The Egyptian Journal of Hospital Medicine (July 2019) Vol. 76 (1), Page 3254-3259

Value of Serum Zinc, Magnesium and Copper in Obese and Normal Weight Children

Hassan Abdel Aziz Gaber, Tarek Abdel Kareim Eldahshan, Sabry Mohammed Ghanem, Mostafa Ahmed Abdo Abdel Fatah

Departments of Clinical Pathology and pediatrics, Faculty of Medicine, Al-Azhar University

Corresponding author: Mostafa Ahmed Abdo Abdel Fatah, **E-Mail:** mostafaeltaroty71@gmail.com, **Mobile:** 01000478283

ABSTRACT

Background: Childhood obesity is one of the most serious public health challenges of 21st century. The problem is global and is steadily affecting many low- and middle-income countries. The rising prevalence of childhood overweight and obesity represent a major health concern, as obesity is an important risk factor for a number of diseases. A strong evidence indicating that a disturbance of serum levels of zinc, copper and magnesium plays important role in the development of obesity and its related diseases. Our aim is to determine the mean zinc, magnesium and copper levels in obese and overweight children as compared to the levels in normal weight controls to study its relationship with overweight and obesity.

Objective: We aimed to assess, evaluate and compare serum zinc, magnesium and copper in obese, overweight and normal-weight children.

Patients and methods: The study was a case-control study conducted on 60 subjects 20 obese children, 20 overweight children and 20 normal weight children. All of them were subjected to full history taking, complete examination, and routine investigation including CBC, SGOT, SGPT, RBS, urea, Creatinine, TSH, lipid profile and specific laboratory investigation including serum zinc, magnesium and copper.

Results: In obese and overweight children, there were increased serum copper levels together with reduced serum levels of zinc and magnesium regardless age and sex when compared to normal weight children.

Conclusion: In obesity, there were increased serum copper levels together with reduced serum levels of zinc and magnesium regardless age and sex. Obese and overweight may be at a greater risk of developing imbalance (mainly deficiency) of trace elements, which may be playing an important role in the pathogenesis of obesity and related metabolic risk factors.

Keywords: childhood, obesity, overweight, normal weight, zinc, magnesium, copper.

INTRODUCTION

Childhood obesity is one of the most alarming challenges developing in today's world. The problem is universal and is steadily affecting many low and middle-income countries, particularly in urban settings. In urban centers, we can see a rise in sedentary lifestyles and unhealthy eating habits at an earlier age [(1)].

There is a dramatic rise in the prevalence of obesity among Egyptian children that has reached alarming levels [(2)].

Our knowledge on abundance of trace elements in human tissues and fluids has increased significantly due to improvements in analytics. Analytical methods have become useful in exploring the relationship between basic composition of body fluids and tissues, pathological conditions, and general nutritional status in humans. However, the literature on trace elements status in obesity in children and adults is scarce [(3)].

Micronutrients and macronutrients have been implicated as an important factor in regulating various metabolic processes and thus playing a role in the etiology of obesity. Many studies are being conducted worldwide that clearly showed a direct link between obesity and micronutrient deficiencies. Deficiencies of various micronutrients associated with increased BMI have an essential role in the metabolism of a variety of nutrients and have a key role in regulating hunger and the hormones that control it [(1)].

Zinc is essential micronutrient for maintaining the structure and form of protein molecules; it is in many cases fundamental to their function as enzymes or structural proteins. Diverse physiological processes including cell replication are impacted by zinc deficiency. Zinc is necessary for immune defense systems, growth, intestinal function, and brain development [(4)].

Zinc insufficiency in humans is demonstrated for the first time in 1960 in Iran and then some cases were reported from Egypt and Turkey. Zinc has shown to be useful for improving appetite and food intake, can affect reduction of anxiety and stress and this may be another mechanism for the effect of zinc on appetite [(5)].

Received:1/4/2019
Accepted:30/4/2019

Low concentrations of zinc in children who were obese were associated with high lipids, inflammation and insulin resistance in a recent Mexican cross-sectional study [6].

Magnesium is the fourth most copious cation found generally and is present abundantly as intracellular cation which exceeded only by calcium, sodium and ranging next to potassium. Magnesium is very essential for body. It can interrupt most of organ systems and can be reason for deadly outcomes such as arrhythmias (ventricular), vasospasm of cardiac arteries or may result in unexpected death [7].

Overweight children have lower serum and intracellular magnesium compared to healthy normal weight controls. Low magnesium levels have also been seen to have an inverse relationship with steady state plasma glucose. Low magnesium levels also lead to insulin resistance [1].

It is speculated that one of the causes for the aforementioned disorders in obese individuals, is magnesium deficiency. Deficiency of magnesium leads to: muscle tremors, convulsions, irritability, tetany, hyperreflexia or hyporeflexia [8].

Copper (Cu) is the third most abundant trace element with only 75–100 mg of total amount in the human body. Copper is an essential and integral component of many metalloenzymes, including ceruloplasmin, cytochrome -c-oxidase, superoxide dismutase, dopamine-B-hydroxylase, ascorbate oxidase and tyrosinase [9].

Serum Cu levels were reported to be significantly higher in obese patients compared to normal body weight controls. Some authors reported a negative correlation between serum copper and High-density lipoprotein (HDL)-cholesterol[10].

Copper imbalance often results in a reduced desire for protein, especially animal protein. Also, high tissue copper aggravates obesity. It is always associated with high serum leptin [11].

SUBJECTS AND METHODS

Subjects:

This study was conducted in collaboration between the Clinical Pathology and Pediatric Departments at Al Hussein University Hospital, Faculty of Medicine, Al-Azhar University.

This study was approved by the Ethics Board of Al-Azhar University.

All patients were collected from Pediatric Department at Al-Hussein University Hospital over a period from December 2018 to May 2019, with appropriate consent to participate in this study after explanation to the parents of participants how much it is helpful in diagnosis and treatment and also explaining to them that it is just a blood sample collection. The present subjects were divided into 2 groups: patients group and control group. The patients group was subdivided into 2 subgroups according to the presence of risk factors as follows:

- Subgroup IA (obese group): This group includes 20 healthy super obese children with age ranged between 2 and 14 years old. Their weight for height are above 95th percentile according to growth charts from National Center for Health Statistic, % ideal body weight (IBW) above 140 percentile of median weight for a given height and BMI greater than the 95th percentile for age and sex.
- Subgroup IB (overweight group): This group includes 20 healthy obese children with age ranged between 2 and 14 years old. Their weight for height are above 90th percentile according to growth charts from National Center of Health Statistic, % IBW in excess of 120 percent of the median weight for height and BMI greater than or equal 85th percentile but less than 95th.

Control group (II): Healthy control group, this group includes 20 apparently healthy and normal-weight children matched in age and sex to group IA and IB with age ranged between 2 and 14 years old.

SAMPLES AND METHODS

Full history taking, clinical examination and laboratory investigations, which included CBC, serum creatinine, urea, RBS, serum cholesterol, triglycerides, high & low density lipoprotein, liver enzymes (ALT & AST), TSH and specific tests (serum level of Zinc, Magnesium and Copper).

Venous blood (4 ml) were withdrawn from all participants of the study and divided into two portions: the first portion (1.5 ml) was taken in EDTA tube for CBC, which was done using cell dyne Ruby automated cell counter. The second portion (2.5 ml) was taken in Lithium-heparin for chemical tests.

Statistical Analysis

- Data were analyzed using Statistical Program for Social Science (SPSS) version 15.0. Qualitative data were expressed as frequency and percentage.
- Descriptive statistics used for quantitative data were mean ± SD, while categorized data were represented as numbers and percentages.

The following test was done: Chi-square test: was used when comparing between non-parametric.

- Friedman One way analysis of variance (ANOVA) and Fisher's least significant difference (LSD) were used to compare means of parametric data of different groups.

- Pearson correlation coefficient was used to check for correlation between two quantitative parametric data.
- For all analysis, P-value < 0.05 was considered significant.

P-value < 0.001 was considered as highly significant.
P-value > 0.05 was considered insignificant.

RESULTS

- Table (1) showed statistically non-significant difference **(p-value > 0.05)** as regard demographic data (gender, age and height) and highly statistical significant difference **(p-value < 0.001)** as regard weight and BMI (Fig 1).

As regard weight, the mean weight was 64.5 ± 14.4 kg in obese group, 48.7 ± 14.9 kg in overweight group and 38.7 ± 11.6 kg in control group.

As regard BMI, the mean BMI was 29.6 ± 4.3 in obese group, 21.9 ± 2.7 in overweight group and 18.7 ± 2.1 in control group.

- Table (2) showed no statistical significant difference **(p-value > 0.05)** between studied groups as regards serum CHOL and T.G while highly statistical significant difference **(p-value < 0.001)** between studied groups as regard LDL (Table 2).

Table (3) showed highly statistical significant difference **(p < 0.001)** between studied groups as regard serum Zinc, Copper and Mg.

As regard serum zinc, copper and Mg, the mean serum zinc was 39.7 ± 17.2 µg/dl in obese group, 54.5 ± 11.4 µg/dl in overweight group and 107.5 ± 15.2 µ/dl in control group. While, the mean serum copper was 124.4 ± 15.7 µg/dl in obese group, 123.7 ± 21.5 µg/dl in overweight group and 96.6 ± 12.9 µg/dl in control group. The mean serum Mg was 2.07 ± 0.17 mg/dl in obese group, 2.07 ± 0.16 mg/dl in overweight group and 2.5 ± 0.13 mg/dl in control group.

- Table (4) showed highly statistical significant difference **(p-value < 0.001) between** studied groups as regard skin fold. The mean skin fold was 21.3 ± 2.3 mm in obese group, 12.6 ± 3.2 mm in overweight group and 9.6 ± 1.4 mm in control group.

Table (1): Comparison between studied groups as regard demographic data

Demographic data / Variables		Obese (N = 20)	Overweight (N = 20)	Control (N = 20)	P-value
Gender	Male	11 (55%)	9 (45%)	9 (45%)	0.76
	Female	9 (45%)	11 (55%)	11 (55%)	
Age (years)	Mean	10.8	10.9	10.6	0.92
	± SD	2.3	2.5	2.7	
Weight (kg)	Mean	64.5	48.7	38.7	**< 0.001***
	± SD	14.4	14.9	11.6	
Height (cm)	Mean	146.7	146.3	140.6	0.32
	± SD	10.7	16.4	15.3	
BMI	Mean	29.6	21.9	18.7	**< 0.001***
	± SD	4.3	2.7	2.1	

Table (2): Comparison between studied groups as regard lipid profile

Variables		Obese (N = 20)	Overweight (N = 20)	Control (N = 20)	P-value
CHOL (mg/dl)	Mean	148.2	153.5	145.2	0.66
	± SD	3.6	2.7	3.7	
T.G (mg/dl)	Mean	134.4	145.9	121.8	0.43
	± SD	7.1	6.7	3.9	
HDL (mg/dl)	Mean	46.6	51.0	50.3	0.57
	± SD	7.01	6.3	6.2	
LDL (mg/dl)	Mean	62.1	57.9	27.6	**< 0.001***
	± SD	2.5	6.01	7.4	

Table (3): Comparison between studied groups as regard Zinc, Copper and Magnesium

Variables		Obese (N = 20)	Overweight (N = 20)	Control (N = 20)	P-value
Zinc (µg/dl)	Mean	39.7	54.5	107.5	< 0.001*
	± SD	7.2	1.4	15.2	
Copper (µg/dl)	Mean	124.4	123.7	96.6	< 0.001*
	± SD	15.7	21.5	12.9	
Mg (mg/dl)	Mean	2.07	2.07	2.5	< 0.001*
	± SD	0.17	0.16	0.13	

Table (4): Comparison between studied groups as regard skin fold

Variables		Obese (N = 20)	Overweight (N = 20)	Control (N = 20)	P-value
Skin fold (mm)	Mean	21.3	12.6	9.6	< 0.001*
	± SD	2.3	3.2	1.4	

DISCUSSION

Obesity in childhood and adolescence is linked with several short-term medical risks, including glucose intolerance, hypertension, hyperlipidemia, sleep apnea and orthopedic complications [12].

In addition, overweight children have a significantly higher risk for becoming overweight adult who is associated with a higher prevalence of cancer, cardiovascular disease and type II diabetes [13].

Trace metals are known to have an important effect on the activity of metalloenzymes and insulin secretion and changes in their levels involved in the etiology of various diseases. Zinc, copper and magnesium are well known essential trace elements in human nutrition; however, the relation between obesity and trace elements is still not clear [10].

Zinc is an essential metabolic and nutritional trace element. It has an important effect on the metabolism and thermoregulation of obese individuals [14]. Copper is known to be an essential component of several copper metalloenzymes including ceruloplasmin, cytochrome -c-oxidase, superoxide dismutase, dopamine-B-hydroxylase, ascorbate oxidase and tyrosinase [9].

Magnesium, the second most abundant intracellular cation, is a critical cofactor in numerous enzymatic reactions. Low serum and dietary magnesium may be related to the etiologies of cardiovascular disease, hypertension, diabetes and atherosclerosis [15].

In our results, there was no significant difference between the studied groups regarding age and sex. This is in accordance with ***Azab et al.*** [16] who reported no significant difference between obese group and non-obese group as regards age and sex.

The body mass index (BMI) showed highly significant increase ($p < 0.001$) in our obese group compared to control group. This is matching with ***Lo et al.*** [17] who suggested that BMI greater than the 95th percentile should be considered a screening criterion for obese children.

In our study, serum zinc levels of obese children were significantly lower than those of the healthy control group ($P < 0.001$). In contrary to our study ***Yakinci et al.*** [18] showed that serum zinc levels in obese children were significantly higher than the healthy control group ($P < 0.01$) and the high serum zinc levels in obese children might be explained by the positive correlation between zinc levels and good appetite and increased taste acuity. These results may reveal a significant metabolic role for zinc in development of obesity. Zinc restriction decreased leptin levels while zinc supplementation of depleted subjects increased circulating leptin level [19].

Zinc is known to have important effects on insulin activity, to increase the body fat deposition and thyroid hormone conversion (T4 to T3). Blood zinc concentration is inversely related to T3 level in diabetics and obese individuals [20]. Therefore, zinc plays a great role in the development of obesity since it stimulates food absorption, protein synthesis and stimulates good appetite and taste acuity [21].

Copper is a trace mineral, which is needed by the body in order to absorb and utilize iron. Its presence is also necessary for the production of adenosine triphosphate (ATP), which is used by the body for energy. It is essential component of cytochrome oxidase enzyme in the respiratory chain. It is also known to be an essential component of several copper metalloenzymes [22].

Copper deficiency or excess have been recognized as potential health problem for infants and children worldwide [23].

Our obese group (group IA) showed highly significant increase in copper levels than healthy control group. This is in agreement with ***Yakinci et al.*** [18] who evaluated serum copper and zinc in 41 obese and 41 healthy control children and found that serum copper and zinc concentrations were significantly higher in obese children than in healthy controls ($p<0.01$). This result was explained by the positive correlation between zinc levels and good appetite and increased taste acuity.

In addition, abnormalities of copper distribution in tissues and serum has been described in obese subject by ***Omar et al.*** [24] who reported that serum copper is significantly elevated in obese subjects than in the healthy subjects ($p < 0.001$).

Our overweight group (group IB) showed highly significant increase in copper levels than healthy control group. Contradictory results were obtained by ***Lopez et al.*** [25] who reported no modification of serum copper level in neither lipid metabolism alterations nor obesity.

Magnesium is one of the most abundant ions present in living cells and its plasma concentration is remarkably constant in healthy subjects. Plasma and intracellular magnesium concentrations are tightly regulated by several factors among them, insulin seems to be one of the most important [26]. Insulin-induced erythrocyte magnesium accumulation is impaired in patients with obesity. Insulin influences both glucose metabolism and magnesium homeostasis in humans. Insulin resistance in non-insulin dependent diabetes mellitus impairs the ability of insulin to stimulate magnesium as well as glucose uptake [27]. The decreased intracellular magnesium might underlie the initial pathophysiologic events leading to insulin resistance and abnormality in platelet coagulation [28].

In our study, serum magnesium levels of obese children were significantly lower than that of the healthy control group ($P < 0.001$). In acceptance with our results, that of ***Yakinci et al.*** [18] who found that serum magnesium levels were significantly lower in obese children than in healthy children ($p < 0.01$). ***Corico et al.*** [29] found that erythrocyte and platelet magnesium levels in normotensive obese patients were significantly lower than those of the control group, while in hypertensive obese patients a reduction of plasma magnesium level has been detected. Therefore, this confirm the existence of a reduction of intracellular magnesium concentrations, which is common in hypertensive and obese patients. The low serum magnesium levels in obese children might be explained by greater preference for fat among children with a higher percentage of body fat or body mass indexes [30]. Oils and fats contain very little amount of magnesium because fatty acids decrease magnesium absorption [31].

In our study, serum zinc showed significant negative correlation with BMI and skin fold thickness. In Acceptance with our results is that of ***Chen et al.*** [32] who showed that zinc level was inversely related to the degree of obesity and that plasma zinc concentrations in overall individuals are inversely correlated to their body mass index.

In our study, serum copper showed highly significant positive correlation with skin fold thickness and significant positive correlation with BMI. This is in agreement with ***Omar et al.*** [24] who showed that levels of serum copper rise with the BMI.

CONCLUSION

In obese and overweight children, there were increased serum copper levels together with reduced serum levels of zinc and magnesium regardless of age and sex when compared to normal weight children. Obese and overweight may be at a greater risk of developing imbalance (mainly deficiency) of trace elements, which may be playing an important role in the pathogenesis of obesity and related metabolic risk factors.

RECOMMENDATION

1- Further studies are needed to clarify if low magnesium levels have an effect on glucose intolerance and cardiovascular disease in obese children.
2- Encouragement of a diet with increased fruit, vegetables and high zinc intake for obese children.
3- Further studies should be continued on large scale to clarify the relationship between obesity and other trace elements as copper.
4-

REFERENCES

1. ***Hassan SA, Ahmed I, Nasrullah A et al. (2017)***: Comparison of serum magnesium levels in overweight and obese children and normal weight children. Cureus, 9 (8): 1607-1616.
2. ***Aboul Ella NA, Shehab DI, Ismail MA et al. (2010):*** Prevalence of metabolic syndrome and insulin resistance among Egyptian adolescents 10 to 18 years of age. Journal of Clinical Lipidology, 4 (3): 185-195.
3. ***Błażewicz A, Klatka M, Astel A et al. (2013):*** Differences in Trace Metal Concentrations (Co, Cu, Fe, Mn, Zn, Cd, and Ni) in Whole Blood, Plasma, and Urine of Obese and Nonobese Children. Biological Trace elements research, 155 (2): 190-200.

4. ***Mary EP (2013):*** Zinc Supplementation in Public Health. Ann Nutr Metab., 62 (1): 31–42.
5. ***Mayo-Wilson E, Junior JA, Imdad A et al. (2014):*** Zinc supplementation for preventing mortality, morbidity, and growth failure in children aged 6 months to 12 years of age. Cochrane Database Syst Rev., 15: 5.
6. ***Zavala G, Long KZ, Garcia OP et al. (2012):*** Specific micronutrient concentrations are associated with inflammatory cytokines in a rural population of Mexican women with a high prevalence of obesity. The British Journal of Nutrition, 55: 1-9.
7. ***Jamali AA, Jamali GM, Jamali AA et al. (2018):*** Association of low serum Magnesium levels in type 2 Diabetes mellitus with & without Hypertension. Open journal of preventive medicine, 8: 57-69.
8. ***Zaakouk AM, Hassan MA, Tolba OA (2016):*** Serum magnesium status among obese children and adolescents. Egyptian Pediatric Association Gazette, 64 (1): 32-37.
9. ***Osredkar J, Sustar N (2011):*** Copper and Zinc, Biological Role and Significance of Copper/Zinc Imbalance. J Clinic Toxicol., 3: 11.
10. ***Fan Y, Zhang C, Bu J (2017):*** Relationship between selected serum metallic elements and obesity in children and adolescent in the U.S. Nutrients, 9 (2): 104.
11. ***Carter S, Caron A, Richard D et al. (2013):*** Role of leptin resistance in the development of obesity in older patients. Clin Interv Aging, 8: 829-844.
12. ***Güngör NK, (2014):*** Overweight and Obesity in Children and Adolescents. J Clin Res Pediatr Endocrinol., 6 (3): 129-143.
13. ***Gallagher EJ, LeRoith D (2015):*** Obesity and Diabetes: The increased risk of cancer and cancer-related mortality. Physiol Rev., 95 (3): 727-748.
14. ***Wang Y, Jia X, Zhang B et al. (2018):*** Dietary zinc intake and its association with metabolic syndrome indicators among Chinese adults: An analysis of the China nutritional transition cohort survey 2015. Nutrients, 10 (5): 572.
15. ***DiNicolantonio JJ, Mangan D, O'Keefe JH (2018):*** Copper deficiency may be a leading cause of ischemic heart disease. Open Heart, 5 (2): e000784.
16. ***Azab SFA, Saleh SH, Elsaeed WF et al. (2014):*** Serum trace elements in obese Egyptian children: a case–control study. Italian Journal of Pediatrics, 40: 20.
17. ***Lo JC, Maring B, Chandra M et al. (2014):*** Prevalence of obesity and extreme obesity in children aged Three to Five years. Pediatric obesity, 9 (3): 167.
18. ***Yakinci C, Pac A, Kucukbay FZ et al. (1997):*** Serum zinc, copper and magnesium levels in obese children. Acta Pediatr Jpn., 39 (3): 339-341.
19. ***El-Mashad GM, El-Gebally EI, El-Hefnawy SM et al. (2018):*** Effect of zinc supplementation on serum zinc and leptin levels in children on regular hemodialysis. Menoufia medical journal, 31 (2): 664-670.
20. ***Abdel Gawad MM, Omar OM, Abo Elwafa RA et al. (2017):*** Serum zinc level and its relation to insulin resistance and lipid profile in childhood and adolescent obesity. Egypt J Obes Diabetes Endocrinol., 3: 46-52.
21. ***Tungtrongchitr R, Pongpaew P, Phonrat B et al., (2003):*** Serum copper, zinc, ceruloplasmin and superoxide dismutase in Thai overweight and obese. J Med Assoc Thai, 86 (6): 543-551.
22. ***Huskisson E, Maggini S, Ruf M (2007):*** The role of vitamins and minerals in energy metabolism and well-being. The journal of international medical research, 35: 277-289.
23. ***Araya M, Koletzko B, Uauy R (2003):*** Copper deficiency and excess in infancy: developing a research agenda J Pediatr Gastroentrerol Nutr., 37 (4): 422-9.
24. ***Omar S, Abdennebi M and Ben Mami F et al. (2001):*** Serum copper levels in obesity: a study of 32 cases. Tunis Med., 79: 370-3.
25. ***Lopez C, Ocon DC, Mengo MS et al. (1991):*** Study of zinc and copper serum levels in dislipemias. Record 10 of 21 therapie, 46 (1): 17-20.
26. ***Birla VH, Dipnaik K, Ingale P et al., (2015):*** Preliminary study of serum magnesium in diabetes mellitus. International journal of research in medical science, 3 (11): 3109-3113.
27. ***Kostov K (2019):*** Effects of magnesium deficiency on mechanisms of insulin resistance in type 2 diabetes: Focusing on the processes of insulin secretion and signaling. Int J Mol Sci., 20 (6): 1351.
28. ***Takaya J, Higashino H, Kotera F et al. (2003):*** Intracellular magnesium of platelets in children with diabetes and obesity. Metabolism, 52 (4): 468-471.
29. ***Corico F, Allegra A, Lentile R et al. (1997):*** Magnesium concentrations in plasma, erythrocytes and platelets in hypertensive and normotensive obese patients. Am J Hypertens, 10 (11): 1311-1313.
30. ***Birch LL, Davison KK (2001):*** Family environmental factors influencing the developing behavioral controls of food intake and childhood overweight. Pediatr Clin North Am., 48 (4): 893-904.
31. ***Schuchardt JP, Hahn A (2017):*** Intestinal absorption and factors influencing bioavailability of magnesium-an update. Curr Nutr Food Sci., 13 (4): 260–278.
32. ***Chen MD, Lin PY, Lin WH (1991):*** Investigation of the relationships between zinc and obesity. The Kaohsiung journal of medical sciences, 7 (12): 628-634.