

CLINICAL PRESENTATION OF LEPTIN LEVELS IN PATIENTS WITH HISTORY OF PARENTAL OBESITY

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Received: 18 October 2016, Revised and Accepted: 17 August 2016

ABSTRACT

Objective: The role of adipose tissue as an endocrine organ is of great interest and leptin seems to be involved in it. The aim of this study is to document the characteristic of participants with respect to leptin and body mass index (BMI), with both parental history of central obesity and to describe the association in it.

Methods: This was a cross-sectional study. The participants fulfilling the criteria were chosen for the study. 83 patients with both parents obese and 55 participants with both parents normal were selected for the study. The participants were divided into four groups based on their status of diabetes and family history of central obesity.

Results: Leptin values obtained was higher in those patients with both parental history of central obesity with a mean difference of 11.1 units ($p < 0.001$) in diabetic patients and 6.44 units ($p < 0.001$) among the normal participants though BMI showed no much difference between the groups.

Conclusion: The data of this study demonstrated the genetic relationship between leptin levels and obesity.

Hence family history information serve as a useful tool in public health and prevention efforts needs to be extended to members who are at risk of developing the complications associated with it.

Keywords: Diabetes, Family history, Leptin, Parental obesity.

INTRODUCTION

The adult onset of diabetes in aged 20-70 years is expected to rise from 285 million in 2010 to 438 million by the year 2030 [1]. Furthermore, obesity has become the strongest risk factors for developing type 2 diabetes (T2D) and is a major clinical problem. The global scenario in the prevalence, incidence, mortality, and burden of obesity and other adverse health conditions has alarmingly raised among the adults. Hence, obesity is now the world's most prevalent disorder. Recent reports show alarming rise in T2D in all ethnicity along with the rise in obesity. This striking increase in obesity and diabetes is prevalent in both adolescents and children [2,3]. Obesity is one of the leading causes of metabolic syndrome and has become an international concern for health risk [4]. The constellation of derangements of the metabolic pathway has associated with it a group of disorders. In 2014, 39% of adults aged 18 years and above (38% of men and 40% of women) were overweight. The worldwide prevalence of obesity was more than doubled between 1980 and 2014 [5]. The prevalence of obesity rose from 2% to 17.1% [6], and as per the National Family Health Survey (NFHS) in Karnataka, the percentage of women aged 15-49 years who were overweight or obese (body mass index [BMI] ≥ 25.0 kg/m²) increased from 15% in (2005-06) NFHS-3 to 23% (2015-16) in NFHS-4 [7]. Similarly, in men who are overweight or obese (BMI ≥ 25.0 kg/m²) with a similar age has increased from 11% in (2005-06) NFHS-3 to 22% in (2015-16) NFHS-4 [8]. Despite the significant understanding of the environmental and genetic factors, its prevalence seems to rise. Although studies suggest lifestyle modification, dietary interventions, and weight loss to be reasonably as health protective barriers for the risk of T2D, little is known about the other prevention strategies. Genetic factors and the susceptible genes have been identified, but the results are not guaranteed. Since diabetes is a chronic disease, there is a long time between the exposure and existence

of clinical features of it. Further family history reflects hereditary component and henceforth an heritable factor [9-15], an knowledge into assessing of family history as a public health tool would be an easy approach in prevention and progress of the risk factor associated. Guidelines from associations and education programs now consider in including family history as a factor in health behavior [16-18] since inherited factors are important in obesity. The central control of energy balance and fat mass is leptin an adipocyte hormone. The adiposity signal to the brain by leptin must also be inherited in due course. Hence, a distinguishable marker for obesity-related diabetes should be used as a standard operational definition for family history. The objective of this study was to investigate the importance of parental history of obesity in diabetic and healthy controls with the leptin profiles in participants with similar BMI.

METHODS

This was a cross-sectional study conducted in Dakshina Kannada district of Karnataka with 229 cases of T2D patients, matched with 205 healthy individuals as the control.

The participants aged between 30 and 70 years (both genders) were recruited for the study. The inclusion criteria for the patients were known case of T2D for at least 1 year, can be only on oral hypoglycemic drugs or diet control, free from any of the vascular disorders such as diabetic nephropathy, neuropathy, and retinopathy. The study participants must also be free from any pre-existing cardiovascular disease, non-pregnant females, and females free from usage of any hormones or oral contraceptives. Self-reported history of presence or absence of central obesity in both the parents was obtained. Parents who did not appear to have central obesity and with a lean body were considered as negative controls and with central obesity were considered as positive

controls, and such participants were selected and grouped. Of the initial 229 cases of diabetic patients, 83 were eligible for the participation and were able to report their parental history of obese or lean stature. Out of 205 healthy individuals, 55 were eligible and participated. Hence, two groups were created in both diabetic and healthy people. Participants with the parents having central obesity were grouped as two plus (++) and without central obesity were grouped as two minus (--). Relevant examination was done to establish the inclusion and exclusion criteria. Clinical examination of pulse beats/minute, blood pressure, and stress test (TMT) was done for the assessment of cardiovascular system, and scan of abdominal system was done.

Diabetic neuropathy was ruled out by filament test and quantitative sensory testing (QST). In our study, we have used 10-g monofilament to find the sensation to the filament. Loss of sensation to this is considered as positive for diabetic neuropathy. QST is used to evaluate a sensory detection threshold or other sensory responses from supra-threshold stimulation. The common physical stimuli were (i) touch-pressure, (ii) vibration, and (iii) coolness, warmth, cold pain, and heat pain. Failure to identify these was considered positive for diabetic neuropathy.

Ophthalmoscope (fundoscopy) is used to diagnose diabetic retinopathy during a dilated eye exam. It is done as a part of an eye examination or routine physical examination. It is crucial in determining the health of the retina and the vitreous humor. A positive case was not included in the study.

Microalbuminuria: Spot-check samples were used along with the albumin/creatinine ratio (ACR). Any participants with ACR ≥ 3.5 mg/mmol (female) or ≥ 2.5 mg/mmol (male) was excluded.

Cardiac stress test (or cardiac diagnostic test) was used to rule out any pre-existing cardiovascular disease (CVD). Here, the stress response is induced by exercise. Walking on a treadmill, any diagnosis of CVD would rule out the criteria as a participant for the study. Work was approved by Yenepoya University ethics committee. Written informed consent was obtained from the selected participants. 5 ml of blood in the fasting state was drawn, and the separated serum was stored at -30°C in the Department of Biochemistry, Yenepoya Medical College and was used within 45 days for the estimation of Leptin with Ray Biotech kit using ELISA instrument at the Department of Biochemistry, Yenepoya Medical College.

Anthropometric variables such as height and weight were measured as per the standard procedure. Measurements of the weight to the nearest 0.1 kg by a weighing machine and height to the nearest of 0.1 cm by an anthropometer rod were done. BMI was calculated as weight (kg)/height (m²).

Statistical analysis: The values were expressed as Mean \pm standard deviation. All the data were analyzed applying two sample *t*-test. The hypotheses of equal means were tested at 5% level of significance. The results were analyzed using SPSS version 15.0.

RESULT

The general characteristics of the diabetic study group and its comparison (corrected for unequal variance) are shown in Table 1. Clearly the leptin levels are increased in subjects with 11.1 units with both parents being obese and the difference was statistically significant though the difference in their BMI was not significant.

Table 2 shows the general characteristics of the Normal subjects of the study group and its comparison (corrected for unequal variance). Subjects with obese parents had a higher leptin levels by 6.4 units even when the BMI showed no variations.

Figure 1 shows levels of leptin among the two study groups. Diabetic subjects had a higher level of leptin when compared to the normal

subjects. Also when family history of obesity was present, a higher level of leptin was noticed.

Figure 2 shows the levels of BMI among the group. The BMI among the study population did not vary much in spite of family history of obesity.

DISCUSSION

Obesity is considered as a serious health complication. Since obesity is linked with high levels of circulating free fatty acid, eventually leading to the progression of insulin resistance, diabetes, and cardiovascular disease. Obesity reflects interaction of genes, environment, and lifestyle. Familial aggregation is one of the strong reasons for increased prevalence of obesity and its associated disorder. The parent-child resemblance in body weight status is now an important factor to be considered hence the need of this study. Multiple studies have suggested to have an association between maternal obesity being the cause with the increase in body weight of the offsprings [19-21]. Studies show that maternal obesity before pregnancy is linked with bigger fetal growth during late gestation [22] and postnatal development [19], but in this study, this has become the limitation since we were not able to get the maternal history during pregnancy. Furthermore, children with obese parents have shown to have more risk associated than those with no obese parents [23-26], one reason being common raising environment, which is true in our study with the finding that a good number of patients in our study population had obese parents which eventually resulted in diabetes. This is because the appetitive traits and familial risk factors are associated with each other. Moreover, the mechanism

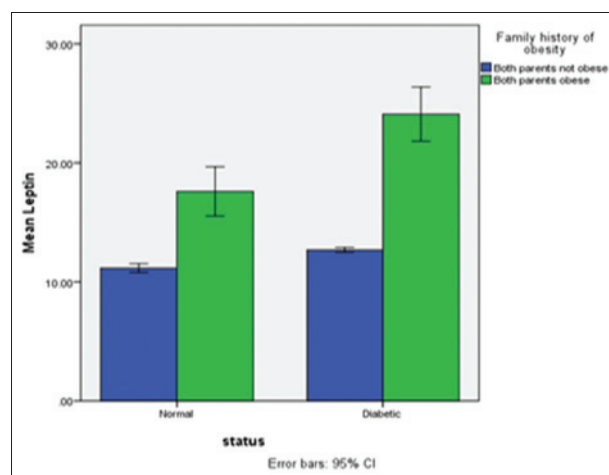


Fig. 1: Levels of leptin among the groups

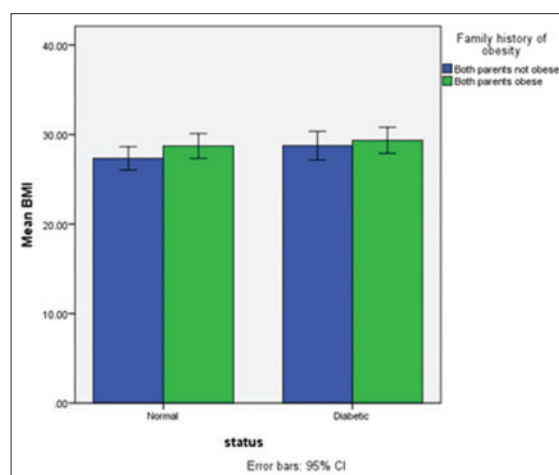


Fig. 2: Levels of body mass index among the groups

Table 1: General characteristics of diabetic subjects with parental history of central obesity

Parameters	Both parents are obese (n=50) (Mean ± SD)	Both parents are not obese (n=33) (Mean ± SD)	t	p
Age	46.28±9.43	46.3±7.89		
Leptin (ng/ml)	24.1±7.79	12.69±0.57	10.07*	<0.001
BMI (kg/m ²)	29.35±5.12	28.75±4.50	0.54	0.59 NS

*Equal variance not assumed, corrected for unequal variance. SD: Standard deviation, NS: Not significant, BMI: Body mass index

Table 2: General characteristics of normal subjects with parental history of central obesity

Parameters	Both parents are obese (n=28) (Mean ± SD)	Both parents are not obese (n=37) (Mean ± SD)	t	p
Age	45.60±8.79	46.81±9.4		
Leptin (ng/ml)	17.60±5.31	11.16±1.09	6.3*	<0.001
BMI (kg/m ²)	28.7±3.56	27.33±3.91	1.46	0.15 NS

*Equal variance not assumed, corrected for unequal variance. SD: Standard deviation, NS: Not significant, BMI: Body mass index

may be genetic or environmental. This shows that parental obesity does interact with the physique and the appetitive traits. Studies by Stunkard and Schachter's speculated that heavier - individuals are to be less sensitive to satiety feeling and more responsive to the presence of food [27,28]. Furthermore, children of heavier parents differ much in their satiety cues and also physical activity [29,30], the mechanistic explanations is that the susceptible genes might have been transferred onto their off spring's which is apparent in this study.

In relation to this, studies have documented the effect of the adipokines to be involved in the energy regulation and implicated in its pathogenesis related disorders. The secretion of an adipokine in relation to this role is leptin which has multiple roles in carbohydrate and lipid metabolism, reproductive system, and inflammatory and immune reactions [31]. The study of leptin interaction with other cytokine is well established. It has become a surrogate marker for atherogenic index, prevalence of metabolic syndrome, intima-media thickness of the common carotid artery, and others [32-35]. Hence, in our study, we observe a higher leptin level (Fig. 1) in patients with both parents obese. This explains the mechanism underlying the associations between parental obesity and associated risk factors along with diabetes.

It is a well-known fact that circulating leptin levels are well associated with the degree of adiposity. However, it is of considerable interest to note that our study population had similar BMI (Fig. 2) which implies the presence of similar adiposity. The major findings in our studies are that though with similar adiposity, families with both parents obese had a higher level of leptin than with those without which rules out the interference of being common raising environment effects. Hence, a secondary regulator is implied in its action which is hereditary factor.

CONCLUSION

We have substantiated that genetic and adiposity relationship does exist and the biological mechanism to which it contributes to the genetic dependent regulation of leptin levels in humans have yet to be elucidated. These areas are clearly the potential topic of future research.

ACKNOWLEDGMENT

We would like to express our gratitude to Dr. G.S Chandrashekar, Senior Physician and Cardio Diabetologist of Adarsha Hospital and Institute of Cardio diabetes, Trauma and Joint Replacement, Udupi, Karnataka, for his support in conducting this study.

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