Medical Science

25(110), April, 2021

Obesity as a threshold of elevating insulin and leptin: A population based cross sectional study

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To Cite:
Samananda L, Govindaraj Y, Kanan W. Obesity as a threshold of elevating insulin and leptin: A population based cross sectional study. *Medical Science*, 2021, 25(110), 853-858

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Peer-Review History
Received: 09 February 2021
Reviewed & Revised: 10/February/2021 to 01/April/2021
Accepted: 02 April 2021
Published: April 2021

Peer-review Method
External peer-review was done through double-blind method.

ABSTRACT

Obesity is often thought to be the result of excessive calorie intake and lack of energy expenditure that leads to negative health impacts such as type 2 diabetes, cardiovascular problems, cancers and other metabolic disorders. Study aimed to evaluate the levels of insulin and leptin in non-obese and obese and its relationships. A total of 331 individuals, age 18 to 65 years (female 212 and male 119) were involved in the study which was conducted in the department of Physiology, Regional Institute of Medical Sciences, Imphal, Manipur, India. Collected blood samples were estimated insulin and leptin levels. All data were calculated the correlations between insulin and leptin. Present study showed significant changes of insulin and leptin levels ($P < 0.01$) among non-obese and obese. Males were found significant increase ($P < 0.01$) in insulin levels as compared to female non-obese and obese group. In contrast, female showed higher leptin levels significantly than male groups of non-obese and obese. Data presents positive correlations between BMI and insulin ($P < 0.05$) as well as between BMI and leptin ($P < 0.01$). Insulin levels had positive relationships with leptin levels ($P < 0.05$) in the obese group. We conclude that with increasing insulin and leptin levels in obese, probability to prone prediabetic and other metabolic disorders might high.

Keywords: Insulin, Leptin, Obese, Manipur

1. INTRODUCTION

The global obesity rate has increased three-fold since 1975, and is now reported to be a leading cause of various immune and metabolic diseases. Therefore, obesity has emerged as a national concern. Based on World Health Organization statistics in 2016, around 2 billion adults worldwide were obese and more than 650 million of them were adults (Hwang et al., 2021). Obesity has been regarded as a behavior-related disease, inappropriate food intake with relative lack of activity. Without exact molecular mechanism to explore the pathology, being obesity was just a lack of will (De Paoli, 2014). Adipose tissue is a type of energy storage tissue which is strongly linked to obesity, this association considered not only as an endocrine gland, but also an immune organ that generates multiple types of immune cells, including eosinophils,

neutrophils, mast cells, macrophages, T and B cells (Huh et al., 2014; Vieira, 2014). Adipocytes produce a various types of cytokines including tumor necrosis factor-alpha (TNF-α), leptin, IL-6, interleukin (IL)-1 and IL-17 (Mohamed et al., 1998; Ahima & Flier, 2000). Leptin was discovered in 1994 (Zhang et al., 1994), as an adipocytokine to regulate food intake, body weight, and fat mass, also a major regulator of the immune and neuroendocrine systems, unleashed a tremendous excitation in the study of obesity as a disorder with a potentially molecular mechanism, as well as many new research areas associated with it (De Paoli, 2014).

In mouse model, insulin resistance, obesity and infertility have been linked with malfunction activity of *ob* gene mutations (Haynes et al., 1998; Dunbar et al., 1997; Pacak et al., 1995). Sex steroid hormones and insulin seem to have an impact on the production of leptin. It has been demonstrated that insulin increases *ob mRNA* gene level in cultured adipocytes and also showing responds to the feeding of rodents and human models, implying that insulin could directly regulate leptin secretion and expression of gene (Saladin et al., 1995). Numerous data suggest that insulin and leptin act in adiposity negative feedback signals of the brain (Morton & Schwartz, 2011). In fact, recent studies have shown that leptin has the effect of normalizing hyperglycaemia and hyperinsulinaemia and increasing insulin sensitivity (Kamohara et al., 1997). Since, the lack of studies related to obesity and its complications among the indigenous people of Manipur, a state in northeast India, this study was aimed to establish the relationship between insulin and leptin in non-obese and obese individuals in Manipuri population.

2. MATERIALS AND METHODS

This cross sectional study was conducted in the department of Physiology, Regional Institute of Medical Sciences, Imphal, Manipur, India from March, 2019 to December, 2020. After taking approval from the Institutional Ethical Board, study consent was obtained from the subjects, age 18 to 65 years. Total of 331 participants (both sex) were recruited. Subjects with the history of any chronic metabolic diseases were excluded from the study. Height was measured using portable Stadiometer and weight was taken using Tanita weighing scale. Based on WHO's BMI (kg/m^2) cut off, study population were grouped as non-obese (< 25 kg/m^2) and obese (≥ 25 kg/m^2). Blood was withdrawn in aseptic condition and centrifuged at 3000 rpm for 10 mins. Separated serum was estimated insulin and leptin levels using Elisa Microplate Reader, Thermoscientific. Statistical analysis was performed using SPSS software version 26. All data were presented as mean ± S.D. Independent student *t* test was calculated to compare the different groups. In addition, the Pearson correlation coefficient (*r*) was used for correlation analysis. $P < 0.05$ was considered significant.

3. RESULTS

Out of 331 subjects, non-obese and obese subjects were 150 and 18, respectively. Table 1 shows the age (in years) and BMI (kg/m^2) of non-obese and obese participants. Insulin levels were increased significantly ($P < 0.01$) in obese (37.42 ± 46.14 μIU/ml) than non-obese (19.00 ± 18.86 μIU/ml), as shown in Figure 1. There was a significant difference ($P < 0.01$) in serum leptin levels between non-obese (6.87 ± 6.53 ng/ml) and obese subjects (12.97 ± 10.45 ng/ml) (Figure 2).

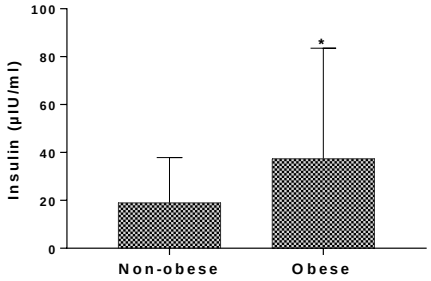

Figure 1. Serum insulin levels in non obese and obese (Values are mean ± S.D.), *($P < 0.01$)

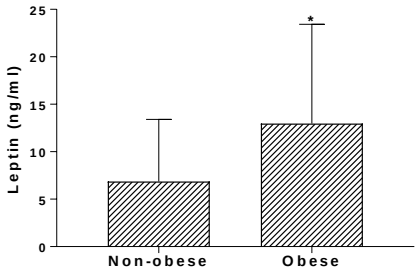

Figure 2. Serum leptin levels in non obese and obese (Values are mean ± S.D.), *($P < 0.01$)

Table 1 Demographic profile in non-obese and obese participants

Variables	Non-obese (n = 150)	Obese (n = 181)	*P*- value
Age (years)	41.48 ±17.59	44.90 ± 14.46	0.00
BMI (kg/m2)	21.78 ± 2.20	28.27 ± 3.22	0.01

Significance at $P < 0.01$

In Table 2, demographic profile of non-obese and obese, according to different gender is shown. In non-obese group, there was a significant change ($P < 0.01$) in insulin levels between female (17.61 ± 14.96 μIU/ml) and male (21.10 ± 23.53 μIU/ml), as shown in Figure 3. Mean leptin levels showed significant differences ($P < 0.01$) between female (9.29 ± 7.07 ng/ml) and male (3.24 ± 3.15 ng/ml) in non-obese group (Figure 3). In obese (Figure 4), insulin level was increased significantly ($P < 0.01$) in male (49.92 ± 60.93 μIU/ml) than female (32.72 ± 37.27 μIU/ml). However, leptin levels showed greater in female (16.35±10.69 ng/ml) than male (6.25 ± 5.29 ng/ml) in obese group ($P < 0.01$).

Table 2 Demographic profile, according to gender participants in non-obese and obese

Groups	Non-obese		Obese	
	Age (years)	BMI (kg/m2)	Age (years)	BMI (kg/m2)
Female (n = 212)	40.91 ± 18.87	21.49±2.30	45.84 ± 14.35	28.69 ± 3.47
Male (n = 119)	42.29 ± 15.70	22.23±1.99	42.88 ± 14.64	27.57 ± 2.45
P-value	0.09	0.16	0.96	0.69

Significance at $P < 0.01$

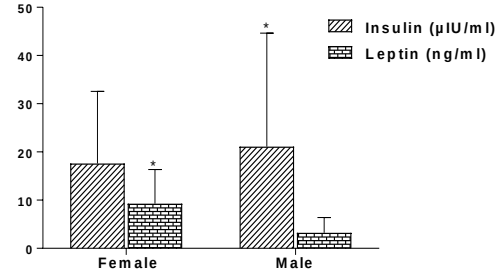

Figure 3. Serum insulin and leptin levels among non-obese female and male (Values are mean ± S.D.), *($P < 0.01$)

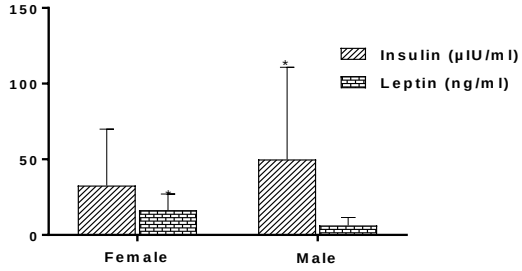

Figure 4. Serum insulin and leptin levels among obese female and male (Values are mean ± S.D.), *($P < 0.01$)

In Pearsons' correlations (Table 3), BMI in obese group was positively correlated with insulin ($P < 0.05$) and leptin ($P < 0.01$). Moreover, leptin showed a positive relation with insulin ($P < 0.05$).

Table 3 Correlations of insulin, leptin and BMI

Variables	Correlation
BMI vs Insulin	$r = 0.12$* $P = 0.02$
BMI vs Leptin	$r = 0.41$** $P = 0.00$
Leptin vs Insulin	$r = 0.17$* $P = 0.01$

*$P < 0.05$ and **$P < 0.01$

4. DISCUSSION

This study was conducted to justify the associations between insulin and leptin levels in relation to adiposity among the groups of non-obese and obese, which was classified based on BMI. Here, male and female differentiation of insulin and leptin concentrations with different BMI also displayed. According to Ferrannini et al., (1997), insulin secretion is more in obesity, thereby suggested that "insulin resistance is not the only mechanism through which obesity enhances insulin secretion." They concluded that "signals

originating in the central nervous system" play a significant role in raising insulin secretion and hyperinsulinemia related with obesity. Previous study of Kim et al., (2015) reported that with increasing insulin secretion developed hyperinsulinemia without reducing insulin clearance in obese individuals, be they insulin-resistant or insulin-sensitive. Serum insulin level is increased in obese subjects in the present study because increased adiposity in obese individuals which may directly lead to elevating the insulin secretion. In different sex, one study reported that men had more fasting insulin levels as compared to women, whether estrogen replacement therapy using women or not (Ferrara et al., 1995).

Our findings correlate with other studies in such way that male group had higher insulin levels than female group that may be the effect of differences in fat distribution of the body within different gender. Enzi et al., (1986) studied that the ratio of visceral adipose tissue (VAT) and subcutaneous fat linked with age and sex, appears higher ratio in women and more in younger than older. In addition, being high concentrations of androgen receptors in VAT and estrogen receptors in subcutaneous fat (Brown et al., 2010), suggest that these sex hormones would reflect to differ in insulin levels in different sex. Moreover, significantly elevated BMI in obese group provides a strong relationship with higher insulin levels, implies that by adjusting overweight should have positive effects against the risk factor arise due to hyperinsulinemia.

Al Maskari et al., (2006) demonstrated that leptin is significantly raised exponentially with adiposity, which exerts endogenous leptin resistance in obesity. With this support, Leptin levels were significantly increased in obese group as compared to non-obese and positively correlate with higher BMI in our study, observing an increasing adiposity influenced in increasing leptin levels. On the other hand, it has been reported that higher level of leptin claimed to be an independent risk factor for development of insulin resistance (Sader et al., 2003). Thereby, suggesting that maintaining body weight could be one of the major positive approaches to control hyperleptinemia, from which may presume abnormalities in other body metabolisms. According to sexual dimorphism, women had higher leptin concentrations than men (Garaulet et al., 2000), an outcome is correlated with higher accumulation of body fat and intracellular contents (Perseghin et al., 2001).

Our study observed higher concentrations of leptin in female than male, may be due to higher body fat distribution in women. Further, it could be the effect of sex hormone, androgens have negatively associated with leptin levels in men (Luukkaa et al., 1998) and estrogen elevates the leptin levels (Margetic et al., 2002). Despite, leptin levels had positive significant correlation with insulin in obese, corroborating with a study showed positive correlations between leptin and insulin levels in healthy population (Yadav et al., 2011) and another which described the relation of insulin and leptin levels (Wallace et al., 2001). This may be because of the mutual role of leptin and insulin in regulating energy metabolism with a close interaction of the regulatory pathways and the insulin axis.

A limitation of the study was lack of study population size that can not represent the whole population and certain parameters like fat percentage needs to be included for precise explanation. However, insulin and leptin were important determinant parameters of each other. The results of the study may provide in dept explanation that metabolic risk factor due to spike of body weight among the study population and may be beneficial to predict predispose condition of several metabolic disorders like diabetes. Finally, analyzing in different sex metabolisms could be a new step approaching in development of therapeutic and preventive measures of metabolic syndromes.

5. CONCLUSION

We conclude the study that insulin and leptin levels are high in obese compared to non-obese. Sexually dimorphism describes males are more prone to increase insulin level whereas females are highly susceptible to elevate in leptin levels. With increasing levels of insulin and leptin in obese subjects, likelihood of prediabetic conditions and other metabolic disorders may be high. Further studies on dynamics of relationships mechanisms between insulin, leptin and adipose tissue may be necessary to clarify the underlying importance in obesity and its complications of this Manipur population.

Acknowledgements

We would like to acknowledge Multi-Disciplinary Research Unit (MDRU), Regional Institute of Medical Sciences, Manipur, India for providing laboratory facilities in this study and special appreciation to Dr. Govindaraj for his kind moral support in this research work.

Author Contributions

L. Samananda did the main work of manuscript writing, data collection and analyzing. Y. Govindaraj advised the work protocol and reviewing the manuscript and W. Kanan supports the same to write this manuscript.

Funding
Study has not received any external funding.

Conflict of Interest
The authors declare that there are no conflicts of interests.

Informed consent
Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval
The study was approved by the Institutional Ethical Board, Regional Institute of Medical Sciences, Manipur, India (ethical approval code: A/206/REB/Prop(SP)70/46/2019).

Data and materials availability
All data associated with this study are present in the paper.

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