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ORIGINAL ARTICLE

Impact of Obesity on Female Reproductive Hormones and Ovulatory Function. A Clinical and Biochemical Evaluation of Endocrine Disruption in Women of Reproductive Age

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ABSTRACT

Background: Obesity is a global health concern that significantly affects female reproductive health. It is strongly associated with hormonal imbalances and ovulatory dysfunction, which may compromise fertility. The present study clinically and biochemically evaluates the impact of obesity on female reproductive hormones and ovulatory patterns in women of reproductive age.

Objective: To assess the endocrine disruption and ovulatory dysfunction associated with obesity in reproductive-aged women through clinical and biochemical evaluation.

Methodology: This cross-sectional clinical study was conducted over six months (January–June 2023) at the Department of Gynecology and Reproductive Endocrinology, Bolan Medical University Hospital, Quetta, and Mayo Hospital, Lahore, Pakistan. A total of 100 women aged 20 to 45 years were enrolled and categorized into obese (BMI ≥30 kg/m²) and non-obese (BMI <30 kg/m²) groups. Clinical data regarding menstrual regularity, ovulation history, and signs of hyperandrogenism were recorded. Biochemical parameters including serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol (E2), progesterone, total testosterone, fasting insulin, and glucose were measured during the early follicular phase. Ovulatory function was evaluated using mid-luteal serum progesterone levels.

Results: Obese women showed a significantly higher incidence of menstrual irregularities and anovulation compared to non-obese women ($p<0.05$). Serum LH/FSH ratio and total testosterone levels were significantly elevated, while mid-luteal progesterone levels were reduced in obese participants ($p<0.01$). A strong correlation was observed between increased BMI and insulin resistance markers, suggesting an interplay between metabolic and reproductive hormonal disturbances.

Conclusion: Obesity in reproductive-aged women is strongly associated with endocrine disruption, particularly involving altered gonadotropin ratios, hyperandrogenism, and ovulatory dysfunction. These findings underscore the need for early screening and weight management strategies to restore reproductive hormonal balance and improve fertility outcomes in obese women.

Keywords: Obesity, Female Reproductive Hormones, Ovulatory Dysfunction, Endocrine Disruption, Infertility, BMI, Hyperandrogenism, Insulin Resistance.

INTRODUCTION

Obesity is a multifactorial chronic disorder characterized by excessive accumulation of adipose tissue and is recognized as one of the leading public health concerns worldwide. The global prevalence of obesity has more than doubled in the past four decades, affecting individuals across all age groups, including women of reproductive age[1]. In females, obesity not only contributes to systemic metabolic complications such as type 2 diabetes mellitus, hypertension, and cardiovascular disease, but also exerts profound effects on reproductive health. Increasing evidence suggests that obesity disrupts the hypothalamic-pituitary-ovarian (HPO) axis, leading to significant hormonal imbalances, menstrual irregularities, and ovulatory dysfunction, thereby compromising fertility potential[2].

In reproductive-aged women, normal ovulatory cycles depend on the precise coordination of gonadotropin-releasing hormone (GnRH) from the hypothalamus, luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the anterior pituitary, and estrogen and progesterone production from the ovaries[3]. Excess adiposity is known to interfere with this finely tuned hormonal cascade. Adipose tissue functions as an active endocrine organ that secretes various adipokines, inflammatory cytokines, and enzymes involved in steroid metabolism, such as aromatase. These factors collectively contribute to an altered hormonal milieu that includes elevated estrogen levels, insulin resistance, and increased androgen production—hallmarks of endocrine disruption seen in obese women[4].

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Furthermore, obesity-induced hyperinsulinemia can potentiate ovarian androgen synthesis and impair hepatic production of sex hormone-binding globulin (SHBG), leading to increased circulating levels of free androgens[5]. This hyperandrogenic environment contributes to follicular arrest, anovulation, and polycystic ovarian morphology. Additionally, central obesity is associated with chronic low-grade inflammation and leptin resistance, which further impair hypothalamic sensitivity to hormonal feedback, ultimately affecting the menstrual cycle and ovulatory function[6].

Several clinical studies have reported higher rates of infertility, delayed conception, spontaneous miscarriage, and poor outcomes in assisted reproductive technologies among obese women. However, there remains a need for comprehensive regional data that correlates obesity with specific hormonal alterations and ovulatory status among reproductive-aged women in local populations[7].

The aims of this study were to fill this gap by conducting a detailed clinical and biochemical evaluation of reproductive hormones and ovulatory function among obese and non-obese women aged 20 to 45 years[8]. By investigating the association between obesity and endocrine parameters such as LH, FSH, estradiol, progesterone, testosterone, insulin, and glucose levels, this research seeks to highlight the mechanisms through which obesity interferes with reproductive health. Understanding these associations is crucial for the development of targeted interventions to restore hormonal balance and improve fertility outcomes in obese women[9].

MATERIALS AND METHODS

Study Design: This study was a cross-sectional, clinical, and biochemical investigation conducted at the Department of Gynecology and Reproductive Endocrinology at Bolan Medical University Hospital, Quetta, and Mayo Hospital, Lahore, Pakistan. The study was carried out over a period of six months, from January 2023 to June 2023. Ethical approval was obtained from the institutional review board, and written informed consent was collected from all participants before enrollment.

Study Population: A total of 100 women aged between 20 and 45 years were recruited from the outpatient gynecology clinic. Inclusion criteria were: (1) reproductive-aged females (20–45 years), (2) not currently pregnant or lactating, (3) no use of hormonal contraception or ovulation induction drugs in the last 3 months, and (4) regular or irregular menstrual cycles for at least six months prior to participation. Exclusion criteria included women with known endocrine disorders (e.g., thyroid dysfunction, hyperprolactinemia, Cushing's syndrome), polycystic ovary syndrome diagnosed per Rotterdam criteria, history of ovarian surgery, or any chronic illness such as diabetes mellitus or liver disease.

Anthropometric Assessment: Each participant underwent a standardized physical examination. Body weight was measured in kilograms using a digital scale, and height was recorded in centimeters. Body Mass Index (BMI) was calculated as weight (kg) divided by height (m²). Based on BMI, participants were divided into two groups:

- **Obese Group:** BMI ≥30 kg/m²
- **Non-Obese Group:** BMI <30 kg/m²

Clinical Evaluation: A detailed menstrual and reproductive history was obtained, including cycle regularity, cycle length, and any symptoms suggestive of anovulation (e.g., amenorrhea, oligomenorrhea). Clinical signs of hyperandrogenism such as hirsutism, acne, and alopecia were noted. Ovulatory status was determined based on mid-luteal serum progesterone levels (days 21–23 in a 28-day cycle), with levels <5 ng/mL suggestive of anovulation.

Biochemical Analysis: Venous blood samples were collected in the early follicular phase (days 2–5 of the menstrual cycle) after an overnight fast of at least 10 hours. The following hormones and biochemical markers were measured using standard enzyme-linked immunosorbent assay (ELISA) and chemiluminescent immunoassay (CLIA) techniques:

- Luteinizing Hormone (LH)
- Follicle-Stimulating Hormone (FSH)
- Estradiol (E2)
- Total Testosterone
- Progesterone (mid-luteal)
- Fasting Insulin
- Fasting Blood Glucose

The LH/FSH ratio was calculated for each participant. Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was also calculated using the formula: HOMA-IR = (Fasting Insulin (μU/mL) × Fasting Glucose (mg/dL)) / 405

Statistical Analysis: Data were analyzed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Independent sample t-tests were used to compare means between obese and non-obese groups. Chi-square tests were used for categorical variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 100 women between the ages of 20 and 45 years participated in this study. Among them, 50 women were classified as obese (BMI ≥30 kg/m²) and 50 as non-obese (BMI <30 kg/m²). The mean age in the obese group was 32.8 ± 5.9 years, and in the non-obese group, it was 31.4 ± 6.2 years, with no significant difference between the groups (p=0.26). Table- 1 summarizes the demographic and clinical features of the study population. Obese women had significantly higher BMI and a greater frequency of menstrual irregularities (76% vs. 24%, p<0.001). Clinical signs of hyperandrogenism (acne, hirsutism) were more common in the obese group.

Table 1: Demographic and Clinical Characteristics of the Study Population (n = 100)

Parameter	Obese Group (n = 50)	Non-Obese Group (n = 50)	p-value
Mean Age (years)	32.8 ± 5.9	31.4 ± 6.2	0.26 (NS)
Mean BMI (kg/m²)	33.7 ± 2.9	24.3 ± 1.7	<0.001
Menstrual Irregularity (%)	38 (76%)	12 (24%)	<0.001
Clinical Hyperandrogenism (%)	30 (60%)	8 (16%)	<0.001
Mean Cycle Length (days)	38.6 ± 10.1	30.2 ± 3.9	<0.001
History of Anovulation (%)	34 (68%)	10 (20%)	<0.001

Obese women had significantly higher serum LH, LH/FSH ratio, total testosterone, fasting insulin, and HOMA-IR levels (p<0.001). Mid-luteal progesterone levels, a marker of ovulation, were significantly lower in the obese group, indicating an increased rate of anovulation as shown in table 2.

Table 2: Hormonal and Biochemical Parameters

Parameter	Obese Group (n = 50)	Non-Obese Group (n = 50)	p-value
LH (mIU/mL)	10.8 ± 2.5	6.9 ± 1.8	<0.001
FSH (mIU/mL)	6.1 ± 1.4	6.3 ± 1.6	0.45 (NS)
LH/FSH Ratio	1.8 ± 0.4	1.1 ± 0.2	<0.001
Estradiol (pg/mL)	75.4 ± 15.7	82.3 ± 13.1	0.02
Total Testosterone (ng/dL)	72.5 ± 21.3	42.8 ± 12.9	<0.001
Mid-Luteal Progesterone (ng/mL)	4.2 ± 2.1	9.8 ± 3.5	<0.001
Fasting Insulin (μU/mL)	18.3 ± 5.6	9.7 ± 3.4	<0.001
Fasting Glucose (mg/dL)	96.2 ± 11.4	89.5 ± 10.2	0.01
HOMA-IR	4.4 ± 1.5	2.1 ± 0.9	<0.001

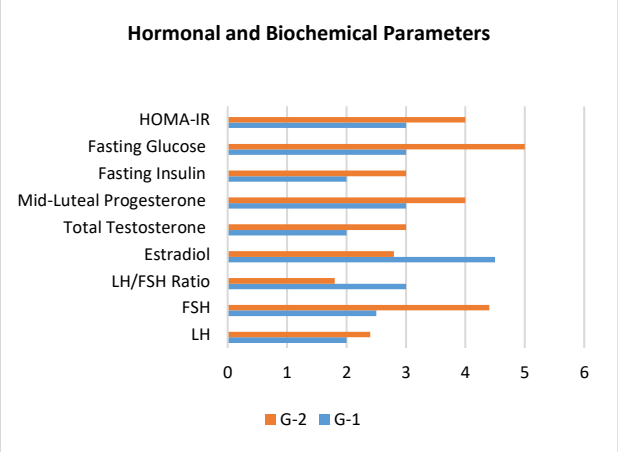

Figure 1: Comparison of Hormonal and Biochemical Parameters Between Obese (G-2) and Non-Obese (G-1) Women of Reproductive Age

The graphically results were highlighted in fig-1, marked hormonal and biochemical differences between obese and non-obese women. Obese participants exhibited significantly elevated luteinizing hormone (LH) levels and LH/FSH ratios, indicating disrupted hypothalamic-pituitary-ovarian axis function. Total testosterone was also markedly higher in the obese group, suggesting a hyperandrogenic state. In contrast, mid-luteal progesterone levels were substantially lower among obese women, reflecting impaired or absent ovulation. Additionally, fasting insulin and HOMA-IR values were significantly increased in the obese group, confirming the presence of insulin resistance,

while fasting glucose was mildly but significantly elevated. These changes collectively illustrate a clear biochemical pattern of endocrine disruption and ovulatory dysfunction in obese women of reproductive age.

These findings confirm a strong association between obesity and disruption of reproductive hormone profiles. The elevated LH/FSH ratio and total testosterone levels, alongside reduced progesterone and increased insulin resistance markers, suggest that obesity significantly impairs normal ovulatory function and contributes to a state of subclinical or overt reproductive endocrine dysfunction.

DISCUSSION

This study described clear evidence that obesity significantly disrupts female reproductive hormone profiles and ovulatory function in women of reproductive age. The findings demonstrate that obese women (BMI ≥30 kg/m²) are more likely to experience menstrual irregularities, clinical hyperandrogenism, and anovulation compared to their non-obese counterparts[10]. These clinical features are supported by biochemical alterations, including elevated LH levels, increased LH/FSH ratios, higher total testosterone, reduced mid-luteal progesterone, and significant insulin resistance all of which are consistent with an endocrine pattern associated with ovulatory dysfunction[11].

The elevated LH and LH/FSH ratio in obese participants suggests hypothalamic-pituitary dysregulation, which can impair follicular maturation and ovulation. This pattern is often seen in women with polycystic ovary syndrome (PCOS), yet our study excluded those diagnosed with PCOS to isolate the effects of obesity alone[12]. The increase in total testosterone levels further supports the presence of obesity-induced hyperandrogenism. Adipose tissue in obese individuals acts as an endocrine organ, producing adipokines and inflammatory mediators that disrupt the hypothalamic-pituitary-ovarian (HPO) axis. Additionally, excessive peripheral aromatization of androgens to estrogens in adipose tissue alters feedback mechanisms on the pituitary and hypothalamus, aggravating the hormonal imbalance[13].

Mid-luteal progesterone levels were significantly lower in the obese group, reflecting inadequate luteal function and confirming a higher prevalence of anovulatory cycles. Progesterone secretion depends on proper ovulation and corpus luteum formation, which are frequently compromised in the context of hormonal dysregulation[14]. Clinically, this is manifested by irregular menses and infertility, both of which were more common among obese women in our study. One of the most notable findings was the presence of marked insulin resistance among obese women, as shown by significantly elevated fasting insulin and HOMA-IR scores. Insulin resistance is a key metabolic disturbance that not only contributes to hyperinsulinemia but also synergistically increases ovarian androgen production and decreases hepatic synthesis of sex hormone-binding globulin (SHBG), resulting in higher levels of biologically active free testosterone. These hormonal shifts reinforce the cycle of anovulation and menstrual dysfunction[15].

These results were in agreement with multiple previous studies that have demonstrated the detrimental effects of obesity on female fertility. For example, research by Pasquali et al. and others has shown that obesity alone, even in the absence of PCOS, is associated with altered gonadotropin dynamics, hyperandrogenism, and impaired ovulation. Furthermore, insulin resistance and chronic inflammation in obese women create an unfavorable intra-ovarian environment for follicular development and oocyte quality[16]. This study added to the growing body of evidence highlighting the importance of weight management in women of reproductive age. Interventions targeting weight reduction, improved insulin sensitivity, and hormonal regulation may restore normal ovulatory cycles and improve fertility outcomes. Lifestyle modifications including dietary control, physical activity, and behavioral therapy remain the cornerstone of treatment. Pharmacological agents such as metformin may also be considered in selected cases to address underlying insulin resistance[17].

However, current study has some limitations. The cross-sectional design limits the ability to establish causal relationships. Additionally, more advanced assessments such as SHBG, anti-Müllerian hormone (AMH), and ultrasound-based ovarian morphology were not included. Despite these limitations, the strength of our study lies in its clear inclusion criteria, appropriate exclusion of PCOS and other confounding endocrine disorders, and comprehensive hormonal and clinical evaluation[18]. Finally, obesity exerts a profound negative impact on the female reproductive system by inducing hormonal imbalances, ovulatory dysfunction, and insulin resistance. These findings underscore the importance of early identification and management of obesity in women of reproductive age to prevent infertility and associated endocrine complications. Future longitudinal studies are warranted to further explore the reversibility of these hormonal disturbances following weight reduction and lifestyle intervention[19].

CONCLUSION

This study provides compelling clinical and biochemical evidence that obesity significantly disrupts reproductive hormonal balance and ovulatory function in women of reproductive age. Obese women demonstrated higher rates of menstrual irregularities, clinical hyperandrogenism, and anovulation, supported by elevated LH, LH/FSH ratios, total testosterone, fasting insulin, and HOMA-IR scores. Additionally, reduced mid-luteal progesterone levels highlight impaired ovulatory activity. These findings underscore the crucial interplay between metabolic and reproductive health and emphasize the need for early identification and intervention strategies, such as lifestyle modification and metabolic control, to improve fertility outcomes in obese women. Addressing obesity is not only essential for general health but also vital for preserving reproductive potential and hormonal homeostasis.

Availability of Data and Materials: The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing Interests: The authors declare that they have no competing interests.

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Authors' Contributions: HH and SI contributed to the conception and design of the study and supervised data collection. SN and MS conducted biochemical assays and statistical analysis. MNN and AWS interpreted the results and contributed to the manuscript writing. SH coordinated clinical assessments and ensured ethical compliance. All authors read and approved the final manuscript.

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