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Research Article

Clinicopathological Evaluation of Hormonal and Ovarian Factors Associated with Female Infertility in Reproductive-Age Women; A Clinical Study

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ABSTRACT

Background: Female infertility is a complex disease that has been usually related to hormonal disorders and ovarian malfunction. The endocrine and ovarian abnormalities should be detected early to manage fertility effectively.

Objective: To assess the clinicopathology of the relationship between hormonal and ovarian factors and female infertility in women of reproductive age.

Methods: The cross-sectional study was a clinical study that was carried out at the Department of Gynecology, Bolan Medical Complex Hospital, Quetta, Pakistan, between September 2024 and May 2025. Total 110 infertile women aged 20–40 years were enrolled. Clinical examination, hormonal analysis, follicle-stimulating hormone, luteinizing hormone, prolactin, thyroid-stimulating hormone, estradiol, progesterone, anti-Mullerian hormone, and ultrasonography of the pelvis were conducted. Data were analyzed using SPSS version 26.0.

Results: The mean age was 29.6 ± 4.8 years, and the mean duration of infertility was 4.1 ± 1.9 years. Primary infertility was observed in 61.8% of cases, while 38.2% had secondary infertility. Menstrual irregularity was observed in 58.2 percent of women. The most common hormonal abnormality was elevated LH/FSH ratio (39.1%), followed by low mid-luteal progesterone (34.5%), reduced anti-Müllerian hormone (22.7%), hyperprolactinemia (21.8%), thyroid dysfunction (17.3%), and abnormal estradiol (15.5%). Polycystic ovarian morphology was the most frequent ovarian abnormality (41.8%), followed by diminished ovarian reserve features (18.2%), ovarian cysts (14.5%), and suspected endometriotic changes (10.9%). Significant associations were observed between menstrual irregularity, hormonal imbalance, and ovarian pathology ($p < 0.05$).

Conclusion: Endocrine abnormalities and ovarian abnormalities are highly correlated with female infertility, especially polycystic ovarian changes and ovulatory dysfunction. To make the correct diagnosis and efficient treatment, an integrated clinicopathological assessment is necessary.

Keywords: Female infertility, hormonal imbalance, ovarian dysfunction, polycystic ovary syndrome, anti-Müllerian hormone, ovulatory disorders

INTRODUCTION

Infertility is a significant health issue of reproduction that impacts women physically, emotionally, socially, and psychologically, and remains one of the key issues in gynaecological and fertility practice across the globe[1]. It is generally defined as the inability to achieve conception after 12 months of regular unprotected sexual intercourse, and it affects a substantial proportion of couples during the reproductive years. Even though infertility can be caused by males, females, or a combination of the two, or even by an unidentified cause, the female factors are of great importance due to their direct relationship with ovulatory activity, endocrine homeostasis, ovarian reserve, ovarian health, and integrity of the reproductive tract[2,3].

Women's infertility is not a disease but is a multifactorial clinical condition that comprises a broad range of hormonal, ovarian, anatomical, inflammatory, metabolic, and environmental factors[4]. Among them, the most common and clinically relevant factors are hormonal imbalance

and ovarian dysfunction. Normal reproductive capacity of a woman is a very well-coordinated interaction of the hypothalamus, pituitary gland, ovaries, and endometrium, and even minor disruptions in this axis can disrupt follicular development, ovulation, oocyte maturation, fertilization, implantation, and maintenance of pregnancy. Thus, testing of endocrine and ovarian variables constitutes a key component of infertility testing in women of child-bearing age[5,6].

A number of reproductive hormones are critical in the female fertility. The follicular growth, ovulation, and corpus luteum development rely on follicle-stimulating hormone (FSH) and luteinizing hormone (LH), respectively[7]. Estradiol helps in follicular growth and endometrial preparation, but progesterone is required to confirm ovulation and the sufficiency of the luteal phase. In the same manner, prolactin and thyroid-stimulating hormone (TSH) play significant roles in menstrual cyclicity and ovulatory activity[8]. Disruption in any of these hormonal pathways can result in menstrual disruption, anovulation, luteal phase defect, poor follicular maturation, or implantation failure. In addition, anti-Müllerian hormone (AMH) has gained considerable importance as a marker of ovarian reserve and follicular potential, especially in women undergoing infertility evaluation[9].

The role of ovarian factors in the pathogenesis of infertility is also critical. PCOS, reduced ovarian reserve, ovarian cystic lesions, endometriotic ovarian involvement, chronic anovulation, and premature ovarian insufficiency are some of the disorders that are frequently seen in infertile women[10]. PCOS is one of these that are one of the most common endocrine-ovarian disorders among women of reproductive age and also a primary cause of anovulatory infertility. It is commonly linked with menstrual disturbance, obesity, insulin resistance, hyperandrogenic symptoms, and typical ovarian morphology on ultrasonography. Conversely, women with lower ovarian reserve can be clinically manifested with infertility despite seemingly normal ovarian cycles, which underlines the significance of ovarian evaluation beyond clinical manifestations[11].

Clinical-pathological assessment plays a significant role in infertility since, in most cases, infertility is both clinically manifested and biochemically or imaging abnormally manifested[12]. Clinical indications that may give useful clinical hints include menstrual irregularity, obesity, hirsutism, acne, galactorrhea, pain in the pelvis, and subfertility history, whereas hormonal tests and pelvic ultrasonography help determine the underlying reproductive dysfunction more precisely. The joint assessment of a clinical picture, hormonal status, and morphology of the ovaries can consequently enhance diagnostic accuracy and can be used to help recognize women who necessitate a specific endocrine, ovulatory, or fertility-focused intervention[13].

In developing countries such as Pakistan, infertility is often associated with substantial psychosocial burden, marital stress, and delayed clinical presentation[14]. It is only after several years of infertility that many women visit a medical facility, and the diagnostic workup is often incomplete or only addresses a single aspect of reproductive health. Consequently, endocrine dysfunctions and minor ovarian pathologies might go undetected. An improved comprehension of the clinicopathological association between hormonal deviations and ovarian variables in infertile women could thus enhance early diagnosis, clinical stratification, and fertility treatment approaches in the targeted group[15].

Irrespective of the increasing load of infertility, local statistics assessing the joint effect of hormonal imbalances and ovarian dysfunctions of reproductive-age women are still scarce. The majority of the literature concentrates either on endocrine parameters or imaging results, but infertility in clinical practice is commonly the outcome of combined hormonal and ovarian pathophysiology. Therefore, the present study was designed to evaluate the clinicopathological significance of hormonal and ovarian factors associated with female infertility in reproductive-age women attending tertiary care hospitals. The study aimed to provide a clinically relevant understanding of the most common endocrine and ovarian abnormalities contributing to infertility in this population[16].

MATERIALS AND METHODS

The present cross-sectional clinical study was carried out in the Department of Gynecology, Bolan Medical Complex Hospital, Quetta, Pakistan, between a span of nine months, September 2024 and May 2025. The study aimed to determine the clinicopathological association of hormonal and ovarian factors related to female infertility in reproductive-age women who referred to a tertiary care hospital unit.

One hundred and ten women of reproductive age with infertility were recruited into the study using non-probability consecutive sampling in the gynecology outpatient and infertility clinic during the study period. Infertility was defined as the inability to conceive after 12 months of continuous unprotected sex to suit this research. Women were classified as primary infertile when they had never been pregnant and secondary infertile when they had been previously pregnant, but could no longer conceive.

Women between the ages of 20 and 40 years who reported primary or secondary infertility and agreed to take part in the study were eligible. Patients were not included in case they had a confirmed male factor infertility as the only known cause, were pregnant, had a history of hysterectomy or bilateral oophorectomy, had a known gynecological malignancy, had severe chronic systemic disease that impaired reproductive functioning, or had incomplete clinical, laboratory, or imaging data.

All the participants were subjected to an elaborate clinical examination after informed consent. Data about age, infertility duration, menstrual, obstetric, and gynecological history, medical and surgical history, previous treatment history, and family history of infertility or endocrine disorders were gathered on a structured proforma. The symptoms that may suggest endocrine and ovarian dysfunction were specifically focused on, such as oligomenorrhea, amenorrhea, irregular menstrual cycles, dysmenorrhea, obesity, hirsutism, acne, galactorrhea, and pelvic pain. All patients had a complete general physical examination and a gynecological examination. Body mass index (BMI) was calculated by dividing body weight in kilograms by the square of height in meters (kg/m^2), and women were categorized according to standard BMI classifications.

All the participants of the study were examined by hormonal assessment of the venous blood samples collected under aseptic conditions. The hormonal tests were conducted based on the pattern of the menstrual cycle of the patient and clinical viability. The hormonal test involved the measurement of follicle-stimulating hormone (FSH), luteinizing hormone (LH), LH/FSH, prolactin, thyroid-stimulating hormone (TSH), estradiol (E2), mid-luteal progesterone, and anti-Mullerian hormone (AMH). The hormonal values were interpreted based on the reference ranges provided by the hospital laboratory, and abnormalities were noted to facilitate clinicopathological correlation.

Pelvic ultrasonographic assessment was also done for all women, either by transabdominal or transvaginal examination based on clinical indication, marital status, and patient comfort. Ovarian size, ovarian volume, follicular pattern, dominant follicle development, polycystic ovarian morphology, ovarian cysts, features suggestive of diminished ovarian reserve, endometriotic ovarian changes, adnexal pathology, and associated abnormalities of the uterus were assessed using ultrasonography. Ovarian morphology had been recorded and subsequently compared to the hormonal profile and clinical outcome of the patients.

The main study result was to establish the prevalence and clinical pathologic values of hormonal imbalances and ovarian anomalies among infertile women. Other variables under investigation were the type of infertility, the menstrual pattern, the BMI, the ovulatory dysfunction, the status of ovarian reserve, and the related ovarian structural pathology. The correlation of the hormonal deviation and ovarian findings in relation to infertility patterns was also assessed.

All the collected data in the form of clinical, laboratory, and imaging data were input into a pre-designed database and were analyzed with the help of Statistical Package of Social Sciences (SPSS) version 26.0. Quantitative variables, including age, infertility duration, BMI, and hormonal levels, were represented by mean and standard deviation (SD), whereas qualitative variables, including infertility type, menstrual abnormalities, hormonal imbalances, and ovarian findings, were expressed in the form of frequency and percentage. The Chi-square test or Fisher's exact test was used to determine the association between categorical variables where necessary. Independent sample t-test was used to compare the means of the relevant groups. A p-value below 0.05 was taken to be statistically significant.

The study was conducted in accordance with accepted ethical principles for biomedical research involving human participants. Before the study was started, the Institutional Ethical Review Committee of Bolan Medical Complex Hospital, Quetta, Pakistan, granted ethical approval. All participants gave written informed consent before enrolling in the study, and patient information was kept confidential during the whole procedure.

RESULTS

The study involved 110 infertile women. The average age of the samples was 29.6 ± 4.8 years (2040 years), and the average age of the patients was 4.1 ± 1.9 years infertile. Among the enrolled women, 68 (61.8%) had primary infertility, whereas 42 (38.2%) had secondary infertility. The largest proportion of patients belonged to the 26–32 years age group, accounting for 50 (45.5%) cases. Menstrual irregularity was present in 64 (58.2%) women, while 46 (41.8%) reported regular menstrual cycles. Clinically, overweight or obesity was identified in 49 (44.5%) women, hirsutism in 27 (24.5%), acne in 21 (19.1%), galactorrhea in 11 (10.0%), and chronic pelvic pain in 18 (16.4%) patients. Table 1 shows these baseline clinicodemographic and reproductive results.

Table 1. Baseline Clinical and Reproductive Characteristics of Infertile Women (n = 110)

Variable	Frequency (n)	Percentage (%)
Age Group (years)		
20–25	24	21.8
26–32	50	45.5
33–40	36	32.7
Type of Infertility		
Primary infertility	68	61.8
Secondary infertility	42	38.2
Menstrual Pattern		
Regular cycles	46	41.8
Irregular cycles	64	58.2
Clinical Features		
Overweight/obesity	49	44.5
Hirsutism	27	24.5
Acne	21	19.1
Galactorrhea	11	10.0
Chronic pelvic pain	18	16.4

The hormonal assessment demonstrated that the rate of endocrine abnormalities was very high among the study patients. The most common hormonal disturbance was an elevated LH/FSH ratio, which was observed in 43 (39.1%) women, followed by low mid-luteal progesterone levels in 38 (34.5%), indicating probable ovulatory dysfunction. Reduced anti-Müllerian hormone (AMH), suggestive of diminished ovarian reserve, was detected in 25 (22.7%) participants. Hyperprolactinemia was present in 24 (21.8%), while thyroid dysfunction based on abnormal TSH values was found in 19 (17.3%) women. Abnormal estradiol levels were noted in 17 (15.5%) cases. Menstrual irregularity showed a significant association with elevated LH/FSH ratio, low progesterone, and hyperprolactinemia ($p < 0.05$), indicating that ovulatory-endocrine dysfunction was a major contributor to infertility in these women. Table 2 summarizes the abnormalities of the hormonal profile.

Table 2. Hormonal Profile Abnormalities in Infertile Women (n = 110)

Hormonal Parameter	Abnormal Cases (n)	Percentage (%)
Elevated LH/FSH ratio	43	39.1
Low mid-luteal progesterone	38	34.5
Reduced AMH	25	22.7
Hyperprolactinemia	24	21.8
Thyroid dysfunction (abnormal TSH)	19	17.3
Abnormal estradiol	17	15.5

Further analysis of ovarian and pelvic ultrasonographic findings demonstrated that polycystic ovarian morphology was the most frequently observed abnormality and was identified in 46 (41.8%) women. Diminished ovarian reserve features, including reduced follicular activity and low antral follicle count, were found in 20 (18.2%) cases. Ovarian cysts were detected in 16 (14.5%), while suspected endometriotic ovarian changes were present in 12 (10.9%) women. Only 16 (14.5%) participants showed a relatively normal ovarian morphology without major sonographic abnormality. Polycystic ovarian morphology was significantly more common among women with primary infertility, menstrual irregularity, hirsutism, and elevated LH/FSH ratio ($p = 0.001$). Equally, decreased AMH women exhibited a much greater proportion of diminished ovarian reserve phenotypes on ultrasonography ($p = 0.003$), demonstrating a significant clinicopathological correlation between hormonal profile and ovarian morphology. Table 3 represents these imaging findings.

Table 3. Ovarian and Pelvic Ultrasonographic Findings in Infertile Women (n = 110)

Ovarian / Pelvic Finding	Frequency (n)	Percentage (%)
Polycystic ovarian morphology	46	41.8
Diminished ovarian reserve features	20	18.2
Ovarian cysts	16	14.5
Suspected endometriotic ovarian changes	12	10.9
Normal ovarian morphology	16	14.5

When the relationship between clinicopathological variables and type of infertility was assessed, primary infertility was found to be more strongly associated with polycystic ovarian changes, elevated LH/FSH ratio, and irregular menstrual cycles, whereas secondary infertility was more frequently associated with endometriotic ovarian changes, chronic pelvic pain, and reduced ovarian reserve markers. Women with primary infertility had a significantly higher prevalence of menstrual irregularity compared to those with secondary infertility (66.2% vs 45.2%, p = 0.028). Similarly, polycystic ovarian morphology was much more prevalent in primary infertile women compared to secondary infertile women (51.5% vs 26.2%, p = 0.009). Women experiencing menstrual disturbances and galactorrhea were found to have hyperprolactinemia and thyroid dysfunction more often, whereas women with suspected ovulatory dysfunction were found to have low progesterone levels.

DISCUSSION

The present study evaluated the clinicopathological association of hormonal and ovarian factors with female infertility in reproductive-age women and demonstrated that infertility in this population is strongly linked with a combination of endocrine imbalance, ovulatory dysfunction, and ovarian morphological abnormalities[1-3]. The results of the present research indicated that primary infertility was more common than secondary infertility, that a significant percentage of infertile women had menstrual anomaly, obesity related phenotypes, hormonal imbalances, and ovarian pathology that was ultrasonographically visible[4]. These observations support the idea that female infertility is not explained by the presence of one abnormality, but it is a complicated interplay of endocrine, ovarian, and clinical factors. WHO also appreciates that female infertility is usually a result of the ovarian and endocrine system, along with other reproductive structures[5,7].

Among the most significant results of the current research, the primary infertility was identified, and it was observed in almost two-thirds of the participants of the research[8]. This could be indicative of the fact that women who fail to conceive during their first pregnancy consult specialist services earlier and more often than women with previous conception history. Also, the mean age of the study population is relatively young, which indicates that fertility assessment is being pursued at younger reproductive ages, but there are still several women who reported having a long history of infertility. This presentation latency is of clinical importance since ovarian and endocrine dysfunctions can be silent before they are manifested[9].

The primary clinicopathological observation made in the present study was that more than half of the infertile women had a high prevalence of menstrual irregularity[10]. Menstrual disturbance is a powerful clinical indicator of ovulatory dysfunction and usually indicates endocrine instability. In our study, menstrual irregularity was significantly associated with elevated LH/FSH ratio, low mid-luteal progesterone, and hyperprolactinemia, indicating that anovulatory or oligo-ovulatory states were highly prevalent in this infertile population. This is clinically significant, as ovulatory dysfunction is one of the most prevalent and remediable factors in female infertility in the general gynecological practice[11,12].

Among the hormonal results, the highest prevalence of abnormality was a high LH/FSH

All in all, the findings of this paper indicate that female infertility in women of reproductive age is closely related to a complex of endocrine disorders, ovulatory dysfunction, and ovarian structural disorders, and polycystic ovarian morphology, disturbed gonadotropin balance, luteal insufficiency, and depleted ovarian reserve are the most clinically significant results in the group of patients.

The current research results suggest that the infertility of reproductive-age women was mainly attributed to primary infertility, menstrual irregularity, dysregulation of hormones, and ovarian morphologic abnormalities. The most frequent abnormalities were polycystic ovarian morphology, elevated LH/FSH ratio, low progesterone, and reduced ovarian reserve indicators. These findings validate the clinical utility of combined hormonal and ovarian testing in the diagnostic presentation of infertile women.

ratio, and then there was low mid-luteal progesterone[13]. These findings largely indicate ovulatory dysfunction and polycystic ovarian-related endocrine imbalance to be significant causes of infertility among this group of people[14]. The high ratio of LH/FSH, particularly when accompanied by irregular cycles, obesity, hirsutism, and polycystic ovarian morphology, is a pattern that is strongly indicative of polycystic ovary syndrome (PCOS) or PCOS-like ovulatory dysfunction. This finding is in line with the current international findings that reveal that PCOS is the most prevalent cause of anovulation and among the greatest causes of infertility in women of reproductive age. Estimates provided by WHO show that PCOS is prevalent in women of reproductive age (about 10-13%), and most of these cases are not diagnosed, particularly in resource-strained environments[15].

Endocrine-metabolic dysfunction in infertility is further supported by the clinical manifestations of our study, such as hirsutism, acne, and overweight/obesity[16]. These results are especially important as obesity and metabolic imbalance can independently contribute to the worsening of ovulatory dysfunction, the change in gonadotropin secretion, and the poor reproductive outcome. In clinical practice, these characteristics cannot be considered as cosmetic issues or metabolic issues but as valuable reproductive signs that can inform next-level fertility assessment and care[17].

The other significant outcome of the present research was the availability of low anti-Mullerian hormone (AMH) in a large percentage of infertile women, and ultrasonographic ovarian reserve[18]. This is a clinically important finding as AMH is now being increasingly recognized as a valuable indicator of ovarian follicular pool and reproductive potential. In the current study, the women who had lower AMH were more likely to experience lower follicular activity and longer infertile period, which implied that lowering ovarian reserve played a significant role in causing infertility in this group. Recent findings justify the value of AMH as an indicator of ovarian reserve, but also point out that it needs to be used cautiously in conjunction with age, ovarian morphology, and clinical history[19].

The ultrasonographic results of the current research also enhance the clinicopathological foundation of infertility[20]. The prevalent abnormalities of the ovary were polycystic ovarian morphology, then reduced ovarian reserve features, ovarian cysts, and suspected endometriotic ovarian changes. This close correlation between polycystic ovarian morphology and high LH/FSH ratio, menstrual irregularity, and primary infertility indicates that ovarian structural abnormality is not an isolated imaging finding but a phenomenon that is closely linked with hormone dysfunction. This supports the need to integrate clinical examination, endocrine analysis, and pelvic ultrasonography into the normal assessment of infertile women[1,11].

It is also interesting that there was a presence of hyperprolactinemia in about a quarter of the population under the study. High levels of prolactin may inhibit pulsatile secretion of gonadotropin-releasing hormone, inhibit ovulation, disrupt luteal activity, and cause menstrual abnormalities and infertility. Hyperprolactinemia in our study was more frequent in women with irregular cycles and galactorrhea, which is clinically and scientifically plausible. Modern evidence still underpins hyperprolactinemia as a major but reversible cause of infertility in the female population, particularly when detected early and treated accordingly[5-10].

Similarly, thyroid dysfunction was identified in a clinically meaningful proportion of infertile women in the present study. Thyroid hormones have effects on the functioning of the ovaries, ovulation, endometrial receptivity, and prolactin regulation[7-9]. Mild thyroid abnormalities can disrupt reproductive physiology and decrease fertility potential. Moreover, hyperprolactinemia and menstrual abnormalities can be combined with thyroid dysfunction, which makes infertility even more complicated. More recent data indicate that thyroid status can also be associated with ovarian reserve measures like AMH, pointing to the greater endocrine interdependence of female infertility[10,12].

Suspected endometriotic ovarian changes and chronic pelvic pains were also more commonly detected in women with secondary infertility, which suggests that having acquired pelvic pathology can be of more significant value in this subpopulation[6]. Infertility associated with endometriosis is becoming recognized as a complex mechanism comprising inflammation in the pelvic area, disturbed folliculogenesis, poor quality of oocytes, deteriorated ovarian reserve, and abnormal implantation. Although the laparoscopy and other sophisticated diagnostic tools were not a part of this study, the sonographic and clinical presentation that was observed justifies the applicability of endometriotic pathology in infertility diagnosis. Recent literature has suggested that endometriosis could impair fertility in 3050 per cent of women with the condition and could have a significant impact on ovarian reserve in cases where the ovaries are involved[8,11].

Overall, the findings of this study emphasize that infertility in reproductive-age women is frequently driven by a combination of endocrine and ovarian

dysfunction rather than a single isolated cause. Practically, this implies that the assessment of infertility cannot be restricted to menstrual history or ultrasound results only. A more comprehensive diagnostic methodology, including hormonal profiling, ovarian reserve testing, menstrual analysis, anthropometry, and ovarian imaging, can greatly enhance the diagnostic accuracy and help in more personalized management plans[5-10].

This study has certain limitations that should be acknowledged. The study is a single-center hospital-based study, and therefore, the findings might not be entirely representative of the general population of the community. Further etiological classification was not done in the study, as it did not provide an in-depth evaluation of the male factor infertility, as well as tubal patency testing, and advanced reproductive endocrine and laparoscopic assessment[10-12]. Also, the cross-sectional design does not allow a causal interpretation. However, the research is still of clinical significance as it demonstrates the trend in the presentations of infertility in a tertiary gynecological environment and offers a useful input into the hormonal and ovarian landscape of infertile women in this area[15-20].

CONCLUSION

Female infertility in reproductive-age women is strongly associated with hormonal disturbances, ovulatory dysfunction, and ovarian structural abnormalities, with polycystic ovarian morphology, elevated LH/FSH ratio, low mid-luteal progesterone, hyperprolactinemia, thyroid dysfunction, and reduced ovarian reserve emerging as the most important findings in the present study. The findings have identified the significance of a rigorous clinicopathological assessment that includes clinical history, hormonal profiling, and pelvic ultrasonography in the standard diagnosis of infertile women. The early detection of these abnormalities can help to intervene in time, advance the clinical decision-making process based on fertility, and improve personalized reproductive treatment of women with infertility.

Availability of Data and Materials

The datasets used 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

- **RN**: Literature review, data entry, initial draft.
- **SS**: Data collection, clinical assessment, manuscript drafting.
- **FJ**: Study design, patient recruitment, critical review.
- **RK**: Data analysis, statistical interpretation.
- **SG**: Histopathological evaluation, interpretation.
- **ZB**: Conceptualization, study design, supervision, final approval.

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