Estimation The Trace Elements And Their Association With Insulin Resistance In Obese Adults.

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ABSTRACT

Background: Trace elements are essential micronutrients in the development of the metabolic complication of obesity , arterial hypertension ,dyslipidemia , and insulin resistance or diabetes . According these it is important to known and measure the trace elements status in obesity.

Aim of the study: A study was performed to estimate serum levels trace elements status Sodium(Na) , Potassium (K) , Calcium (Ca) ,and, Chloride (Cl)in the adults obese comparison with normal weight controls , and to evaluate their potential association with insulin resistance .

Material and Methods: Eighty obesity with Body Mass Index(BMI) 35-39.5 Kg/m2and twenty health person with (BMI) 18 -24.5 Kg/m2 as control group aged 20-40 years were assessed the serum levels trace elements and also were evaluated the insulin resistance in the obesity and control groups, according to Homeo- static Model Of Assessment for Insulin Resistance (HOMA-IR) protocol.

Results : Compared to the control group Ca and K serum levels were significantly lower (all P<0.05) and Na and Cl serum levels were significantly higher (P< 0.05) in the adults obese group in all age groups . Also   significant inverse correlation was found between HOMA-IR and Ca level.

Conclusion : Obesity adults have higher mineral serum levels especially Na and Cl than control group in all age groups, and lower Ca and K which contributed with insulin resistance.

INTRODUCTION

The trace elements are sodium , copper, iron , magnesium , potassium and zinc which have been identified as essential for human health (1) . In these study we estimation the serum levels of the trace elements changes that include Na , K , Ca , and , Cl in obesity compare with normal persons , and to elevate their potential association with insulin resistance.Trace elements can be involved their production or in the protection against inflammation and peroxidation which are important key factors in the development of metabolic complication of obesity(2).

Dietary with high amounts of sodium , calories and fats considered one of the etiology of chronic disease , including obesity and high blood pressure (3).Many studies on animals indicated that a diet with high sodium may increase adipose tissue mass, and this is lead to alteration in insulin and glucose metabolism which promote fat accumulation (4).

Obesity caused of restrict sodium excretion , which leads to elevated blood pres-sure .In a study on obese adolescents with age 10-16 years, increased blood pressure could directly be related with a volume dependent of increased stroke volume and which decreased with a low sodium diet (5). High levels of salt in the body may lead to increased circulatory volume , this can lead to increase fluid pressure on the blood vessel walls .This process can cause thickening of the blood vessel walls and leave less space for the blood flowing within the vessels (6).

Several mechanisms may contribute to the pathogenesis of obesity induced hyp-ertension , these mechanisms are the sodium retaining effects of catecholamine and insulin , disorders in transmembrane fluxes of sodium and altered carbohydrate metabolism , also some of these mechanisms can alter the urinary excretion of sodium and that effect on the serum sodium level (7).

Potassium can be defined as intracellular cationic electrolyte which is essential for normal cellular function , also it was easily excreted by the kidneys instead of stored in the body and the average of potassium consumption was insufficient (8). Many studies showed that higher potassium can be reduced the obesity and meta – bolic syndrome risk (9).

Potassium contributed in the protein synthesis and carbohydrate metabolism later was excreted , in the urine instead of storage in the body , the human body requires a constant quantity of potassium , also it has important role in insulin secretion from pancreatic beta cells (10) . Potassium consumption can be alterable to the activation of the renin – angiotensin system (RAS) in response to the volume contraction , promoted potassium exchange with sodium in the distal tubule when potassium enters the cell lead to diuretic-induced alkalosis , the (RAS) activation can be considered an important system contributes to hypertension in obese individuals, sodium retention in the body and volume expansion can be enhanced sympathetic activity , also high levels of circulation components of(RAS) were observed in obese subjects , which had shown a reduction in weight loose (11) . In insulin – resistance obese patients an elevated Na$^+$ / K$^+$ ratio was found in skeletal muscles , pointing to reduction pump ability , also the some study showed a positive association between skeletal muscle Na$^+$/ K$^+$ and BMI (12).

Calcium constitutes about 1.5% - 2% of total body weight and mostly found in bones and teeth (13) , also calcium is the most abundant in the human body, which participated in many physiology processes such as muscle contraction , hormones , and , neurotransmitters release, glycogen metabolism , cell proliferation and differe-ntiation , nerve impulse transmission and structural support of the skeleton (14) .

Calcium concentration controlled by three hormones ; parathyroid hormones , calcitriol, and calcitonin hormones, these hormones work to increase calcium conce-ntration by interaction with kidneys , intestines , and bones (13) . Many data have proved the regulation

of adipocyte energy storage can be controlled by intracellular Ca^{2+} which lead to increase circulating calcitrophic hormones and /or parathyroid hormone and low Ca^{2+} diets induce adipocyte Ca^{2+} flow and thereby increase lipid storage (15).

Loos et al. (2004) showed an association between fat – free mass and calcium intake in black women and also indicated that lower Ca^{2+} intake can be linked with higher adiposity (16) . In a study performed on Chines women showed that calcium is inversely associated with BMI , weight change , waist to higher ratio , and fat mass , they also indicate when dairy calcium is increased , the risk for abdominal obesity was significantly decreased (17).

Trace elements is involved in the pathogenesis of obesity and obesity related disease , we tried to assess trace elements status (Na, K ,Ca ,and Cl) serum levels and insulin resistance in obese adults compare to the control group.

MATERIAL AND METHODS

Subjects : This study conducted between July 2020 continued through September 20202 in Al-Diwaniah Teaching , Hospital , The study included 100 individuals , subjects with history of chronic medication use , history of chronic disease ,drug use and other disorder were excluded from this study.The total samples 100 blood samples were taken from men in this study ,which divided according BMI into control group (20 sample) which BMI 18-24.5Kg/m^2 and obesity group (80 sample) which BMI 35 -39.5 Kg /m^2 and according to age divided into four groups (20 - 25 year) , (26 – 30 year) , (31 – 35 year) , and (36 - 40 year). Obese male groups examined to estimate the serum trace elements levels and evaluated the insulin resistance according to the (HOMA-IR) protocol and compare with control group.The hospital ethical committee approved the human study, control and obese were told about the importance, and other detail of research and explain the aim of this study and protocol of ethics.Many of subjects refused to give the blood samples.

Blood Collection: Blood were collected by vein puncture at 8 – 10 am after overnight fast .Separated into 3 ml untreated gel tube for serum and 2 ml EDTA treated tube for plasma. The serum were frozen at -20 C° in two replicate until thawed for assay.

Trace Elements Measurements : Trace elements levels in the serum (Na ,K ,Ca ,Cl) were detected for all subjects and control by using Opti – Lion analyzer (Optimedical, U.S.A.) by using available cassette which taken the serum 200 microliter , after 2 minutes, the result was given in m mol /L .

Glucose and Insulin Resistance Measurements : Fasting glucose level was estimated by using Reflotron plus automated analyzer (Roche ,Germany). Plasma insulin was determined by immunoradiometric assay (DIA- Source Immunoassays S.A. Nivelles, Belgium).

The diagnosis of insulin resistance was determined by Homeostasis Model Assessment index for Insulin Resistance (HOMA-IR) protocol , which the product of fasting insulin (µUI/mI) and fasting glucose (mmol/L) divided by 22.5 . Insulin resistance was defined when P values were above 3.16 (18).

Data are shown as mean ± SD , all calculations and statistics were performed using analyzed Statistical Package for the Social Science(SPSS) , version 20. Compari- sions between groups were carried out using the Mann –Whitney U test . Simple correlations between variable were calculated as the Spearman Coefficient of corre- lation at P Value <0.001 was regarded as significant.

RESULTS

One way ANOVA analysis showed significant increased (P <0.05) the Na serum level in obese compare with the control group in all age groups . Statistical analysis demonstrated no significant difference (P < 0.05) between obesity and control group k serum level in age group (20-25 year) , while significant decrease (P<0.05) K serum level in obesity compared with control group in age groups (26 – 30 year) , (31 – 35 year) , and (36 – 40 year).

Results showed significant decreased (P < 0.05) the Ca serum level in obesity in all age groups compare with control groups. Studied reveal significant increased (P < 0.05)in Cl serum concentration level in obesity compare with control group in all age groups (Table 1).

Subject	Parameter	Mean ± SD(age groups)				L.S.D
		20 - 25 Year N=20	26 - 20 Year N=20	31- 35 Year N=20	36 - 40 Year N=20	
Obesity BMI 35-39.9 Kg/ m^2 N=80	Na m mol/L	140.62±1.789**	142.31±2.074**	140.61±3.103**	143.71±3.032**	
	K m mol/L	4.240±0.409	4.110±0.577	3.822±0.317	3.876±0.680	
	Ca m mol/L	1.021±0.036	1.001±0.028	1.098±0.045	1.036±0.041	
	Cl m mol/L	104.22±2.831	105.20± 2.864	106.20±2.550	105.40±1317	
		20-25 Year N=5	26-20 Year N=5	31-35 Year N=5	36-40 Year N=5	

Control BMI 18-24.9 Kg/ m^2 N=20	Na m moI/L	133.13±2.578	135.27±2.219	136.27±2.251	134.60±3.158
	K m moI/L	4.760±0.408	4.627±0.459	4.747±0.612	4.353±0.052
	Ca m moI/L	1.143±0.065	1.148±0.048	1.165±0.071	1.125±0.052
	Cl m .moI/L	103.27±2.245	103.30±2.651	102.47±2.557	104.80±3.189

*Significant(p>0.05)

Table 1: Comparison mean ±SD trace elements serum levels in obesity and control in different age groups.

In present study we found significant increase (P < 0.001) insulin resistance in obesity as represent by HOMA- IR indices , serum insulin and glucose concentration levels compare with the control group in all age groups (Table 2 , Table 3) Also result indicate significant correlation between obesity and poor trace elements Ca and K with control group in all age groups.

Subjects	Parameter	Mean ± S.D (age groups)				L. S. D
Obesity BMI 35-39.9 Kg/m^2 N=80	Glucose (m mol/L) Insulin (µUI/ml)	**20 – 25 Year N = 20**	**26 – 30 Year N = 20**	**31 – 35 Year N = 20**	**36 – 40 Year N = 20**	
		90.860±5.409* 14.3±3.4 *	97.920±3.091* 16.8±4.8*	93.180±6.414* 13.7±3.8*	121.601±7.394 * 14.1±4.1*	
Control BMI 18-24.9 kg/m^2 N=20	Glucose (m moI/L) Insulin (µUI/mI)	**20 – 25 Year N = 5**	**26 – 30 Year N = 5**	**31 – 35 Year N = 5**	**36 – 40 Year N = 5**	
		81.800±5.611 8.1±6.1	84.610±2.590 9.2±5 .2	83.201±6.900 8.7±3.2	87.4± 5.221 9.1± 3.5	

*Significant (P<0.05)

Table 2 : The comparison mean ±SD fasting Glucose and Insulin concentration in obesity and control in different age groups.

Parameter	Obesity N=80	Control N=20	P
Glucose (m mol/L)	100.89±5.577*	84.252±5.080	P<0.001
Insulin (µUI/ml)	14.725±4.025*	8.775±4.5	P<0.001
HOMA-IR	66.026±1.7*	32.858±0.58	P<0.001

*Significant(P<0.001)

Table 3 : Comparison mean ± SD Glucose , insulin concentration and , insulin resistance level in the obesity and control groups.

The mean ± SD HOMA-IR was significantly higher (P< 0.01) in obesity with Ca and K deficiencies as well as correlation analyses showed significant invert relation between Ca serum level in obesity with HOMA-IR (P < o.o1) (Table 4).

	Subjects Parameter	(20-25 year) N=20	(26-30 Year) N=20	(31-35 Year) N=20	(36-40 years) N=20	R	P
Obesity	**Ca-HOMA-IR**	0.347*	0.469*	0.428*	0.387*		P*

*Significant(P<0.01)
R (Spearman Coefficient)

Table 4 : Significant correlation between Ca trace element in obesity relation with HOMA-IR in different age groups.

DISCUSSIONS

Our data showed that sodium serum level was increased in obese adult indiv-iduals compared with control group . The insulin resistance can increased the activity of central sympathetic nervous system which increased the peripheral resistance and increased the reabsorption of sodium in the kidney tubules (19) . The increasing risk factors of blood pressure and cardiovascular diseases related with the consumption of salt which increasing in the risk of stroke and renal diseases which associated with obesity (20).

Our study reveal   that potassium serum level were decreased in obese indivi-duals in age groups (26 - 30 year) , (31 -35 year) , and (36 -40 year) , so that our suggestion about the decreased of potassium in these age groups may be related with the reduction of muscle mass or increase the glucose metabolism in those indiv-duals , while no significant differences potassium level in obese age group (20 -25 year) compare with control may be related with high dietary of potassium . Cai et al. (2016) showed that potassium intake was related to metabolic syndrome and also performed a protective influence of potassium intake on metabolism syndrome and obesity , sodium to potassium ratio was considered a sensitive marker to obesity.We finding significant differences in calcium serum level between obese and control group in all age groups , while no significant differences between age groups in control an obesity groups . Our suggestion that the decrease of calcium level in obesity groups may be related with many factors such as   affected in   the future with hypertension , diabetes type II   , insulins tolerance , high cholesterol levels and other complication of obesity as well as increasing cytokines and interleukins and deficien-cy of Vitamin D . The mechanism which explain the influence of calcium on the body weight alteration that calcium was considered a regulatory for lipid metabolism because the increasing levels of intracellular calcium can stimulate the activity of lip- ogenic enzyme and inhibit the lipolysis with elevated the accumulation of fat (16). May study confirm with our result data , calcium intake as calcium only or in the dairy food was related with weight loss (21), also Huang et al. (2011) showed that dietary calcium intake   , but not calcium supplement was negatively related with abdominal obesity and body composition. The absence of some micronutrients were associated with fat accumulation and obesity , such as overweight and   obese individual had lower levels of minerals and vitamins compared   with   non-overweight   and   non-obese individuals (21).

In the cross sectional study , elevated the degree of obesity higher BMI and weight were associated with higher sodium intake and low calcium (22).

Our data demonstrated a significant differences in glucose concentration in obese individual compare with control group in all age groups , our suggestion about increasing levels of glucose in obese may be related with their insulin resistance and dyslipidemia which increasing the risk factors of obesity and metabolic syndrome. The increasing of plasma insulin is associated with increasing obesity and with incre-ing the decline of insulin sensitivity , while the glucose levels not raised in the men with BMI >25 without metabolic syndrome , but the levels of insulin elevated in the men with metabolic syndrome (23-24).

The elevated levels of fatty acids in the liver lead to increase triglycerides , hepatic gluconeogenesis and the synthesis of Very Low Density Lipid (VLDL) which can cause the abnormalities in glucose metabolism (25) . Obesity , metabolism syndrome and the risk factor of cardiovascular disease was increased when the blood glucose increased (26) . The immunoassay of serum insulin was caused a con-founding results about insulin secretion in individuals with abnormalities of glucose tolerance, so that many researchers showed that glucose induced insulin can release in mild diabetes while others showed that it was increased in obesity (27 -28).

CONCLUSIONS

Obese adult individuals were have significant increased Na and Cl serum levels, and significant decreased Ca and K mineral compare with control in all age groups , also invert correlation between Ca and K serum levels deficiencies with insulin resistance.

REFERENCES

1. Wang Y , Chen X , Song Y , Caballero B , and Cheskin L (2008) Association between obesity and kidney disease : A systematic review and meta-analysis .Kidney Inter. 73 (1) : 19-33.
2. Azab S F , Saleh   S H , Elsaeed   WF, et al. (2014)Serum trace elements in obese Egy –tian children : a case –control study .Italian J of Pediatrics .40 (1):20.
3. Berenbaum E , Bocking N , O"Brien M ,Wu JH (2014)Evidence brief :Impacts of and relationship between excessive dietary sodium consumption and childhood obesity . Public Health Ontrio .

4. Grimes CA , Boluis DP , He FJ , and Nowson CA (2016)Dietary sodium intake and overweight and obesity in children and adults: a protocol for a systematic review and meta- analysis .Systematic Reviews .5(1): 7.
5. Staboulie S, Papakatasika S, and Kotsis V (2011)The role of obesity , salt and exerc- ise on blood pressure in children and adolescents .Expert Revi of Cardiovasc Therapy. 9 (6):753-761.
6. Schellhardt TA(2012) The relationship between the sodium / potassium ratio and vascular function . (Doctoral dissertation), The University of Delaware. ,1-90.
7. Nanji AA and Freeman JB (1985) Relationship between serum sodium and blood pressure in morbid obesity . Clin and Exper Hyperten .Part A : Theory and Practice . 7 (7) : 933-937.
8. Chae JS , Paik JK , Kang R , et al. (2013) Mild weight loss reduces inflammatory cytokines , leukocytes count , and oxidative stress in overweight and moderately obese participants treated for 3 years with dietary modification. Nutri Res .33 (3):195 -203.
9. Cai X , Li X , Fan W , et al. (2016) Potassium and obesity / metabolic syndrome : A systematic review and meta-analysis of the epidemiology evidence. Nutri.8(4):183.
10. Shin D , Joh HK , Kim KH and Park SM (2013) Benefits of potassium intake on metabolic syndrome : The fourth Korean National Health and Nutrition Examination Survey .Atherosclerosis .230 (1) : 80 -85.
11. Mariosa LSS , Ribeiro-Filho FF , Batista MC , et al. (2008) Abdominal obesity is associated with potassium depletion and changes in glucose homeostasis during diuretic therapy . The J Of Clin Hyper.10 (6) : 443-449.
12. Djurhuus MS , Vaag A and Klitagaard NAH (2001) Muscle sodium , potassium and {H-3} Ouabain binding in identical twins , discordant for type 2 diabetes. J of Clin End
13. Metab .86(2): 859-866.
14. Ewoldt LP (2013) The relationship between calcium intake and body mass index in the participants of HUB City Steps.
15. De Oliveira Freitas DM , Martino HSD , Ribeiro SMR , and et al. (2012) Calcium ingestion and obesity control. Nutri Hospita .27 (6) : 1758-1771.
16. Vilarroel B , Villalobos E , Reyes M and Cifuentes M (2014) Calcium , obesity , and the role of calcium – sensing receptor. Nutri Revi .72 (10) : 627-637.
17. Zemel M B , Shi H , Greer B and et al. (2000) Regulation of adiposity by dietary calcium . The FASEB J : Official Publication of the Federation of American Societies for Experimental Biology . 14 (9): 1132-1138.
18. Loos R , Rankinen T , Leon A and et al. (2004) Calcium intake associated with adiposity in black and white men and white women of the Heritage Family Study .
19. Huang L , Xue J , He Y and et al. (2011) Dietary calcium but not elemental calcium from supplements is associated with body composition and obesity in Chines women .PLos ONE. 6 (12) :1-7.
20. Keskin M , Kurtoglu S, Kendirci M et al. (2005) Homeostasis model assessment is more reliable than the fasting glucose / insulin ration and quantative insulin sensitiv-ity check index for assessing insulin - resistance among obese children and ado-lescents . Pediatrics . 115 : e 500-503.
21. Vilarrasa N , Maravall J , Estepa A , and et a l. (2007) Low 25- hydroxyl vitamin D concentrations in obese women : their clinical significant and relationship with anthropometric and body composition variables . J of Endo Inves .30 (8):653-658.
22. Garcia OP ,Long KZ , and Rosado JL (2009) Impact of micronutrient deficiencies on obesity . Nutri Revi .67 (10):559-572.
23. 22-Stella SY and Kansagra SM (2014)Association of sodium intake with obesity , body ,mass index ,waist circumference, and weight .Americ J of Preven Medi .46(6):53-55.
24. Suliburska J , Bogdaski P , Pupek-Muslalik D and Krespcioo Z(2011) Dietary intake and serum and hair concentrations of minerals and their relationship with serum lipids and glucose levels in hypertensive and obese patients with insulin resistance . Biol Trace Elem Res .139:137-150.
25. Goncharov NP , Katsya GV , Chagina NA and Gooren L J (2009) Testosterone and obesity in men under the age of 40 years . Andrologia .41(2):76-83.
26. Phillips GB , Olaizola I , AIastrue A , and et al.(2006)The metabolic syndrome and glucose intolerance .Hospital Physician. 71:26-38.
27. Kadota A , Hozawa A ,Okamura T and et al. (2007) Relationship between metabol-ism risk factor clustering and cardiovascular mortality stratified by higher blood glucose and obesity NIPPON DATA90, 1990-2000. Diabetes Care .30(6):1533-1538.
28. Cercato C , Mancin i MC , Arguello AMC, and et al.(2004) Systemic hypertension, diabetes mellitus , and dyslipidemia in relation to body mass index: evaluation of a Brazilian population. Revista do Hospital das Clinicas. 59(3):113-118.
29. Ortega RM , Rodriguez E , Aparicio A,and et al.(2012)Poor zinc status is associated with increased risk of insulin resistance in Spanish children .Br J Nutr .107:398-404.