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SOME SELECTED TRACE METALS (ESSENTIAL AND TOXIC) AND MACRO-METAL MG AS PROBABLE BIOMARKERS OF OBESITY-ASSOCIATED COMPLICATIONS

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Keywords:

Obesity, Diabetes Mellitus, Hypertension, Trace metals, Macro-metal Mg.

Abstract

Background: Trace metals and Mg metabolism may play a role in adiposity which contributes to inflammation and oxidative stress; two potential mechanisms proposed to play a major role in the morbidity/mortality associated with obesity hence this study.

Methods: We investigated trace metals-essential and toxic (Zn, Cu, Mn, Fe, Se, Cr, Pb, Cd and macro-metal Mg) in two hundred and sixty-four (264) subjects. They consist of group NONDH (60 non obese non diabetic/hypertensive or normal control); Group ONDH (45 Obese Non Diabetic/ Hypertensive- obese only), Group OD (59 Obese Diabetic); Group OH (59 Obese Hypertensive); Group ODH (41 Obese Diabetic/Hypertensive). Using standard procedures, weight, height, blood pressure and fasting blood glucose were measured and mineral trace metals and macro-metal Mg were analyzed spectrophotometrically.

Results: showed that Obesity has a diminution effect on trace metals and Mg and obesity-associated complications (diabetes mellitus/hypertension) worsen this effect. Also Trace metals and Mg correlated positively with BMI in the obesity only subjects. But as soon as complications develop (OD and OH groups), the metals correlated negatively showing that the levels of the metals may be a useful biomarker in determining when obesity-associated complication(s) develop(s). Also All metals correlated negatively in obese non complicated (ONDH) and control (NONDH) groups with age showing that as age advances, there is reduction in the levels of trace metals and macro-metal Mg.

Conclusion: These trace metals and macro-metal Mg studied may be probable useful biomarkers for identifying when obesity associated complications develops.

Introduction

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy and/or increased health problems.[1] Obesity is a leading preventable cause of death worldwide, with increasing prevalence in adults and children, as authorities view it as one of the most serious public health problems of the 21st century.[2] Obesity has been found to shorten the life expectancy and increase the risk of diseases such as cardiovascular disease, type 2 diabetes, obstructive sleep apnea, cholelithiasis, kidney diseases, certain types of cancer, osteoarthritis.[3-5] There is increasing prevalence of obesity [2] and obesity-related morbidity and several other chronic conditions such as diabetes, hypertension, cardiovascular diseases, obstructive sleep apnoea, certain type of cancers and osteoarthritis [1] among adults and children in both developed and developing countries. The prevalence of such obesity-related conditions is likely to increase as obesity continues to rise. The factor that dominates in obesity is the permanent elevation of plasma free fatty acid (FFA) and the predominant utilization of lipids by muscles inducing a diminution of glucose uptake and insulin resistance.

For normal biological functioning, metals are required (e.g., zinc, cobalt, iron, copper, manganese, chromium, and molybdenum) but a subset of them have been shown to have negative effects on the normal physiological and biochemical functions in humans and are considered toxic or heavy metals (e.g., lead, mercury, cadmium and the metalloid arsenic). Metals that pose a human health risk are the metals with no known beneficial role in normal

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human physiology as majority have been reported to have negative effects on physiology and associated with metabolic syndromes.[6-12]

Exposure levels of many environmental toxicants have risen in the same time-frame as disease incidence and some of these widely distributed chemicals have been shown to interact with biological systems to result in deleterious metabolic and/or endocrine effects.[13] In daily life, the general population is commonly exposed to multiple metals through dietary intake, water drinking, inhalation of ambient air, and dermal contact of consumable goods.[14-15] There are evidence supporting environmental exposure to dangerous chemicals including toxic metals to influence obesity,[8 ,16] hypertension,[17] diabetes [18] and the metabolic syndrome.[13, 19]

The relationship between the concentration of some metals in blood and body mass has been investigated in children, adolescents and adults, however, the fundamental mechanisms still need exploration.[20] There are currently emergence of new **hypotheses to explain the aetiopathogenesis of these conditions, including environmental chemicals, stress, immunological alterations, micronutrient deficits, and gut microbiota.[21-22]** In fact, well-documented dramatic increase in the incidence of diabetes has been thought to be primarily due to coincident alterations in general lifestyle factors and yet another potential contributing factor in industrialized countries is exposure to environmental pollutants and industrial chemicals.[13] The underlying mechanisms for the association of obesity with diabetes and/or hypertension are still not fully known.[3, 5] One opportunity for elucidating these mechanisms most likely involves identifying biomarkers that result from obesity and that independently enhance susceptibility for diabetes and/or hypertension. Such biomarkers will further refine risk assessment and aid in diabetes and hypertension prevention in an obese individual. This study is focused on mechanisms of current interest: mineral trace metals and macro-metal Mg metabolism in obesity as a probable biomarker in determining when obesity associated complication(s) develop(s).

Materials and methods

2.1. Study design and area

This study is a cross-sectional study. This study was conducted in in the south-south zone of Nigeria with the following areas selected; Ekpoma, Benin City, Kwale and Asaba. Subjects were selected via simple random sampling and cohort sampling.

2.2. Ethical consideration

Ethical approval was sought and given by the Research and Ethic Review Committee of the Ambrose Alli University, Ekpoma. The intervention and control community gave their permission after the aims and objectives of the study were explained to them. Also, informed consent was sought and obtained from the subjects before enrollment into the study. At the end of the study the control group was also given the same intervention, for ethical reasons. Written informed consent/ questionnaire were administered to all subjects and blood sample collected.

2.3. Subjects and grouping

A total of two hundred and sixty-four (264) subjects were recruited and were distributed as follows into five (5) grou ps to meet the set goals of this research. Group A (60 Non Obese Non Diabetic/hypertensive or normal control), Group B (45 Obese Non Diabetic/Hypertensive ie obese only), Group C (59 Obese Diabetic); Group D (59 Obese Hypertensive); Group E (41 Obese Diabetic/Hypertensive). They were classified as obese using BMI ≥ 30 kg/m2, non-obese using BMI ≤ 24.5 kg/m2, diabetic using fasting plasma glucose (FBG) ≥ 7mmol/l (126mg/dl) and hypertensive at blood pressure ≥ 140mmHg/90mmHg.

2 .4. Inclusion and Exclusion criteria

All Subjects with BMI ≤ 24.9kg/m^2 (control group), ≥30kg/m^2 (obese groups) BP ≥ 140/90mmHg (hypertensive group) and not on any form of medication were recruited. All Subjects who are overweight (BMI ≥ 25 to ≤ 29.9kg/m^2) and non obese and obese who are hypertensive or diabetic on medications or with any co morbid conditions were excluded from this study.

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2.5. BMI measurement
Heights were measured in standing position, with shoulder and buttocks against the wall, the subject looking straight ahead with joined feet, and arms hanging on both sides with a graduated tape. In addition, body weights were measured with a calibrated beam scale. These were used to calculate the BMI which is weight (kg)/height (m^2).

2.6. Fasting blood glucose (FBG) and blood pressure measurement
Preliminary measurements of FBG and BP in all the subjects were done respectively using Glucometer and sphygmomanometer (at least two different times) with the mean value recorded. Subjects were asked to fast overnight (no food, drink, alcohol or smoking).

2.7. Sample collection and analysis
About 5mls of fasting blood was collected from each subject with 0.5ml immediately used for preliminary FBG estimation and 2.0mls immediately placed in fluoride oxalate container for FBG estimation spectrophotometrically as described by Trinder,[23] and these served as basis for comparing FBG levels. Two (2.0) mls was placed in lithium heparin container for the trace metals analysis using Atomic Absorption Spectrophotometer as described by Kaneko.[24]

2.8. Duration of study
The study was conducted within a thirty months period (from July, 2009 to June, 2012). The first 0-6mths was selection of subjects and baseline measurements of BP and FBG, 7-12mths was repeat measurements of BP and FBG, 13-18mths was repeat measurements of BP and FBG, 19-24mths was final measurements of BP and FBG and collection of sample for analysis and 25-3 0mths was analysis, collation and processing of data.

2.9. Statistical analysis
Data were presented as mean±S.D (standard deviation) and then analyzed using Statistical Package for Social Sciences (SPSS) at a P value of 0.05 and 95% level of confidence and results presented in suitable tables.

Results
Two hundred and sixty four subjects participated in this study comprising 169 males and 95 females. The total numbers of male subjects in the groups namely non-obese non-diabetes/hypertensive (control group), obese non-diabetes/hypertensive, obese diabetes, obese hypertensive and obese diabetes/hypertensive were 30, 26, 42, 41 and 30 and female were 30, 19, 17, 18 and 11 respectively.

Table 1 showed the mean ± standard deviation of ages, systolic and diastolic blood pressure, fasting blood glucose levels and BMI of the different groups in the sampled population. The obese hypertensive and obese diabetic and hypertensive groups had significantly higher ($p<0.05$) mean age between the groups. There were significantly higher ($p<0.05$) blood pressure and fasting blood glucose in the obese diabetes and hypertensive groups compared to the control and the obese non-diabetic/hypertensive. Body mass index was significantly higher in the obese groups compared to the control with the obese diabetic group presenting the highest BMI.

Table 1: Mean of age, systolic BP, Diastolic BP, FBG and BMI for all the groups

Parameter	NONDH	ONDH	OD	OH	ODH
AGE (years)	42.33± 14.64 ^{a}	43.73± 14.78 ^{a}	42.86± 15.78^{a}	51.32± 15.09 ^{b}	49.29± 15.92^{b}
BP systolic (mmHg)	125.5± 10.14^{a}	127.8± 11.47^{a}	138.9± 7.01^{b}	163.1± 13.90^{c}	157.7± 7.07^{d}
BP diastolic (mmHg)	70.77± 11.29^{a}	70.09± 9.20^{a}	79.81± 8.15^{b}	94.39± 4.53^{c}	92.39± 6.89^{c}
FBG (mmol/L)	3.93± 0.85^{a}	4.09± 0.93^{ab}	10.91± 4.65^{c}	4.97± 1.37^{b}	12.50± 6.41^{c}

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BMI (kg/m^2)	23.62± 2.03^{a}	33.69± 3.80^{b}	36.09± 5.28^{c}	33.28± 4.79^{b}	34.73± 5.06^{bc}
Number of Subjects	60	45	59	59	41

Values are expressed as mean ± standard deviation. Means in a row with different superscripts are significantly different at the p<0.05 level. Key: NONDH= Non Obese Non Diabetic/Hypertensive [normal control(C)], ONDH = Obese Non Diabetic/Hypertensive, OD= Obese Diabetic, OH= Obese Hypertensive, ODH= Obese Diabetic/Hypertensive.

Table 2 presents the **Mean± S.D** of some selected essential trace metals (Fe, Zn, Cu, Mn, Se and Cr), macro-metal Mg and some selected toxic trace metals (Pb and Cd) of the study population. Fe levels, when compared with control (NONDH) group, all the groups were found to be significantly higher (P<0.05) except group OD where Fe levels was significantly lower (P<0.05). Mean Fe levels was highest in group ONDH. Zinc, Cu and Mn levels follow the same pattern as iron levels when compared with the control group (NONDH) but Mn levels in group OD was higher than the control. When compared with the control group (NONDH), all the groups' levels were found to be lower and mean level of Se was significantly different between control group (NONDH) and group OD. When compared with control group (NONDH), Cr levels in groups OD and ONDH were found to be lower while those of groups OH and ODH were higher although not statistically significant (p>0.05). Although not significant, when compared with control group (NONDH), Mg levels in all the groups were found to be higher except groups OD and ODH which were lower. Serum levels of lead and cadmium were higher in the control group (NONDH) but there was no significant difference (p>0.05) between the groups.

Table 2: Mean of some selected trace metals- essential (Fe, Zn, Cu, Se, Cr) and toxic (Pb, Cd) and Macro-metal Mg in the groups

Parameter	NONDH	ONDH	OD	OH	ODH
Fe (µg/dl)	58.33± 14.01^{a}	60.4± 10.91^{ab}	56.97± 18.01^{a}	58.66± 16.37^{a}	58.54± 16.96^{a}
Zn (µg/dl)	101.3± 15.23^{a}	105.9± 16.62^{ab}	99.54± 20.22^{a}	102.2± 19.10^{ab}	101.6± 19.88^{ab}
Cu (µg/dl)	57.08± 14.33^{a}	57.93± 12.57^{a}	56.21± 14.94^{a}	57.88± 14.24^{a}	58.57± 14.73^{a}
Mn (µg/dl)	53.25± 16.43^{b}	56.07± 8.84^{ab}	55.83± 10.36^{ab}	55.44± 10.72^{ab}	56.37± 12.01^{ab}
Se (µg/dl)	28.36± 9.31^{b}	28.21± 5.74^{ab}	25.44± 6.43^{a}	26.94± 6.76^{ab}	26.98± 6.53^{ab}
Cr (µg/dl)	35.83± 10.56^{a}	35.07± 8.64^{a}	34.85± 9.45^{a}	36.19± 11.07^{a}	36.56± 9.44^{a}
Mg (mg/dl)	15.42± 3.79^{a}	15.70± 2.84^{a}	14.72± 3.43^{a}	15.55± 4.03^{a}	15.29± 3.39^{a}
Pb (µg/dl)	8.70± 4.93^{b}	7.78± 1.43^{ab}	7.40± 2.02^{a}	7.72± 2.15^{ab}	7.33± 1.72^{ab}
Cd (µg/dl)	45.59± 11.55^{a}	44.84± 8.76^{a}	43.42± 10.46^{a}	44.94± 11.43^{a}	43.37± 8.66^{a}
Number of Subjects	60	45	59	59	41

Values are expressed as mean ± standard deviation. Means in a row with different superscripts are significantly different at the p<0.05 level. Key: NONDH= Non Obese Non Diabetic/Hypertensive [normal control(C)], ONDH = Obese Non Diabetic/Hypertensive, OD= Obese Diabetic, OH= Obese Hypertensive, ODH= Obese Diabetic/Hypertensive.

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In tables 3a and b shown the Sex variation of mean values of some selected essential trace metals (Fe, Zn, Cu, Mn, Se and Cr), macro-metal Mg and toxic trace metals (Pb and Cd) among the groups. The mean levels of trace metals (essential and toxic) and Mg studied were found to be significantly higher ($P<0.05$) in females than males in the control (NONDH) group. Among the other groups, the mean levels of trace metals and Mg studied was found to be significantly higher ($P<0.05$) in males than in females except in ODH in which case mean levels in female was higher than in males.

Table 3a: Sex variation of mean values of some selected essential trace metals among the groups

Group	sex	N	Fe (µg/dl) Mean±SD	Zn (µg/dl) Mean±SD	Cu (µg/dl) Mean±SD	Mn (µg/dl) Mean±SD	Se (µg/dl) Mean±SD	Cr (µg/dl) Mean±SD
NONDH	**M**	30	58.17±2.42[a]	101.13±3.49[a]	56.16±2.70[a]	49.10±2.27[a]	26.67±1.03[a]	34.93±1.80[a]
	F	30	58.50±2.73[a]	101.37±1.88[a]	58.00±2.57[a]	57.40±3.46[b]	30.04±12.16[b]	36.73±2.07[a]
ONDH	**M**	26	62.15±1.86[a]	108.42±2.73[a]	59.19±2.13[a]	56.12±1.69[a]	29.31±0.93[a]	36.19±1.43[a]
	F	19	58.00±2.86[a]	102.47±4.50[b]	56.21±3.38[a]	56.00±2.15[a]	26.72±1.54[a]	33.53±2.35[a]
OD	**M**	42	58.72±3.10[a]	99.57±3.20[a]	57.46±2.48[a]	56.02±1.75[a]	25.48±1.06[a]	35.62±1.53[a]
	F	17	52.64±2.60[b]	99.47±4.73[a]	53.12±2.78[b]	55.35±1.89[a]	25.35±1.33[a]	32.94±1.97[a]
OH	**M**	41	60.76±2.86[a]	103.88±3.14[a]	60.22±2.42[a]	56.05±1.82[a]	27.64±1.14[a]	37.87±1.84[a]
	F	18	53.88±2.28[b]	98.28±3.89[a]	52.56±2.18[a]	54.06±1.99[a]	25.36±1.22[a]	32.39±1.95[a]
ODH	**M**	30	62.78±3.91[a]	104.37±4.04[a]	61.74±2.93[a]	56.40±2.56[a]	27.10±1.21[a]	37.18±1.76[a]
	F	11	61.16±2.37[a]	109.27±3.51[b]	57.82±2.37[a]	60.46±1.51[a]	29.55±1.16[a]	38.46±2.02[a]

Values are expressed as mean ± standard deviation. Means in a row with different superscripts are significantly different at the $p<0.05$ level. Key: NONDH= Non Obese Non Diabetic/Hypertensive [normal control(C)], ONDH = Obese Non Diabetic/Hypertensive, OD= Obese Diabetic, OH= Obese Hypertensive, ODH= Obese Diabetic/Hypertensive.

Table 3b: Sex variation of mean values of Mg and some selected toxic trace metals among the groups

Group	Sex	No. subjects	of Mg (mg/dl) Mean±SD	Pb (µg/dl) Mean±SD	Cd (µg/dl) Mean±SD
NONDH	**M**	30	15.21±0.71[a]	7.94±0.36[a]	44.52±1.83[a]
	F	30	15.64±0.68[a]	9.47±1.22[b]	46.67±2.37[a]
ONDH	**M**	26	16.13±0.45[a]	7.96±0.24[a]	45.85±1.45[a]
	F	19	15.11±0.78[a]	7.55±0.39[a]	43.47±2.38[b]
		17	16.94±0.75[a]	8.47±0.37[a]	49.71±2.48[a]
OD	**M**	42	14.84±0.56[a]	7.44±0.34[a]	43.64±1.79[a]
	F	17	14.43±0.73[a]	7.31±0.37[a]	42.88±1.97[a]
OH	**M**	41	16.09±0.69[a]	8.04±0.38[a]	46.87±1.98[a]
	F	18	14.33±0.64[a]	6.99±0.28[b]	40.56±1.44[b]

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ODH	**M**	30	15.59±0.67[a]	7.96±0.48[a]	46.38±2.46[a]
	F	11	16.18±0.57[a]	7.98±0.25[a]	46.18±1.24[a]

Values are expressed as mean ± standard deviation. Means in a row with different superscripts are significantly different at the p<0.05 level. Key: NONDH= Non Obese Non Diabetic/Hypertensive [normal control(C)], ONDH = Obese Non Diabetic/Hypertensive, OD= Obese Diabetic, OH= Obese Hypertensive, ODH= Obese Diabetic/Hypertensive.

All trace metals both essential and toxic (Fe, Zn, Cu, Mn, Se, Cr, Pb and Cd) and the macro-metal Mg in group ONDH significantly correlated positively with BMI while in obesity-associated complications groups (OD, OD, ODH), the metals correlated negatively and also in the control group BMI correlated positively with all the metals studied as shown in table 4.2d. The levels of Zn, Mn, Mg, Se, Cu and Cr correlated positively with age among the obese complicated groups (groups OD, OH and ODH) except Mg, Cr and Cu which correlated negatively in group OH while Fe, Pb and Cd correlated negatively except Fe which correlated positively in group ODH (see table 4.2d). Also shown in table 4, all metals correlated negatively in obese non complicated group (ONDH) with age and in the control group, all metals correlated negatively with age.

Table 4: Correlation between Age, BMI with Some selected trace metals (essential and toxic) and macro-metal Mg in all the groups

		Group NONDH		**Group ONDH**		**Group OD**		**Group OH**		**Group ODH**	
Dependent Variable	**Independent Variable**	**R**	**p-value/ Remark**	**R**	**p-value/ Remark**	**r**	**p-value/ Remark**	**r**	**p-value/ Remark**	**r**	**p-value/ Remark**
AGE	Fe	-0.209	NS	-0.202	NS	-0.05	NS	-0.184	NS	0.053	NS
AGE	Zn	-0.122	NS	-0.216	NS	0.142	NS	0.11	NS	0.407	S
AGE	Cu	-0.104	NS	-0.24	NS	0.109	NS	-0.036	NS	0.313	S
AGE	Mn	-0.007	NS	-0.257	NS	0.006	NS	0.094	NS	0.142	NS
AGE	Se	-0.051	NS	-0.218	NS	0.107	NS	0.002	NS	0.391	S
AGE	Cr	-0.098	NS	-0.289	NS	0.034	NS	-0.091	NS		
AG	Mg	-	N	-	N	0.1	NS	-	NS	0.359	S

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E		0.237	S	0.253	S	21		0.029			
AGE	Pb	-0.014	NS	-0.261	NS	-0.134	NS	-0.208	NS	-0.144	NS
AGE	Cd	-0.075	NS	-0.283	NS	-0.131	NS	-0.226	NS	-0.171	NS
BMI	Fe	0.281	S	0.478	S	-0.201	NS	-0.185	NS	-0.318	S
BMI	Zn	0.268	S	0.533	S	-0.386	S	-0.313	S	-0.572	S
BMI	Cu	0.295	S	0.515	S	-0.338	S	-0.235	NS	-0.482	S
BMI	Mn	0.146	NS	0.578	S	-0.132	NS	-0.077	NS	-0.036	NS
BMI	Se	0.335	S	0.484	S	-0.37	S	-0.283	S	-0.554	S
BMI	Cr	0.376	S	0.457	S	-0.285	S	-0.167	NS	-0.357	S
BMI	Mg	0.149	NS	0.481	S	-0.358	S	-0.275	S	-0.524	S
BMI	Pb	0.277	S	0.46	S	-0.195	NS	-0.175	NS	-0.219	NS
BMI	Cd	0.351	S	0.444	S	-0.17	NS	-0.134	NS	-0.132	NS

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Discussion

While genetic predisposition and energy imbalance are the main established risk factors reported to be fueling the obesity epidemic, caloric excess and physical inactivity alone has failed to fully account for the magnitude and the steep trajectory following the obesity epidemic. There is however a growing consensus suggesting the exposure to some lipophilic or metalloid contaminants is obesogenic.[25-29] Obesity increases the risk of diabetes and/or hypertension.[3, 5] Worrisome, the obesogenic potential of ubiquitous inorganic metals (essential and toxic) and macro-metal Mg are still largelly unclear and the underlying mechanisms for the association of obesity with diabetes and/or hypertension are still not fully known.[3, 5] Hence the present study, in which we assessed the serum levels of some selected essential trace metals (Fe, Zn, Cu, Mn, Se and Cr), macro-metal Mg and some selected toxic trace metals (Pb and Cd).

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There were some clinical and metabolic differences in blood pressure, blood glucose level and body mass index between obese-patients who were diagnosed with diabetes and those diagnosed with hypertension compared with the control in this study (table 1). Indeed many disorders occur with greater frequency in obese people than in others.[30] The most important and prevalent being hypertension, type 2 diabetes mellitus (both well studied in the course of this study), hyperlipidaemia, coronary artery disease, degenerative joint disease, and psycho-social disability.[31-32]

All metals correlated negatively in obese non complicated (ONDH) group and also in the control (NONDH) group with age showing that as age advances, there is reduction in the levels of trace metals and macro-metal Mg. According to Bloniarz and Zareba, [33] metabolism of carbohydrate and fats in human organism is connected with some trace metals (microelements) and macro-metal Mg and the occurrence of obesity may indirectly be connected with the disturbances of homeostatic mechanisms involving these trace metals. Changes in the enzymatic activities of several metabolic pathways are seen in obesity induced type 2 DM as a result of relative magnesium deficiency.[34] It is therefore obvious that microelements disturbances, irrespective of the cause or the gene involved are associated with hypertension and diabetes. By implication, a link exists between dietary microelement intake and development of metabolic diseases such as obesity and diabetes and cardiovascular disease such as hypertension. Hence, the balance of the intake of microelements is helpful for the prevention and management of hypertension, diabetes and obesity and in cases where they co-exist. Selenium showed a significant decrease ($p<0.05$) and this decrease in serum Se levels has been described in an earlier study by Burt.[35] Selenium is known to act as an antioxidant and peroxynitrite scavenger when incorporated into selenoproteins.[36] The low concentration of selenium in serum could potentially expose the subjects to oxidative stress which is known to be associated with the pathogenesis of diseases such as diabetes mellitus[37]. This decrease in serum selenium levels could contribute to oxidative stress and low selenium level has been shown to reduce insulin secretion and increased insulin resistance in some experimental models, thereby possibly playing a causal role in the development and pathogenesis of type 2 diabetes.[38]

We found that blood Pd and Cd levels were non-significantly lower in obese subjects with and without diabetic and or hypertension compared to the control (table 2). The possible association between lead and cardiovascular disease has been recognized for many years.[39-41] In correspondence with a finding of this study, Babalola et al.[42] has reported lead to be significantly high in obese non diabetic individuals compared to obese diabetic individuals. Some literatures suggested that these metals (cadmium) mainly locate on blood cells and the implication was the report in a previous study by Yuan et al.[43] to examine the correlations of metals between plasma, whole blood, or urine, it was found that plasma cadmium were poorly correlated with both whole blood and/or urine levels. For this reason, Yuan et al. [43] assumed plasma cadmium were not reliable biomarkers to reflect internal exposure and as such was excluded from further analyses. This decreased in blood Pd and Cd level in this study may be due to its utilization in its various toxic actions/processes with it lowest levels in complicated obesity playing a role in the pathogenesis of the complication such as hypertension by affecting hormone metabolism, vasoconstriction and renal tubular function. Blood lead accounts for only 1% to 5% of total body lead burden, however, as most lead in the body is contained in bone and other calcified tissues.[44] Once in the chronic storage compartment, bone lead leaches out over time, serving as an endogenous source of blood lead and resulting in ongoing, years long low-level lead exposure to the cardiovascular system, neural tissues, and kidneys.[45] Also, once ingested, cadmium is stored predominantly in the kidneys, liver, lungs, pancreas, and central nervous system, with a half-life for excretion of over 15 to 45 years.[46-47] By implication, the observed lower levels of Pd and Cd in this study may be due to the metal been internalized by body organs and tissue.

From this study, trace metals (Fe, Zn, Cu, Se, Mn, Cr, Pb and Cd) and macro-metal Mg levels were found to be higher in the control (NONDH) and obese only (ONDH) groups although significant only with Mg when compared with other groups. This showed that obesity has a reducing effect on trace metals and the macro-metal Mg. Further comparisons among the obese (ONDH, OD, and OH) groups showed that obesity-associated complications (diabetes mellitus/hypertension) worsen this effect of obesity on trace metals. BMI correlated negatively with the metals suggesting that these metals may play an important metabolic role in the development of obesity, hypertension and diabetes mellitus singly or in combination. This is also corroborated by the fact that, trace metals and macro-metal

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Mg correlated positively with BMI in the obesity only (ONDH) group. But as soon as complications set in (groups OD, OH and ODH), the metals correlated negatively showing that the levels of the metals may be a useful biomarker in determining when obesity-induced complication(s) set in.

Conclusively, Obesity has a diminution effect on trace metals and the macro-metal Mg and obesity-induced complications (diabetes mellitus/hypertension) worsen this effect of obesity on trace metals. Trace metals and macro-metal. Mg correlated positively with BMI in the obesity only subjects. But as soon as complications develops (OD and OH groups), the metals correlated negatively showing that the levels of the metals may be a useful biomarker in determining when obesity-induced complication(s) develops. We therefore recommend more research on the role of trace metals and macro-metal Mg on the aetiopathogenesis of obesity.

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