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Original Research Article

Frequency of Hyperprolactinemia in Infertile (Primary and Secondary) Women Presenting at OPD of Gyneacology

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Abstract: ***Background:*** *Infertility is a major reproductive health concern affecting up to 15% of couples globally. Among its multiple etiologies, endocrine abnormalities, particularly hyperprolactinemia, are recognized as frequent yet treatable causes of anovulation and menstrual irregularities.* ***Objective:*** *To determine the frequency of hyperprolactinemia among infertile women presenting to the gynecology outpatient department and to compare its occurrence between primary and secondary infertility.* ***Methodology:*** *This cross-sectional descriptive study was conducted at Shaikh Zaid women hospital Larkana from August 2023 to Jan 2024. A total of 135 infertile women aged 18–45 years were included using non-probability consecutive sampling. Women with thyroid or pituitary disorders, chronic illnesses, or recent use of dopamine-modulating drugs were excluded. After informed consent, demographic and clinical data were recorded, and fasting serum prolactin levels were measured using a chemiluminescent immunoassay.* ***Results:*** *The mean age of participants was 29.7 ± 5.1 years. Primary infertility was observed in 82 (60.7%) and secondary infertility in 53 (39.3%) women. Hyperprolactinemia was detected in 46 participants, yielding a frequency of 34.1%. The condition was significantly more prevalent in women with primary infertility (43.9%) compared to secondary infertility (18.9%) ($p = 0.002$). Mean serum prolactin levels were 32.4 ± 17.9 ng/mL in primary infertility and 20.6 ± 10.8 ng/mL in secondary infertility. Menstrual irregularities (95.6%) and galactorrhea (28.2%) were significantly more common among hyperprolactinemic women ($p < 0.05$). No significant association was found with age or BMI.* ***Conclusion:*** *Hyperprolactinemia is a prevalent and reversible cause of infertility, particularly among women with primary infertility.*

Keywords: Hyperprolactinemia, Infertility Female, Infertility Primary, Infertility Secondary, Prolactin

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Introduction

Infertility, defined as the inability to conceive after 12 months of regular unprotected intercourse, affects an estimated 10–15% of couples worldwide (1). It is not just a medical condition but a psychosocial crisis which is having a significant toll to the mental health of a woman, her marriage stability, and social identity particularly in societies where motherhood is greatly associated with the role and self esteem of a woman (2). Infertility can create stigma and emotional strain in South Asia and other developing countries with the need to carry out correct diagnosis and treatment strategies based on evidence. Out of the many factors that lead to female infertility, tubal blockage, endometriosis, ovarian dysfunction and uterine pathology hormonal disorders have a special place (3). Among them, one of the most common yet treatable endocrine abnormalities linked with reproductive failure has developed to hyperprolactinemia. Prolactin is a 198-amino-acid polypeptide hormone that is produced by lactotroph cells of the anterior pituitary gland (4). It is known to control mostly lactation and breast growth, yet it has a far-reaching effect on metabolism, immune regulation, and reproductive physiology. In a normal situation, hypothalamic dopamine personifies the inhibition of prolactin secretion (5). But a number of physiological and pathological processes like pituitary adenoma (prolactinoma), hypothyroidism, stress, some drugs (antipsychotics, antidepressants, antihypertensives) and chest wall defects may disrupt this regulatory process, resulting in the continuously high level of serum prolactin (6). Hyperprolactinemia interferes with the pulsatile secretion of gonadotropin-releasing hormone (GnRH), suppresses luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and inhibits the normal development and ovulation of ovaries. This results in women being exposed to anovulation, luteal phase defects, amenorrhea or oligomenorrhea- each of which leads to infertility (7).

There are varying clinical manifestations of hyperprolactinemia, and this condition has varied symptoms based on the severity and duration of hormonal increase. It is characterized by common manifestations such as menstrual irregularities, galactorrhea, low libido, dyspareunia and infertility. In other instances, only subtle indications like premenstrual bleeding or infertility can be the only indicators (8). As such, serum prolactin testing has now become one of the routine elements of the diagnostic work-up of infertile or menstrually abnormal women. Notably, the condition is reversible in nature, and proper treatment with dopamine agonists and even surgical resection of prolactinomas can restore the fertility of many individuals hence the importance of early diagnosis (9). Both primary and secondary infertility have been reported to have hyperprolactinemia, although the occurrence and etiologies might vary. Primary infertility is the term used to describe women who have never conceived and secondary infertility to describe those who have previously managed to conceive but could no longer do so (10). Research has suggested that hyperprolactinemia has been more common among women with primary infertility, which may be because of previous endocrine malfunction or inborn pituitary lesions (11). Nonetheless, secondary infertility can also be acquired due to factors like stress, drug use, or post-partum pituitary alterations (e.g. Sheehan syndrome). The recognition of these differences is important, as it will inform targeted assessment and treatment approaches (12). The topicality of this issue is mentioned in a number of studies in South Asia. A study in India and Bangladesh showed that around a quarter of infertile women had a high level of prolactin and a large percentage has shown normalization and restored menstruation following administration of bromocryptine or cabergoline (13).

Objective

To determine the frequency of hyperprolactinemia among infertile women presenting to the gynecology outpatient department and to compare its occurrence between primary and secondary infertility.

Methodology

This was a cross-sectional descriptive study conducted at Shaikh Zaid women hospital Larkana from August 2023 to Jan 2024. A total of 135 infertile women were included in the study. Non-probability consecutive sampling was used to recruit participants who met the inclusion criteria.

Inclusion Criteria

Women of reproductive age (18–45 years) presenting to the gynecology OPD with a history of infertility for at least one year were included. Both primary infertility (no previous conception) and secondary infertility (previous conception but inability to conceive again) were eligible for inclusion.

Exclusion Criteria

Women with known thyroid disorders, previously diagnosed pituitary tumors, those on dopamine antagonists or hormonal medications during the last three months, and those with chronic systemic illnesses such as renal or hepatic disease were excluded from the study.

Data Collection

After obtaining informed written consent, detailed demographic and clinical information was collected using a structured questionnaire. Data included age, duration and type of infertility, menstrual pattern, and presence of galactorrhea or other symptoms. Blood samples were drawn between 9:00 and 11:00 a.m. after overnight fasting to minimize diurnal variation. Serum prolactin levels were measured using a chemiluminescent immunoassay in the hospital's diagnostic laboratory. A serum prolactin level greater than 25 ng/mL was considered diagnostic of hyperprolactinemia.

Data Analysis

Data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS) version 26.0. Quantitative variables such as age, BMI, infertility duration, and serum prolactin levels were expressed as mean ± standard deviation (SD). Categorical variables such as type of infertility, presence of hyperprolactinemia, and menstrual irregularities were presented as frequencies and percentages. The chi-square test was used to determine associations between categorical variables, while the independent t-test compared means of continuous variables. A p-value ≤ 0.05 was considered statistically significant.

Results

Data were collected from 135 patients, mean age of the participants was 29.7 ± 5.1 years, with the majority (68.9%) falling in the 25–35-year age group, while 22.2% were younger than 25 years and 8.9% were older than 35 years. Most women (60.7%) presented with primary infertility, whereas 39.3% had secondary infertility. The average duration of infertility was 3.4 ± 1.5 years. Menstrual irregularities were reported in 112 women (82.9%), and galactorrhea was observed in 17 women (12.6%). The mean BMI of the participants was 26.7 ± 3.2 kg/m², indicating that a considerable proportion were overweight.

Table 1. Baseline Characteristics of Infertile Women (n = 135)

Variable	n (%) / Mean ± SD
Age (years)	29.7 ± 5.1
Age Group	
• <25 years	30 (22.2)
• 25–35 years	93 (68.9)
• >35 years	12 (8.9)
Type of Infertility	
• Primary	82 (60.7)
• Secondary	53 (39.3)
Duration of Infertility (years)	3.4 ± 1.5
Menstrual Irregularities	112 (82.9)
Galactorrhea	17 (12.6)
BMI (kg/m²)	26.7 ± 3.2

Hyperprolactinemia was detected in 46 women, giving an overall frequency of 34.1%. Among those with primary infertility, 36 out of 82 (43.9%) were hyperprolactinemic, compared to 10 out of 53 (18.9%) with secondary infertility.

Table 2. Frequency of Hyperprolactinemia According to Type of Infertility (n = 135)

Type of Infertility	Total (n)	Hyperprolactinemia n (%)	Normal Prolactin n (%)	p-value
Primary Infertility	82	36 (43.9)	46 (56.1)	0.002
Secondary Infertility	53	10 (18.9)	43 (81.1)	
Total	135	46 (34.1)	89 (65.9)	

When stratified by age and BMI, hyperprolactinemia was observed in 33 women (36.7%) under 30 years and in 13 women (29.4%) aged 30 years or older. Similarly, it was found in 17 women (30.9%) with BMI <25 kg/m² and in 29 women (36.3%) with BMI ≥25 kg/m². However, neither age nor BMI showed a statistically significant association with hyperprolactinemia (p = 0.31 and p = 0.45, respectively).

Table 3. Association of Hyperprolactinemia with Age and BMI (n = 135)

Variable	Hyperprolactinemia n (%)	p-value
Age <30 years (n = 90)	33 (36.7)	0.31
Age ≥30 years (n = 45)	13 (29.4)	
BMI <25 kg/m² (n = 55)	17 (30.9)	0.45

BMI ≥25 kg/m² (n = 80)	29 (36.3)	

The mean serum prolactin level was significantly higher among women with primary infertility (32.4 ± 17.9 ng/mL) compared to those with secondary infertility (20.6 ± 10.8 ng/mL), with a p-value of 0.001. This suggests that elevated prolactin plays a more dominant role in primary infertility cases.

Table 4. Comparison of Mean Serum Prolactin Levels Between Primary and Secondary Infertility (n = 135)

Type of Infertility	Mean ± SD (ng/mL)	95% CI	p-value
Primary Infertility (n = 82)	32.4 ± 17.9	28.5 – 36.3	0.001
Secondary Infertility (n = 53)	20.6 ± 10.8	17.6 – 23.6	
Total (n = 135)	28.1 ± 15.8	25.4 – 30.8	

Menstrual disturbances were present in 95.6% of women with hyperprolactinemia compared to 76.4% of those with normal prolactin (p = 0.01). Similarly, galactorrhea was markedly more frequent among hyperprolactinemic women (28.2%) than those with normal prolactin (4.5%) (p < 0.001). Headaches were also more common in the hyperprolactinemia group (21.7%) compared to the normal group (7.9%) (p = 0.03). However, visual disturbances and longer infertility duration (>3 years) did not show statistically significant differences between the two groups (p = 0.22 and p = 0.09, respectively).

Table 5. Distribution of Clinical Features Among Women with and Without Hyperprolactinemia (n = 135)

Clinical Feature	Hyperprolactinemia (n = 46)	Normal Prolactin (n = 89)	p-value
Menstrual Irregularities	44 (95.6)	68 (76.4)	0.01
Galactorrhea	13 (28.2)	4 (4.5)	<0.001
Headache	10 (21.7)	7 (7.9)	0.03
Visual Disturbance	3 (6.5)	2 (2.2)	0.22
Duration of Infertility >3 years	22 (47.8)	30 (33.7)	0.09

Discussion

This study looked at the relationship between the type of infertility and the frequency of hyperprolactinemia in infertile women who went to the gynecology outpatient department. One of the most common endocrine causes of infertility, hyperprolactinemia continues to be one of the most common endocrine causes of infertility, as 46 out of 135 women (34.1%) had elevated serum prolactin levels. Prolactin elevation may play a more direct role in impairing ovulatory function before the first conception occurs, as the condition was significantly more prevalent among women with primary infertility (43.9% versus 18.9%). The overall prevalence in this study aligns with several regional findings. For instance, Tahir et al. (Pakistan) reported that 34.2% of infertile women had hyperprolactinemia, while Kumar et al. (India) observed a prevalence of 30.5%. Similar results were seen in studies by Kaur et al. and Fatima et al., where one-third of infertile females had raised prolactin levels. Western data, on the other hand, typically show frequencies between 10 and 15%, which are indicative of improved early detection, variations in stress levels, and the effects of environmental and lifestyle factors. The high prevalence observed in South Asian studies suggests that stress, nutritional deficiencies, and delayed hormonal testing may contribute to increased rates of prolactin-related infertility (14).

The women in this study had a mean serum prolactin level of 56.2±18.4 ng/mL, which was significantly higher than the 15.9±5.6 ng/mL found in women with normal levels. Moreover, mean prolactin values were significantly greater in women with primary infertility (32.4 ± 17.9 ng/mL) than those with secondary infertility (20.6 ± 10.8 ng/mL). The physiological mechanism by which hyperprolactinemia disrupts the hypothalamic-pituitary-ovarian axis is supported by these findings. The pulsatile release of gonadotropin-releasing hormone (GnRH) is stifled by excess prolactin, resulting in decreased LH and FSH secretion, anovulation, and luteal phase defects (15). Endometrial receptivity, cervical mucus quality, and follicular development all suffer as a result of the hypoestrogenic state. Clinical symptoms in this study strongly reflected the hormonal dysfunction underlying hyperprolactinemia. Menstrual irregularities were reported in 95.6% of hyperprolactinemic women, compared with 76.4% of those with normal prolactin levels (16). Similarly, galactorrhea was found in 28.2% of hyperprolactinemic women but only 4.5% of those with normal levels. The fact that these correlations were statistically significant (p=0.05) demonstrates how useful these symptoms are for diagnosing endocrine causes of infertility. Comparable trends were observed in studies by Ranjana et al. and Nidhi et al., who also reported that menstrual abnormalities and galactorrhea were highly predictive of raised prolactin levels (17).

Although a higher frequency of hyperprolactinemia was observed in women younger than 30 years (36.7%) compared with those 30 years or older (29.4%), this difference was not statistically significant. This suggests that prolactin-related infertility is not strongly influenced by age alone. In a similar vein, there was no significant correlation found between hyperprolactinemia and body mass index (BMI), which is in line with the findings of Babu et al. but stands in contrast to some studies that claim obesity causes mild prolactin elevation due to altered estrogen metabolism (18). This study's higher prevalence of hyperprolactinemia in primary infertility compared to secondary infertility supports previous findings that prolactin excess primarily affects ovulation and follicular maturation prior to a woman becoming pregnant. Acquired factors like pelvic inflammatory disease, endometriosis, tubal damage, and postpartum pituitary changes may have a greater impact on cases of secondary infertility. In cases of primary infertility, therefore, screening for hyperprolactinemia should take precedence, particularly if irregular periods or galactorrhea are present. The clinical relevance of this finding is substantial because hyperprolactinemia is both detectable and treatable. Dopamine agonists such as bromocriptine and cabergoline effectively normalize prolactin levels, restore ovulation, and significantly improve conception rates (19,20). Up to 70%–80% of women with prolactin-related infertility can conceive with medical treatment alone, according to evidence. As a result, early detection through straightforward biochemical testing can keep affected women from having to undergo invasive fertility treatments that aren't necessary and lessen their physical and mental stress. The present study has several strengths. It adds updated local data from a tertiary care center, includes both primary and secondary infertility groups, and integrates clinical symptom analysis with biochemical findings. However, it also comes with restrictions. The study was cross-sectional and single-centered, which may limit generalizability. Long-term follow-up after treatment was excluded, and other hormonal parameters such as TSH, LH, FSH, and estradiol were not analyzed concurrently. In order to evaluate treatment outcomes and pregnancy rates

following hyperprolactinemia correction, subsequent multicenter longitudinal studies are required.

Conclusion

It is concluded that hyperprolactinemia is a common endocrine disorder among infertile women, with a significantly higher frequency in those with primary infertility compared to secondary infertility. The strong association of elevated prolactin levels with menstrual irregularities and galactorrhea emphasizes its role as a major reversible cause of anovulation and infertility. Since hyperprolactinemia is both easily diagnosable and treatable, routine screening for serum prolactin levels should be integrated into the initial infertility work-up of all women presenting to gynecology clinics. Early identification and prompt management can restore normal ovulatory cycles, enhance the chances of conception, and reduce the psychological and financial burden associated with infertility treatments.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-MMS-033-24)
Consent for publication
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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

M (FCPS-II Trainee)
Manuscript drafting, Study Design,
SS (Professor and Head)
Review of Literature, Data entry, Data analysis, and drafting articles.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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