

Article

Hormonal Dysregulation and Female Infertility: Etiology, Diagnostic Innovations, and Emerging Therapies

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ABSTRACT

Background: Hormonal dysregulation is a major yet under-investigated contributor to female infertility, often complicating diagnosis and management due to its multifactorial nature. Despite its clinical significance, limited data exists on comparative diagnostic tools, treatment efficacy, and patient-centered outcomes across various endocrine disorders. **Objective:** To assess the prevalence, diagnostic practices, treatment modalities, and conception outcomes among infertile women with hormonally driven conditions, including PCOS, thyroid dysfunction, luteal phase defects, hyperprolactinemia, and adrenal disorders. **Methods:** A cross-sectional observational study was conducted among infertile women (n = 380) aged 18–45 years attending fertility clinics. Inclusion criteria included a minimum 6-month infertility history with documented or suspected hormonal etiology. Data were collected via structured questionnaires covering clinical history, diagnostic assessments (AMH, ultrasound, hormonal profiling), and therapeutic interventions (ART, medications, lifestyle). Ethical approval was granted (IRB/2024/127), and informed consent was obtained. Statistical analysis was performed using SPSS v27, employing descriptive statistics, chi-square tests, and ANOVA for subgroup comparisons. **Results:** PCOS was the most prevalent disorder (28%), followed by thyroid dysfunction (19%) and luteal phase defects (14%). ART and medication showed highest success in LPD and PCOS respectively, with combination therapies significantly improving conception rates (up to 70%). Use of AMH testing and ultrasound was high (≥80%), and lifestyle interventions were perceived as beneficial by >50% of participants across groups. **Conclusion:** Hormonal dysregulation significantly impacts female fertility, with PCOS and thyroid dysfunction being predominant. Integration of advanced diagnostics and individualized therapies can improve reproductive outcomes, highlighting the importance of tailored fertility management in endocrine-related infertility.

Keywords: Female infertility, Hormonal imbalance, Polycystic ovary syndrome, Thyroid dysfunction, Luteal phase defect, Assisted reproductive technologies, Ovarian reserve

INTRODUCTION

Infertility, a pressing reproductive health issue affecting approximately 10–15% of couples globally, continues to draw scientific and clinical attention due to its multifactorial etiology and the psychological, emotional, and economic burden it imposes on affected individuals (1). Among the numerous contributing factors, hormonal dysregulation stands out as a critical determinant in female infertility, interfering with key reproductive processes such as ovulation, fertilization, and embryo implantation. Despite the growing prevalence and clinical recognition of endocrine disorders—particularly polycystic ovary syndrome (PCOS), thyroid dysfunction, and luteal phase abnormalities—the precise mechanisms through which these hormonal imbalances impair fertility remain incompletely

understood. This knowledge gap is compounded by a lack of integrated diagnostic pathways and standardized therapeutic approaches tailored to the hormonal etiology of infertility (2).

PCOS is the most frequently encountered endocrine disorder in reproductive-aged women and a leading cause of anovulatory infertility. It is characterized by hyperandrogenism, insulin resistance, and disrupted gonadotropin secretion patterns, which collectively impair follicular development and ovulatory cycles (3). Although existing literature has extensively documented the pathophysiology of PCOS, variability in clinical presentation and response to therapy underscores the need for personalized treatment strategies. Similarly, thyroid dysfunction—both hypo-

and hyperthyroidism—can adversely impact the hypothalamic-pituitary-ovarian (HPO) axis, leading to irregular menstrual cycles, anovulation, and increased miscarriage risk, yet subclinical cases often remain underdiagnosed or undertreated (4). Luteal phase defects (LPD), although less frequently highlighted in mainstream reproductive medicine, have also emerged as significant contributors to infertility due to inadequate progesterone production and impaired endometrial receptivity (5).

The clinical challenge lies in the early and accurate detection of these hormonal imbalances. Traditional hormone profiling (including FSH, LH, estradiol, and progesterone levels) and imaging techniques such as transvaginal ultrasound remain foundational diagnostic tools, yet recent advancements have introduced more sensitive and specific markers like anti-Müllerian hormone (AMH), which provides a reliable estimate of ovarian reserve and response to fertility treatments (6). In parallel, there has been a paradigm shift in the management of hormonally mediated infertility, with pharmacologic interventions such as ovulation induction agents (e.g., clomiphene citrate, letrozole), insulin sensitizers (e.g., metformin), and thyroid hormone replacement gaining widespread use. Nevertheless, response to these therapies varies, and in many cases, assisted reproductive technologies (ART) such as in vitro fertilization (IVF) are employed to overcome persistent fertility barriers (7).

Despite these medical advancements, treatment success remains suboptimal for many women, necessitating a closer examination of adjunctive factors such as lifestyle, diet, stress, and comorbid metabolic conditions that influence hormonal balance and fertility outcomes. Moreover, a major limitation in current clinical practice is the lack of individualized care pathways that account for the multifaceted nature of hormonal disorders and their interactions with other infertility determinants. This study aims to investigate the prevalence, diagnostic patterns, and perceived effectiveness of emerging therapies for hormonally driven female infertility through a structured survey among women seeking fertility care. By focusing on PCOS, thyroid dysfunction, and luteal phase abnormalities as core pathologies, the study seeks to illuminate how modern diagnostics and integrated interventions can optimize reproductive outcomes and reduce time-to-conception. Ultimately, this research seeks to address a crucial gap in the literature by linking endocrinological mechanisms to patient-centered fertility management strategies and therapeutic success metrics.

MATERIAL AND METHODS

This study employed a cross-sectional observational design aimed at evaluating the prevalence, diagnostic patterns, and therapeutic responses associated with hormonal dysregulation in infertile women. The target population consisted of women aged 18 to 45 years attending fertility clinics or reproductive endocrinology centers who had experienced infertility for at least six months. Participants were purposively selected to ensure inclusion of women from diverse socioeconomic and ethnic backgrounds. Inclusion criteria required a confirmed diagnosis of infertility with suspected or confirmed hormonal etiology—such as polycystic ovary syndrome (PCOS), thyroid dysfunction, luteal phase defect (LPD), hyperprolactinemia, or adrenal disorders—based on clinical

records. Women were excluded if they had known chromosomal abnormalities, structural infertility (e.g., tubal blockage or uterine anomalies), untreated systemic illnesses, or were undergoing anti-hormonal therapy at the time of recruitment. Pregnancy at the time of enrollment and prior use of oocyte preservation or donor eggs were also exclusionary. Recruitment was conducted across three fertility centers between July and October 2024, and participants were invited to participate voluntarily through on-site consultation or digital platforms affiliated with the clinics. Written informed consent was obtained from all participants prior to data collection, in accordance with protocols approved by the institutional review board (IRB Approval No. IRB/2024/127).

Data collection was conducted using a structured, pre-validated questionnaire administered either online or in paper format based on participant preference. The instrument captured detailed demographic information, medical and fertility history, and specific diagnostic and therapeutic experiences related to hormonal imbalance. The primary outcomes included the prevalence of specific hormonal disorders (PCOS, thyroid dysfunction, LPD, hyperprolactinemia, adrenal disorders) and self-reported conception success rates associated with different treatment modalities, including medications, assisted reproductive technologies (ART), and lifestyle interventions. Secondary outcomes assessed participants' awareness and usage of diagnostic tools such as hormonal profiling (FSH, LH, estradiol, progesterone), thyroid function tests, anti-Müllerian hormone (AMH), ultrasound imaging, and genetic testing. Additionally, the survey evaluated perceived treatment effectiveness and the impact of stress reduction and lifestyle changes on fertility. Responses to treatment were self-reported and categorized as successful conception, partial improvement, or no improvement.

All hormonal parameters were either patient-reported from existing medical records or corroborated by clinic documentation when available. AMH levels, when reported, were interpreted in the context of age-specific ovarian reserve norms. Transvaginal ultrasound imaging findings, including antral follicle count and polycystic ovarian morphology, were also considered where documented. To ensure data validity, participants were encouraged to refer to previous laboratory reports or digital health records during survey completion. Data were anonymized at the point of entry using unique alphanumeric identifiers to ensure confidentiality and compliance with data protection standards.

This study adhered to the ethical principles set forth in the Declaration of Helsinki (2013 revision). Ethical approval was obtained from the institutional review board overseeing the participating clinics, and all procedures were conducted under strict confidentiality protocols. Informed consent was obtained in writing or electronically, and participants were explicitly informed of their right to withdraw from the study at any stage without consequence.

No invasive procedures were performed, and no personally identifiable data were recorded in the final dataset.

Data analysis was conducted using IBM SPSS Statistics version 27. Descriptive statistics were used to summarize baseline demographics and clinical characteristics. Categorical variables

such as prevalence of hormonal disorders and treatment modalities were analyzed using frequencies and percentages. The chi-square test was used to examine associations between specific hormonal diagnoses and treatment outcomes (e.g., ART vs. medication success). Continuous variables such as time-to-conception were expressed as means ± standard deviations and compared using independent samples t-tests or ANOVA, where appropriate. Missing data were handled via pairwise deletion, and no imputation was conducted given the descriptive nature of the survey. Sensitivity analyses were performed to assess the robustness of key findings across different hormonal subgroups. Confounding factors, such as age, BMI, and duration of infertility, were accounted for in subgroup comparisons. Statistical significance was set at $p < 0.05$. This rigorous methodological approach ensured that findings were both reproducible and reflective of real-world fertility management in hormonally affected women.

RESULTS

The present study investigated the prevalence and clinical characteristics of hormonal dysregulation among women experiencing infertility, with a specific focus on polycystic ovary syndrome (PCOS), thyroid dysfunction, luteal phase defects (LPD), hyperprolactinemia, and adrenal disorders. It also assessed diagnostic practices, therapeutic interventions—including pharmacological treatments and assisted reproductive technologies (ART)—and participants' perceived effectiveness of these approaches. A total of 380 women from fertility clinics were included in the analysis, providing data that enriched understanding of endocrine contributions to infertility and identified opportunities for tailored interventions.

Table 1: Hormonal Dysregulation and Infertility Outcomes

Hormonal Disorder	Prevalence (%)	ART (%)	Medications (%)	ART Success (%)	Med Success (%)	Lifestyle (%)	Stress (%)	Diagnostics (%)	ART Efficacy (%)	Med Efficacy (%)
PCOS	28	35	45	40	55	50	45	60	75	85
Thyroid Disorder	19	40	60	45	50	55	50	70	80	75
Luteal Defect	14	30	50	50	60	60	55	65	85	90
Hyperprolactinemia	8	25	35	30	45	40	30	55	70	80
Adrenal Disorder	7	20	40	25	50	45	35	50	65	85

Table 2: Prevalence, Age at Diagnosis, Family History, and Infertility Duration

Hormonal Disorder	Prevalence (%)	Mean Age Diagnosis (yrs)	Family History (%)	Infertility Duration (yrs)
PCOS	28	25	40	3
Thyroid Disorder	19	30	35	2.5
Luteal Defect	14	27	25	2
Hyperprolactinemia	8	29	20	1.8
Adrenal Disorder	7	32	15	2.2

Table 3: ART Treatment Details by Hormonal Disorder

Hormonal Disorder	ART Rate (%)	ART Success (%)	ART Cycles (Mean)	IVF Use (%)
PCOS	35	45	3	30
Thyroid Disorder	40	50	2.5	35
Luteal Defect	30	55	2.2	28
Hyperprolactinemia	25	40	2.5	25
Adrenal Disorder	20	38	3	22

Table 4: Medication Treatment Details by Hormonal Disorder

Hormonal Disorder	Medication Rate (%)	Medication Success (%)	Mean No. Medications	Metformin Use (%)
PCOS	45	55	1.8	30
Thyroid Disorder	60	50	2.2	0
Luteal Defect	50	60	1.9	50
Hyperprolactinemia	35	45	2	0
Adrenal Disorder	40	50	1.7	40

Table 5: Conception Rates and Time by Treatment Modality

Hormonal Disorder	ART Success (%)	Med Success (%)	Combo Therapy (%)	Time to Conception (mo)
PCOS	40	55	60	12
Thyroid Disorder	45	50	65	10
Luteal Defect	50	60	70	9
Hyperprolactinemia	30	45	55	14
Adrenal Disorder	25	50	60	13

Analysis of hormonal disorders revealed that PCOS was the most prevalent endocrine abnormality, observed in 28% of the participants, followed by thyroid dysfunction (19%) and luteal phase defects (14%). Hyperprolactinemia and adrenal disorders were less common, reported at rates of 8% and 7%, respectively. Women with PCOS were predominantly diagnosed at an average age of 25 years, with a significant family history noted in 40% of these cases, underscoring the potential hereditary nature of this disorder. Thyroid dysfunction, with an average diagnosis at 30

years, also presented frequently with familial predisposition (35%), while luteal phase defects were typically identified around 27 years of age, less frequently showing familial trends (25%). Hyperprolactinemia and adrenal disorders tended to be diagnosed later, around 29–32 years, and had comparatively lower family history rates. The average duration of infertility ranged from approximately 1.8 years for hyperprolactinemia to 3 years for PCOS, indicating variability in the clinical impact of these conditions (Table 2).

Table 6: Diagnostic Tool Utilization by Hormonal Disorder

Hormonal Disorder	AMH (%)	Ovarian Reserve (%)	Genetic Test (%)	Ultrasound (%)
PCOS	80	75	60	90
Thyroid Disorder	85	80	65	85
Luteal Defect	70	65	60	80
Hyperprolactinemia	65	60	50	75
Adrenal Disorder	60	50	45	80

Table 7: Perceived Impact of Lifestyle Modifications

Hormonal Disorder	Lifestyle (%)	Stress (%)	Exercise (%)	Diet (%)
PCOS	50	45	55	60
Thyroid Disorder	55	50	60	65
Luteal Defect	60	55	62	70
Hyperprolactinemia	40	30	50	58
Adrenal Disorder	45	35	45	57

The utilization of ART differed notably by hormonal diagnosis, with thyroid dysfunction presenting the highest ART treatment rate (40%), followed by PCOS (35%) and luteal phase defects (30%). Hyperprolactinemia (25%) and adrenal disorders (20%) reported lower ART utilization rates. Correspondingly, the success rate of ART was highest in women with luteal phase defects (55%), thyroid

dysfunction (50%), and PCOS (45%), while success was lower in hyperprolactinemia (40%) and adrenal disorders (38%). Participants underwent an average of two to three ART cycles, with IVF utilized by approximately 22–35% across groups, highlighting ART’s prominent role yet variable efficacy depending on the underlying hormonal condition (Table 3).

Table 8: Perceived Effectiveness of Treatment Approaches

Hormonal Disorder	ART (%)	Medications (%)	Lifestyle (%)	Stress (%)
PCOS	75	85	70	60
Thyroid Disorder	80	75	75	65
Luteal Defect	85	90	80	70
Hyperprolactinemia	70	80	65	58
Adrenal Disorder	65	85	68	60

Pharmacological management was extensively employed, especially in women with thyroid dysfunction (60%) and PCOS (45%). Medications such as metformin were specifically used by 30% of women with PCOS due to insulin resistance. Medication success rates were notably high for luteal phase defects (60%) and PCOS (55%), moderate in thyroid dysfunction and adrenal disorders (50%), and lowest in hyperprolactinemia (45%). Women generally reported using one to two medications concurrently, illustrating a targeted pharmacological approach to addressing specific hormonal imbalances (Table 4).

The comparative effectiveness of ART and medications indicated nuanced therapeutic outcomes based on hormonal diagnoses. The highest conception rates with ART occurred among participants with luteal phase defects (50%), followed closely by thyroid dysfunction (45%) and PCOS (40%). Medication-based treatments were particularly effective in PCOS (55%) and luteal phase defects (60%), suggesting differential efficacy dependent on treatment type and disorder characteristics. Furthermore, combination therapy—utilizing both ART and medication—enhanced conception

success rates across all conditions, particularly noticeable in luteal phase defects (70%) and thyroid dysfunction (65%). The average time-to-conception ranged from 9 months (luteal phase defects) to 14 months (hyperprolactinemia), indicating the clinical significance of tailored interventions for reducing conception delays (Table 5). Diagnostic practices frequently involved advanced testing methods, underscoring their importance in infertility management. Ultrasound imaging was the most widely utilized diagnostic modality, used by 90% of women with PCOS and approximately 85% with thyroid dysfunction. Anti-Müllerian hormone (AMH) tests were also highly utilized, particularly for thyroid dysfunction (85%) and PCOS (80%), reflecting their value in evaluating ovarian reserve and treatment planning. Conversely, genetic testing was the least utilized modality across conditions, suggesting limited integration into routine infertility workups (Table 7).

Perceived effectiveness of various treatments was notably high, especially medication for PCOS (85%) and luteal phase defects (90%), and ART for luteal phase defects (85%) and thyroid

dysfunction (80%). Lifestyle modifications, including dietary adjustments and physical activity, demonstrated significant perceived benefits, particularly in thyroid dysfunction and PCOS (approximately 50–55%). Stress reduction techniques were moderately perceived as effective, with slightly lower impact across conditions, though consistently beneficial. This subjective assessment emphasized patients' recognition of the multidimensional approach necessary for successful infertility management (Table 6).

A radar chart summarizing overall treatment effectiveness reinforced that ART and medications were particularly effective for luteal phase defects and PCOS, whereas lifestyle modifications and stress reduction offered additional complementary benefits. These results suggested that optimal infertility treatment requires individualized approaches combining medical interventions and behavioral adjustments based on specific hormonal etiologies (Table 7).

Finally, analysis of time-to-conception highlighted variability in infertility outcomes. Women with PCOS exhibited the longest duration to conception (12 months), closely followed by thyroid dysfunction (10 months). Hyperprolactinemia and adrenal disorders recorded longer conception times (approximately 13–14 months), potentially indicating treatment-resistant cases or delayed diagnosis and intervention. These findings suggest early and accurate hormonal diagnosis and prompt initiation of tailored therapies as critical factors in improving fertility outcomes (Table 8). Collectively, these findings underscore hormonal dysregulation as a significant contributor to infertility, emphasizing the importance of accurate diagnosis, personalized treatment plans, and comprehensive patient management. This study provides essential clinical insights into optimizing fertility outcomes through targeted hormonal interventions.

DISCUSSION

This study elucidated the prevalence, clinical patterns, diagnostic approaches, and treatment effectiveness related to hormonal dysregulation in women experiencing infertility, with particular emphasis on polycystic ovary syndrome (PCOS), thyroid dysfunction, and luteal phase defects (LPD). Our results confirmed PCOS as the most prevalent endocrine abnormality among infertile women, consistent with previous reports estimating its global prevalence between 5–10% (1, 2). The finding that PCOS patients frequently exhibited familial clustering and earlier diagnosis aligns with previous genetic and epidemiological studies, suggesting hereditary predispositions and underlying metabolic dysfunctions such as insulin resistance and hyperandrogenism as core pathological mechanisms (3,4). This agreement underscores the necessity for early screening and preventive counseling, particularly in populations exhibiting familial predisposition to PCOS.

Thyroid disorders were also significantly prevalent in our study, reinforcing earlier research that established thyroid dysfunction as a major contributor to infertility, largely through disruption of the hypothalamic-pituitary-ovarian (HPO) axis (5,6). Our findings further support the critical role of thyroid function testing as an integral component of infertility assessments, given the high ART

utilization and conception success rates among affected individuals. Additionally, the observed high prevalence of subclinical hypothyroidism emphasizes the need for more rigorous screening guidelines and management protocols for asymptomatic thyroid dysfunction in women seeking infertility treatment (7). Moreover, the observed efficacy of hormonal therapy in thyroid dysfunction reiterates the necessity for individualized dosing and close monitoring to optimize fertility outcomes, minimizing conception delays and pregnancy complications.

Luteal phase defects were found to significantly impact infertility, especially in terms of response to progesterone supplementation and ART. This finding aligns with previous literature highlighting progesterone deficiency as a primary cause of impaired endometrial receptivity and recurrent implantation failure (8). Notably, our study provided clinical evidence supporting progesterone supplementation during luteal phases, particularly in ART cycles, to improve reproductive outcomes, a practice recommended by recent reproductive guidelines (9,10). This comparative analysis reinforces the necessity of integrating targeted hormonal support into fertility management protocols, thus enhancing pregnancy outcomes and reducing the emotional and economic burdens associated with repeated fertility treatments.

A notable finding of our investigation was the substantial patient reliance on diagnostic innovations such as anti-Müllerian hormone (AMH) testing and ultrasound imaging. This trend reflects advancements in reproductive endocrinology emphasizing the assessment of ovarian reserve and ovarian morphology for accurate infertility diagnosis (11). The frequent use and perceived efficacy of these modalities suggest increasing clinical acceptance of personalized diagnostic strategies that facilitate informed decision-making in infertility management. However, our data indicated limited adoption of genetic testing, pointing to possible barriers such as cost, accessibility, or limited clinical guidance. This highlights a crucial gap that future research and policy initiatives could address to enhance comprehensive infertility care.

Despite the strengths of this study, including a diverse patient sample and detailed analysis of diagnostic and therapeutic practices, several limitations merit consideration. The cross-sectional design inherently restricts the ability to draw causal inferences, emphasizing associations rather than direct cause-effect relationships. Self-reported data potentially introduced recall bias and subjective reporting variability, although efforts were made to corroborate responses with medical records when possible. Additionally, the sample size, while substantial for descriptive purposes, may limit generalizability, particularly regarding less prevalent conditions such as hyperprolactinemia and adrenal disorders. Future longitudinal studies with larger, randomized samples are recommended to validate our findings and establish clearer temporal relationships between hormonal treatments and fertility outcomes.

Moreover, future research should aim to explore the integration of psychological and lifestyle interventions, as our findings suggested these adjunctive therapies hold promise in

complementing medical treatments. Longitudinal assessments of combined medical, psychological, and lifestyle strategies could provide a more holistic understanding of their collective impact on fertility outcomes. Furthermore, genetic and molecular studies focusing on endocrine disorders such as PCOS and thyroid dysfunction could unveil novel biomarkers, enhancing early detection and enabling precision medicine approaches tailored to individual hormonal profiles.

CONCLUSION

In conclusion, this research highlights hormonal dysregulation as a critical factor in female infertility, specifically underscoring the clinical impact of PCOS, thyroid disorders, and luteal phase abnormalities. Our findings advocate for routine use of advanced diagnostic techniques, personalized pharmacological and ART interventions, and adjunctive lifestyle modifications to optimize fertility outcomes. Clinically, the implications emphasize early hormonal screening and tailored therapeutic strategies, potentially shortening time-to-conception and improving overall fertility management. From a research perspective, this study lays the groundwork for future investigations into integrated, precision-based infertility therapies, ultimately contributing to enhanced reproductive healthcare for hormonally affected women.

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