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Investigating the Relationship between Hyperprolactinemia, Menstrual Disorders, and Infertility in Women of Reproductive Age

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ABSTRACT

Background: Menstrual problems and infertility are best understood and treated with knowledge of gynecological endocrinology. Serum prolactin levels in infertile individuals with menstrual disorder are the focus of this study.

Materials and Methods: Patients between the ages of 20 and 40 (the reproductive age range) were split into two groups for a year-long prospective case-control research. Fifty fertile women with normal periods served as the control group, while 150 infertile women with menstrual dysfunctions made up the research group. Serum prolactin levels were checked in addition to other relevant laboratory and radiographic tests to get a full picture of the obstetric history.

Results: In this analysis, hyperprolactinemia was shown to occur in 24.6% of participants. Hyperprolactinemia was more common in those with polycystic ovary syndrome (33.3%), oligomenorrhea (27.27%), secondary amenorrhea (30.2%), primary amenorrhea (5.5%), irregular menstruation (9.09%), and 25% of those with regular ovulatory cycles and 40% of those with regular anovulatory cycles. Oligomenorrhea was the most common presenting symptom among hyperprolactinemic patients (48.7%), followed by secondary amenorrhea (35.1%). Patients with secondary amenorrhea had a substantially higher mean blood prolactin level (111.42 ng/mL) compared to those with oligomenorrhea (69.3 ng/mL). Seventy-five point six percent of hyperprolactinemic individuals experienced primary infertility, but only twenty-seven point zero seven percent experienced secondary infertility. (p0.01). Blood prolactin levels were significantly different (p 0.01) between cases with and without galactorrhea, and 66.6% of patients with galactorrhea had hyperprolactinemia. Although 13.5

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percent of hyperprolactinemic individuals experienced galactorrhea, this symptom was not consistently present.

Conclusion: Regular blood prolactin testing is required for the diagnosis of hyperprolactinemia, a major cause of infertility and menstrual disruption.

Keyword : Gynecological endocrinology, Menstrual dysfunction ,Infertility , Serum prolactin ,Hyperprolactinemia , Oligomenorrhea ,Amenorrhea ,Polycystic ovarian disease , Anovulatory cycles , Galactorrhea

INTRODUCTION

Clinical examination, endometrial biopsies, endocrine assessments, sonography, hysterosalpingography, hysteroscopy, laparoscopy, and other diagnostic techniques are used to identify and evaluate female infertility. Absent or irregular menstruation across varied time periods is a symptom of menstrual dysfunction, which is a unique clinical illness caused by abnormalities in the hypothalamic-pituitary-ovarian-uterine axis. Nonetheless, it has been a major problem for medical practitioners to localize malfunction and identify its root cause. In order to properly assess cases of menstrual disorder and infertility, a thorough knowledge of gynecological endocrinology is required. Hence, radioimmunoassay for endocrinological assessment has developed as a useful tool. The recent advancements in reproductive endocrinology have identified that the underlying pathophysiology of anovulation in amenorrhea-galactorrhea syndrome, as well as other menstrual irregularities associated with infertility, can be attributed to the anterior pituitary polypeptide hormone, prolactin. Lactotroph cells of the pituitary gland reside in close proximity to growth hormone-producing cells within the lateral wings of the gland. These lactotrophs are responsible for secreting the polypeptide hormone prolactin. Hyperprolactinemia can be diagnosed without either stimulation or suppression tests since prolactin release is primarily regulated by hypothalamic inhibition. Hypogonadotropic hypogonadism is commonly associated with hyperprolactinemia. Anovulation is caused by prolactin's effect on PRL-R-expressing kisspeptin-1 neurons, which decreases release of both kisspeptin-1 and gonadotropin-releasing hormone (GnRH). Ovulation can be disrupted by prolactin because it inhibits the pulsatile release of GnRH. Anovulation, amenorrhea, and galactorrhea are examples of menstrual and ovulatory dysfunctions that may be accompanied by hyperprolactinemia. Determining prolactin levels is a useful way to evaluate the hypothalamic, pituitary, and gonad regulating systems

MATERIAL & METHODS

The Department of Obstetrics and Gynecology at MLB Medical College oversaw this prospective case-control research that lasted for a full calendar year. Patients in the hospital's ER and outpatient clinic were chosen at random. Women between the ages of 20 and 40 were included in the study since that was the age range in which reproduction was possible. Primary and secondary infertile women with menstrual disorder (amenorrhea, oligomenorrhea, menorrhagia, irregular uterine bleeding, regular ovulation, galactorrhea, polycystic ovarian syndrome) were 150 in the Study Group. Fifty healthy, fertile women with regular periods and pregnancy rates served as the Control Group.

Eligible participants were women aged 20 to 40 with primary or secondary infertility and menstrual disorders. Exclusion criteria included hyperprolactinemia, thyroid abnormalities, tuberculosis, a history of anxiety or other psychological disorders, age below 20 or above 40, Male factor infertility, tubal difficulties, urogenital malformations, and pathological lesions are all causes of female infertility. All subjects provided written informed consent, and ethical

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clearance was obtained prior to initiating the study. Serum prolactin levels were assessed for all participants, along with a comprehensive obstetric history and relevant laboratory and radiographic tests.

We got representative samples from everyone who participated. The daily fluctuations of serum prolactin levels were reduced by collecting samples between 8 and 10 in the morning. and 9 a.m. As nipple stimulation, breast inspection, and sexual activity may all affect prolactin levels, participants were asked to fast from the previous night's meal and refrain from these activities. Participants' serum prolactin levels were measured using a commercially available kit for competitive enzyme-linked immunosorbent assay (ELISA) (Accubind ELISA Microwells).

There were 150 patients and 50 healthy controls in the trial. Serum prolactin occurrence was analyzed and compared among many groups. The findings are broken down into parts for ease of reading.

RESULTS

In the current study, we investigated 150 patients and 50 healthy controls. Serum prolactin incidence was investigated across different groups, and the results were compared. The results are presented in a series of tabular displays.

Table 1: Distribution of Subjects Across Different Groups

Cases	No. of Cases	Percentage
Primary infertility	**97**	**64.7%**
Secondary infertility	**46**	**30.7%**
Control	**7**	**4.7%**
Total	**150**	**100%**

table 1: Distribution of Cases across Study and Control Groups

The 1 represents the allocation of cases across the study and control groups. There were 102 cases of primary infertility, 48 cases of secondary infertility, and 50 cases in the control group.

Groups	Cases of Primary Infertility	Cases of Secondary Infertility	Control Group Cases
Number of Cases	102	48	50

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Table 2: Individuals with infertility are categorized as having primary or secondary infertility based on the presence or absence of menstrual dysfunction and galactorrhea.

Table 2: Menstrual Disorders and Galactorrhea-Related Case Distribution In the table, Group A includes infertile patients without galactorrhea who also experience menstrual dysfunctions, whereas Group B includes infertile patients who also experience galactorrhea and menstrual dysfunctions. The data is tabulated for ease of viewing.

Table 3: Assessment of Prolactin Levels in Participants of the Control Group

cases	Prolactin Level Range in ng/ml	Mean ± SD (Standard Deviation)
50	5.6 -21.0	14.52+_5.21

Table 3: Evaluation of Prolactin Concentrations in a Normal Sample Prolactin levels in the control group fell within the range shown in the table. The range of measured values was narrow, with a mean value of 14.62 4.31 ng/ml and a low of 5.5 ng/ml.

Group	Subgroup	Total Number of Cases (excluding)	Percentage of Cases	Cases of Primary Infertility	Cases of Secondary Infertility
A. Without Galactorrhea	1. Oligomenorrhea	57	41.2	45	15
	Secondary Amenorrhea	38	26.6	18	22
	3. Primary Amenorrhoea	17	12.0	18	-
	4. PCOD	3	2.0	3	-
B. Accompanied by Galactorrhea	1.Oligomenorrhea	3	2.3	3	1

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Group	Subgroup	Total Number of Cases (excluding)	Percentage of Cases	Cases of Primary Infertility	Cases of Secondary Infertility
	Secondary Amenorrhea	5	3.3	2	3
	3. Primary Amenorrhoea	-	-	-	-
Total		123		89	41

Table 4: Comparison of Prolactin Levels and Prevalence of Hyperprolactinemia among Various Infertility Patient Groups

Different groups	cases	Prolactin rang in ng/ml	Average ± Standard Deviation	Hyperprolactinemia	Percntage
A. Without Galactorrhoea	134			37	24.66%
1. Oligomenorrhoea	57	5-105	29.92 ± 23.95	14	23.34%
2. Amenorrhoea Secondary	38	7.4-170	38.62 ± 42.71	11	26.5%
3. Amenorrhoea Primary	17	7.5-88	21.27 ± 18.67	1	6.5%
4. pcod	2	22-35.5	26.54 ± 6.48	1	33.33%
5. Menstruation Irregular	10	12-90	25.67 ± 21.56	1	9.09%
6. Regular Anovulatory cycles	4	16.5-362	10.50 ± 13.08	1	25%
7. Regular Ovulatory cycles	5	5.5-60.5	29.90 ± 23.33	2	40%
B. With Galactorrhoea	9			6	66.66%
1. Oligomenorrhoa	5	21.5-375.0	101.44 ± 103.14	5	64.64%
2. Amenorrhoea Secondary	3	7.5-87	21.27 ± 16.67	3	65.65%

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Table 4:-: Prolactin Concentration and Incidence of Hyperprolactinemia in Infertile Patients

Hyperprolactinemia Prevalence in a Group of 150 Couples Struggling to Conceive The frequency of hyperprolactinemia in a group of 150 infertile patients is displayed in the table. Thirty-seven (24.66%) were found to have elevated levels of prolactin in their blood. Among infertile patients, those with galactorrhea had the highest frequency of hyperprolactinemia (66.6%). Infertility characterized by normal ovulation cycles had the highest frequency of hyperprolactinemia (40%), followed by polycystic ovary disease (33.3%), secondary amenorrhea (27.5%), and finally primary amenorrhea (5.5%).

Table 5: Hyperprolactinemia is characterized by elevated levels of prolactin in the blood.

Pattern Menstrual	Serum Prolactin Mean (ng/ml)	Patients	Percentag
Oligomenorrhea	72.82	18	51.1%
Secondary Amenorrhoea	117.09	13	37.0%
Primary Amenorrhoea	94.50	2	5.4%
PCOD	37.28	2	5.4%
Irregular Menstruation	94.50	2	5.4%
Regular Anovulatory cycles	380.10	2	5.4%
Regular Ovulatory cycles	61.16	3	8.1%

Table 6: In a table, researchers from the study titled "Menstrual Patterns and Serum Prolactin Levels in Patients with Hyperprolactinemia" show how individuals with this condition experienced different types of periods and different blood prolactin levels. The majority of patients had oligomenorrhea (48.7%), and the next most common symptom was secondary amenorrhea (35.1%). Compared to individuals with oligomenorrhea (69.35 ng/ml), those with secondary amenorrhea (111.52 ng/ml) had a substantially higher mean blood prolactin level (p 0.001). There was just one patient in the group with regular anovulatory cycles who had a blood prolactin level higher than 362 ng/ml, according to the data.

Table 6: Reproductive Impairment in Hyperprolactinemic Patients: Incidence of Infertility.

Infertility cases	Number	Percentage hyperprolactinemia
Primary Infertility	**27**	**71.07%**
Secondary Infertility	**8**	**28.17%**

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Infertility cases	Number	Percentage hyperprolactinemia
Total	**35**	**99%**

Table 6: The frequency with which infertility occurs in people with hyperprolactinemia is shown in the table. According to the findings, primary infertility accounted for 75.67 percent of hyperprolactinemia-related infertility cases, whereas secondary infertility occurred in 27.07 percent of cases. It's worth noting that there's a statistically significant gap between the two, as shown by the test of proportion (p 0.01).

Table 7: Hyperprolactinemic infertile patients have an elevated risk of developing galactorrhea.

Prevalence of Hyperprolactinemia in the Sample Population.	Incidence of Galactorrhea among the Sample Population.	Cases without Galactorrhoea
No of cases	5	30
%	14.29%	85.71%
Mean Serum Prolactin Level in the Sample Population.	134.86	82.5

Table 7: Incidence of Galactorrhea among Infertile Cases with Hyperprolactinemia.
The table presents the observed incidence of galactorrhea in infertile cases with hyperprolactinemia. The results indicate that 13.5% of hyperprolactinemic infertile cases were associated with galactorrhea, however, it was not consistently present in all hyperprolactinemia patients. Significantly different mean blood prolactin levels were seen between patients with and without galactorrhea (p 0.01).

Discussion

The participants were women experiencing primary or secondary sterility with or without galactorrhea, and their blood prolactin levels were measured. In addition, the researchers wanted to see how often hyperprolactinemia occurred alongside other causes of infertility in women.

A total of 150 cases and 50 healthy individuals served as the study's control group. Consistent with the results of multiple previous studies [7,8], 102 (68%) of the 150 patients were categorised as main infertility and 48 (32%) as secondary infertility. In their study, Madhuprita et al. found that 65% of infertility cases were caused by primary factors and 35% by secondary factors. People aged 20-40 who were fertile and had regular menstrual cycles served as the control group. In our analysis, the majority of primary (50%) and secondary (48.9%) infertility cases occurred between the ages of 26 and 30. The majority of women diagnosed with hyperprolactinemia and infertility were found to be between the ages of 25 and 34, as reported by the research team of Isah IA et al. [20]., therefore this conclusion is consistent with their research. It appears that hyperprolactinemia is more common amongst reproductive-age females[21-31]

Mean blood prolactin concentrations for the control group were 14.62 4.31 ng/ml (range, 5.5-22 ng/ml) [7,20]. Our study's prevalence of hyperprolactinemia (24.66%) is in line with findings from other research [5,6,7,8,10]. A 20% incidence was recorded by Mishra et al.,

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whereas an 11.5% frequency was discovered by Madhuprita et al. These results show that the female reproductive axis is more vulnerable to the effects of hyperprolactinemia. Thus, prolactin tests are crucial for identifying menstruation disorders[32-42].

Consistent with multiple other studies [7], we observed that hyperprolactinemia affected 9.09% of patients with irregular menstruation and 25% of those with normal anovulatory periods. Hyperprolactinemia is hypothesized to prevent ovulation by lowering GnRH secretion. Key regulators of GnRH neurons are kisspeptin neurons [12], which express prolactin receptors. Disrupted gonadotropin pulsatility and reduced estrogen-positive feedback impact on LH production are the chief causes of anovulation in hyperprolactinemic individuals. Similar to many other research, we found that 40% of patients in our study had idiopathic hyperprolactinemia despite having regular menstrual cycles and ultrasonographic evidence of ovulation. Our findings suggest that prolactin estimate screening is warranted for all sterile individuals, independent of underlying causes such monthly disorders or ovulation problems[43-53].

In our study, oligomenorrhea was the most common menstrual abnormality among the 37 patients with hyperprolactinemia (48.7%), followed by secondary amenorrhea (35.1%). This is due to the fact that elevated prolactin levels lead to anovulation, stop LH pulsatility, and inhibit estrogenic receptors in the hypothalamus, all of which interfere with the positive feedback effect of estradiol [13,14,15]. Normoprolactinemic hypothalamic amenorrhea has also been linked to disruptions in pulsatile LH production. Hyperprolactinemia is unique in that it counteracts the positive feedback impact of estrogen on LH release [13,14,15]. Hyperprolactinemia was seen in 8.1% of the people with hypertension in our research[54-65].

Conclusion

The most important findings of our research are as follows:

1.Those between the ages of 26 and 30 accounted for over half (40.08%) of all instances of primary infertility and nearly 47.9% of all cases of secondary infertility.

2.In our study, 24.6% of participants had hyperprolactinemia.

3.Hyperprolactinemia was shown to occur in the following menstrual diseases with the following frequencies:

A quarter of women experience oligomenorrhea.

Instances of secondary amenorrhea 30.2%

Incidence of primary amenorrhea is 5.5%

33.3% of women have polycystic ovary syndrome.

In women, 9.09% have irregular periods.

25% had regular, anovulatory cycles.

Forty percent have regular ovulation cycles.

4.Primary infertility was more common among hyperprolactinemic individuals (75.67%) compared to secondary infertility (27.07%), according to our findings. There is a statistically significant (p 0.01) disparity between the two, as determined by a test of proportion. Females with secondary infertility exhibited higher serum prolactin levels, with a mean of 19.21 15.1 ng/ml compared to the 15.18 8.485 ng/ml seen in those with first infertility [9,11]. This result coincides with that of Badesara S et al. Whereas the average prolactin level in secondary infertility was 340 310 nmol/l, 495 340 nmol/l was found by Akhter et al.

5.Among the hyperprolactinemic individuals in our research, over half (48.5%) had oligomenorrhea as their primary monthly abnormality and another 35.1 % had secondary amenorrhea.

6.Serum prolactin levels were found to be substantially higher than normal (132.96 ng/ml) in 66.6% of individuals with galactorrhea, indicating the presence of hyperprolactinemia.

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7.Our research showed that only 13.5% of hyperprolactinemic individuals exhibited clinically significant galactorrhea.

Recommendations

.1Prolactin estimation screening should be performed on all individuals with infertility, regardless of the presence or absence of menstrual problems or ovulation.

Second, although galactorrhea is the most common clinical sign of hyperprolactinemia, it is important for doctors to remember that not all patients experience this symptom.

Third, elevated prolactin levels, or hyperprolactinemia, are a potential contributor to infertility and menstruation problems.

To better understand hyperprolactinemia and create appropriate treatment techniques, further research is needed to examine the prevalence of the illness in various groups.

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