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Correlation between Serum Prolactin and Thyroid Profiles among the Infertile Women of Eastern India- A Cross-Sectional Study

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Abstract

In today's environment, infertility is a worldwide health concern. It is a social stigma in countries like India. The etiology behind it is multifactorial. Disorders related to thyroid gland and hyper prolactinemia have substantial contribution towards the causation of female infertility. The current research was conducted to evaluate the prolactin and thyroid profiles of infertile females in the reproductive age group, as well as any association between the two, in light of the aforementioned results. One hundred infertile women had their serum levels of prolactin, thyroid stimulating hormones (TSH), free tri-iodothyronine (FT3), and free thyroxine (FT4) evaluated. The findings were compared to those of one hundred age-matched women. Among the infertile individuals, correlations between blood prolactin and serum TSH, FT3, and FT4 were also found. When compared to controls, infertile patients have a large rise in TSH and prolactin and a considerable drop in FT4. Serum prolactin has a substantial negative connection with both FT3 and FT4, and a significant positive correlation with TSH in infertile cases. Hyperprolactinemia and abnormal thyroid profiles have a major impact on a childbearing woman's fertility.

Keywords: Infertility, Prolactin, Tri-Iodothyronine, Thyroxine.

Introduction

A worldwide problem affecting the reproductive system is infertility. Many regions still fail to notice the issue, even if it is enormous. This is especially true in emerging nations like ours (1). Infertility is defined as a woman's inability to conceive after a year of frequent, unprotected sexual activity (2). Both spouses are affected by this condition. The underlying cause can be identified in 85% of instances, but in the other cases, the concealed agent remains a mystery. Even though both spouses are often at blame, the disease has far-reaching effects on the female partner's mental health in addition to her physical, social, and cultural well-being. So, it is important to carefully assess these instances whenever possible before making a diagnosis or prescribing medication (1, 3). Multiple factors may contribute to the underlying cause of infertility. It may be the result of a chronic illness or ovulatory disorders, or it may be caused by environmental and lifestyle factors (2). According to several studies, ovulatory disorders are the leading cause of female infertility. In cases of infertility, it is crucial to thoroughly assess the underlying endocrine dysfunctions since the ovarian functions primarily are regulated by these organs (4-6). Faulty functioning of the hypothalamic pituitary ovarian (HPO) axis is associated with Group II ovulatory diseases, which constitute 85% of ovulation-related illnesses. An essential part of a woman's reproductive process is the highly controlled HPO axis (7). The HPO axis is heavily influenced by a number of hormones, such as prolactin and thyroid hormones (8). Infertility and reproductive physiology are impacted when the thyroid gland malfunctions, which in turn affects the gonads and a host of other organs (9). All steroid hormones, including sex steroids, have lipophilicity and intracellular nuclear receptors, which is similar to the way thyroid hormone works. Therefore, fertility depends on the thyroid gland operating normally so that the ovaries can do their job (10, 11). The anterior pituitary gland secretes the polypeptide hormone prolactin, which plays an

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important role in the maturation of the mammary gland and the production of milk. Defects in its secretion may lead to a wide range of diseases (12). Due to suppression of gonadotropin releasing hormone through hyperprolactinemia, it leads to amenorrhoea and contributes to infertility (13-16). Hyperprolactinemia is more prevalent in hypothyroidism than in other thyroid conditions (17). Elevated prolactin levels may explain the thyroid follicular alterations seen in hypothyroidism. When these individuals take thyroid hormone supplements, their prolactin levels may return to normal, reversing its impact (18, 19). Since thyroid hormone is necessary for the generation of progesterone and oestrogen, menstruation irregularities and infertility are symptoms of both hypothyroidism and hyperthyroidism (6, 20, 21). Therefore, the foundation of assessing a case of female infertility is the assessment of serum prolactin in addition to thyroid profiles, particularly the TSH (11). In light of these results, the current research set out to examine the prolactin and thyroid profiles, as well as any link between the two, in infertile women of childbearing age.

Methodology

A tertiary care teaching hospital in eastern India collaborated with the department of biochemistry to carry out a 2-year, hospital-based cross-sectional case-control research. The Institutional Ethics Committee gave its stamp of approval to the research plan. A sample size of 100 people per group was enough to detect a significant difference in thyroid and prolactin profiles, assuming a medium effect size (Cohen's d = 0.5) and power 80%. This research therefore comprised one hundred instances of female infertility, with participants ranging in age from twenty to forty, who had visited the gynaecology department either as an outpatient or an inpatient. As a control group, the research included 100 fertile female individuals of similar age. A questionnaire was administered to all respondents, and all case data were gathered using a specified proforma. All participants gave their written, informed permission. Cases were women diagnosed with infertility between the ages of 20 and 40 who had been married for at least a year, could read and sign an informed consent document unique to the research, and consented to participate. Exclusion criteria for this research included a history of thyroid surgery, a current or past diagnosis of thyroid illness, an apparent organic lesion, a congenital defect of the urogenital tract, or infertility caused by male or tubal causes. People who were likely to change their prolactin or thyroid hormone status due to their medication use were also not included in the research.

Fasting blood sugar (FBS) and regular biochemical parameter assessment were performed using venous blood collected in fluoride vials and plain vials, respectively. We also use serum from plain vials to estimate thyroid profiles and prolactin levels. We used standard kits to estimate routine biochemical parameters in the Toshiba FA120 auto-analyzer, including FBS, serum urea, creatinine, triglycerides (TG), total cholesterol, and high density lipoproteins (HDLc). Using standard kits, the Beckman Coulter chemiluminescence immunoassay was used to assess hormone parameters such as serum TSH, free tri-iodothyronine (FT3), free thyroxine (FT4), and prolactin.

A normal range for TSH is 0.27 to 4.20 μIU/ml. Individuals were deemed to be experiencing sub-clinical hypothyroidism if their TSH value was high, even when their FT3 and FT4 levels were within normal ranges. A case was considered hyperthyroidism if the TSH was low but the FT3 or FT4 levels were high or hypothyroidism if the TSH was high but the FT3 or FT4 levels were low.

Statistical Analysis

Kolmogorov-Smirnov test was used to test the normality. Data that did not follow a normal distribution is shown as median± interquartile ranges (IQR), whereas continuous data that did follow a normal distribution is shown as mean±standard deviation (SD). To compare variables with normal distribution, an unpaired t-test was used. Since these variables did not have a normal distribution, we performed the Mann-Whitney U test to find out how they differed, and we used Spearman's correlation coefficient to see whether there was any relationship between them. Statistics was deemed significant when the P value was less than 0.05.

Results

Table 1 show the results of the statistical analysis, which demonstrated that routine biochemical measures were not significantly different between the infertile patients and the controls. The research population's age distribution reveals that the highest number of infertility cases occur in the 31–35 age bracket, followed by the 26–30 age bracket, as outlined in Figure 1. Table 2 shows that among the hormonal measures, infertility patients had significantly lower FT4 levels than controls, whereas infertility cases have significantly higher serum TSH and prolactin levels. Subclinical hypothyroidism affects approximately 50% of infertility cases as shown in figure 2, whereas overt hypothyroidism affects 24%.

Table 1: Biochemical Parameters in Study Groups

Parameters	Controls (n=100) MEAN ± S.D.	Cases (n=100) MEAN ± S.D.	p-value
FBS (mg/dl)	84.93 ± 9.54	88.33 ± 12.61	0.053
Urea (mg/dl)	25.18 ± 4.49	25.94 ±5.02	0.263
Creatinine (mg/dl)	0.91 ± 0.15	0.90 ± 0.15	0.638
Total Cholesterol (mg/dl)	142.48 ± 16.36	148.60 ± 31.41	0.087
TG (mg/dl)	105.61 ± 34.32	114.26 ± 35.55	0.082
HDLc (mg/dl)	38.35 ± 8.25	38.32 ± 8.76	0.981

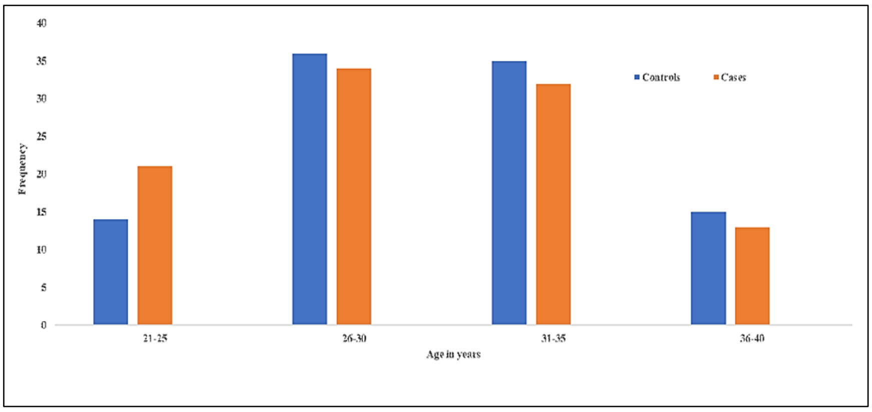

Figure 1: Age Distribution of Study Population

Table 2: Hormonal Parameters in Study Groups

Parameters	Controls (n=100) MEDIAN ± IQR	Cases (n=100) MEDIAN ± IQR	p-value
FT3 (pg/ml)	2.99 ± 0.607	2.97 ± 0.47	0.680
FT4 (ng/ml)	0.87 ± 0.25	0.78 ± 0.27	0.007*
TSH (µIU/ml)	3.90 ± 2.54	4.80 ± 5.53	0.002*
Prolactin (ng/ml)	16.42 ± 6.98	21.38 ± 25.54	< 0.001**

*p value <0.05, **p value <0.001

According to the research, there is a strong positive link between TSH and prolactin as depicted in table 3 and figure 3, and a strong negative correlation between serum prolactin and both FT3 and FT4 as represented in table 3, figure 4 and figure 5.

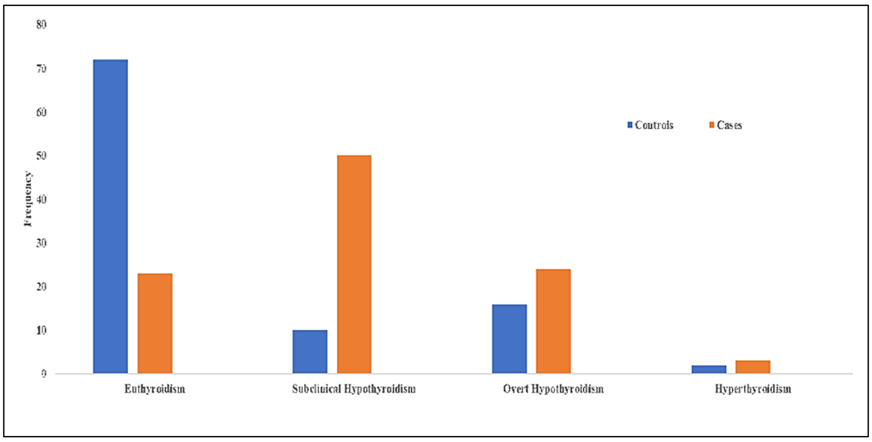

Figure 2: Thyroid Hormone status in Cases and Controls

Table 3: Correlation of Prolactin with Thyroid Profile in Infertile Cases

Parameters	Prolactin	
	r-value	p-value
FT3	- 0.27	0.006*
FT4	- 0.43	< 0.001**
TSH	0.54	< 0.001**

*p value <0.05, **p value <0.001

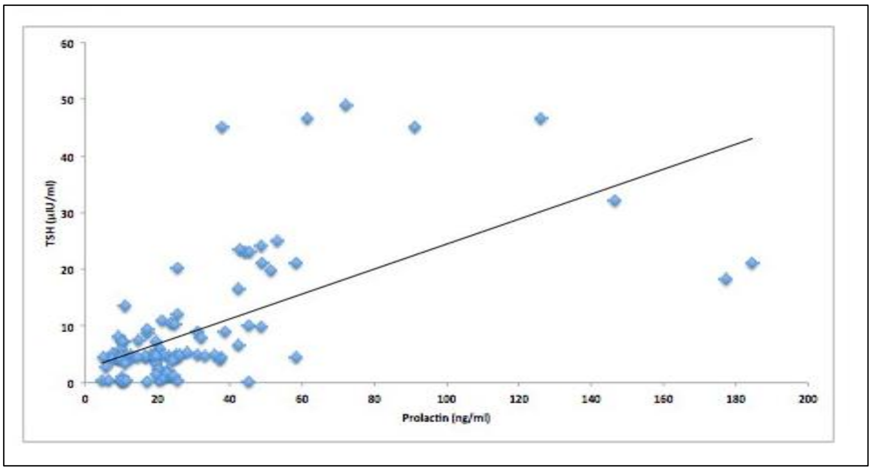

Figure 3: Correlation between Prolactin and TSH among Cases (r 0.54, p < 0.001)

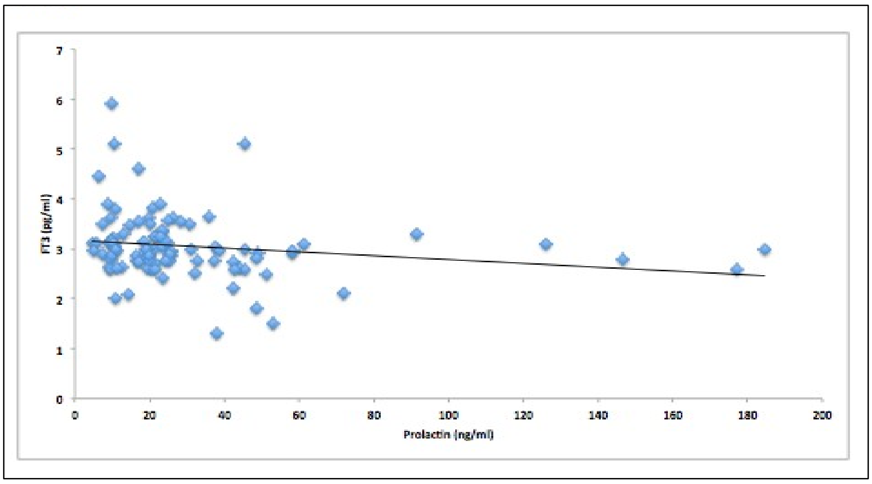

Figure 4: Correlation between Prolactin and FT3 among Cases (r – 0.27, p < 0.05)

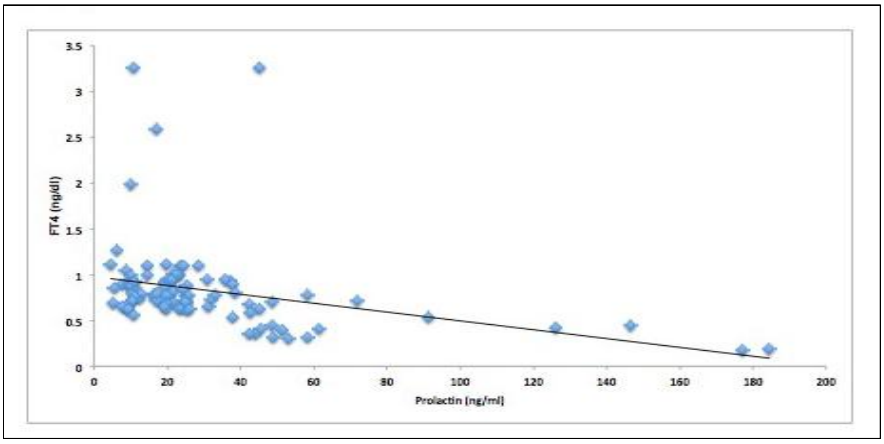

Figure 5: Correlation between Prolactin and FT4 among Cases (r – 0.43, p < 0.001

Discussion

There was no statistically significant variation in lipid profiles between the patients and controls, suggesting that metabolic variables are not likely to be the cause of the observed hormonal imbalance. It is possible that the high desire to have a family occurs between the ages of 26 and 35, as this is when the majority of female infertility cases occur. When comparing infertile patients to controls, this research found that FT4 levels were significantly lower and TSH levels were much higher'. When comparing infertile patients to controls, there is a statistically significant rise in prolactin levels. These findings resemble findings of many other researches done previously (22, 23). In addition, the research found that serum prolactin was positively correlated with TSH and negatively correlated with FT3 and FT4. Many existing data also are in line with these findings (3, 8, 9). This study has shown half of infertile women had subclinical hypothyroidism, which is consistent with earlier research (24).

Hormones produced by the thyroid also play an important role in the whole reproductive process, including pregnancy. Ovulation, the luteal phase, sex hormone imbalance, and hyperprolactinemia are among ways in which hypothyroidism affects fertility. Since hyperprolactinemia counteracts the effects of gonadotropin releasing hormone and follicle stimulating hormone, it further hinders fertility. Additionally, it disrupts the production of gonadal steroid hormones (8, 22). Reduced levels of sex hormone-binding globulin and disruptions to peripheral estrogen metabolism are additional symptoms of hypothyroidism. When these processes come together, they cause infertility by sending a negative signal back to the pituitary gland (10).

Thyroid hormone abnormality should be considered as very crucial parameter while evaluating a case of thyroid abnormality. As both low and high thyroid profile can be unfavourable for the pregnancy outcome. In women with decreased thyroid hormone, there are irregular menstrual cycles which are frequently associated with anovulation. In women with hyperthyroidism there are impairment of quality of oocytes along with follicular atresia. These things together poorly influence the fertility (25). Abnormal thyroid status also negatively affects the endometrium interfering with implantation which further aggravates the problem. There is study that has been shown that hypothyroidism adversely affect serum progesterone and genes related to implantation (26). Abnormal thyroid function also associated with much pregnancy related complications like repeated abortion and hypertensive disorder of pregnancy. Infertile cases when found to have abnormal thyroid function status respond very well to proper treatment and proven to be clinically essential. Treatment of thyroid problem can reverse the infertility (25). All these problems gears up when associated with increased prolactin value, which is also a common finding in inferlity and hypothyroidism.

Conclusion

Infertility is a global health issue with multifactorial etiology. Thyroid abnormalities are among the treatable causes, which is commonly associated with abnormal prolactin values. Such women often found to have subclinical hypothyroidism. The reproductive status of a woman who is pregnant might be greatly affected by abnormal thyroid profiles and hyperprolactinemia. This study demonstrated a significant relationship between hypothyroidism and hyperprolactinemia with infertility. Out of the total thyroid abnormalities a maximum number of cases belong to subclinical hypothyroidism. Therefore, anytime a woman is presented with infertility, it is imperative that these characteristics be assessed thoroughly irrespective of her clinical features. When evaluated early it can show the outcome in a more positive way. However more prospective study with large sample size can further validate the findings of present study.

Abbreviations

FBS: Fasting blood sugar, FT3: free tri-iodothyronine, FT4: free thyroxine, HDLc: High density lipoprotein, HPO: Hypothalamic pituitary ovarian axis, IQR: Interquartile range, SD: Standard deviation, TG: Triglycerides, TSH: Thyroid stimulating hormones.

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None.

Author Contributions

All authors contributed equally.

Conflict of Interest

The authors declare no competing interest.

Declaration of Artificial Intelligence (AI) Assistance

The authors declare that they did not use AI-assisted tools (ChatGPT, OpenAI) during the writing process.

Ethics Approval

The study protocol was approved by Institutional Ethics Committee (ECR/84/Inst/OR/2013, IEC/IRB:148/7/9/15).

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