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ORIGINAL ARTICLE

Exploring the Association Between Hyperprolactinemia and Infertility in Women: Insights From a Study of 170 Patients

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ABSTRACT

Background: Hyperprolactinemia is a common endocrine disorder in women that is closely associated with infertility. Elevated prolactin levels can disrupt reproductive functions, particularly ovulation, and menstrual cycles, leading to challenges in conception. This study aims to examine the association between hyperprolactinemia and infertility in women, analyzing the clinical characteristics, causes, and treatment outcomes of 170 patients.

Methods: A retrospective study was conducted involving 170 women diagnosed with hyperprolactinemia and infertility. Clinical data, including prolactin levels, menstrual history, causes of hyperprolactinemia, and treatment outcomes, were collected. Dopamine agonists such as bromocriptine and cabergoline were the main treatment options. The effects of treatment on prolactin levels and subsequent fertility outcomes were analyzed.

Results: The majority of the patients presented with irregular menstrual cycles (65%) and anovulation (55%). Prolactinomas were the leading cause of hyperprolactinemia (40%), followed by medication-induced hyperprolactinemia (25%) and hypothyroidism (20%). Following treatment with dopamine agonists, 72% of patients experienced normalization of prolactin levels, and 55% achieved successful conception.

Conclusion: Hyperprolactinemia is a significant cause of infertility in women, with dopamine agonists proving effective in restoring normal prolactin levels and improving fertility outcomes. Early diagnosis and appropriate treatment are essential for improving reproductive health.

Keywords: Hyperprolactinemia, Infertility, Dopamine agonists, Prolactin, Anovulation, Prolactinoma, Menstrual irregularities, Fertility

INTRODUCTION

Hyperprolactinemia is defined as elevated levels of prolactin in the bloodstream, a condition that can significantly affect female fertility. Prolactin, a hormone produced by the pituitary gland, plays a critical role in breast milk production post-delivery. However, abnormal levels of prolactin, not associated with pregnancy or breastfeeding, can cause disturbances in the menstrual cycle and ovulation, leading to infertility[1]. Hyperprolactinemia has been implicated in various causes of infertility, including anovulation, luteal phase defects, and impaired endometrial development[2].

The condition can arise from a variety of etiologies, including prolactin-secreting pituitary tumors (prolactinomas), medications that interfere with dopamine production, hypothyroidism, and other endocrine imbalances[3,4]. Prolactinomas, benign tumors of the pituitary gland, account for a significant proportion of hyperprolactinemia cases, while medications such as antipsychotics and antidepressants are also common causes[5]. The impact of hyperprolactinemia on fertility can be profound, as it can lead to the cessation of ovulation, making conception difficult[6].

Dopamine agonists, such as bromocriptine and cabergoline, are the primary treatment for reducing prolactin levels. These medications work by stimulating dopamine receptors in the pituitary gland, which inhibits prolactin secretion and restores normal reproductive function[7]. Studies have shown that treatment with dopamine agonists often results in normalization of prolactin levels and improved fertility outcomes[8,9]. However, the success rate of treatment and subsequent conception varies depending on the underlying cause of hyperprolactinemia and the patient's response to therapy[10].

This study aims to assess the relationship between hyperprolactinemia and infertility in a cohort of 170 women, analyzing the clinical features, causes, and treatment outcomes.

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METHODOLOGY

This multicenter retrospective study was conducted at PNS Shifa Hospital/BUHSC Karachi/ Jacobabad Institute of Medical Sciences, Jacobabad between September 2022 and August 2023. A total of 170 women who presented with infertility and were diagnosed with hyperprolactinemia were included. The inclusion criteria were women aged 20-40 years who had a confirmed diagnosis of hyperprolactinemia (serum prolactin >25 ng/mL) and infertility, defined as the inability to conceive after 12 months of unprotected intercourse.

Clinical data were collected from medical records, including demographic information, menstrual history, prolactin levels, causes of hyperprolactinemia, treatment modalities, and outcomes. All patients had undergone a thorough endocrine evaluation, including thyroid function tests, magnetic resonance imaging (MRI) for the detection of prolactinomas, and a detailed medication history to identify any potential drug-induced causes.

Treatment Protocol: The treatment for hyperprolactinemia was primarily dopamine agonists (bromocriptine or cabergoline). The choice of medication was based on the severity of the condition and the patient's tolerance. Dosage adjustments were made based on the patient's prolactin levels and clinical response.

Outcome Measures: The primary outcome was the normalization of prolactin levels, defined as prolactin levels ≤25 ng/mL. The secondary outcome was pregnancy achievement, defined as a positive pregnancy test confirmed by ultrasound. Patients were followed for a period of 12 months after starting treatment.

Data Analysis: Statistical analysis was performed using SPSS version 26 (IBM Corp., Armonk, NY, USA). Descriptive statistics, including mean and standard deviation, were used to summarize continuous variables. Categorical variables were expressed as frequencies and percentages. To assess associations between clinical variables (cause of hyperprolactinemia, treatment type, etc.) and pregnancy outcomes, chi-square tests were performed. A p-value <0.05 was considered statistically significant.

To identify factors influencing fertility outcomes, logistic regression analysis was conducted. The dependent variable was pregnancy achievement, while independent variables included

age, cause of hyperprolactinemia, prolactin normalization, and treatment type. Odds ratios (OR) with 95% confidence intervals (CI) were reported.

RESULTS

Among the 170 women, the mean age was 32.4 ± 4.5 years. The most common cause of hyperprolactinemia was prolactinomas, which were found in 68 patients (40%). Medication-induced hyperprolactinemia accounted for 25% of cases, while hypothyroidism was identified in 20% of patients. The remaining 15% had idiopathic hyperprolactinemia, where no underlying cause was identified.

Table 1: Demographic and Clinical Characteristics of the Study Population

Cause of Hyperprolactinemia	Number of Patients (n = 170)	Percentage (%)
Prolactinoma	68	40
Medication-induced	43	25
Hypothyroidism	34	20
Idiopathic	25	15

To evaluate the association between clinical characteristics and pregnancy outcomes, a chi-square analysis was performed. The results showed that women with medication-induced hyperprolactinemia had a significantly higher pregnancy rate ($p < 0.05$) compared to those with prolactinomas. Additionally, a significant association was found between the normalization of prolactin levels and pregnancy achievement ($p < 0.01$).

Table 2: Association Between Cause of Hyperprolactinemia and Pregnancy Outcomes

Variable	Pregnancy Rate (%)	p-value
Prolactinoma	50	0.032
Medication-induced	65	0.045
Hypothyroidism	45	0.105
Idiopathic	55	0.072

Logistic Regression Analysis: A logistic regression analysis was performed to determine the factors that significantly affect the likelihood of achieving pregnancy. The analysis showed that normalization of prolactin levels and medication-induced hyperprolactinemia were significantly associated with higher pregnancy rates (OR = 2.35, 95% CI 1.42-3.78, $p < 0.01$). Age was not found to be a significant predictor of pregnancy (OR = 1.08, 95% CI 0.96-1.21, $p = 0.207$).

Table 3: Logistic Regression Analysis for Predictors of Pregnancy Achievement

Variable	Odds Ratio (OR)	95% CI	p-value
Normalized Prolactin	2.35	1.42-3.78	<0.01
Medication-induced	2.12	1.18-3.86	0.019
Age	1.08	0.96-1.21	0.207

Treatment with dopamine agonists led to normalization of prolactin levels in 122 out of 170 patients (72%). Of the patients who had prolactinomas, 80% experienced normalization of prolactin after treatment. For medication-induced cases, 70% responded to treatment, while 60% of those with hypothyroidism achieved normal prolactin levels after thyroid hormone replacement.

Table 4: Treatment Response and Pregnancy Outcomes by Cause of Hyperprolactinemia

Cause of Hyperprolactinemia	Pregnancy Rate (%)
Prolactinoma	50
Medication-induced	65
Hypothyroidism	45
Idiopathic	55

Out of the 122 patients who achieved normalized prolactin levels, 67 (55%) successfully conceived within 12 months of treatment. The pregnancy rate was highest in patients with medication-induced hyperprolactinemia (65%) and lowest in those with prolactinomas (50%).

DISCUSSION

The results of this study confirm that hyperprolactinemia is a significant cause of infertility in women. Prolactinomas, as expected, were the most common cause of elevated prolactin levels, consistent with previous studies[11]. Medication-induced hyperprolactinemia is also an important factor to consider, particularly given the increasing use of antipsychotics and antidepressants in clinical practice[12].

The effectiveness of dopamine agonists, such as bromocriptine and cabergoline, in normalizing prolactin levels and improving fertility outcomes is well-supported by the findings of this study[13]. The response rate was highest in patients with medication-induced hyperprolactinemia, suggesting that treatment of the underlying cause is crucial for fertility restoration[14].

The pregnancy rate of 55% in this study is consistent with other reports in the literature, where treatment with dopamine agonists has led to pregnancy rates ranging from 40% to 60% in women with hyperprolactinemia[15]. The lower pregnancy rate in patients with prolactinomas may be attributed to the severity of the condition, as larger tumors may require more intensive treatment or surgical intervention[16].

Thyroid dysfunction was another contributing factor in hyperprolactinemia, with hypothyroidism leading to elevated prolactin levels in 20% of patients. In these cases, correction of thyroid function resulted in normalization of prolactin and improved fertility outcomes[17].

It is worth noting that early diagnosis and treatment of hyperprolactinemia are critical to improving reproductive outcomes. Patients who are treated promptly with dopamine agonists have a significantly higher chance of achieving pregnancy than those who delay treatment[18].

CONCLUSION

Hyperprolactinemia is a common cause of infertility in women, with prolactinomas being the most frequent underlying cause. Treatment with dopamine agonists is highly effective in normalizing prolactin levels and improving fertility outcomes. Early diagnosis and appropriate management are essential for enhancing the chances of conception in women affected by this condition.

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