



ORIGINAL RESEARCH PAPER

Obstetrics & Gynaecology

CORRELATIONS OF HYPOTHYROIDISM AND PROLACTIN LEVEL IN FEMALE INFERTILITY PATIENTS

KEY WORDS: Infertility, hypothyroidism, Hyperprolactinemia

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ABSTRACT

Introduction: Both thyroid and prolactin hormones play key role in fertility among women. Disturbances in these hormones leads to infertility by causing menstrual irregularities and anovulatory cycles. Early detection of these hormonal imbalances can help in better outcome in patients of infertility. This study showed correlations of Prolactin level and Hypothyroidism in female infertility patients. **Materials and Methods:** In this study, we studied the thyroid profile and prolactin levels in 60 infertile women who visited the obstetrics and gynecology department or in vitro fertilization center of a tertiary care hospital. The frequency of hypo and hyperthyroidism along with hyperprolactinemia was studied, and the association between thyroid dysfunction and levels of serum prolactin was analyzed. **Results:** The majority of the infertile women were having normal thyroid function tests and normal serum prolactin level. Thyroid dysfunction was noted in 41.66% of infertile women, with 8.33% showing hyperthyroidism and 33.33% showing hypothyroidism. Hyperprolactinemia was observed in 31.66% of infertile females. Hypothyroidism was found to be positively associated with hyperprolactinemia. **Conclusion:** Thyroid function test and prolactin level is important routine workup in female infertility patients so that appropriate measures can be taken to improve results.

INTRODUCTION-

Infertility is failure to conceive after 1 year of regular intercourse without contraception. It is a global problem affecting people of all over world. About 60–80 million couples suffer from infertility every year, of which between 15 and 20 million are in India alone^[1].

While primary infertility is infertility in a couple who have never conceived, secondary infertility is an inability to conceive after a previous pregnancy.

The causes of infertility are due to female factors, male factors, combined factors, or unexplained. Under female factors, the important causes of infertility include hormonal conditions such as thyroid problems, diabetes, hyperprolactinemia, and polycystic ovary syndrome^[2].

Thyroid hormone imbalance is prevalent in the female population and is known to affect reproductive function and pregnancy. Thyroid hormones (triiodothyronine T3 and tetraiodothyronine T4) are responsible for the normal growth, sexual development, and reproductive physiology. Undiagnosed and untreated thyroid disease can be a cause for infertility as well as subfertility.^[3] Prolactin is another hormone playing an important role in female infertility. Hyperprolactinemia causes infertility by primarily interfering with ovulation. Furthermore, increased levels of thyroid-stimulating hormone (TSH) seen in hypothyroidism are often associated with increased prolactin levels, which leads to a delay in luteinizing hormone (LH) response and abnormal ovulation.

Previously many studies showed that thyroid dysfunction and hyperprolactinemia are common endocrine abnormalities in females. We consider the importance of these hormones in infertility. This study aims at studying the correlations of thyroid hormonal disorder and increased prolactin levels in female infertility cases in our institute.

MATERIALS AND METHODS

This was a prospective study conducted at a tertiary care postgraduate teaching hospital. All female infertility cases, both primary and secondary, who visited the hospital over a period of 8 months from September 2023 to April 2024 were included in the study. Informed, written and valid consent of all participants was taken. The study was approved by the institutional ethical committee.

history, duration of infertility, and obstetrics history was recorded in detail.

All female infertility patients registered at obstetrics and gynecology department or in vitro fertilization center of the same hospital and sending their blood sample to the pathology department were included in the study irrespective of age, duration of infertility, and semen analysis findings of husband. Rest of the patients in which samples were received for evaluation of other hormones were excluded from the study.

Thyroid profile analysis and serum prolactin levels were measured by a fully automated chemiluminescence immunoassay analyzer. The normal reference range for various hormones tested was serum T3: 0.8–2.1 ng/dl, serum T4: 5.5–11 ug/dl, serum TSH: 0.4–4.5 uIU/ml, and serum prolactin: 2.7–19 ng/ml according to standard protocol.

RESULTS

The present study was conducted on 60 female patients of infertility. Out of the 60 cases studied, 36 (60%) cases were of primary infertility and 24 (40%) cases were of secondary infertility. Included females had an age range of 18–42 years. The maximum number of cases (60%) belonged to 28–32 years of age group, followed by 20% of cases in the age group of 22–27 years.

It was observed that the total duration of infertility in the present study group ranged from 2 to 13 years and 36.66% of the cases had infertility for 5–7 years. [Table 1]

Abnormal menstrual pattern was seen in 50% of cases. Most had complaints of irregular menses seen in 33.33% of cases, followed by oligomenorrhea in 8.33% of cases, polymenorrhea in 5% of cases, and menorrhagia in 3.33% of cases. [Table 2]

Table 1: Duration of infertility in years of female infertility patients

Duration infertility	Total cases (%)
2-4	20(33.33)
5-7	22(36.66)
8-10	11(18.33)
11-13	5(8.33)
Total	60

Table 2: Menstrual complaints of female infertility patients

Relevant clinical history including menstrual history, family

Menstrual Complaints	Number of cases (%)
Normal	30 (50)
Irregular	20 (33.33)
Menorrhagia	2 (3.33)
Oligomenorrhea	5 (8.33)
Polymenorrhea	3 (5)
Total	60

In the present study, euthyroidism was the most common and was seen in 35 (58.33%) cases. Thyroid dysfunction was seen in the remaining 25 (41.66%) cases comprising hyperthyroidism and hypothyroidism in 5 (8.33%) and 20 (33.33%) cases, respectively [Table 3].

On studying serum prolactin levels, it was found that most females had normal levels of hormone, and hyperprolactinemia was seen in 19 (31.66%) cases [Table 3].

Of the nineteen cases of hyperprolactinemia, twelve were having hypothyroidism [Table 4]. Chi-square statistics is 21.5918 and showed a significant association between prolactin level and thyroid status ($P < 0.00001$) with a phi coefficient of < 0.05 indicating a strong positive relationship between the two parameters.

Table 3: Thyroid profile and serum prolactin in infertile females

Number of Cases (%)	Thyroid Status			Serum Prolactin	
	Hypothyroidism	Hyperthyroidism	Euthyroidism	Normal	Hyperprolactinemia
100(100)	20 (33.33)	5 (8.33)	35 (58.33)	41 (68.33)	19 (31.66)

Table 4: Distribution of cases showing correlation of thyroid and prolactin levels

	Hypothyroidism	Euthyroidism/Hyperthyroidism
Hyperprolactinemia (n=19)	12	7
Normal prolactin (n=41)	3	38

DISCUSSION

Thyroid disorders including overproduction of thyroid hormones (hyperthyroidism) and underproduction of the hormones (hypothyroidism) can cause significant reproductive problems in women. Human oocytes and granulosa cells express thyroid receptors, and thus abnormal hormone production is associated with delayed onset of puberty, menstrual disorders, anovulatory cycles, infertility, and early pregnancy loss.^[2]

Prolactin, a peptide hormone produced by the anterior pituitary gland, is primarily associated with breast development during pregnancy and milk production during lactation. Increased blood levels decrease the secretion of gonadotropin-releasing hormone in the hypothalamus, thereby decreasing the secretion of LH and follicle-stimulating hormone in the pituitary gland which in turn leads to decreased production of estrogen and progesterone by the ovaries. Decreased hormone production in the ovaries leads to disruption of the normal follicular development causing atresia of the dominant follicle, which interferes with ovulation. Hyperprolactinemia could be physiological like in pregnancy or pathological like hypothalamic-pituitary disease or idiopathic in origin.^[1]

There is also a close interrelation between hypothyroidism and hyperprolactinemia. Increased thyrotropin-releasing hormone seen in hypothyroidism stimulates both thyrotrophs and lactotrophs, thus increasing the level of both TSH and prolactin. Morphological changes observed in the follicles in hypothyroidism can be a consequence of higher prolactin production.^[5] Adequate thyroid supplementation can restore prolactin levels to optimal range and normalize ovulatory

function.

Our study consisted of 60 infertile women with a maximum number of women in the age group of 28–32 years followed by 22–27 years. Such findings have also been reported by Mehra *et al.* ($n = 100$) with most infertile women in the age group of 28–32 years and Saxena *et al.* ($n = 50$) as 22–30 years.^[6,7] Biradar SM *et al.* ($n = 50$) also reported most infertile women in the age group of 24–28 years.^[8] Kundu, Sonia *et al.* studied 100 patients of age group 18 -42 years just like in our study. In our study, the maximum duration of infertility ranged from 5 to 7 years. Most infertile women in the study by Mehra *et al.* had a duration of infertility of < 3 years, while Biradar SM *et al.* have reported most cases with an average duration of infertility of < 5 years. The duration of infertility in both these studies was found to be lesser in comparison to our study.^[8] In our study, 50% of the infertile women complained of menstrual disturbances. In other studies, a higher number of cases with menstrual abnormalities were reported with Binita *et al.* ($n = 160$) as 61.2% and Mehra *et al.* as 57%.^[9,6]

This study was directed to evaluate how many infertile females have an imbalance in thyroid and prolactin hormone levels. In the present study, out of 60 cases studied, abnormal thyroid hormone levels were seen in 41.66% of infertile females with 8.33% showing hyperthyroidism and 33.33% showing hypothyroidism. This is comparable to the prevalence of thyroid dysfunction found in infertile women as 33.3% in a study by Rahman *et al.* ($n = 30$) and 25.5% by Keerthanaa and Hiremath ($n = 200$).^[11,12] Majority of the patients in our study as well as most other studies were in a euthyroid state, which may be attributable to other causes of infertility.

In our study, hypothyroidism was seen in 20 (33.33%) of female infertility cases. In a study conducted by Verma *et al.* on 394 infertile women, the frequency of hypothyroidism was higher being 23.9%.^[13] Another work published by Keerthanaa and Hiremath ($n = 200$) reported 23.5% of infertile females were hypothyroid.^[12] This is lower in comparison to our results. This discordance can be probably due to the smaller sample size of our study. Few other studies also reported a higher number of female infertile patients with hypothyroidism with Mehra *et al.* ($n = 100$) observing hypothyroidism in 22% of cases, whereas Priya ($n = 95$) and Hivre MD *et al.* ($n = 50$) found occurrence of 53.7% and 20%, respectively.^[10,14] Our study was having more number of hypothyroid infertile patients as reported by Biradar SM *et al.* ($n = 50$) Rahman *et al.* ($n = 30$), Rijal *et al.* ($n = 735$) where the occurrence of hypothyroidism was found to be 6%, 6.7% and 7.6% respectively.^[8,11,15]

Hyperthyroidism was seen in 8.33% of our cases. and Mehra *et a and* Binita *et al.* reported lower prevalence as 1% and 5% cases of hyperthyroidism, respectively, while a study by Hivre MD *et al.* and Biradar SM *et al.* reported hyperthyroidism in 34% and 26% of infertile women, respectively.^[6,8,9,14] This was more in comparison to our study.

Vidhyalakshmi did a prospective study that was undertaken to determine the frequency of hyperprolactinemia in a group of infertile women. Among 100 infertile patients, 10 (10%) had elevated levels of serum prolactin.^[16] These findings does not correlate to our study, where 31.66% showed increased prolactin. Other studies showed a higher prevalence of infertility cases showing elevated prolactin levels with Sharma *et al.* and Binita *et al.* 41% cases, Verma *et al.* 37% cases, Keerthanaa *et al.* 31% cases, Mehra *et al.* 26% cases, and Verma *et al.* reporting 18.3% of cases^[5,9,10,12,13].

Just like in our study, Mehra *et al.* also observed a highly significant association between prolactin levels and thyroid status among infertile women^[6]. Case-control study done by Hivre MD *et al.* and Binita *et al.* reported that the infertile

women with hypothyroidism had significantly higher prolactin levels in comparison to the control group.^[9,14] Similarly, Saxena *et al.* ($n = 50$) also noted a strong positive correlation between serum TSH and prolactin in infertile women ($P < 0.05$).^[7]

CONCLUSION

It is imperative to check the thyroid status and prolactin levels in all infertile females as a part of their diagnostic protocol. Hypothyroidism combined with or without hyperprolactinemia is proved to be one of the important causes of female infertility and therefore should be ruled out before other therapeutic options.

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Conflicts of interest

There are no conflicts of interest.

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