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Weight Gain and Leptin Level in Normal and High BMI Pregnant Women

Marzieh Faghani Aghoozi[1], Najmeh Tehranian[2,*], Fahimeh Ramezani Tehrani[3]

[1]Department of Midwifery, School of Nursing and Midwifery, Shahroud University of Medical Sciences, Shahroud, Iran
[2]Department of Reproductive Health and Midwifery, Medical Sciences Faculty, Tarbiat Modares University, Tehran, I.R.Iran
[3]Reproductive Endocrinology Research Center, Research Institute for Endocrine Sciences, ShahidBeheshti University of Medical Sciences, Tehran, I.R. Iran

***Corresponding author:** Najmeh Tehranian**,** Department of Reproductive Health and Midwifery, Medical Sciences Faculty, Tarbiat Modares University, Tehran, I.R.Iranfah Email: n_tehranian@yahoo.com

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Abstract

Introduction and Objective: Leptin plays a key role in the regulation of body fat mass. In the case of calorie restriction and weight loss, serum leptin level will decrease rapidly. decreased leptin sensitivity causes weight gain and obesity and a compensatory increase in serum leptin levels. Hence, the aim of the current study was to investigate the relationship between maternal weight gain and changes in leptin levels during pregnancy.

Methodology: In this study, 45 pregnant women were classified into two groups, such as normal BMI (n=22) and high BMI group (n=23). The peripheral blood obtained from pregnant women in 6-12 and 15-20 weeks of pregnancy and Leptin levels were analyzed by ELISA.

Findings: there were statistically significant differences between maternal leptin levels in the first and second trimester and weight gain in each group. Correlation of changes in maternal serum leptin levels with total weight gain was significantly higher in obese pregnants The number of abortion ($P<0.001$) and the number of parturition ($P= 0.012$) had a significant effect on pregnancy BMI.

Conclusion: Increased serum leptin levels during pregnancy were directly related to their weight gain. This study is a preliminary step to determining and using indicators for appropriate weight gain, which in turn guarantees the health of mothers and the future generation.

Keywords: Leptin; Pregnancy; BMI

Introduction

Leptin is a basic hormone which is secreted by the adipose tissues and it was discovered by Zanck in 1994 [1]. It is a 4-stranded long-chain spiral protein belonging to the cytokines superfamily Group I and product of the obese (ob) gene (located on chromosomes 6 and 7), which is structurally similar to the growth hormones such as prolactin, granulocyte-colony stimulating factor (G-CSF), oncostatin M (OSM), and some interleukins (ILs). This 16-kDa non-glycosylated adipokine is found in the white adipose tissue [2, 3]. Leptin as a dual hormone with cytokine nature, has a wide range of biological activities such as: regulation of body weight and balance of energy through adjustment of food intake, satiety, affecting basal metabolism of glucose and fatty acids, increase insulin sensitivity, angiogenesis, ossification, synaptic transitions, homeostasis, oxidative stress, cardiovascular function, regulation of the hypothalamic-pituitary–adrenal axis, development of infant [4] especially at the maturity of Type II pulmonary cells for producing surfactants, onset of puberty, fertility and pregnancy [5-9].

Nowadays, obesity, cardiovascular diseases, and diabetes are common among people and specifically in pregnant women [10]. Maternal obesity is associated with increased risks of pregnancy complications. Many factors affect postpartum weight maintenance such as: preconception obesity, maternal weight during pregnancy, pregnancy duration, weight gain during the first trimester of pregnancy, maternal age, level of education, and economic status, which increase the risk of maternal and fetal mortality and morbidity [11]. Therefore, the serum level of leptin should be logically high in cases of obesity. However, according to previous studies, resistance to leptin activity can be seen in the cases of chronic overeating and obesity, which can lead to severe cellular hunger such as nervous anorexia [1]. In non-pregnant females, leptin is mainly secreted from several tissues such as fat cells, bone marrow, gastric fundus epithelium, muscles, granulosa and cumulus cells in mature ovarian follicles and mammary epithelial cells [12]. During pregnancy, leptin is secreted in the form of autocrine and paracrine by maternal, fetal, and placental trophoblastic adipose tissues. In addition, specific leptin receptors in the uterine endometrium, and maternal, syncytiotrophoblastic, and fetal decidua cause this hormone to affect implantation, maternal-fetal exchange, placental endocrine function, and fetal development [5, 13]. The main serum leptin level is produced by the placenta (115 ng/min), which is mainly released into the maternal blood circulation [14]. Several studies on pregnant women in weeks 15-20 of pregnancy have shown that the maternal blood fat had a greater effect on the serum leptin concentration than the number or size of twin [5, 14]. Thus, the presence of adipokines in adults led to the development of a theory stating that changes in adipokines found in maternal blood circulation in a normal pregnancy can be effective in the occurrence of pregnancy complications, such as: gestational diabetes [15-17], preeclampsia [18-21], gestational nausea and vomiting [23], cardiovascular diseases, late fetal deaths, preterm labor [24] macrosomia [25], LGA [26], SGA [27], cesarean delivery [28], childhood obesity [29-31] and Type II diabetes in adulthood, through making changes in maternal weight gain. Accordingly, the aim of this study was to investigate the prognostic role of serum leptin level in the determination of maternal weight gain during pregnancy, toward decreasing the pregnancy complication.

Methodology

Study subject

Peripheral blood was obtained from 45 pregnant women who attended the prenatal clinics in Tehran (Mahdiyeh Hospital and healthcare centers) during the first trimester of pregnancy, and who had met the inclusion criteria for the study. Written informed consents were obtained from all participants and the study was approved by the Ethics Committee of Tarbiat Modares University of Medical Sciences. Subjects between the ages of 18-40 years and with singleton pregnancies, and in the first trimester of pregnancy were included in the study. However, subjects with pregnancy complications such as preeclampsia, moles, ectopic pregnancy, diabetes, placenta previa, and placental abruption, who had been taking any medication other than pregnancy supplements, or who had adhered to certain diets, such as vegetarianism or high-protein diets, were excluded from the study. Patients according to BMI were divided into two groups such as normal BMI (n=22) and high BMI groups (n=23). Then, routine prenatal care questionnaire which was recommended by the Ministry of Health was completed through direct interview. All pregnant women food protocol was recorded in the questionnaire using the Food Protocol recommended by the Ministry of Health for pregnant mothers.

BMI calculation and serum leptin measurement with ELISA

BMI was calculated as weight at the first trimester of pregnancy (kg), divided by height (m) squared. The subjects were divided into two groups according to maternal BMI, including normal BMI (BMI < 25) and obese BMI (BMI ≥ 25) using the Food Protocol recommended by the Ministry of Health.

Nine to ten milliliters of peripheral blood were obtained from all subjects and transfer to the clinical laboratory center and plasma was separated with centrifuged (3000 rpm for 10 min) and frozen at a low temperature (-20 °C to -70 °C) until tested. Then, the serum leptin level was measured through the ELISA method using a kit specific for human leptin (Mercidia Company, Sweden, Uppsala, 10_1199_01), with a sensitivity of 0.024 ng/ml.

Statistical analysis

All statistical analyses were performed using IBM SPSS Version 22.0. Normality distribution of the obtained data was determined by Kolmogorov-Smirnov test. Independent T-test was considered to compare the mean differences between groups. Pearson correlation analysis was used to calculate the correlation coefficients. Univariate general linear model (GLM) analysis was used to compare the effects of every variable on pregnancy BMI separately and P-values less than 0.3 were considered for multiple GLM analysis. Data were expressed as means ± standard deviation of the mean (SD) and p-values less than 0.05 were considered significant. All graphs were prepared using the Graphpad Prism 6 software.

Results

The mothers (N=45) were categorized into two groups including normal and obese BMI (n=15, 30, respectively). The mean ± SD of the old age in mothers was 27.47 ± 5.55 (range= 19-37). The studied mothers were mostly in the age group of 21 to 30 years. Our data showed that the mean maternal weight was 67.25 ± 11.98 kg at the first round of serum leptin sampling, and 69.91 ± 11.68 kg at the second round of sampling. The mean maternal weight gain (n = 45) was reported to be 1.33 ± 1.79 kg at the first trimester, 4.92 ± 2.58 kg at the second trimester, and 5.05 ± 2.66 kg at the third trimester. The mean total maternal weight gain during pregnancy (n = 45) was measured to be 11.45 ± 4.44 kg with a minimum weight gain of 4 kg and a maximum of 21 kg, which was 12.5 ± 4.3 kg in group A, and 11 ± 4.63 kg in group B. Other demographic characteristics are shown in Table 1.

Also, the mean ± SD of the leptin levels in normal and obese BMI were 4.54 ± 6.14 and 3.32 ± 8.80, respectively. The relationship between the leptin level and normal BMI groups was not statistically significant (r (15) = -0.08, P=0.75). Moreover, the comparison between leptin level and obese BMI group did not show any statistical significance (r (30) = 0.16, p=0.37). The independent sample T-test indicated that leptin level was not significant in the comparison between normal and obese BMI groups in pregnancy period (t (45) = 0.48, p= 0.63). However, there were no statistically significant differences between the correlation of maternal leptin levels and weight gain at the first, second, and third trimester of pregnancy in two group.

The parameter estimates of the general linear model indicated that the number of abortion (P<0.001) and a number of parturition (P= 0.012) had a significant effect on BMI (figure 1). The value of -1.504 for the number of parturition indicates that for every additional number of parturition, we expected that mothers' BMI will decrease by 1.504 on average. Also for every additional number of abortion, mothers' BMI increases by 1.524 on average, holding all other variables constant (Table 2)

Table 1: Demographic information of mothers

Factors	Categories	Normal group	Obese group	p-value
Education	Elementary school	9(40%)	11(47.8%)	0.54
	Diploma or higher	13(60%)	12(52.2%)	
Income	Poor economic class	1(4.5%)	2(8.7%)	0.87
	Middle economic class	16(72.2%)	20(87%)	
	Desirable economic class	5(21.7%)	1(4.3%)	
Sex of newborns	Boy	8(36.4%)	12(52.2%)	0.29
	Girl	14(63.6%)	11(47.8%)	
Type of deliveries	Vaginal	12(54.5%)	13(56.5%)	0.89
	Cesarean	10(45.5%)	10(43.5%)	

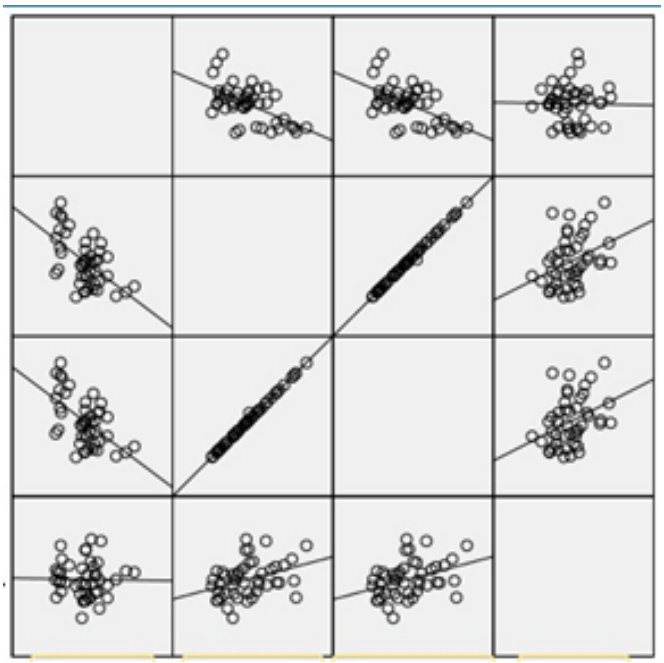

Figure 1. The scatter plot of correlation of leptin changes with body mass index, birth weight, and total weight gain.

Parameter	Categories	B	Std. Error	t	Sig.
Intercept	-	4.330	2.343	1.848	.073
Husband's job	Services industry	-0.785	0.459	-1.711	0.096
	clerk	-	-	-	-
Number of a family member	2	0.390	1.178	0.331	0.743
	3	-0.010	0.703	-.014	0.989
	≥4	-	-	-	-
Infant's gender	Boy	-0.615	0.343	-1.791	0.082
	girl	-	-	-	-
BMI before pregnancy		-0.039	0.052	-0.742	0.463
Number of parturition		-1.504	0.565	-2.661	**0.012**
Number of pregnancy		1.372	0.686	2.002	**0.053**
Number of abortion		1.524	0.362	4.208	**<0.001**

Table 2: General linear model result of factors affecting BMI during pregnancy

Weight gain

There were statistically significant differences between maternal leptin levels in the first and second trimester and weight gain in each group. Correlation **of** changes in maternal serum leptin levels with **total** weight gain was significantly higher **in obese pregnants** which confirms the main hypothesis of the study (Table.3).

Discussion

Leptin as a basic hormone, which is produced by the adipose tissues, is functionally similar to a dual hormone and cytokine. Leptin as a multifunctional hormone, has a wide range of activities such as: body weight and energy adjustment, angiogenesis, ossification, synaptic transitions, homeostasis, oxidative stress, cardiovascular function, regulation of the hypothalamic-pituitary-adrenal axis, development of infant, onset of puberty, fertility and pregnancy, maternal-fetal exchange, placental endo-

Weight(kg) / Leptin (ng/ml)	Modified total weight gain				Lambda test	
	Pierson test					
	Normal group(22)		Obese group (23)			
	P value	R	P value	R	P-Value	Lambda
Leptin(first trimester)	P<0/01	R= -0/371	P<0/01	R= -0/148	P=0/07	-1/8
Leptin(second trimester)	P=0/01	R=-0/109	P=0/728	R=-0/014	P=0/47	-0/7
Leptin changes	P<0/01	R= 0/527	P<0/01	R=0/254	P=0/01	2/64

Table 3. correlation of leptin levels and total weight gain

crine function, fetal development and etc. [4-13]. Interestingly, the main serum leptin level is produced by the placenta, which is mainly released into the maternal blood circulation [14]. Several previous studies have shown that maternal blood fat has a greater effect on the serum leptin concentration than the number or size of twin [5, 14]. Accordingly, this study aimed to investigate the relationship between changes in serum leptin levels and weight gain during pregnancy in Iranian women.

In Isfahan in 2012, Sharifirad et al. reported the mean weight gain during pregnancy to be 11.73 kg, which was 13.24 ± 4.34 kg in the normal-weight group, 12.76 ± 5.13 kg in the overweight group, and 10.22 ± 7.51 kg in the obese group [32]. In a study by Koohdani et al. in 2010, this mean value was reported to be 10.1 kg in the case group and 13.9 kg in the control group [33, 34]. Moreover, in a prospective cohort study conducted in Japan in 2010 on 2,989 Vietnamese pregnant women, Ota et al. reported the mean weight gain during pregnancy to be 12.5 ± 3.6 kg in the low-weight group, 12.2 ± 3.8 kg in the normal-weight group, and 11.5 ± 4.7 kg in the overweight and obese group [35]. Thus, the mean weight gain in the present study was similar to that in the study conducted by Sharifirad in Isfahan. Different mean values for weight gain during pregnancy in different studies can be attributed to differences in race, climate, dietary habits and cultures, traditional customs governing maternal nutrition during pregnancy, and lifestyles in different cities in Iran and around the world [32]. Similarly, Kim et al. conducted a study in South Korea in 2008 on plasma leptin levels after a 12-hour fast in 75 pregnant women at the first and third trimesters of pregnancy and six months after delivery using the ELISA method. The results of the study showed that the first-trimester leptin was significantly correlated with pre-pregnancy BMI, and predicted maternal birth weight [36]. In a study conducted by Nitert in Australia in 2015 on blood leptin levels after an overnight fast in 35 pregnant women in weeks 12, 20, 28, and 36, the maternal serum leptin levels obtained through the ELISA method showed no significant differences from the total maternal weight gain during pregnancy. However, the results of a review study by Faghani and Tehranian in 2015 showed a strong potential relationship between serum leptin levels and weight gain during pregnancy, which was independent of BMI [37, 38]. Finally, we analyzed the correlation between BMI and demographic characteristic of all subject. Our result showed that BMI correlated with the number of abortion in obese BMI women. These result highlighted the critical role of BMI in pregnancy. However, the leptin level was not correlated with these parameter.

Conclusion

Our results indicated that the preliminary determinant factor in maternal plasma leptin levels during pregnancy is pre-pregnancy BMI. It can be concluded that pre-pregnancy BMI, plays an important role in the determination of maternal plasma leptin level. It can be used as a predictive factor for serum leptin level. Due to a large number of pregnancy complication caused by unsuitable weight gain, the serum leptin level can be used as a novel indicative factor for control of weight gain in pregnant women, which plays an essential role. Pre-pregnancy BMI can be a predictive factor for maternal serum leptin levels and the total weight gain during pregnancy, which in turn guarantees the health of mothers, infants, and eventually the future generation.

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Ethics approval and consent to participate

The Ethics Committee of study Tarbiat Modares University with an ethics code of IR.TMU.REC.1393.600 in medicine approved the study. The aims and procedures of the study were explained to all participants and informed written agreement was obtained from them. Then they were given directions on how to complete the questionnaires.

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