ClinicSearch

International Journal of Clinical Case Studies

Chro Najmadin Fattah *

Open Access

Research Article

The Level of Serum Leptin in Non-Obese Women with And Without Gestational Diabetes in Sulaimaniyah City, Iraq

Chro Najmadin Fattah [1*], Polia Habeeb Rashid [2]

[1] University of Sulaymaniyah, Republic of Iraq.

[2] Maternity Teaching Hospital, Directorate of Health, 0046 Sulaimaniyah, Republic of Iraq.

***Correspondence Author:** Chro Najmadin Fattah, University of Sulaymaniyah, Republic of Iraq.

Received Date: September 01 2023 | Accepted Date: September 15 2023 | Published Date: September 29 2023

Citation: Chro Najmadin Fattah, Polia Habeeb Rashid, (2023), The Level of Serum Leptin in Non-Obese Women with And Without Gestational Diabetes in Sulaimaniyah City, Iraq, *International Journal of Clinical Case Studies*,2(5); **DOI:**10.31579/2835-9291/023

Abstract:

Background:

Obesity in pregnancy is correlated with pregnancy complications, including gestational diabetes mellitus (GDM).

Objective:

The present work was carried out to compare serum leptin levels in non-obese pregnant women with and without GDM.

Keywords: serum leptin; pregnancy; gestational diabetes mellitus;obesity, case-control study

Introduction

Leptin, an adipocyte-based hormone that is mainly synthesized by stomach, intestine, and placenta, decreases food intake and increases energy consumption through its effect on the receptors of the hypothalamus1 as well as assists energy/glucose homeostasis, blood vessel growth, and reproductive/immune systems regulation2. Also, it can play a role in hyperemesis gravidarum (severe morning sickness during the first trimester of pregnancy), affects metabolism, adiposity, fertility, puberty, and satiety, as well as functions as an anti-obesity agent3.

Most obese individuals are resistant to the leptin effect due to their negative response to central feedback mechanisms. For instance, obese peoples possess lower amounts of central nervous system (CNS) leptin than thin peoples4; thus, the quantity of stored energy in fat tissues are reflected by serum leptin concentrations5. In normal-healthy adult peoples, serum leptin levels are directly associated with the amount of body fat; however, it's not associated with reduced energy intake/energy stored in fatty tissues6.

Maternal/fetal adipose tissues and the placental trophoblast produce leptin (7). During pregnancy, leptin has a significant role in regulating maternal energy metabolism and regulates conceptus development and fetal growth. Serum leptin levels are believed to associate with body mass index (BMI) and body fat mass and are normally linked to adipose tissue mass in both pregnant and non-pregnant adults7. The leptin secretion is highest at midnight and down-regulates corticosteroid production in the adrenal glands8.

Reduced leptin amount in the body stimulates high glucose synthesis in the liver and affects brain systems varieties that change mood and behavior9. Like insulin resistance in type 2 diabetes (T2DM), a decreased sensitivity to leptin is associated with obesity, which fails to diagnose satiety despite high levels of leptin and high energy stores10. The adipokine leptin plays a significant role in regulating maternal energy metabolism during pregnancy. It is generally thought that serum leptin levels are associated with BMI and body fat mass in pregnant and non-pregnant women 7.

Hormone synthesis in the maternal-fetoplacental chain, embryonic hematopoiesis, fetal/placental angiogenesis, and the conceptus growth and development are the physiological roles of leptin during pregnancy. Compared with non-pregnant women, pregnant ones have greater maternal serum leptin concentrations that increase mainly in the second trimester and remains high until parturition11. An association between maternal obesity and hyperleptinemia and other biomarkers of placental dysfunction and insufficiency was found. In addition, there is an association between lower adiponectin levels and an increase in the risk of gestational diabetes12. In recent years, leptin has been indicated to change insulin sensitivity and secretion. It is vivid that there is a positive correlation between circulating leptin and different measures of adiposity; however, the relationship of diabetes to serum leptin level, independent of adiposity, is not clear13.

Pregnancy can be complicated by glucose metabolism disorders that result in gestational diabetes mellitus (GDM) and gestational impaired glucose tolerance (IGT). Although there is unclear explanation about GDM pathogenesis, GDM might result from reduced insulin sensitivity and increased anti-insulin hormones (such as progesterone, glucocorticoid, prolactin, and lactogen) that are produced by the placenta during pregnancy14.

Increased maternal plasma leptin might be caused by increased adipocyte leptin production due to increased insulin resistance and hyperinsulinemia in the second trimester of pregnancy. Hence, leptin might directly affect insulin

sensitivity by regulating insulin-mediated glucose metabolism in skeletal muscle and by gluconeogenesis regulation in the liver10. Therefore, the present study was carried out to compare the serum leptin level in non-obese GDM women with non-obese normal pregnant women.

Materials And Methods

Methods:

This study included 160 pregnant women with gestation ages of 28 – 35 weeks, of which 80 were in a study group (pregnant women with GDM) and the rest were in a control group (pregnant women without GDM). Participants' age, family health history (Hx), previous Hx, gestational age, parity, and body mass index (BMI) were collected from the women using a questionnaire. Serum leptin level and fetal amniotic index (FAI) were also measured.

Study design

This case-control study was performed in Sulaimaniyah Maternity Teaching Hospital and Diabetic Center in Sulaimaniyah City, Iraq from March 2020 to June 2021.

Study Sample

The study sample comprised 2 groups of pregnant women whose gestation age was 28 to 35 weeks. The first group was 80 women with GDM, and another group was a control group of 80 pregnant women without GDM.

Inclusion Criteria

Women with confirmed GDM having gestation age of 28–35 weeks and those who were not obese were included in this study.

Exclusion Criteria

Obese women with BMI ≥ 30 and those with intrauterine growth restriction (IUGR) or having T1DM/T2DM were excluded from this study. Women who had pregnancy-induced hypertension (PIH) and preeclampsia (PET) were also not included.

Experimental

A well-designed questionnaire was used to record participant's age, family health history (Hx), previous Hx, gestational age, and parity. Simultaneously, anthropometric measures (height and weight to determine BMI) were obtained from each participant. On the other hand, blood samples (3.0 mL) were obtained into plain tubes from patients and serum were collected to determine leptin level using Human Leptin ELISA kit (ab179884, UK). Additionally, amniotic fluid index (AFI) was measured using ultrasound (US) to determine the depth of the fluid in four quadrants in the gravid uterus. A depth of 5.0–25 cm AFI was considered as normal, while < 5.0 cm was considered oligohydramnios, and > 25 cm were considered polyhydramnios.

Statistical analysis

The collected data were analyzed through the Statistical Package for the Social Sciences (SPSS, version 25.0). For this purpose, descriptive and inferential statistical tests were utilized. The level of statistically significant data was considered at a p-value < 0.05.

Results:

Significant differences were seen between both groups in terms of their age ($p<0.001$), parity ($p=0.05$), BMI ($p<0.001$), and leptin level ($p<0.001$) in which women with GDM had higher BMI and leptin levels. The results also indicated that leptin level in the GDM women was correlated with their parity ($p=0.04$) and BMI ($p<0.001$), such that multiparous women and overweight women had higher levels of serum leptin.We found a significant different ($p < 0.001$) in the age between the studied group and the control group in which the women without GDM were younger than those with GDM. Also, there was a significant difference ($p = 0.05$) in the parity between the two groups, as multiparity was observed in 85% of the women with GDM while 72.5% of those without GDM were multiparous. Moreover, primiparous was found in 27.5% of women without GDM and 15% of women with GDM. There was also a significant difference ($p < 0.001$) in BMI between both groups, as 78.8% of women with GDM were overweight while 52.5% of those without GDM were overweight. However, 47.5% and 21.3% of women without GDM and with GDM had normal BMI, respectively (Table 1).

Variable		Group		Total	P-value
		Study Group (%)	Control Group (%)		
Age group (Year)	20–30	22(27.5)	53(66.3)	75(46.9)	< 0.001
	31–40	48(60.0)	27(33.8)	75(46.9)	
	> 40	10(12.5)	0(0.0)	10(6.3)	
Total		80(100.0)	80(100.0)	160(100.0)	
Parity	Primipara	12(15.0)	22(27.5)	34(21.3)	0.05
	Multipara	68(85.0)	58(72.5)	126(78.8)	
Total		80(100.0)	80(100.0)	160(100.0)	
BMI	Normal (18.5–24.9) kg/m^2	17(21.3)	38(47.5)	55(34.4)	< 0.001
	Overweight (25.0–29.9) kg/m^2	63(78.8)	42(52.5)	105(65.6)	
Total		80(100.0)	80(100.0)	160(100.0)	
BMI: Body Mass Index					

Table 1: Comparison between the studied and control groups regarding their demographics and medical profile.

Further comparison between two groups of pregnant women revealed that there was a significant difference ($p < 0.001$) in their serum leptin level as the mean serum leptin level in the studied group was significantly higher (33.42 ± 24.99) than the control group (20.86 ± 12.58) (Table 2).

Group	Leptin (Mean ± SD)	95% CI	P-value
GDM (N = 80)	33.42 ± 24.99	6.39–18.74	< 0.001
Normal pregnant (N = 80)	20.86 ± 12.58	6.37–18.76	

Table 2: Comparison between the studied and control groups regarding their leptin level.

Moreover, our outcomes demonstrated that the leptin level significantly correlates ($p < 0.05$) with parity and BMI of studied pregnant women with/without GDM. In this regard, multiparous (35.77 ± 25.56) women had a higher level of serum leptin than primiparous (20.13 ± 16.71). Additionally, overweight women showed higher (38.45 ± 25.58) serum leptin levels than women with normal body weight (14.78 ± 16.71) in both groups. However, family history, amniotic fluid index (AFI), previous history of GDM, and age groups did not have any significant difference ($p > 0.05$) with serum leptin levels in both groups (Table 3).

GDM Group	No.	Leptin (Mean ± SD)	95% CI	P-value
Family Hx				0.89
Yes	50	33.11 ± 25.59	-12.40–10.72	
No	30	33.95 ± 24.37	-12.30–10.62	
AFI				0.57
≥ 25	55	34.49 ± 25.60	-8.64–15.46	
< 25	25	31.07 ± 23.92	-8.44–15.27	
Parity				0.04
Primipara	12	20.13 ± 16.71	-30.91 - -0.36	
Multipara	68	35.77 ± 25.56	-27.54 - -3.73	
BMI				< 0.001
Normal (18.5–24.9) kg/m^2	17	14.78 ± 8.87	-36.28 - -11.08	
Overweight (25.0–29.9) kg/m^2	63	38.45 ± 25.58	-31.40 - -15.95	
Previous Hx GDM (Multipara)				0.21
Yes	58	31.08 ± 23.57	-20.89–3.87	
No	22	39.6 ± 28.01	-22.2–5.17	
Gestational age (Week)				0.02
28–30	29	25.29 ± 19.53	-24.03–1.46	
31–34	51	38.04 ± 26.69	-23.13– 2.37	
Age group (Year)				0.29
20–30	22	32.23 ± 25.61	20.87–43.58	
31–40	48	36.21 ± 25.65	28.75–43.65	
> 40	10	22.67 ± 18.37	9.53–35.18	

AFI: Amniotic Fluid Index, BMI: Body Mass Index, GDM: Gestational Diabetes Mellitus

Table 3: Association between leptin level and other variables in women with GDM.

Furthermore, we revealed a significant association ($p < 0.001$) between gestational age and serum leptin level. However, leptin level had no significant correlation ($p > 0.05$) with parity, age groups, and BMI in both groups of women (Table 4).

Normal Pregnant Group	No.	Leptin (Mean ± SD)	95% CI	P-value
Age group (Year)				0.5
20–30	53	20.26 ± 13.14	-7.68–4.20	
31–40	27	22.00 ± 11.54	-7.46–3.99	
Parity				0.2
Primipara	22	18.25 ± 12.61	-9.85–2.6	
Multipara	58	21.84 ± 12.53	-9.97–2.79	
Gestational age (Week)				< 0.001
28–30	27	12.22 ± 9.23	-18.21 – -7.84	
31–34	53	25.25 ± 11.80	-17.84 – -8.22	
BMI				0.5
Normal (18.5–24.9) kg/m^2	38	19.90 ± 12.77	-7.27 – 3.99	
Overweight (25.0–29.9) kg/m^2	42	21.63 ± 12.50	-7.27– 3.99	
BMI: Body Mass Index				

Table 4: Association between serum leptin level and other variables in women with normal pregnancy.

Discussion

Gestational diabetes that develops more commonly in the second or third trimester of pregnancy period and often disappears after giving birth seems to be directly related to maternal age during pregnancy.15 In this respect, the results of our study showed that older women were at a higher risk of developing GDM during pregnancy than younger ones, whereas a conducted research on 17,145 pregnant women in Qingdao, China by Li et al. 2020 showed the highest rate of women with GDM in the age group of 30–34 years with a BMI > 30 kg/m2 .16

Additionally, we found 2/3 of primiparous women had normal pregnancies while 1/3 of primiparous women had GDM. In this regard, Laine et al. 2018 in Finland reported the prevalence of GDM in primiparous women to be < 10%, while the rate of GDM was 15% for multiparous women.17 Based on NICE guidelines, the most important risk factors for developing GDM during pregnancy are BMI > 30, pregnancy weight of > 11% than ideal body weight, prediabetes, polycystic ovary syndrome (PCOS), particular race/ethnicity, high maternal age (> 35 years), previous history of GDM, pre-existing diabetes, fetal death, and macrosomic childbirth with a weight of 4.5 kg or above.18

In this study, about 80% of GDM women were overweight, which is consistent with the results of a cohort study conducted on 3172 Chinese pregnant women by Sun et al., 2020 who concluded that extreme gestational weight gains and pregnancy obesity/overweight enhanced the possibility of GDM, large gestational age, fetal macrosomia, and gestational hypertension. 19 Besides, they recommended that controlling body weight across and before pregnancy could reduce the adverse outcomes of pregnancy, especially for ethnic minorities. Also, they concluded that pregnant women with a BMI > 25 kg/m2 at pregnancy might develop GDM sooner and faster than those with less BMI. Thus, public health attempts, such as encouraging women of childbearing age to exercise and eat a healthy diet, should be stepped up to reduce pregnancy BMI.

The current study also revealed that the level of maternal serum leptin was associated with maternal weight. In line with this finding, a similar study conducted by Serapio et al. 2019, on Sweden pregnant women and a maternal weight was observed to have different effects on maternal serum leptin. However, they could not find any significant relationships between the level of maternal serum leptin and infant birth weight neither in normal or overweight women.20

Moreover, our results showed that the serum leptin level of women with GDM was significantly different from women without GDM. Hence, the mean level of leptin was significantly lower in women without GDM than in those with GDM. In this respect, Calan et al. 2013 study conducted on pregnant women in Turkey was reported that GDM caused higher levels of serum leptin and positively affected insulin resistance.21 On the other hand, Thagaard et al. 2017 studied adiponectin and leptin as first trimester biomarkers for GDM among 2590 pregnant women in Denmark and observed the highest serum leptin level in women with GDM than non-GDM women. Their study also showed that women with a higher BMI had higher levels of leptin concentration.22 These findings indicate that serum leptin levels are correlated with glucose metabolism in patients with GDM.Our results also revealed the significant correlation between multiparity and leptin levels in women with GDM. In line with this finding, Rodriguez et al. 2020 conducted a study on 973 pregnant women in the USA. They realized that adjusting lifestyle and demographic factors results in higher serum leptin levels in women with grand multiparity (≥ 5 births).23 Additionally, we revealed that leptin levels were significantly higher in overweight women than normal-weight women with GDM. In this regard, Misra et al. 2011 studied the effect of overweight/obesity on maternal serum leptin levels during the gestation period in 143American pregnant women. They found that leptin profiles of overweight/obese women are significantly different from those with normal weight during gestation.7Regarding the association between leptin level and gestational age in both studied groups of women with and without GDM, we observed that women with a gestational age of 31–34 weeks had significantly ($p < 0.05$) higher leptin levels. In agreement with our study, another research was conducted by Lacroix et al. 2016 on Canadian pregnant women to determine the correlations between maternal leptin and gestational age during the second trimester and reported that leptin levels increased drastically during the second trimester and later in pregnancy.24 However, we have not seen any significant correlation between serum leptin level and AFI or a previous history of GDM in the studied women or their families. Similarly, Lackovic et al. 2021 studied GDM among 203 mother-infant pairs in Belgrade and reported that based on the multivariate logistic regression model, only motoric development

suspension of infants at the first three months and AFI had a significant association with GDM.25

Conclusion

Higher serum leptin was found in GDM women, and an increased gestational age was associated with increased leptin in both GDM and non-GDM women.Finally, we concluded that women with GDM had higher serum leptin levels than those without GDM. Increased gestational age was associated with an increased serum leptin level in women with/without GDM. Compared to women with normal weight in both normal pregnancy and GDM groups, overweight women had higher serum leptin levels. Thus, we concluded that serum leptin levels could be effectively regulated by controlling weight gain during the prenatal period, which might prevent subsequent complications in the future. Consequently, we recommend serum leptin measurement in early pregnancy to predict easily detected GDM in later pregnancy.

Declarations

Ethical approval and consent to participate Our experiments on pregnant women were followed the appropriate guidelines and regulations belonging to the declaration of Helsinki. Additionally, the study protocol was approved by the Ethical Committee of College of Medicine, University of Sulaimani, Republic of Iraq with No. 07/21072020-CoM-UoS. Furthermore, informed written consent was obtained from all subjects.

Consent to publish

Consent to publish was obtained from the study participants.

Data availability

The data used to support the findings of this study are included within the article.

Competing interest

Both authors reported no conflicts of interest.

Funding

This work was not funded by any national/international agency, company, or organization.

Acknowledgments

The author appreciates the help and assistance from the healthcare staff of Maternity TeachingHospital/Diabetic Center, Sulaimaniyah Health Directorate, Sulaimaniyah city, Iraq.

Author contribution

CNF: Conceptualization, methodology, data analysis, writing the original manuscript

PHS: Resources, validity, visualization, revision/submission of the original manuscript

References

1. Zou G, Zhang Y, Yu L. (2013). Natural selection and adaptive evolution of leptin. *Chin Sci Bull,* 58(18):2104-2112.
2. Pérez-Pérez A, Sánchez-Jiménez F, Vilariño-García T, Sánchez-Margalet V. (2020). Role of leptin in inflammation and vice versa. *Int J Mol Sci*, 21(16):5887-5912.
3. Miehle K, Stepan H, Fasshauer M. (2012). Leptin, adiponectin and other adipokines in gestational diabetes mellitus and preeclampsia. *Clin Endocrinol*, 76(1):2-11.
4. Park HJ, Lee SE, Kim HB, Isaacson R, Seo KW, Song KH. (2015). Association of obesity with serum leptin, adiponectin, and serotonin and gut microflora in beagle dogs. *J Veterinary Intern Med*, 29(1):43-50.
5. Ramanand SJ, Ramanand JB, Jain SS, et al. Leptin in non PCOS and PCOS women: a comparative study. Artigo em Inglês; 2014.
6. Jafari-Vayghan H, Tarighat-Esfanjani A, Jafarabadi MA, Ebrahimi-Mameghani M, Ghadimi SS, Lalezadeh Z. (2015). Association between dietary patterns and serum leptin-to-adiponectin ratio in apparently healthy adults. *J Am Coll Nutr*, 34(1):49-55.
7. Misra VK, Trudeau S. (2011). The influence of overweight and obesity on longitudinal trends in maternal serum leptin levels during pregnancy. *Obesity*, 19(2):416-421.
8. Morton GJ, Schwartz MW. (2011). Leptin and the central nervous system control of glucose metabolism. *Physiological Reviews*, 91(2):389-411.
9. Pan H, Guo J, Su Z. (2014). Advances in understanding the interrelations between leptin resistance and obesity. *Physiol Behav*, 130:157-169.
10. Sanchez-Garrido MA, Tena-Sempere M. (2013). Metabolic control of puberty: roles of leptin and kisspeptins. *Horm Behav*, 64(2):187-194.
11. Liu Y, Wang W, Hitomi M. (2000). Serum leptin levels in normal pregnant women and their babies. *Zhonghua fu Chan ke za zhi*, 35(7):392-395.
12. Hedderson MM, Darbinian J, Havel PJ, et al. (2013). Low prepregnancy adiponectin concentrations are associated with a marked increase in risk for development of gestational diabetes mellitus. *Diabetes Care*, 36(12):3930-3947.
13. Mente A, Razak F, Blankenberg S, et al. (2010). Study of the Health Assessment and Risk Evaluation; Study of the Health Assessment and Risk Evaluation in Aboriginal Peoples Investigators. Ethnic variation in adiponectin and leptin levels and their association with adiposity and insulin resistance. *Diabetes Care*, 33(7):1629-1634.
14. Myers MG Jr, Heymsfield SB, Haft C, et al. (2012). Challenges and opportunities of defining clinical leptin resistance. *Cell Metabolism*, 15(2):150-166.
15. Hinkle SN, Buck Louis GM, Rawal S, Zhu Y, Albert PS, Zhang C. (2016). A longitudinal study of depression and gestational diabetes in pregnancy and the postpartum period. *Diabetologia*, 59(12):2594-2602.
16. Li G, Wei T, Ni W et al. (2020). Incidence and risk factors of gestational diabetes mellitus: a prospective cohort study in Qingdao, China.*Frontiers in Endocrinology*, :636.
17. Farley D, Choi J, Dudley D, et al. (2010). Placental amino acid transport and placental leptin resistance in pregnancies complicated by maternal obesity. *Placenta*, 31(8):718-724.
18. NCCf W. (2008). Health Cs. Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period.
19. Sun Y, Shen Z, Zhan Y, et al. (2020). Effects of prepregnancy body mass index and gestational weight gain on maternal and infant complications. *BMC Pregnancy and Childbirth*, 20(1):1-13.
20. Serapio S, Ahlsson F, Larsson A, Kallak TK. (2019). Second trimester maternal leptin levels are associated with body mass index and gestational weight gain but not birth weight of the infant. *Hormone Res Pædiatrics*, 92(2):106-114.
21. Calan M, Yilmaz O, Altindag T et al. (2013). Maternal serum fetuin-A, leptin, and hs-CRP concentrations in gestational diabetes. Paper presented at: *Endocrine Abstract*.
22. Thagaard IN, Krebs L, Holm J-C, Lange T, Larsen T, Christiansen M. (2017). Adiponectin and leptin as first trimester markers for gestational diabetes mellitus: a cohort study. Clin Chem Lab Med 55(11):1805-1812.
23. Rodriguez CP, Ogunmoroti O, Quispe R, et al. (2021). The Association Between Multiparity and Adipokine Levels: The Multi-Ethnic Study of Atherosclerosis. *J Women's Health*, 142(:13525.
24. Lacroix M, Battista M-C, Doyon M, et al. (2016). Higher maternal leptin levels at second trimester are associated with

subsequent greater gestational weight gain in late pregnancy. *BMC Pregnancy and Childbirth*, 16(1):1-9.

25. Lackovic M, Milicic B, Mihajlovic S, et al. (2021). Gestational Diabetes and Risk Assessment of Adverse Perinatal Outcomes and Newborns Early Motoric Development. *Medicina*,57(8):741.