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Adiponectin and Leptin of Maternal Serum Predict the Sexual Function in Women with Normal Vaginal Delivery and Cesarean Section? A Prospective Study

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ABSTRACT

Background: Postpartum sexual function may be affected by various endocrine and paracrine factors such as testosterone and adipokines, and environmental and delivery aspects.

Objectives: This study aimed to investigate the relationship between maternal serum Adiponectin and Leptin level with sexual function after Normal Vaginal Delivery (NVD) and CS.

Methods: This prospective cohort study was performed in pregnant women in the third trimester who met the inclusion criteria. Serum concentrations of maternal adiponectin and leptin were measured during the first 24 hours after delivery. Then, women's sexual function was assessed by Female Sexual Function Index (FSFI) at 8 and 12 weeks of postpartum.

Results: The results showed no significant relationship between the delivery type and sexual function ($P > 0.05$). However, the mean score of sexual function during the three times in two delivery groups indicated statistically significant changes ($P<0.001$). Also, comparing the levels of Leptin and Adiponectin with the delivery type showed that the levels of these two hormones in NVD were higher than in CS (NVD = 14.48 ± 6.75 and CS = 8.27 ± 5.6; NVD = 17.75 ± 11.85 and CS 14.58 ± 12.20, respectively). However, this association was only significant at leptin ($p <0.001$). Finally, the results showed a significant inverse relationship between Adiponectin level and sexual function at the 12th week postpartum NVD group ($P = 0.014$ $r = -0.362$).

Conclusion: Serum leptin and adiponectin levels in the first 24 hours after vaginal delivery were higher than cesarean delivery. However, regarding the importance of leptin and adiponectin, vaginal delivery is preferred.

Keywords: Adiponectin; Leptin; Sexual Function; NVD; CS

Abbreviations: NVD: Normal Vaginal Delivery; CS: Cesarean Section; BMI: Body Mass Index; DHEAS: Dehydroepiandrosterone-Induced Adiponectin; ACTH: Adrenocorticotropic Hormone; 5α-DHT: 5α-dihydrotestosterone; E2: Estradiol; T: Testosterone; WHO: World Health Organization; CRP: C-Reactive Protein

Introduction

Adiponectin and leptin are adipose members secreted by the proteins called adipocytokines or adipokines [1]. Leptin plays an essential function in the central nervous system in regulating energy balance. Also, it signals the body's preparation for sexual maturation and reproduction to the brain. Leptin level is high in pregnancy and at birth such that to provide the energy needed for pregnancy, childbirth, and full breastfeeding [2]. Adiponectin modulates metabolic processes such as glucose regulation and acid oxidation. Adiponectin is highly important in the perinatal period regarding the strong correlation between adiponectin concentration in the mother and breastfeeding [3]. Some studies have demonstrated that the synthesis and expression of adiponectin and leptin are altered in systemic inflammation [4,5]. Several factors are associated with differences in the level of inflammatory markers postpartum, including formula versus breastfeeding, and Normal Vaginal Delivery (NVD) versus Cesarean Section (CS) [6]. The number of CS has increased worldwide. Interestingly, in Iran, this rate is three times more than the world standard [7]. However, this surgery is associated with a higher risk rate in current and subsequent pregnancies [8]. Fear of losing vaginal tightness and its negative impact on postpartum sexual life is one of the main reasons for preferring the cesarean by many women or couples [9].

Sexual function becomes an important issue for couples in the postpartum as their sexual activity decreases during this period [10]. In this respect, more than one-ninth of women may not have resumed sexual activity until six months after delivery [11]. Therefore, according to the World Health Organization (WHO), women's sexual function is an important aspect that should be considered [12]. The authors' hypothesized that levels of adiponectin and leptin would differ concerning types of delivery and sexual function. Regarding the increasing cesarean section and its complications and insufficient evidence supporting adiponectin and leptin's potential role in postpartum and maternal health outcomes, including sexual function, the present study aimed to evaluate the relationship between sexual function, Leptin, and Adiponectin in CS and NVD.

Methods

Study Design and Participants

This prospective cohort study was performed on healthy pregnant women in their third trimester of pregnancy who referred to Mahdieh Hospital in Tehran for NVD and CS from June 2021 to January 2022. The sample size was calculated using the following formula and the study of Nuamah, et al. [13]. With 95% confidence and 80% power, the number of samples required in each group was determined to be 41. With an almost 10% probability of withdrawal rate, 45 women were selected to participate in each study group, making 90 samples in total.

$$N = (Z1 - {}^{a}/_{2} + Z1 - B)2 \times (S1\,2 + S2\,2) \div (\bar{X}1 - \bar{X}2)2$$

First, 122 pregnant women who met the inclusion criteria were included in the study. Twenty-four of them were excluded from the study due to pregnancy complications such as preterm delivery, instrumental vaginal delivery or large grade 3 or 4 perineal rupture, fetal or infant death, or fetus's congenital malformations. Also, eight women were excluded from the study due to not participating in follow-ups in weeks 8 and 12 (6 participants) and suffering from postpartum depression (2 participants). Finally, the present study was carried out on 90 women (45 in the vaginal delivery group and 45 in the cesarean delivery group).

Inclusion Criteria: Age 18-40 years, gestational age 38-42 weeks, and elective CS (the cause of CS included a previous cesarean section, maternal request, or breech delivery). Moreover, they had Iranian ethnicity, no previous history of psychiatric disorders or use of relevant drugs, no prior history of systemic or chronic disorders (e.g., lupus, thyroid disorders, liver, kidney, heart disease, and diabetes), were not a smoker or did drink, and had sexual function score 28 and above. Furthermore, they had a reading and writing literacy, no history of infertility, a normal Body Mass Index (BMI) before pregnancy checked at the first prenatal visit, and a depression score less than 17(study at third trimester by Beck questionnaire).

Exclusion Criteria: dystocia, congenital fetal malformations, fetal death, neonatal and infant death, preterm delivery, chorioamnionitis, instrumental vaginal delivery, large grade 3 or 4 perineal muscles rupture, postpartum depression score more than 17 (study at 8th week postpartum by Beck questionnaire), and not participating in follow-ups. In the first visit, a checklist of demographic and obstetric characteristics along with FSFI and Beck questionnaires were completed by the samples to assess the inclusion criteria. All pregnant women received standard prenatal care.

Data Collection Instruments

Blood samples for measuring leptin and adiponectin were collected from the mother during the first 24 hours after delivery. Blood samples were centrifuged immediately at 4,000 rpm at 4℃ for 10 min, and the serum amount was frozen without delay at 70℃ until decomposition. According to the standard chain, it was transferred to the Endocrinology Research Institute of Shahid Beheshti University of Medical Sciences laboratory. The concentrations of adiponectin and leptin (µg/ml) were measured by using an enzyme-linked immunosorbent assay (ELISA) using a commercial kit according to the protocol (Human Adiponectin & Leptin, Zell Bio GmbH, Ulm, Germany) according to the manufacturer's instructions. Serum adiponectin was measured with an intra-assay and interassay coefficient of variation (CV) of <5.4% and <8.5%, respectively, while serum leptin was measured with an intra-assay and interassay CV of <7.4% and <9.3%, respectively.

Data Collection was Performed Using the Following Measures: The demographic and obstetric questionnaire includes age, education level, occupational status, number of gravidities, parity and abortion, gestational age at the time of delivery, history of pregnancy, and infant characteristics. The FSFI was designed by Rosen, et al. [14] to assess sexual performance in women over the past four weeks. The 19-item questionnaire is classified into six sub-categories, including sexual desire (2 items), arousal (4 items), hydration (4 items), orgasm (3 items), satisfaction (3 items), and pain (3 items). Each question is scored with a response range of 0 to 5. Here, the score 0 is considered when they do not have sexual activity, and 5 is equivalent to better sexual performance (except for the first and second questions, which are assigned with a score of 1 to 5). The minimum score for the total number of questions is 2 and the maximum score is 36 [14]. The Persian version of this tool was localized, and the cut-off point for the Persian version of tool 28 was reported in [15]. Beck Depression Inventory (BDI–II) is a self-assessment questionnaire consisting of 21 questions developed by Beck, et al. [16]. The questionnaire is rated in the range of 0 to 3, with 0 = mental health in the subject, 1 = mild disorder, 2 = moderate disorder, and 3 = acute and severe disorder. The sum of the scores varies from 0 to 63 [16]. In Iran, the psychometric properties were defined by Ghasemzadeh, et al. [17] and factor analysis results indicated the questionnaire's effectiveness [17].

The FSFI was completed in the third trimester and the 8th and 12th weeks postpartum. Also, BDI-II was completed in the third trimester and the 8th week.

Ethical Considerations

Before data collection, ethical approval was obtained from the Research Committee of the Faculty of Medical science, Tarbiat Modares University, Tehran, Iran (IR.MODARES.REC.1397.013). All procedures were in accordance with the ethical standards of the Regional research committee and with the Declaration of Helsinki 1975 and its later amendments. At the first of the questionnaire page, the informed consent form was put to participants. Participants were convinced that in this study they could leave the study at any time without being reprimanded or losing benefits. In addition, participants were reassured that the information was confidential and anonymous.

Data Analysis

The data normality was assessed by Kolmogorov-Smirnov and Shapiro-Wilk tests. Also, descriptive statistics were used to examine the data. Moreover, parametric independent chi-square and nonparametric Mann-Whitney U were used for intergroup comparisons. The Pearson parametric test was performed to evaluate the relationship between serum level of leptin, adiponectin, Leptin-to-Adiponectin ratio, and sexual function. Friedman test and repeated measures analysis of variance were used to analyze the effect of time on sexual function in vaginal delivery and cesarean section. In addition, ROC curve analysis was used to examine whether serum levels of leptin and adiponectin could predict sexual function in both vaginal delivery and cesarean section. The accuracy of the forecast was estimated through the Area under the Curve (AUC) and its 95% CI. The analysis was performed using SPSS version 22. A P-value of less than 0.05 was considered statistically significant.

Results

The demographic characteristics of the participants are presented in Table 1. The mean age of women in the vaginal delivery and elective cesarean section was 25.9 ± 4.7 and 29.5 ± 4.5, respectively. Most participants were housewives (87%), and their education level was diploma (44.4%). The results showed that most of the samples in the two groups of vaginal delivery and cesarean section in BMI variables before pregnancy, infant weight, education, number of abortions, method of breastfeeding at 8 and 12 weeks postpartum, having a vaginal infection at 8 and 12 weeks postpartum, and time of onset of postpartum sexual activity were homogeneous (P >0.05). However, the results showed a significant difference in age, the number of delivery, and pregnancy between the two groups (P <0.05). Table 2 shows a statistically significant difference between serum leptin level and delivery type (P<0.001) NVD 14.48 ± 6.75, CS 8.27 ± 5.6). However, there is no relationship between the delivery types and serum adiponectin level (P = 0.26) (NVD 17.75 ± 11.85, CS 14.58 ± 12.20). Furthermore, the leptin-to-adiponectin ratio in NVD and CS was 0.82 and 0.57, respectively. Also, the Independent t-test showed no significant difference between sexual function in the third trimester of pregnancy and 12 weeks postpartum (P = 0.19 and P = 0.78, respectively). The Mann-Whitney U test showed no significant relationship between sexual function at week 8 and the delivery type (P = 0.53).

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Table 1: Comparison of the frequency distribution of demographic and obstetric characteristics of the studied samples in the two groups of vaginal delivery and cesarean section.

	NVD	CS	P-Value
Age Mean (SD)	25.9(4.7)	29.5(4.5)	< 0.001*
BMI Mean (SD)	24.1 (3.38)	24.96(2.72)	0.067*
number of Parity N %			
one	29 (64.4)	4(8.9)	< 0.001**
two	11(24.4)	31(68.9)	
Tree and more	5(11.1)	10(22.1)	
Gravidity number of			
one	25(55.5)	3(6.7)	< 0.001**
two	13(28.9)	26(57.8)	
Tree and more	7(15.5)	16(35.5)	

*Independent T Test, p<0.05 considered as statistically significant

**Mann-Whitney, p<0.05 considered as statistically significant

NVD: Normal Vaginal Delivery

CS: Cesarean Section

BMI: Body Mass Index

Table 2: Comparison of serum levels of adiponectin and leptin in the two groups of vaginal delivery and cesarean section.

	C/S	NVD	
	Mean ± SD	**Mean ±SD**	**P-Value**
Serum Adiponectin levels	14.58 ±12.20	17.75 ± 11.85	0.26*
Serum Leptin levels	8.27 ± 5.6	14.48± 6.75	< 0.001**

*Mann-Whitney, p<0.05 considered as statistically significant

**Independent T Test, p<0.05 considered as statistically significant

Nevertheless, studying the effect of time on sexual function in vaginal delivery and cesarean section revealed that the mean score of sexual function had statistically significant changes (P<0.001) during the three times in the group of vaginal delivery and the cesarean section (Table 3 & Figure 1). Also, two-by-two comparison tests were performed on the mean sexual function scores at three times using the Ben Foroni post hoc test and repeated measure analysis of variance. The results showed that the mean score of sexual function is statistically significant (P <0.05) in all two-by-two comparisons at studied times. The Pearson correlation test results between Serum Leptin level and Leptin-to-Adiponectin ratio with sexual function (third trimester of pregnancy, weeks 8 and 12 postpartum) in NVD and CS showed no statistically significant relationship between these variables and any of the variables. Also, according to the Pearson Correlation Test results between serum Adiponectin level and sexual function in the two groups, only the relationship between serum Adiponectin level and sexual function at 12 weeks postpartum in NVD was significantly related (P = 0.014, r = -0.362) (Table 4). In addition, the multiple linear regression used to determine the relationship between the type of delivery and the sexual function of the third trimester, 8 weeks and 12 weeks after delivery and the serum level of leptin and adiponectin.

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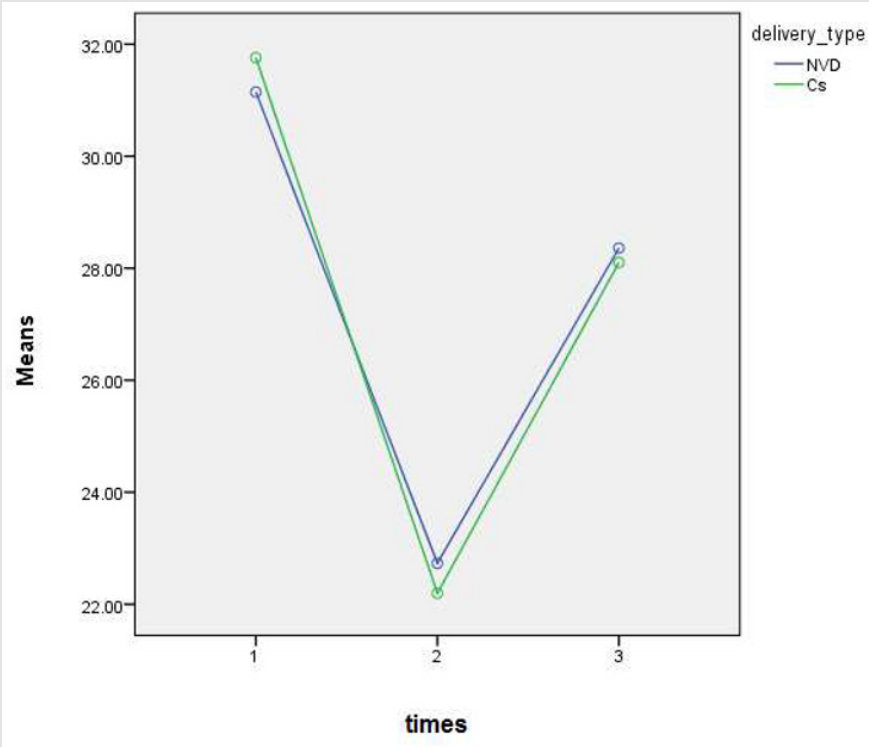

Figure 1: Graph of analysis of variance with repeated measures to examine changes in sexual function at three times between the two groups of vaginal delivery and elective cesarean section. 1=third trimester, 2= 8th week postpartum, 3= 12th postpartum.

Table 3: Comparison of sexual function at three times in the two groups of vaginal delivery and cesarean section.

Sexual function	NVD Mean ± SD	C/S Mean ± SD	p- value
Third trimester	31.13 ± 2.16	31.75 ± 2.28	0.19*
8th week	22.86 ± 10.55	22.05 ± 10.30	0.55**
12th week	28.4 ± 5.8	28.05 ± 5.93	0.78*
*Independent T Test, p<0.05 considered as statistically significant **Mann-Whitney, p<0.05 considered as statistically significant			

Table 4: Relationship between serum Leptin and Adiponectin levels and sexual function at three times in the two groups of vaginal delivery and cesarean section.

Serum level	Sexual function	NVD P-value r		CS P-value r	
Leptin	Third trimester	0.817	-0.35	0.274	0.166
	8th week postpartum	0.292	0.160	0.729	-0.053
	12th week postpartum	0.111	0.241	0.182	0.203
Adiponectin	Third trimester	0.081	-0.263	0.266	-0.169
	8th week postpartum	0.261	-0.171	0.127	0.231
	12th week postpartum	0.014	-0.362	0.404	0.128
Leptin-to-Adiponectin ratio	Third trimester	0.511	0.101	0.21	0.191
	8th week postpartum	0.46	0.113	0.78	-0.043
	12th week postpartum	0.106	0.244	0.714	0.056

The results showed that only serum levels of leptin were significantly related to the type of delivery, so that the amount of leptin in women who performed normal delivery was 1.2 times higher than women who had cesarean delivery (Table 5). ROC curve analysis showed that serum Leptin level could predict about 71% of sexual function in women in the 12 weeks postpartum (Area Under Roc = 0.769 p <0.001, 95% CI: 0.671- 0.867) (Figure 2).

Table 5: Prediction of serum levels of hormones and sexual performance at different times in two groups of vaginal delivery and elective cesarean section.

	Odds Ratio	p-value	CI 95%	
			Lower	Upper
SF- Third trimester	.899	0.369	0.711	1.135
SF- 8th week	1.013	0.675	0.955	1.074
SF- 12th week	0.975	0.633	0.881	1.080
Adiponectin	1.036	0.106	0.992	1.098
Leptin	1.201	< 0.001	1.098	1.314
SF: Sexual Function				

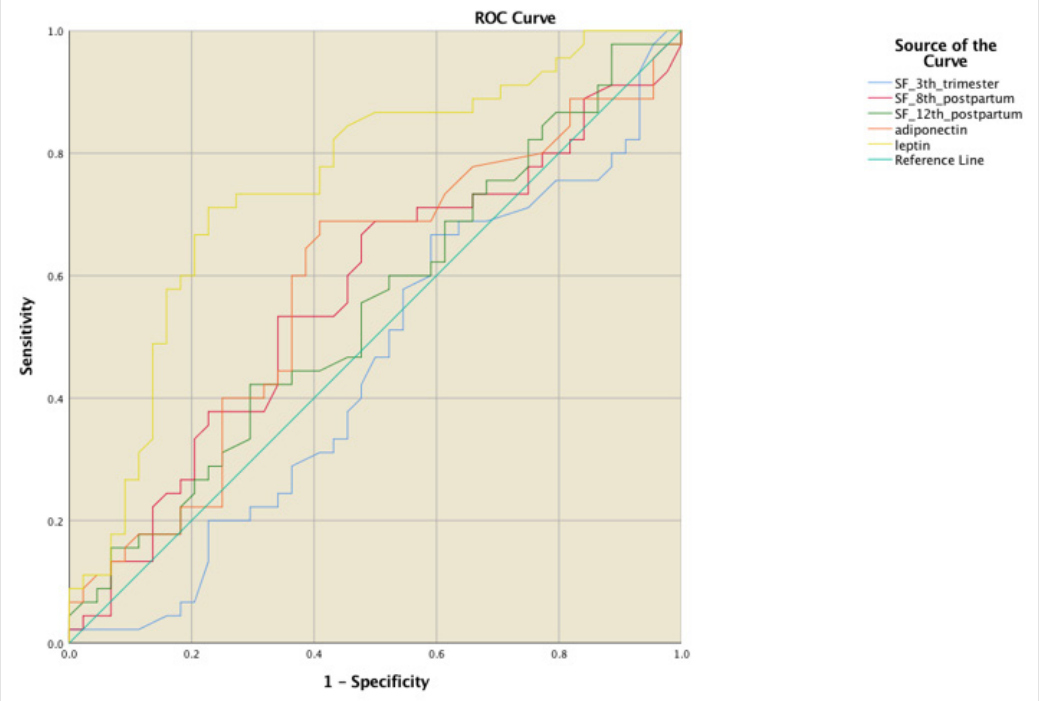

Figure 2: ROC curve to display serum levels of leptin and adiponctin and sexual function at different times in two types of vaginal delivery and cesarean section.

Discussion

This study aimed to evaluate the role of serum levels of adiponectin and leptin in sexual function in two types of NVD and CS. To the authors' knowledge, the number of studies comparing the relationship between sexual function and serum levels of Leptin and Adiponectin with the delivery type is very low or even non-existent. In the present study, in the CS group, the samples had higher age, pregnancies, and deliveries. The results of some studies are in line with those of our research [18,19]. However, Lurie, et al. [20] have provided contradictory results in this regard [20]. This heterogeneity can be justified according to the country's health policy on reducing the number of CS and avoiding performing CS without indication, especially in moth-

ers who are in their first pregnancy. Most repeated cesarean sections are performed in multiparous pregnant women. Also, in the present study, primiparous and multiparous women have participated as well. In contrast, the participants of other studies included only primiparous women, which may explain the heterogeneity of the two groups in our study. The results of the present study showed that there was no significant relationship between sexual function and delivery type. The results of Baghdadi, et al. and Lurie, et al. [20] are in line with the present study results [18,20]. A systematic review to discover the effect of delivery and postpartum factors on postpartum sexual function concluded that the delivery mode had no significant short- or long-term impact on postpartum sexual function [21].

However, in the survey conducted by Kahramanoglu, et al. [9] and Moghadam, et al. [22] sexual function was lower in the vaginal delivery group than CS group [9,22]. On the other hand, Moghimi, et al. [23] showed that women with vaginal delivery had higher sexual function than those with cesarean delivery [23]. In general, there seems to be a disagreement between various studies about the effect of delivery mode on sexual function. Postpartum women's sexual activity may be influenced by socio-cultural differences that lead to diverse outcomes. Also, other factors affecting postpartum sexual function include body dissatisfaction, physical discomfort, decreased physical ability, vaginal dryness, incompatibility with the maternal role, disorders in sleep patterns, fatigue, and lack of privacy due to the child's presence [9,20,21]. Since the postpartum questionnaire has not been developed yet and the factors mentioned in the sexual function questionnaires are not explicitly examined, it seems logical to attribute the discrepancies in the results of different studies to this cause. This study showed a statistically significant difference between sexual function at different times in NVD and CS. Thus, in both delivery types, at the 8th week, a statistically significant decrease in sexual function was observed. In line with our study, Samuel Lurie et al. showed that the sexual function had the lowest score at week 6 postpartum; also, as the postpartum period proceeded, the sexual function score increased [20].

Banaei, et al. [24] stated that the highest dysfunction rate occurs in the first two months postpartum, and the rate of dysfunction gradually decreases [24]. Also, according to Kahramanoglu, et al. [9] in both groups, NVD and the CS had increased sexual function scores over time [9]. Early in the postpartum period, fear and pain of episiotomy and scar CS reduces libido, arousal, and moisture, leading to decreased sexual function [21]. Also, maternal fatigue, stress, and sleep disturbance decreased libido [24]. However, over time, by being accustomed to their role as mothers, they can balance between sexual activity and the child's sleep. The present study results showed that serum leptin in the NVD group was significantly higher than CS group. The results of Hajimirzaie, et al [7,13]. are consistent with those of the present study [7,13,25]. However, in the study of Faghani Aghoozi, et al. [26] the leptin level in the two groups was not different [26]. The higher serum leptin level in NVD can be explained by the delivery stage. In this respect, a hypoxic condition develops during labor following uterine contractions and increases leptin secretion. Also, during NVD, the fetus is exposed to stress and stress hormones such as cortisol. some studies have shown the increase in leptin levels in a dose-dependent manner with cortisol. The mother's need for energy also increases during labor because of active uterine contractions.

Since fetal energy metabolism may also be affected during labor, it seems logical that placental leptin plays an important role in maternal and fetal energy metabolism during labor. Furthermore, stimulation of the sympathetic system during labor may increase maternal serum leptin levels [7]. The present study results also showed that the adiponectin level in the NVD group was higher than in the CS group, although this relationship was not statistically significant. Consistent with our study, Rebelo et al. and Fazeli Daryasari, et al. [27] showed that serum adiponectin levels in NVD were higher than CS [4,27]. In this regard, Logan, et al. [28] stated that the lowest adiponectin was an elective CS [28]. Delivery, regardless of its type, is an inflammatory process. But some studies have shown that CS is more inflammatory than NVD. In addition, CS can be considered the source of "long-term" inflammation. C-Reactive Protein (CRP) is a reactive protein inflammatory marker in clinical practice often used as a screening test for inflammation. Since plasma CRP levels are negatively correlated with plasma adiponectin levels [6,29], in CS, adiponectin levels may be lower than in NVD. The present study showed an inverse relationship between adiponectin and sexual function at week 12 after vaginal delivery. Although we did not find a study investigating these two variables, Parvanevar, et al. examining the relationship between marital satisfaction and adiponectin, reported the lack of any significant relationship between these two variables [25].

In the present study, women in the NVD group had a lower age and number of deliveries. Therefore, the amount of body fat in these women may be lower than in the CS group. It is generally accepted that adiponectin, unlike other adipose-related cytokines, is negatively correlated with body fat percentage [9]. Adiponectin levels appear to depend on body fat distribution, which is strongly influenced by sex hormones. Thus, some studies have shown an inverse relationship between androgens and plasma adiponectin levels [29]. Testosterone (T) modulates critical biochemical signaling pathways directly, either by converting it to the more potent metabolite 5α-dihydrotestosterone (5α-DHT) or by aromatization to estradiol (E2). Some studies have suggested the inhibitory role of estrogen in adiponectin secretion [30]. As a result, the inverse relationship of adiponectin with sexual function can be explained by the inverse effect of estrogen and androgen with adiponectin and their impact on sexual function.

Limitation

The study's main limitation is the small sample size in each group, making it difficult to generalize the study results. Also, due to financial problems, we could not measure the rest of the effective hormones such as CRP, testosterone, estrogen, etc.

Conclusion

The present study results showed that serum levels of Adiponectin and Leptin were higher in NVD, although there was a significant relationship only between leptin and the delivery type. On the other hand, there was no significant relationship between the hormone level of leptin and adiponectin with sexual function (except in week 12 postpartum). Overall, regarding the wide effects of leptin and adiponectin on the physiology and pathophysiology of pregnancy, neonatal and maternal outcomes, NVD is recommended as the preferred method. Besides, we concluded lack of any significant relationship between the delivery type and sexual function. It should be noted that the results of various studies on sexual function and type of delivery are contradictory, which may be due to the lack of a specific questionnaire on the sexual function of Postpartum.

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Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

All authors have fulfilled all three conditions (substantial contributions to the concept and design, the execution of the work, or the analysis and interpretation of data; drafting or revising the manuscript; and final approval of the manuscript at the time of submission).

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None.

Availability of Data and Materials

The data sets generated and analyzed during this study are not publicly presented because of a desire to protect the participants' anonymity; they are, however, available from the corresponding author on advisable request.

Ethics Approval and Consent to Participate

The present study was originated from the Ph.D. thesis of the first author at the Department of Reproductive Health. Before data collection, ethical approval was obtained from the Research Committee of the Faculty of Medical science, Tarbiat Modares University, Tehran, Iran. The ethics code number is IR.MODARES.REC.1397.013. The present study only involved persons who gave their informed consent. For this, verbal informed consent was obtained from all participants before the start of the study. All participants completed informed written consent after being informed about the objectives of the interview. Participants were reassured that the information was confidential and anonymous; they were guaranteed that all records files would be deleted after completing the study. Also, Participants were convinced that they could leave the study at any time without being reprimanded or losing benefits in this study.

Consent for Publication

Not applicable.

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