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Original Research Article

COMPARATIVE STUDY OF SERUM LEPTIN, LIPID PROFILE AND FBG IN OVERWEIGHT, AND OBESE SUBJECTS IN NNEWI SOUTH-EAST NIGERIA

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ABSTRACT

Introduction. Obesity is caused by an imbalance between food intake and energy expenditure, leading to excessive fat accumulation in organs. Leptin, an adipokine, reflects adiposity and its levels increase with weight gain and decrease with weight loss. The purpose of this study was to compare of serum leptin, lipid profile and FBG in overweight. **Methods.** This is a cross-sectional study. A total of 90 healthy obese, overweight, and normal-weight participants who met the inclusion criteria were enrolled in the study. They were grouped using their body mass index of 18.5 to 24.9 kg/m2 (normal weight), 25 to 29.9 kg/m2 (overweight) and ≥30 kg/m2 (obese). The measured parameters were analyzed using standard methods. **Results and Analysis.** There was an increased difference in the mean level of Leptin (ug/l) of the obese participants compared to normal weight participants (0.63±0.29 vs 0.25±0.26, 0.001) and overweight when compared to normal weight (0.51±0.27 vs 0.25±0.26, 0.003). A significant positive correlation was observed when the leptin and BMI of obese subjects were compared. Mean fasting very low-density lipoprotein (VLDL) and triglyceride (TG) (mmol/l), were significantly higher ($p<0.05$) in overweight compared to normal weight participants (0.76±0.31 vs. 0.47±0.22) and (1.72±0.60 vs. 1.09±0.51) and obese participants (0.82±0.23 vs. 0.47±0.22) and (1.85±0.59 vs. 1.09±0.51) when compared to normal weight subjects respectively. **Discussions.** The level of leptin was increased in the overweight and obese groups when compared to the control groups and correlates positively with the BMI of the overweight and obese groups.

Keywords: FBG, Leptin, Lipid Profile, Obesity.

INTRODUCTION

Leptin is a hormone derived from Greek word *leptos* meaning thin. It is a molecule with approximately 16KDa and located on chromosome 7. It is also known as ob gene. (Jeanrenaud and Jeanrenaud, 1996). Leptin was the first fat cell-derived hormone (adipokine) to be discovered. (Conde *et al.*, 2011).This ob gene has several other endocrine functions, which include the regulation of immune and inflammatory response as well as in angiogenesis and wound

healing. Brennan *et al*, observed that leptin is the important hormone that is derived from white adipose tissue. Leptin, discovered more than 13years ago, its function is to decrease food intake and increase nerve activity to both thermogenic and non-themogenic tissues. It was believed that leptin is an anti-obesity hormone and plays a major role in the development of hypertension in obesity (Bravo *et al*., 2006).

Leptin is an important component in the long term regulation of body weight. Recent studies with obese and non-obese humans demonstrated a strong positive correlation of serum leptin concentration with percentage of body fat. It appears that, as adipocytes increase in size due to accumulation of triglyceride, they synthesize more and more leptin. Leptin effects on body weight are mediated through effects on hypothalamic centers that control feeding behavior and hunger, body temperature and energy expenditure. (Hafizuallah, 2006).

The role of leptin in the regulation of energy homeostasis was demonstrated by observing leptin-deficient patients, who develop hyperphagia and obesity in which the alterations in the transport of leptin to the brain through the blood–brain barrier (BBB) was observed, but the mechanism that has not been completely deciphered (Rodriguez *et al.*, 2010), obesity can generate pathological changes in the cellular integrity of the BBB, independently of the transporters, which can aggravate the pathological situation at the level of the central nervous system. Obesity and chronic consumption of a high-fat diet (HFD) produce important changes at the level of the BBB as well as in different regions of the brain, especially in the regions of neuronal populations with high metabolic demands, such as the hippocampus. (Moraes *et al*., 2009 and Kim *et al.*, 2016).

Lipids are ubiquitous in the body tissue as they have an important role in virtually all aspects of life, acting as energy stores (Triglycerides), important structural component of cells (Cholesterol) and they could also have special functions (Hormones) (Rifai and Warnick, 2006). The serum concentrations of cholesterol and triglycerides have been observed to positively correlate with obesity. (Young and Bermes, 2006). In this current study we looked at the level of leptin, some lipid fractions and FBG in over weight and obese subjects randomly recruited from Nnewi metropolis, south east Nigeria.

METHOD AND ANALYSIS

This is a cross-sectional study, designed to compare the serum level of leptin, some lipid fractions and FBS in

normal, overweight and obese participants. Based on the calculated sample size, 90 consenting participants that fulfill the inclusion criteria were recruited for the study. Informed consent of the participants was sought and obtained before the enrollment into the study. Ethical approval was sought and obtained from the Ethics Committee (NAUTH/CS/66/VOL.11/154/2018/088) of Nnamdi Azikiwe University Teaching Hospital Nnewi. Questionnaires were administered and it served as a primary instrument for this study. The questionnaires were structured to reflect the health issues relevant to the objectives of the study. The study comprised of 90 obese and non-obese subjects, among them, 30 participants were known obese, 60 participants were non-obese and between 20-50 years of age. The participants were labeled Normal weight (BMI 18.5-24.9 kg/m^2), over-weight (BMI 25.0-29.9kg/m^2) Obese (≥30kg/m^2). BMI was measured as weight in kilogram (0.01), divided by height squared (m^2), WC was measured with a tape to the nearest 0.1cm at the end of a normal expiration at the midpoint between the subcostal plane and the iliac crest of an exposed abdomen. HC was also measured at the largest standing horizontal circumference of the buttock to determine the waist to hip ratio (WHR=WC/HC). Hypertension was defined to be systolic blood pressure≥140mmHg, diastolic blood pressure≥90mmHg. A fasting blood sample was obtained in the morning between 0800-0900 hours, about 7ml, through venipuncture from each participant. Aliquot was drawn into appropriate containers for biochemical analysis.

The quantitative determination of serum leptin was performed using the sandwich Enzyme-Linked Immunosorbent Assay (ELISA) Technique, with commercially available reagent kit MONOCENT Leptin (sandwich) ELISA, (CAT NO. EL9-1059) (LOT NO. 200610) by, Monocent USA. Fasting lipid profile was assessed using commercially available kits (Randox) serum total cholesterol and high density lipoprotein HDLc, was determined by cholesterol oxidase method Allain, *et al.*, serum triglyceride by glycerol kinase method. Trinder, (Trinder, 1969) and LDLc was calculated using Friedwald formula (Friedwald et al., 1972). Fasting blood glucose was determined using the enzymatic colorimetric method of Trinder, (Trinder, 1969). Statistical analysis was performed to compare the two groups using ANOVA. The values were expressed as the Mean ± S.D. Values were regarded as significant if p is ≤ 0.05. Pearson correlation coefficient was used to correlate the parameters

estimated.

RESULTS

Table 1. Anthropometric Maker and Indices Of Obesity. It Highlights The BMI, WHR, Diastolic Blood and Systolic Blood Pressures (Mean±SD)

GROUPS	SBP (mmHg)	DBP (mmHg)	BMI (Kg/m^2)	WHR
NORMAL WEIGHT (A) (n=30)	115.28±11.89	75.59±10.03	21.75±1.82	0.85±0.05
OVER WEIGHT (B) (n=30)	118.92±25.02	78.40±9.55	27.11±1.02	0.86±0.07
OBESE (C) (n=30)	127.00±10.86	85.64±12.25	33.85±4.51	0.96±0.10
f-test	3.310	6.246	123.387	18.038
p-value	0.042*	0.003*	<0.001*	<0.001*
A vs B	1.000	1.000	<0.001*	1.000
A vs C	0.040*	0.003*	<0.001*	<0.001*
B vs C	0.287	0.056	<0.001*	<0.001*

Table 1 shows the mean anthropometric markers of all participants. There was no significant difference in the diastolic and systolic blood pressures. There were significant increase in the body mass index of all the participants (<0.001). There was also significance difference in the waist to hip ratio of the participants.

Table 2 shows the mean of the various fasting biochemical parameters of obese, overweight and normal weight group. Significant change was observed in the fasting plasma Triglyceride (TG) and very low-density lipoprotein (VLDL). (p<0.001) in the obese subjects when compared with the corresponding control values. No significant change was observed in other lipid parameters.

Table 2 Levels of Fasting HDL-C, LDL-C, VLDL-C, TG, And TC in Normal Weight, Overweight and Obese Groups (Mean±SD)

GROUPS	HDL-C (mmol/L)	LDL-C (mmol/L)	VLDL-C (mmol/L)	TG (mmol/L)	TC (mmol/L)
NORMAL WEIGHT (A) (n=30)	1.00±0.21	1.77±0.67	0.47±0.22	1.09±0.51	3.39±0.66
OVER WEIGHT (B) (n=30)	0.95±0.09	1.52±0.34	0.76±0.31	1.72±0.60	3.47±0.42
OBESE (C) (n=30)	1.00±0.17	1.84±0.38	0.82±0.23	1.85±0.59	3.45±0.53
f-test	0.816	3.006	9.391	8.638	0.135
p-value	0.446	0.055	<0.001*	<0.001*	0.874
A vs B	0.732	0.201	<0.001*	<0.001*	1.000
A vs C	1.000	1.000	<0.001*	<0.001*	1.000
B vs C	0.906	0.067	0.019*	0.030*	1.000

Table 3 The Mean Serum Leptin, Fasting Blood Glucose, in The Obese, Overweight and Normal Weight Participants (Mean±SD)

GROUPS	LEPTIN (ug/l)	FBG (mmol/L)
NORMAL WEIGHT (A) (n=30)	0.25±0.26	3.46±0.79
OVER WEIGHT (B) (n=30)	0.51±0.27	4.46±1.82
OBESE (C) (n=30)	0.63±0.29	4.94±1.26
F-value	13.038	8.740
p-value	<0.001*	<0.001*
A vs B	0.003*	0.021*
A vs C	<0.001*	<0.001*
B vs C	0.337	0.647

Table 3 show the mean serum leptin, fasting blood sugar, in the obese, overweight and normal weight participants. There was a significant difference in the serum leptin level between the normal weight participants (0.25±0.26) and overweight participants (0.51±0.27) at (P<0.003). Also there was a significance difference between the normal weight (0.25±0.26) and obese participants (0.63±0.29) at (P<0.001). There was statistical significance in the

fasting blood sugar level between the normal weight participants (3.46±0.79) and overweight (4.46±1.82) at (P<0.021), Also between the normal weight and obese participants (3.46±0.79 vs 4.94±1.26) at (P<0.001).

Table 4 Correlation of BMI with Lipid Profile, And Leptin In Normal Weight, Overweight And Obese Individuals

PARAMETRS	NORNAL WEIGHT (n=30)		OVERWEIGHT (n=30)		OBESE (n=30)	
	r	p-value	r	p-value	r	p-value
BMI vs HDL mmol/l	-0.202	0.293	0.083	0.693	0.217	0.298
BMI vs LDL mmol/l	-0.041	0.831	-0.108	0.607	0.089	0.672
BMI vs VLDL mmol/l	-0.087	0.654	0.223	0.285	0.085	0.685
BMI vs TG mmol/l	-0.134	0.490	0.024	0.909	0.031	0.882
BMI vs TC mmol/l	-0.181	0.348	-0.141	0.502	0.141	0.503
BMI vs FBG mmol/l	-0.103	0.593	0.010	0.962	0.021	0.919
BMI vs LEPTIN µg/l	-0.259	0.175	0.185**	0.002*	0.119**	0.004*

** Correlation is significant at 0.01 level (2tailed).
* Correlation is significant at 0.05 level (2tailed)

Table 4 shows the correlation of the measured parameters with BMI in normal weight, overweight and obese subjects. Serum leptin correlated positively and significantly with BMI in the overweight (r=0.185**, p<0.002*) and obese (r=0.119**, p<0.004*) participants.

DISCUSSIONS

High levels of leptin was observed in obese participants when compared with normal weight participants (0.63±0.29 vs 0.25±0.26, p<0.001*). There was increased significant difference in the leptin level between the overweight participants when compared to the normal weight participant (0.51±0.27.vs 0.25±0.26, p<0.003*). Leptin expression and secretion have been correlated with body fat and adipocyte as reported by Sone *et al*., 2001. Leptin reduces appetite and body weight, the paradoxical co-existence of obesity and hyperleptinemia suggest the pathology of leptin resistance. Leptin resistance may be due to the defect in intracellular mechanism, or due to impairment in transport through

the blood brain barrier. Several pathways related to the developments of leptin resistance have been studied in animal models such as the, Fat mass and Obesity-related Gene, Oestradiol(E2) and Peroxisomes Proliferator-Activated Receptor Y, Phosphodiesterase-3B (PDE3B)-Camp, and AKT-Pathways of leptin signaling in the hypothalamus. (Farr *et al*., 2015) The fact that obese individuals have leptin levels two times higher (on average) than non-obese individuals (Mohamed and Hassan, 2017) as reflected from the findings obtained from this study confirms the general hypothesis that obese adults with greatest leptin concentration has a higher level of overall circulating leptin as previously reported in literature. Obese individuals exhibit high levels of leptin expression in adipose tissue and have elevated circulating leptin levels (Park and Ahima, 2015) but appetite is not effectively suppressed in these individuals, implying cellular resistance rather than deficiency (Crujeiras et al 2015,Park and Ahima, 2015 and Riccioni et al., 2004) the mechanisms implicated in this leptin resistance may include disruption of leptin signaling in the hypothalamic and other CNS neurons, impaired leptin transporter across the blood brain barrier, hypothalamic inflammation, endoplasmic reticulum stress and hyperphagia. It can also be due to impaired receptor sensitivity or due to change in receptor expression or changes in post-receptor signal transduction (Herrick et al., 2016).

The levels of fasting serum TG and VLDL-C where observed to be significantly higher in overweight (1.72±0.60, 0.76±0.31 p<0.001*,0.001*) and obese (1.85±0.59, 0.82±0.23 p<0.001*,0.001*) participants respectively when compared to normal healthy controls which was in accordance to the study findings of Gupta and Mukherjee, 2018 and Haddad *et al.,* 2017, that observed higher TG and VLDL-C in obese subjects when compared with the controls, and contradicted the study by Zavorini *et al*., 1985, who found no increase significant difference between the normal weight and overweight subjects. There was no observed significant change in other lipid fraction (TC, LDL-C and HDL-C) amongst all the different groups. Obesity is associated with many deleterious changes in lipid biosynthesis or metabolism, the significant of this finding in the elevation of TG is usually associated with reduced levels of HDL-c suggesting a possible metabolic interaction between these two lipid fractions. The mechanism to this

relation may be due to the increase in fat deposition in obese subjects which is associated to leptin resistance in the peripheral tissues and which might also involve insulin resistance, as stipulated by Howard *et al*, leading to varied alterations in intracellular signaling and changes in substrate handling resulting to increase in the synthesis and secretion of TG enriched VLDL particles (Howard et al., 2003).

From the results, all the participants has normal TC, LDL-C, while normal HDL-C was observed only in the control group within the National Cholesterol Education Program (NCEP) reference range, furthermore, dyslipidemia is an abnormal lipid metabolism and defined by the presence of one or more abnormal concentration of serum lipid biomarker, obese individuals with hypertriglyceridemia are considered dyslipidemic subject.(NCEP, 2002).

There was also an increased significant difference in the fasting blood glucose among the groups; there is positive correlation of BMI with the level of FBG but not significant, this finding is in agreement with the study by Prema *et al.,* 2016, and Agrawal *et al*., 2017, whom observed a positive correlation of blood glucose with BMI.

CONCLUSION

It could be assessed that the increased in serum leptin associated with anthropometric indices are indications that it is increased as body adiposity increases. From these findings brings in the knowledge of the pathophysiology of leptin and the congenital leptin deficiency which is associated with hyperphagia and early onset obesity as observed from our results, progressive increase of leptin levels in the groups.

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