Abe A *et al.* Cline chem .1989: 3514
11. Lowry DH, Rosebrough NJ, Farr AL, Randal RJ. (1, 15):J.Biol.chem; 139:265
12. International Head quarters Randox Loeborateriel Lta, Diamond Road, Randox- Cu 2340, and Cu 2341.
13. Lee, GR; William, D.M. Cartwright, G.E (1976). The role of copper in iron metabolism and human biosynthesis. Trace Element in Human Health and Disease. Vol. (1) Zinc and copper. Eds Pressed A, S & Oberlin's, D. Academic press, New York ch. 23, pp: 373 - 388.
14. Haris, ED (1983) Copper in Human and animal health IN: Trace

- Element in Health A review of current issues, ED Rose, J, Butter, Worth & Co Publishers. Ch .3, pp: 44-73.
15. Watts D.L: Trace Elements and Glucose Disorders TEI Newsletter 11:2, 1999
 16. Noto R , Alicata R, Sfoglain L, Neri S , Bifarella M. Study of copper in a group of elderly diabetics. Acta Diabet. lat.1983; 20:81-5.
 17. Frank A, Sell DR , Danielsson R , Fogarty JF, Monnier VM : copper deficiency and type 2 diabetes in the moose population of south-west Sweden , Scitotal Environ 2000 Apr 17; 249,(1-3) : 123-31 .
 18. Main Uliyar, Desai swati, Deshmukh, S hilpa Rai vandana & Iyer Uma: Zinc and Human Health. [Http //www.iza.com / conferences Conf - 02- abstracts.](http://www.iza.com/conferences/Conf-02-abstracts)
 19. Ibrahim, H.M (2002): Risk factors for late diagnosis of retinopathy .j. Kufa .Med 5(1):141-144.
 20. Ekin .S. Meral I, Gundus , H; Mert , N (2003): Comparative study of total protein and total lipid associated sialic acid levels in patients with type 2 diabetes mellitus. J clin lab. Anal, 17(4):124 - 6.
- Kareem I; Jawed, S.A, Bardapurkar, V.D; Patil (2004) study of magnesium, glycosylated hemoglobin and lipid profile in diabetic retinopathy. Clin. Biochem 19(2):124-12.