Association between Leptin and Lipid Profile among Women

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Authors' contributions

This work is a collaborative effort of all the three authors. Author KK performed the experimental work, presented the results, searched the literature and carried statistical analysis. Authors SS and GK designed the study, supervised it and prepared the draft of the paper which was finalized by collective effort of all of them. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Aim: The present study was aimed to assess the association between leptin and lipid profile among non-obese and obese women subjects.
Method: 60 non-obese and 60 obese women working in various educational institutes and hospitals in the age group of 30-60 years were selected. Their body measurement like height and weight were taken with standardized methods and BMIs were calculated as per World Health Organization guidelines. After ensuring fasting for 12 hours, blood sample of 5 ml was collected in sterile tubes from anti-cubital vein under aseptic conditions. Blood samples were allowed to stand and then centrifuged immediately at room temperature. Serum was separated, aliquots were made and samples were stored in freezer at -20° C for further analysis. Lipid profile and leptin levels were assessed as per protocols mentioned in the kits.
Result: Dyslipidemia coupled with hyperleptimia was observed among the obese subjects as compared to their non-obese counterparts. Correlation was observed among different components of lipid profile and leptin and this association was stronger in the obese subjects.
Conclusion: Hyperleptimia and dyslipidemia might be playing role in obesity. It is difficult

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to say if higher leptin levels leads to worsen the lipid profile or vice versa. Efforts to normalize lipid profile may lead to lower leptin levels and check obesity.

Keywords: Leptin resistance; hyperleptimia; obese; dyslipidemia.

1. INTRODUCTION

Overweight and obesity" are defined as abnormal or excessive fat accumulation that presents a risk to health. Being overweight and obese poses major risk factors for a number of chronic diseases, including diabetes, cardiovascular diseases and cancer. Once considered a problem only in high income countries, overweight and obesity are now dramatically on the rise in low and middle-income countries, particularly in urban settings. The latest data from World Health Organization (WHO) shows that worldwide there are some 1.6 billion adults who are overweight with a body mass index (BMI) above $25kg/m^2$. Of these, at least 400 million adults are obese, with a BMI above $30kg/m^2$ (http://www.who.int/topics/obesity/en/ retrieved on April 6th, 2010). Data from the National Health and Nutrition Examination Survey (2009–2010) reports that more than 2 in 3 adults are considered to be overweight or obese [1,2]. According to van der Merve [3], the prevalence figures for obesity within the European region confirm that in most countries, the number of obese women surpasses the number of obese men, sometimes as much as 2 to 1.

Developing countries are now facing a "double burden" of disease as they continue to deal with the problems of infectious disease and under-nutrition. They are also experiencing a rapid upsurge in chronic disease risk factors such as obesity and overweight, particularly in urban settings. BMI provides a benchmark for individual assessment, but experts suspect that the risk of chronic disease in populations increases progressively from a BMI of 21 upwards (http://whqlibdoc.who.int/fact_sheet/2006/FS_311, retrieved on October 20th, 2010).

Maintenance of body weight depends on the balance between the energy intake and the energy expenditure. The energy intake is food intake; the energy expenditure is derived from complex thermogenesis processes that include basal metabolism, adaptive thermogenesis, and physical activity. The energy balance is regulated by peripheral signals (hormones) that are integrated in the brain centers, including the hypothalamus, brainstem, and reward centers, which in turn modulate feeding and energy expenditure [4,5]. Leptin is secreted primarily by adipocytes and is present in serum in direct proportion to the amount of adipose tissue [6,7]. However, the accumulating evidence suggests that the role of leptin is much broader than that of an anti-obesity hormone. Leptin also affects several neuroendocrine mechanisms and regulates multiple hypothalamic-pituitary axis.

Obesity is associated with leptin resistance as supported by hyperleptinemia. Resistance arises from impaired leptin transport across the blood-brain barrier (BBB), defects in leptin receptor signaling, and blockades in downstream neuronal circuitries. Obesity in humans and rodents is almost always associated with a resistance to, rather than a deficiency of leptin [7,8,9]. Leptin resistance has been implicated in the pathogenesis of obesity-related complications involving abnormalities of lipid metabolism. According to Li et al. [10], leptin resistance coupled with the changes of blood lipids and inflammatory responses are found in children with obesity.

Leptin on one hand is known as an anti-obesity hormone and on the other hand obese people develop leptin resistance. Women have higher leptin levels than men that pose great threat to them if they become obese. Leptin resistance and dyslipidemia together may make the situation worst as both are related to metabolic disorders. The present study was aimed to assess the levels of leptin and lipid profile among the non-obese and the obese women and further assess if any association exists between these two. If such relationship exists between the two, it will help the clinicians to formulate possible measures to control obesity.

1.1 Hypothesis

Taking our previous findings and literature into consideration where leptin resistance and dyslipidemia has been observed among obese, it is hypothesized that certainly some relationship occurs among the duo which could have been a major cause of obesity and its related morbidities.

2. MATERIALS AND METHODS

For the present study, 60 non-obese and 60 obese women working in various educational institutes and hospitals in the age group of 30-60 years were selected randomly after following the criteria given by WHO [11]**.** Their height and weight were taken with standardized methods [12] and BMI [weight (kg)/height (m^2)] was calculated. Subjects with BMI 18.5 to <23 were considered as non-obese and BMI ≥23 and less than 25 were considered as overweight whereas subjects with BMI ≥ 25 were considered as obese. Only obese subjects were considered for the present study. Fifty percent of them were in their premenopausal and rest fifty percent were in their postmenopausal phase of life. Both the groups were combined. Every detail was noted down in a pre-designed questionnaire. After ensuring overnight fasting for 12 hours, blood sample of 5 ml was collected in sterile tubes from anti-cubital vein under aseptic conditions the next morning before the breakfast. Blood samples were allowed to stand and then centrifuged at room temperature. Serum was separated, aliquots were made and serum samples were stored in freezer at -20ºC untill further analysis. The study was approved by the Guru Nanak Dev University Ethical Review Committee. Lipid profile was assessed by kit manufactured by Crest Biosystems, Goa, (India). Total serum Cholesterol (TC), triglycerides (TG) and lipoproteins; heavy density lipoproteins (HDL-C) and low density lipoproteins (LDL-C) were estimated. The absorbance in each case was measured with semi-autoanalyser RA-50 (Bayer India Limited). TC was determined by enzymatic (CHOD-PAP) colorimetric method [13] and TG by enzymatic (GPO-PAP) method [14]. HDL-C was estimated by precipitation method [15] and LDL-C by Friedewald formula [16]. Leptin was estimated by sandwich ELISA, using Leptin ELISA Kits manufactured by Bio-Line, S.A., Brussels (Belgium). The intra-assay and inter-assay coefficients of variation in case of leptin were 3.6 and 5.2%, respectively.

2.1 Statistical Analysis

Data was maintained on excel spread sheet. Analysis was performed using SPSS (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA)) version 16. Results were presented as mean ± Standard deviation. The differences between the non-obese and the obese subjects were analysed with 't-test'. Pearsons correlation was computed to observe the correlation of leptin with lipid profile. Additionally, multiple regression was performed to find out the best suitable predictor of leptin taking all the variables like BMI, weight, TC, TG, LDL-C and HDL-C into consideration.

3. RESULTS

Table 1 presents mean values of age, BMI, leptin and different components of lipid profile. It is observed that both the non-obese and the obese subjects are of matching age, whereas there is significant difference in BMI (p<0.001) of the non-obese and the obese subjects, as expected. The levels of leptin, TC, TG and LDL-C are significantly higher (p<0.001), whereas, level of HDL-C is significantly lower (p<0.001) in the obese subjects as compared to the non-obese women. We additionally performed normality test on our data and the data passed the normality test.

Table 1. Mean ± Standard Deviation of Age, BMI, Leptin, Total Cholesterol (TC), Triglycerides (TG), Low Density Lipoproteins Cholesterol (LDL-C) and High Density Lipoproteins Cholesterol (HDL-C) among Non-Obese and Obese Women.

Variable	Non-Obese	Obese	Normality test	*t*-value	*P*-value
Age (yrs.)	45.28±7.42	47.26±5.64	<0.05	-0.43	NS
BMI (kg/m^2)	20.42±1.37	30.74±3.60	Passed P=.182	-20.61	<.001
Leptin (ng/ml)	10.57±5.57	44.36±18.93	Passed P=.327	-7.08	<.001
TC (mg/dl)	176.96±23.02	206.75±33.40	Passed P=.222	-5.45	<.001
TG (mg/dl)	111.72±23.33	142.62±33.40	Passed P=.412	-5.80	<.001
LDL-C (mg/dl)	110.63±26.30	141.19±24.60	Passed P=.170	-6.52	<.001
HDL-C (mg/dl)	60.10±12.72	39.69±8.90	Passed P=.222	4.77	<.001

NS- Non-Significant

Table 2 depicts the correlation coefficient (r) of leptin with BMI, weight, TC, TG, LDL-C and HDL-C among the non-obese and the obese women. It is evident from table that leptin is positively correlated with BMI, weight, TC, TG, LDL-C and negatively correlated with HDL-C. It is further reflected from the table that the association of leptin with different components of lipid profile is statistically stronger among the obese subjects as compared to their non-obese counterparts.

Table 2. Correlation Co-efficient (r) of Leptin with BMI, weight, Total Cholesterol (TC), Triglycerides (TG), Low Density Lipoproteins Cholesterol (LDL-C) and High Density Lipoproteins Cholesterol (HDL-C) among Non-Obese and Obese Women.

Variable	Non-Obese		Obese	
	r	*P*-value	r	*P*-value
BMI	0.842	.002*	0.895	<.001*
Weight	0.679	.044*	0.755	.02*
TC	0.371	.130	0.849	<.001*
TG	0.294	.236	0.550	.02*
LDL-C	0.302	.152	0.661	<.001*
HDL-C	-0.223	.256	-0.665	<.001*

*Significant values

Additionally, the multiple linear regression was performed to find the best suitable predictor of leptin in these subjects and it was observed that TC came out as best suitable predictor for leptin among obese subjects, independent of BMI, weight and other components of lipid profile (Table 3).

4. DISCUSSION

Dyslipidemia coupled with leptin resistance was observed among the obese subjects. The significant correlation was seen between leptin and lipid profile in the obese women. Linear regression model projected that TC is the most suitable predictor of leptin. Complex physiological systems equalize the energy expenditure with the energy intake. The energy balance is regulated by peripheral signals of hormones that are integrated in the brain centers. The primary role of leptin is to provide the central nervous system with a signal of energy stores in the body to enable the brain to make the adjustments necessary to balance the energy intake and expenditure [17]. On the contrary, it is observed that the obese people usually have very high plasma leptin concentrations. However, this endogenous hyperleptinemia may not reduce appetite or increase energy expenditure. This state has been termed "leptin resistance." The postulated leptin resistance is one major target in the search for a better understanding of obesity and the development of pharmacological tools to treat this wide-spread disease.

In the present study, we observed the higher levels of leptin coupled with significantly higher levels ($p<0.001$) of TC, TG, LDL-C, the non-friendly components of lipid profile and lower level of HDL-C ($p<0.001$), the friendly component of lipid profile among the obese women (Table 1). It is further reflected from Table 2 that obesity is associated with leptin resistance and dyslipidemia among the obese women as reported in literature also. The results of multiple linear regression model predicted that TC is the best suitable predictor of leptin among the obese subjects (Table 3). Literature reports association between leptin and different components of lipid profile [18,19]. Although the autocrine or paracrine role of leptin in fatty acid metabolism has not yet been fully elucidated at the molecular level, it is known that leptin in adipocytes inhibits the synthesis of ACC, an enzyme essential (and rate-limiting) in the conversion of carbohydratees to long-chain fatty acids and hence in the storage of energy as triacylglycerol. In addition, long-term treatment of wild-type mice with large leptin doses increases mRNA levels of the key lipolytic enzyme hormone-sensitive lipase but reduces those of the lipogenic enzyme fatty acid synthase [20,21]. In animal models, it has been postulated that the leptin resistance occurs due to inability of the leptin to get transported across BBB. Although, the actual mechanism is not clear, yet the studies have shown that serum TG impair the ability of the BBB to transport leptin. TG are likely a major cause of the leptin resistance seen in both starvation and obesity [22,23,24,25].

Table 3. Linear Regression Co-efficient (β) and Standard Error (S.E.) with test statistic (t) and probability (*P*) values for different variables in Multiple Regression Model for Leptin in Non-Obese and Obese Women

Variable	Non-Obese				Obese			
	β	S.E.	t	*P*-value	B	S.E.	t	*P*-value
BMI	0.04	0.68	0.06	0.95	0.07	0.96	0.08	0.93
Weight	-0.32	0.10	-3.16	0.00	0.38	0.22	1.75	0.10
TC	0.23	0.116	2.02	0.06	0.32	0.12	2.57	0.02*
TG	0.03	0.11	0.33	0.74	-0.00	0.09	-0.00	0.99
LDL-C	-0.08	0.08	-1.01	0.32	0.17	0.10	1.68	0.11
HDL-C	0.22	0.144	1.52	0.15	-0.30	0.36	-0.82	0.42

*-Significant value

So, the lowering TG may be therapeutically useful in enhancing the effects of leptin on weight loss. The studies have reported the improvement in plasma lipids and the decrease in plasma leptin concentrations following a 16 week weight reduction program or after an exercise intervention associated with weight loss [26]. A recent study conducted by Iftikhar et al. [27] in women with pre-eclampsia has reported that serum leptin levels during pre-eclampsia are strongly associated with TC whereas association with other variables is insignificant. The correlations between the changes in plasma lipids and changes in plasma leptin concentrations have been observed by Cordero-MacIntyre et al. [28]. The association between leptin and lipid profile has also been reported in women with different grades of obesity [29].

Though, it is difficult to say if leptin affects lipid profile or vice versa, but it is certain that to check obesity, lipid profile should be given the main priority. It may be improved by changing life style and incorporating good food habits. The literature reports that the weight control measures like exercise, etc. improve lipid profile [26]. As leptin and lipid level are associated with each other [22,23,24,25,28], it can be assumed that if the status of lipid profile is improved, leptin resistance may be checked which can further lead to weight control and lower obesity. This field needs to be thoroughly studied as the obesity is a major health problem in today's scenario and people find it difficult to control weight in spite of their all efforts. It will help the clinicians to trace the measures to check the body weight among the obese patients.

5. CONCLUSION

It is concluded from the present work that hyperleptimia and dyslipidemia might be playing a role in obesity. It is difficult to say if the higher leptin levels leads to worsen the lipid profile or vice versa. The efforts to normalize the lipid profile may lead to lower leptin levels and check obesity.

LIMITATIONS OF THE STUDY

Ours is a cross-sectional study which can simply bring association but can not predict the effect of individual variables.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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