

## Association of Hyperprolactinemia with Hypothyroidism in Infertile Women: A Cross Sectional Observational Study

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### Abstract

**Background:** Thyroid and prolactin hormone levels are associated with fertility disorders among women. This study aims to find out the correlation between hyperprolactinemia and its correlates with hypothyroidism in female infertility.

**Aims & Objectives:** To assess the biochemical association of hyperprolactinemia in infertile women with hypothyroidism.

**Material & Methods:** This cross-sectional observational study recruited 100 infertile women who came to the Department of Obstetrics & Gynecology, of our tertiary care hospital from April 2022 to March 2023. Women diagnosed with primary infertility & marriage span of >2 year were included in the study. Complete history taking, general & medical examination was conducted by an experienced gynecologist. Venous sample was collected & sent to lab for assessment of Complete blood count, haemoglobin level, renal function test, blood sugar levels, and serum TSH & Prolactin levels. Normal serum TSH levels considered were 0.35-5.5 µIU/ml. Hyperprolactinemia was considered if prolactin levels were >25 microgram/L.

**Results:** A total of 100 patients were enrolled in this study, out of which 21% were <24 yrs. age, 36% were 25-29 yrs of age, 33% were 29-39 yrs of age, 26% were of 30-34 yrs age & 17% were in 35-40 yrs of age. The mean age, duration of marriage, mean serum TSH levels & serum Prolactin levels were observed to be higher in infertile women (p value <0.05). No statistically significant difference in the mean serum TSH levels & serum Prolactin levels were observed in primary & secondary infertility groups (p value >0.05). A positive correlation was observed between the age of women, the number of years of marriage & infertility was observed (p value <0.05). A positive correlation between mean serum TSH levels & serum Prolactin levels were observed (p value >0.05).

**Conclusion:** Abnormally high prolactin levels & low thyroid levels were observed in infertile women. Infertile couples should be regularly screened for evaluation of prolactin and TSH levels for an early intervention & conception.

**Keywords:** Hyperprolactinemia, Hypothyroidism, Infertility.

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### Introduction

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Primary Infertility is defined as failure to conceive within one or more years of regular unprotected coitus. Patients suffering from primary infertility have never conceived, while patients suffering from secondary infertility became pregnant but failed to conceive later.[1] 80-90% of fertile couples conceive within the first year of attempting pregnancy. In about 30-40% of cases, males & 40-55% of cases, females are responsible. Male factors causing infertility could be attributed to hypothalamic pituitary disease, testicular disease, and post testicular defects in sperm transport & idiopathic. Female factors attributing to infertility could be ovulatory & ovarian factors, peritoneal /tubal factors, endometriosis, and uterine /cervical factors. [2]

Normal thyroid levels in the body are essential for fertility & sustain pregnancy after conception. Abnormalities in the thyroid function can be a cause for anovulatory cycles, luteal phase defect, high prolactin (PRL) levels, and sex hormone imbalances. Thus, thyroid function tests should be conducted in women with menstrual irregularities, family history of thyroid, previous miscarriages & not able to conceive after one year of unprotected coitus.[3] Krassas GE et al 2000 study noted the prevalence of hypothyroidism to be 2-4% in the reproductive age group & main cause of infertility & abortion.[4] Subclinical hypothyroidism is considered when there is a slight increase in TSH levels with normal T3 and T4 indicates whereas clinical hypothyroidism occurs when high TSH levels are accompanied by low T3 and T4 levels.[5]

Prolactin hormone is secreted by the pituitary gland; it has an important role in the reproductive system & promoting lactation in women. It also regulates human behaviour & immune system. Hypothalamus secretes Prolactin Inhibitor Factor which controls the prolactin secretion High serum levels of prolactin in the blood is known as Hyperprolactinemia

which normally occur in pregnancy and lactation. High serum prolactin levels in non- pregnant females hamper the production of estrogen and progesterone & disturb the ovulation cycle. [6] In men, Hyperprolactinemia causes galactorrhoea, decreased libido, impotence & infertility. Etiology behind Hyperprolactinemia could be disrupted hypothalamic-pituitary axis due to pituitary tumours, hypothyroidism, stress & drug induced. Increased levels are also observed when vasoactive inhibitory peptide (VIP) and Thyrotropin releasing hormone (TRH) levels are high.

TRH stimulates the production & secretion of thyrotropin (Thyroid stimulating hormone -TSH) & prolactin by the anterior pituitary gland. Thus, individuals could suffer from galactorrhea. [7] Cooper DS 1984 reported higher levels of serum prolactin in 30% cases with primary hypothyroidism. [8]

Hyperprolactinemia may develop in occur in individuals with primary hypothyroidism, as in hypothyroidism, a compensatory increase in the secretion of central hypothalamic TRH occurs, resulting in stimulation of prolactin secretion.[9] Thus this cross-sectional observational study was designed to assess the biochemical association of hyperprolactinemia in infertile women with hypothyroidism.

## Material & Methods

This cross-sectional observational study recruited 100 infertile women who came to the Department of Obstetrics & Gynecology, of our tertiary care hospital from April 2022 to March 2023. Women diagnosed with primary infertility & marriage span of >2 year were included in the study. Women with age >35 yrs, abnormality of the urogenital tract, tubal blockage, genital tract, thyroid disease, thyroid surgery, any other comorbid illnesses, with husbands having abnormal semen analysis were excluded from the study. A written informed consent was

taken from all the participants. Institutional ethical approval was obtained. Complete history taking, general & medical examination was conducted by an experienced gynaecologist.

On the third day of menstrual cycle, venous sample was collected & sent to biochemistry lab for assessment of Complete blood count, haemoglobin level, renal function test, blood sugar levels, and serum TSH & Prolactin levels. Normal serum TSH levels considered were 0.35-5.5  $\mu$ IU/ml. Hyperprolactinemia was considered if prolactin levels were >25 microgram/L. Semen analysis was conducted to check for Volume, appearance, Liquefaction time, Ph, total sperm count, colour, viscosity, motility, pus cells, RBCs, morphology. Semen sample was collected in a collection cup following period of abstinence of at least 72 hours. Hysterosalpingogram to rule out tubal blockade & ultrasound was conducted.

### Statistical analysis

The data collected was tabulated & analyzed using SPSS version 22.0 for Windows (IBM Corp, India). Quantitative data are presented as mean  $\pm$  SD or proportions. Values were expressed as

number (n) and percentage (%). Spearman correlation test was utilized to find the correlation between infertility, serum TSH levels and serum prolactin levels. P-value 0.05 at 90% confidence interval was considered to be statistically significant.

### Results

A total of 100 patients were enrolled in this study, out of which 21% were <24 yrs. age, 36% were 25-29 yrs of age, 33% were 29-39 yrs of age, 26% were of 30-34 yrs age & 17% were in 35-40 yrs of age. The mean age, duration of marriage, mean serum TSH levels & serum Prolactin levels were observed to be higher in infertile women (p value <0.05). No statistically significant difference in the mean serum TSH levels & serum Prolactin levels were observed in primary & secondary infertility groups (p value >0.05). (Table 1) The incidence of hypothyroidism in hyperprolactinemia was 32.69%. A positive correlation was observed between the age of women, the number of years of marriage & infertility was observed (p value <0.05). A positive correlation between mean serum TSH levels & serum Prolactin levels were observed (p value >0.05). (Table 1)

**Table 1: Clinical and biochemical profile of infertile women.**

Variables	Groups	N	Mean $\pm$ SD	P value
Age (yrs)	Primary infertility	72	26.32 $\pm$ 3.71	<0.05
	Secondary infertility	28	28.45 $\pm$ 4.76	
Duration of marriage (yrs)	Primary infertility	72	4.78 $\pm$ 2.24	<0.05
	Secondary infertility	28	6.1 $\pm$ 1.81	
TSH ( $\mu$ IU/ml)	Primary infertility	72	3.13 $\pm$ 3.02	>0.05
	Secondary infertility	28	5.61 $\pm$ 7.24	
Prolactin (microgram/L)	Primary infertility	72	25 $\pm$ 10.2	>0.05
	Secondary infertility	28	28 $\pm$ 18.67	

### Discussion

Fertility is a major health issue globally, impacting the social, mental, financial aspect of married couples. [10] According to World health organization every one in six people experience infertility in their lifetime. In Katole & Saoji et al 2019 study,

8.9% of women in 25-39 yrs age in urban population of Central India experienced infertility.[11] Romero Ramos R 2008 noted the rising incidences of female infertility from 10-20%. [12]

In the present study, 100 patients were enrolled, out of which 21% were of <24 yrs

age, 36% were of 25-29 yrs of age, 33% were of 29-39 yrs of age, 26% were of 30-34 yrs age & 17% were in 35-40 yrs of age. Out of 100, 72 % of the patients experienced primary infertility while 28 % patients experienced secondary infertility. Accordingly, in Kumar D et al 2007 study primary & secondary infertility occurred in 15% of all women globally. [13] Unuane D et al 2011 noted female infertility in around 37% of all infertile couples. [14]

In the present study, the mean age, duration of marriage, mean serum TSH levels & serum Prolactin levels were observed to be higher in infertile women (p value <0.05). No statistically significant difference in the mean serum TSH levels & serum Prolactin levels were observed in primary & secondary infertility groups (p value >0.05). (Table 1) A positive correlation was observed between the age of women, the number of years of marriage & infertility was observed (p value <0.05). A positive correlation between mean serum TSH levels & serum Prolactin levels were observed (p value >0.05). (Table 1)

In the present study, the incidence of hypothyroidism in hyperprolactinemia was observed to be 32.69%. Similarly, Kumar MP, Yadav MK 2019 study noted hyperprolactinemia in 18% of women exhibiting hypothyroidism.[15] Goswami Binita et al. 2009 study observed hyperprolactinemia in 46.1% infertile women with hypothyroidism.[16] Ambreena AR 2020, observed that the hyperprolactinemia was more common in overt hypothyroidism (33%) than in subclinical hypothyroidism (12%). This could be attributed to high levels of TRH in primary hypothyroid patients. Also, females with Hypothyroidism had higher prevalence of hyperprolactinemia than males. Thus, suggesting the role of estrogen as stimulus. Such hormonal changes can cause infertility in women with emotional and financial burden. [17]

Similar observations were reported by Meir et al. [18] and Bahar et al. study [19]. Noor ul Ain et al 2017 study concluded a higher rate of infertile women with unusually high prolactin levels than with low thyroid levels. Hypothyroidism is noted to be correlated to hyperprolactinemia & thus suffering women exhibit ovulatory collapse resulting in infertility. [20]

Hormonal imbalances of female reproductive system result due to malfunctioning of hypo-thalamic-pituitary ovarian axis leading to infertility. Thyroid function affects the male and female gonads & decreases the chances of conceiving. [8] Moreover many a times infertile females have normal menstrual cycle in spite of high serum prolactin level. Hormones released from pituitary gland like TSH & prolactin acting synergistically with follicle stimulating hormone & luteinizing hormone enhance the entry of non-growing follicles into the growth phase.[9] Structural changes observed in the follicles can be attributed to high prolactin levels & production, which inhibits the action & secretion of gonadotropins. The serum levels of prolactin should be assessed in the cases of women with hypothyroidism & a timely treatment should be ensured to prevent or treat infertility. [11]

## Conclusions

The study concluded high incidence of hyperprolactinemia was observed in infertile women. A positive correlation was noted between hyperprolactinemia and hypothyroidism. Thus, early detection of hypothyroidism and hyperprolactinemia in infertile women is essential, as it could be treated & help infertile couples in early conception.

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