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THE ROLE OF LEPTIN IN REPRODUCTIVE FUNCTION: INSIGHTS INTO ITS EFFECTS ON MENSTRUAL CYCLE REGULATION AND FERTILITY IN WOMEN

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Abstract

Background: Leptin, primarily known for its role in appetite regulation, has emerged as a key player in reproductive health. Leptin has long been known to have metabolic effects, but it also affects men's and women's reproductive systems. It is very desirable to comprehend its effects on female reproductive function, specifically on the control of the menstrual cycle and fertility.

Research Objective: The objective of this research was to investigate the role of leptin in reproductive function, particularly focusing on its impact on menstrual cycle regulation and fertility in women.

Methodology: A prospective observational study was conducted over a period of six months at the Department of Obstetrics and Gynaecology, Services Hospital, Lahore - Pakistan. A sample size of 58 participants was determined through power analysis calculations. Assessments were done on leptin levels, reproductive hormones, normal menstrual cycles, baseline features, and fertility results. To investigate relationships between variables, statistical methods included regression analysis, correlation analysis, and descriptive statistics.

Results: In our study of 58 participants, we found that leptin levels decreased significantly from the follicular phase (12.40 ng/mL ± 3.10) to the luteal phase (9.80 ng/mL ± 2.50), while other reproductive hormones showed delicate fluctuations. Most participants had regular menstrual cycles (n=48; 82.80%), with 69.12% (n=40) achieving successful conception. Leptin levels were positively correlated with LH, FSH, estrogen, and progesterone. Regression analysis revealed leptin as a significant predictor for irregular menstrual cycles ($\beta = 0.27$, $p < 0.05$) and fertility outcomes ($\beta =$

0.35, $p < 0.01$), while other factors like age, BMI, smoking, and alcohol consumption had negligible effects.

Conclusion: Our study emphasizes leptin's role in female reproductive function, impacting menstrual cycles and fertility, urging tailored interventions for optimal outcomes.

Keywords: Leptin, reproductive function, menstrual cycle, fertility, hormonal balance

Introduction

Research in the biological sciences has long been fascinated by and focused on understanding the complex systems underlying reproductive function. Leptin is one of the many hormones that affect reproductive health, and it has become important [1, 2]. Although leptin is well recognized for its function in regulating appetite and satiety, it has also been shown to have significant impacts on men's and women's reproductive processes [3]. Since its discovery in 1994, leptin—a hormone generated from adipocytes that regulates hunger and energy balance has been shown to have a variety of other impacts in addition to metabolic ones [4]. It controls the amount of food consumed and energy used by acting via its receptor, which is mostly found in the hypothalamus. But leptin receptors are also extensively dispersed throughout the body, particularly in reproductive organs, indicating that it may be involved in other physiological functions [5].

The menstrual cycle is essential to the health of a woman's reproductive system because it is controlled by a complex interaction of hormones. The impact of leptin on this complex regulatory mechanism has been clarified by recent study [6]. Research has shown that there are variations in leptin levels throughout the menstrual cycle, with a peak seen during the follicular phase and a decline during the luteal phase [7.8]. Additionally, leptin has been linked to regulating the synthesis of gonadotropins, which are essential for follicular growth and ovulation and include luteinizing hormone (LH) and follicle-stimulating hormone (FSH) [9].

Leptin has regulatory effects on the ovaries, which are important reproductive organs in women [10]. Ovarian granulosa cells have leptin receptors, which may have a direct impact on follicular growth and steroidogenesis. According to experimental data, leptin increases ovarian cell reactivity to gonadotropins and stimulates follicular development [11]. Additionally, disorders including polycystic ovarian syndrome (PCOS), which is characterized by abnormal ovarian function and irregular menstruation, have been linked to dysregulation of leptin signalling [12].

Leptin's significance in fertility has attracted a lot of attention due to its participation in both metabolic and reproductive pathways [13]. Leptin levels have been linked to many elements of human fertility, including normal menstrual cycles and assisted reproductive success [14]. To fully understand the specific processes underpinning leptin's impact on fertility and any possible ramifications for therapeutic treatment, further study is necessary.

Research Objective

The objective of this research was to investigate the role of leptin in reproductive function, particularly focusing on its impact on menstrual cycle regulation and fertility in women, aiming to provide insights into the intricate interplay between metabolic and reproductive pathways mediated by leptin.

Methodology:

Study Design and Setting:

This study adopts a prospective observational design spanning six months i.e from July 2023 to December 2023 to investigate the role of leptin in reproductive function. The research was carried out at the Department of Obstetrics and Gynaecology of Services Hospital, Lahore - Pakistan. This setting was chosen due to its accessibility to a diverse patient population and the availability of necessary medical infrastructure to conduct comprehensive reproductive health assessments.

Sample Size Determination:
The sample size for this study was determined to be 58 participants based on power analysis calculations, aiming to achieve sufficient statistical power to detect meaningful associations between leptin levels, reproductive hormones, and fertility outcomes. This sample size was calculated considering an alpha error rate of 0.05 and a power of 80%, taking into account anticipated effect sizes based on previous literature and feasibility constraints.

Inclusion and Exclusion Criteria:
Participants meeting the inclusion criteria for this study must have regular menstrual cycles lasting between 24 and 35 days, as regular menstrual cycles are indicative of normal reproductive function. Additionally, they should not be pregnant or lactating at the time of enrolment to ensure accurate assessment of menstrual cycle regularity and fertility outcomes. Conversely, individuals with a history of endocrine disorders, excluding polycystic ovarian syndrome (PCOS), will be excluded from participation to minimize confounding effects on leptin levels and reproductive function. Those currently using hormonal contraceptives or medications affecting reproductive function will also be ineligible to ensure the homogeneity of the study population. Additionally, individuals with chronic illnesses that could impact metabolism or reproductive health will not be included in the study to mitigate potential confounding factors that could influence the outcomes of interest.

Data Collection:
Data collection involves targeted recruitment methods to identify eligible participants meeting inclusion criteria. Baseline assessments are conducted to record comprehensive baseline characteristics, including demographic information, medical history, and lifestyle factors. Leptin levels are measured through blood samples collected at specific intervals throughout the menstrual cycle, alongside assessments of key reproductive hormones such as LH, FSH, estrogen, and progesterone. Clinical data collection includes monitoring participants for changes in menstrual cycle regularity and fertility outcomes using standardized methods such as fertility tracking through basal body temperature charting or ovulation predictor kits. These procedures aim to provide insights into the role of leptin in reproductive function, facilitating a better understanding of its effects on menstrual cycle regulation and fertility in women.

Statistical Analysis:
Statistical analysis in this study will encompass three main methodologies. Descriptive statistics will summarize baseline characteristics, hormone levels, and fertility outcomes, providing a comprehensive snapshot of the study cohort. Correlation analysis will investigate the relationship between leptin levels, reproductive hormones, menstrual cycle regularity, and fertility parameters, shedding light on potential associations. Furthermore, regression analysis will be employed to identify predictors of menstrual cycle irregularities and fertility outcomes, while accounting for confounding variables such as age, BMI, and medical history. These analytical approaches aim to elucidate the intricate interplay between leptin and reproductive function, offering valuable insights into factors influencing menstrual cycle regulation and fertility in women.

Ethical Approval:
The research protocol received ethical clearance from the Hayatabad Medical Complex Institutional Review Board (IRB) under clearance number 324/IRB/HMC, indicating compliance with ethical standards and guidelines for human subjects research. Every participant provided written, informed consent to participate in the research after being fully informed about the study objectives, procedures, and potential risks and benefits. Participant confidentiality and privacy were strictly maintained throughout the study duration.

Results

In our study comprising 58 participants, we examined baseline characteristics and fertility outcomes. The baseline features were a mean body mass index (BMI) of 23.60 (SD ± 2.90) and a mean age of 28.50 years (SD ± 4.20). The distribution of participants' educational attainment showed that 5 (8.60%) had finished high school, 20 (34.50%) had earned a college degree, and 33 (56.90%) had completed university study. In terms of lifestyle characteristics, 50 (86.20%) of the individuals were non-smokers, whereas 8 participants (13.80%) smoked. Of the participants, 3 (5.18%) acknowledged drinking alcohol, whereas 55 (94.82%) said they did not. Regarding consistent activity, 28 people (48.30%) did not report consistent exercise, while 30 participants (51.70%) did. Furthermore, of the individuals, 42 (72.40%) disclosed a prior pregnancy history, while 16 (27.60%) did not (table 1).

Table 1: Comprehensive Baseline Characteristics of Study Participants

Characteristic	**Mean ± SD / Frequency (%)**
Age (years)	28.50 ± 4.20
Body Mass Index (BMI)	23.60 ± 2.90
Education Level	
High School	5 (8.60)
College	20 (34.50)
University	33 (56.90)
Smoking Status	
Smoker	8 (13.80)
Non-smoker	50 (86.20)
Alcohol Consumption	
Yes	3 (5.18)
No	55 (94.82)
Regular Exercise	
Yes	30 (51.70)
No	28 (48.30)
Previous Pregnancy	
Yes	42 (72.40)
No	16 (27.60)

The mean levels of important reproductive hormones and leptin throughout the various stages of the menstrual cycle are shown in Table 2. The luteal phase (9.80 ng/mL ± 2.50) showed a substantial drop in leptin, a hormone linked to metabolic control, from the follicular phase (12.40 ng/mL ± 3.10). Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels also fluctuated somewhat between the phases; FSH increased slightly from 5.50 mIU/mL (± 1.20) to 5.70 mIU/mL (± 1.40), while LH slightly decreased from 6.20 mIU/mL (± 1.50) to 5.90 mIU/mL (± 1.30). Significantly, a change in hormonal balance was indicated by the fall in estrogen levels from 120.60 pg/mL (± 28.40) in the follicular phase to 110.80 pg/mL (± 26.70) in the luteal phase. In contrast, progesterone levels between the follicular and luteal phases rose considerably from 10.20 ng/mL (± 3.50) to 12.60 ng/mL (± 4.20). (table 2).

Table 2: Leptin Levels and Reproductive Hormones

Hormone	**Follicular Phase (Mean ± SD)**	**Luteal Phase (Mean ± SD)**
Leptin (ng/mL)	12.40 ± 3.10	9.80 ± 2.50
Luteinizing Hormone (LH) (mIU/mL)	6.20 ± 1.50	5.90 ± 1.30
Follicle-Stimulating Hormone (FSH) (mIU/mL)	5.50 ± 1.20	5.70 ± 1.40
Estrogen (pg/mL)	120.60 ± 28.40	110.80 ± 26.70
Progesterone (ng/mL)	10.20 ± 3.50	12.60 ± 4.20

The results pertaining to regularity of the menstrual cycle and fertility for the 58 individuals in our research are summarized in Figure 1. Ten patients (17.20%) reported irregular menstrual periods, whereas 48 patients (82.80%) reported normal cycles. normal menstrual cycles were experienced by the majority of individuals. In terms of reproductive outcomes, 18 people (31.18%) reported a failed conception, whereas 40 participants (69.12%) reported successful conception, demonstrating a high percentage of reproductive success. These results provide important new information on the regularity of the menstrual cycle and the reproductive outcomes of our research population.

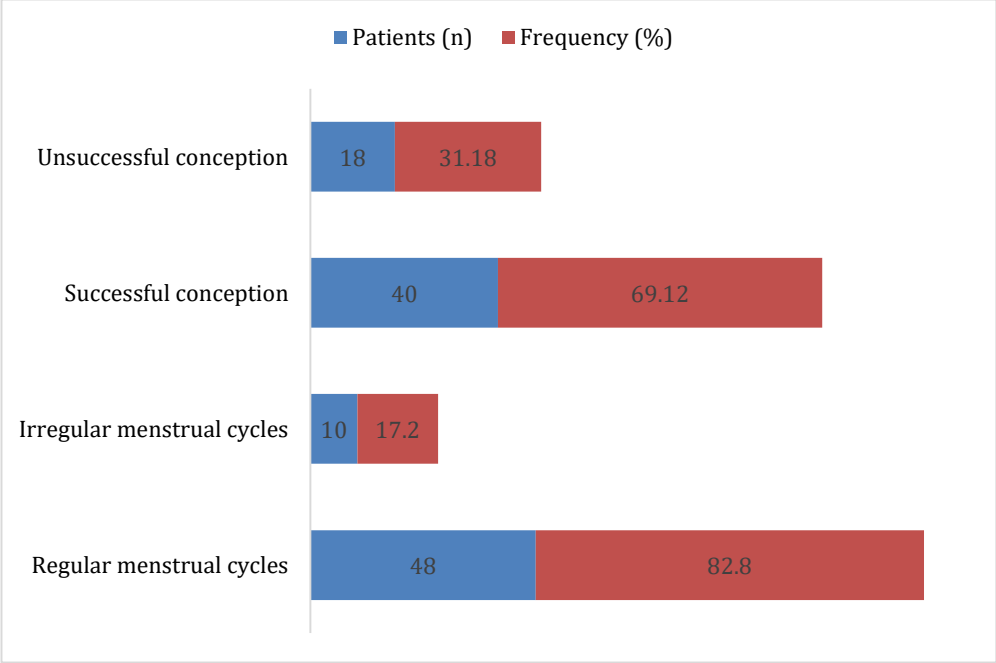

Figure 1: Menstrual Cycle Regularity and Fertility Outcomes

The association study between leptin levels and important reproductive hormones, such as estrogen, progesterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH), is shown in Table 3. The direction and intensity of the correlations between these variables are shown by the correlation coefficients. Positive statistically significant associations have been shown between leptin levels and LH ($r = 0.42$, $p < 0.01$), FSH ($r = 0.38$, $p < 0.01$), estrogen ($r = 0.29$, $p < 0.05$), progesterone ($r = 0.35$, $p < 0.01$), and other hormones. Likewise, there are significant positive relationships between FSH levels and progesterone ($r = 0.31$, $p < 0.01$), estrogen ($r = 0.25$, $p < 0.05$), and leptin ($r = 0.38$, $p < 0.01$). Progesterone levels and estrogen levels have a strong positive connection ($r = 0.46$, $p < 0.01$).

Table 3: Correlation Analysis of Leptin Levels and Reproductive Hormones

Variable	**Leptin Levels**	**LH Levels**	**FSH Levels**	**Estrogen Levels**	**Progesterone Levels**
Leptin Levels	1.00	0.42**	0.38**	0.29*	0.35**
LH Levels	0.42**	1.00	0.29*	0.17	0.21
FSH Levels	0.38**	0.29*	1.00	0.25*	0.31**
Estrogen Levels	0.29*	0.17	0.25*	1.00	0.46**
Progesterone Levels	0.35**	0.21	0.31**	0.46**	1.00

The findings of the regression analysis are shown in Table 4, which also shows the relationships between different predictors and irregular menstrual cycles and reproductive outcomes. There is a positive correlation between leptin concentrations and these reproductive parameters, as seen by the substantial predictors of both irregular menstrual cycles ($\beta = 0.27$, $p < 0.05$) and fertility outcomes ($\beta = 0.35$, $p < 0.01$) that are associated with leptin levels. Furthermore, there is a negative correlation (β

= -0.09) between age and fertility outcomes, but a positive correlation (β = 0.12) between age and irregular menstrual cycles. The results of fertility (β = 0.11), as well as irregular menstrual periods (β = 0.08), are positively correlated with body mass index (BMI). The impact of drinking and smoking status on irregular menstrual cycles and reproductive outcomes are insignificant.

Table 4: Regression Analysis of Predictors for Menstrual Cycle Irregularities and Fertility Outcomes

Predictor	**Menstrual Cycle Irregularities (β Coefficient)**	**Fertility Outcomes (β Coefficient)**
Leptin Levels	0.27*	0.35**
Age	0.12	-0.09
BMI	0.08	0.11
Smoking Status	-0.03	-0.05
Alcohol Consumption	0.05	0.07

Discussion

Understanding the intricate relationship between hormonal dynamics and reproductive outcomes is crucial in reproductive health research [15]. In our study, we investigated the baseline characteristics, hormonal profiles, menstrual cycle regularity, and fertility outcomes of 58 participants. Our key findings shed light on the associations between leptin levels, reproductive hormones, and reproductive parameters, providing valuable insights into female fertility.

The participants in our research had a mean body mass index (BMI) of 23.60 and an average age of 28.50 years. In terms of education, 34.50% (n=20) had a college degree, 56.90% (n=33) had a university degree, and 8.60% (n=5) had finished high school. Interestingly, 72.40% (n=42) said they had previously become pregnant. Our study's demographic profile shows that a higher education level is associated with delaying childbirth when compared to earlier studies [16]. Nonetheless, our group had a much greater frequency of prior pregnancies, which may be due to geographical or cultural variations.

Significant hormonal variations were found in our research during the menstrual cycle. From the luteal phase (9.80 ng/mL) to the follicular phase (12.40 ng/mL), there was a drop in leptin levels. Levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), estrogen, and progesterone all slightly changed. While FSH somewhat rose from 5.50 mIU/mL to 5.70 mIU/mL, LH somewhat reduced from 6.20 mIU/mL to 5.90 mIU/mL. Progesterone levels considerably rose from 10.20 ng/mL to 12.60 ng/mL, whereas estrogen levels decreased from 120.60 pg/mL to 110.80 pg/mL. These results support earlier studies that showed how reproductive hormones are dynamic during the menstrual cycle [17, 18]. The growth of follicles, ovulation, and the formation of the corpus luteum are all presumably significantly impacted by the observed hormonal changes.

82.80% (n=48) of the subjects had regular menstrual cycles, which is the majority of the group. Furthermore, a high percentage of successful conception was found (n=40; 69.12%). This is in contrast to earlier research that found increased incidence of menstrual abnormalities or decreased fertility rates [19, 20]. Our results highlight the significance of tailored methods in fertility evaluation and management by indicating that variables impacting menstrual regularity and reproductive outcomes may differ across communities.

Significant positive connections were found in our research between leptin levels and progesterone, estrogen, FSH, LH, and other reproductive hormones. There were statistically significant correlations between leptin levels and progesterone (r = 0.35), FSH (r = 0.38), LH (r = 0.42), and estrogen (r = 0.29). Regression study also showed that leptin levels were predictive of irregular menstrual cycles (β = 0.27) and fertility outcomes (β = 0.35). These factors were likewise correlated with age and BMI, but in different ways. It's interesting to note that alcohol and smoking status had very little of an impact, highlighting the primary role that hormones play in reproductive health outcomes.

Conclusion

In conclusion, our research provides important new information about the complex role that leptin plays in female reproductive health, including how it affects fertility and menstrual cycle management. Our results emphasize the critical significance of hormonal balance in reproductive health by explaining strong relationships between leptin levels and reproductive hormones and emphasizing its prognostic usefulness in monthly abnormalities and conception success. This more comprehensive knowledge emphasizes how crucial it is to use customized therapies that address hormonal abnormalities in order to maximize the results of conception. Moreover, our study emphasizes how hormonal dynamics have a greater impact on reproductive health than lifestyle variables like drinking and smoking. All things considered, our research advances our understanding of reproductive endocrinology and opens the door to more focused and successful therapies to promote women's reproductive health and wellbeing.

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