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Original Research Article

Correlation between prolactin, thyroid, LH, FSH, estradiol and progesterone in the infertile women

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ABSTRACT

Background: An important global health issue, infertility affects a couple's social, psychological, economic, and sexual well-being. A variety of issues stemming from abnormal hypothalamus pituitary ovarian axis dysfunction make up the hormonal diseases of the female reproductive system. The aim of the study was to find correlation between prolactin, thyroid, LH, FSH, estradiol and progesterone in the infertile women.
Methods: Present study was hospital based descriptive, cross-sectional study. 150 infertile women were required in sample size. Serum LH, FSH, estradiol was measured on day 2 of menstrual cycle and also serum TSH and serum progesterone on day 21.
Results: Around one third (38%) of the cases was married since more than 10 years. Majority 108 (72%) had primary infertility and 50% of the women had history of irregular menstrual cycles. There was significant positive correlation between TSH and prolactin (p value <0.05) and significant negative correlation of TSH with FSH and LH (p value <0.05) and there was insignificant negative correlation of TSH with estrogen (D2) and progesterone (D21). The mean value of TSH in our study was 7.47±1.82 µIU/ml.
Conclusions: TSH has strong positive co-relation between prolactin, FSH and LH indicating role in female infertility. These hormonal evaluations allow a routine etiological approach to the diagnosis of infertility.

Keywords: Estradiol, FSH, LH, Progesterone, Prolactin, Thyroid, Women infertility

INTRODUCTION

An important global health issue, infertility affects a couple's social, psychological, economic, and sexual well-being. When a couple is unable to conceive within a year of getting married despite having frequent, unrestricted sex, they are said to be infertile.[1]

A variety of issues stemming from abnormal hypothalamus pituitary ovarian axis dysfunction make up the hormonal diseases of the female reproductive system. Infertility is frequently brought on by these rather typical illnesses. A significant psychological strain is caused by infertility or difficulty conceiving. A multidisciplinary diagnostic strategy is necessary for an accurate diagnosis of these illnesses, with clinical laboratories playing a crucial role.[2]

The hypothalamic-pituitary-ovarian axis, which is functionally intact, coordinates and controls ovulation in females. This axis is regulated by several hormones, including follicle-stimulating hormone, luteinizing hormone, prolactin (PRL), and thyroid hormones. Prolactin and thyroid hormone measurements, particularly thyroid stimulating hormone (TSH), have been regarded as crucial measures in the evaluation of female infertility.[3]

It has been suggested that abnormal FSH and LH secretion in women with insufficient luteal rises in plasma

progesterone may contribute to poor follicular growth and poor corpus luteum function. Measurements of plasma estradiol and progesterone, appropriately timed during the menstrual cycle, are frequently used to detect anovulation or ovulatory malfunction in these patients, who frequently struggle with infertility issues or recurrent abortions.[4]

The ovary is made up of two cellular components that are separately activated by LH and FSH to produce ovarian steroids.[5] FSH is in responsible of follicular development and estrogen production. Estradiol, the main estrogen in humans, augment FSH's effects in the later stages of follicular development.[6]

Despite the fact that follicle growth can be induced by FSH even in the absence of LH, there is evidence that the follicles may have developmental abnormalities, such as abnormally low estradiol synthesis and a lack of luteinization and rupture upon hCG stimulation.[7]

The most frequent cause of female infertility is anovulatory infertility, which is frequently characterised by irregular menstruation, amenorrhea, or oligomenorrhoea. In order to release and maintain a normal amount of estrogen and progesterone during a menstrual cycle, thyroid hormone works synergistically with FSH and LH on the ovary. Thyroid disease has been linked to anovulatory cycles with lower fecundity and, as a result, infertility.[8]

Increased prolactin may have an adverse effect on reproduction by inhibiting the hypothalamus GnRH neurons and/or the pituitary gland's ability to secrete the gonadotropins luteinizing hormone (LH) and follicle stimulating hormone (FSH), which reduces the amplitude and frequency of LH pulses.[9]

As there is little information on the effects of various endocrine hormones, including TSH, FSH, LH, estrogen, progesterone, and prolactin, on female fertility, this study aims to evaluate and determine the correlation between the same in the diagnostic and management aspects of women who are presenting to gynaecological clinics with primary or secondary infertility, so that management can be planned accordingly.

METHODS

Present study is hospital based descriptive, cross-sectional study which was conducted in department of obstetrics and gynaecology, SMS Medical College and Hospitals Jaipur from May 2021 to June 2022. Sample size of 150 would be adequate at 95% confidence and 80% power to verify the expected correlation coefficient of 0.68 between various hormones in infertile women.

Inclusion and exclusion criteria

The study was conducted on infertile women fulfilling the inclusion and exclusion criteria. Inclusion criteria were infertile females of age between 20-40 years, women who were cooperative and willing to give consent for the study. Exclusion criteria were male factor infertility, tubal pathology factors, uterine factors, any congenital or acquired anomaly of female genital tracts, history of any thyroid surgery or patient already on any thyroid medication and drug affecting thyroid and prolactin level. We selected first 60 infertile women who attend OPD in our hospital during the study period by convenience sampling after fulfilling inclusion and exclusion criteria.

All the cases were subjected to detailed history taking regarding their age, active married life, menstrual and obstetric history, presenting complaint (if any) along with general, physical, gynecological and systemic examination with complete infertility work up. Serum LH, FSH, estradiol was measured on day 2 of menstrual cycle and also serum TSH and serum progesterone on day 21 in fasting state and at same time. Early morning samples were more preferred. Fasting 4 ml venous blood samples were collected from all participants in there early follicular phase of menstrual cycle i.e. between days 3rd to 5th in plane bulbs were evaluated for serum LH, FSH, estradiol, prolactin and serum progesterone on day 21. If indicated then only endometrial sampling, hysterosalpingography and diagnostic laparoscopy were done.

Data analysis

Continuous data was summarized in form of mean and standard deviation. Difference in mean of two groups was analysed using student t-test. Discrete data was expressed in form of proportions and difference in proportion was analysed using chi square test. The p value of <0.05 was considered as statistically significant.

RESULTS

The baseline characteristics of the whole Study cohort are given in Table 1. Mean age of participants was 28.62±5.29 years. In our study, almost half 78 (52%) of cases belonged to urban area and other half 72 (48%) belonged to rural area. Around 50 (33.3%) women are graduate. Around one third (38%, 57/150) of the cases were married since more than 10 years, followed by 4-6 years since marriage in 45 (30%) cases. In present study, family history of infertility was present among 69 (46%) of the women. Half of the women (50%, 75/150) of the women had history of irregular menstrual cycles. Majority 108 (72%) had primary infertility and only 42 (28%) had secondary infertility.

The mean level of pregnancy related hormones includes TSH, Prolactin, FSH, LH, estrogen and progesterone was shows in Table 2. In our study, 21 (14%) out of 150 had hypothyroidism. The mean value of TSH in our study was 7.47±1.82 µIU/ml which is more than the normal range, that is, 0.5-5 µIU/ml. In our study, the mean value of prolactin was 45.36±20.69 (6-30 ng/ml normal range).

Table 1: Baseline characteristics of the whole study cohort.

Baseline characteristics	Value
Mean women age	28.62±5.29 years
Residence	
Rural	72 (48)
Urban	78 (52)
Educational status	
Illiterate	12 (8)
Primary school	23 (15.3)
10th class pass	23 (15.3)
12th class pass	42 (28)
Graduate	50 (33.3)
Active married life (years)	
1-3	24 (16)
4-6	45 (30)
7-9	24 (16)
>10	57 (38)
Family history of infertility	
Present	81 (54)
Absent	69 (46)
History of irregular cycles	
Present	75 (50)
Absent	75 (50)
Type of infertility	
Primary	108 (72)
Secondary	42 (28)

Table 2: Different hormones level in infertile cases.

Variables	Mean	Standard deviation
TSH	7.47	1.82
Prolactin	45.36	20.69
FSH	3.69	1.89
LH	11.73	11.15
Estrogen	86	47.18
Progesterone	13.76	4.77

Table 3: Correlation of TSH with different hormones.

Hormones	Spearman's correlation coefficient	P value
Prolactin	0.4	0.004
FSH	-0.461	0.001
LH	-0.39	0.005
Estrogen (D2)	-0.199	0.166
Progesterone (D21)	-0.147	0.307

Table 3 depicts that there was significant positive correlation between TSH and prolactin (p value <0.05) and significant negative correlation of TSH with FSH and LH (p value <0.05) and there was insignificant negative correlation of TSH with estrogen (D2) and progesterone (D21) (p value >0.05) i.e. with increase in TSH value there was increase in prolactin value and with increment of TSH value there was decrement in FSH, LH, estrogen (D2) and progesterone (D21).

Table 4: Correlation of FSH with different hormones.

Hormones	Spearman's correlation coefficient	P value
Prolactin	-0.243	0.089
TSH	-0.461	0.001
LH	0.676	<0.001
Estrogen (D2)	-0.003	0.985
Progesterone (D21)	-0.063	0.666

In our study, there was significant positive correlation between FSH and LH (p value <0.05) i.e. with increase in FSH value there was increase in LH value and significant negative correlation of FSH with TSH and LH (p value <0.05). and there was insignificant negative correlation of FSH with prolactin, estrogen (D2) and progesterone (D21) (p value >0.05) i.e. with increment of FSH value there was decrement in TSH, prolactin, estrogen (D2) and progesterone (D21) (Table 4).

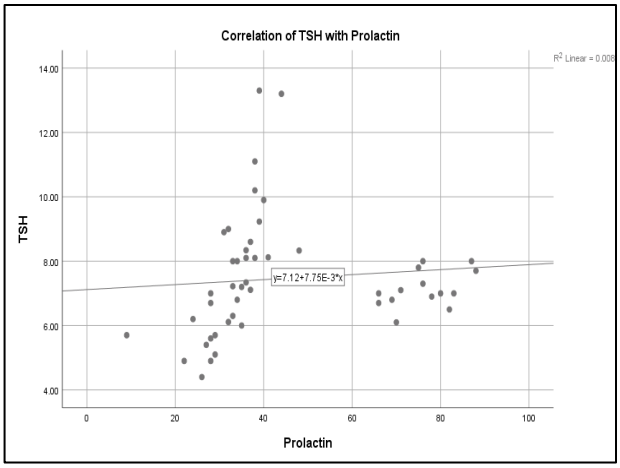

Figure 1: Correlation of TSH with prolactin.

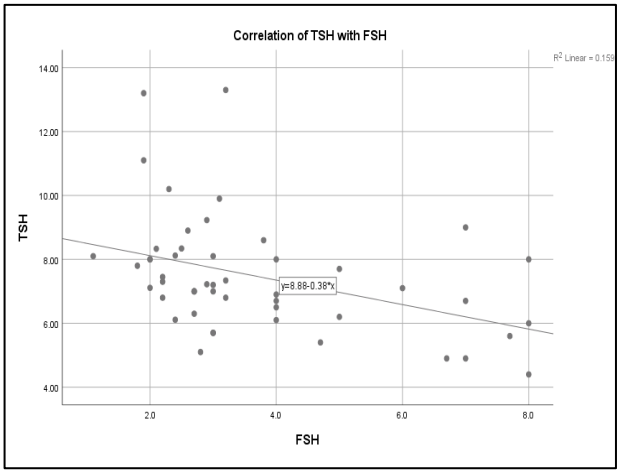

Figure 2: Correlation of TSH with FSH.

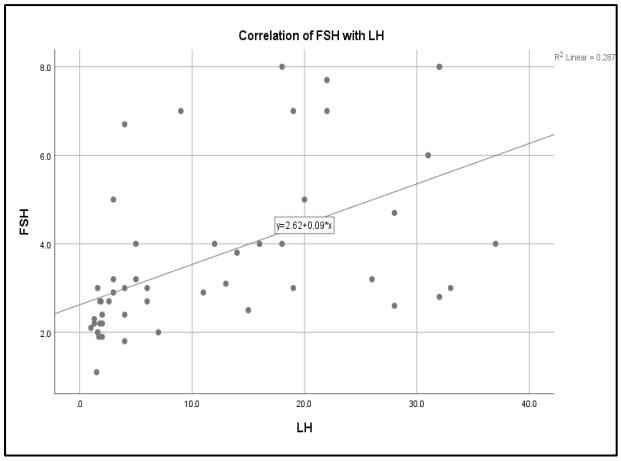

Figure 3: Correlation of FSH with LH.

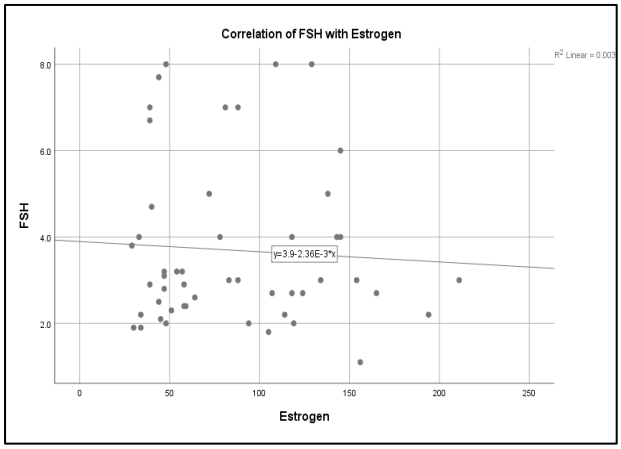

Figure 4: Correlation of FSH with estrogen.

DISCUSSION

The thyroid gland's thyroid hormones, prolactin, FSH, and LH, as well as the anterior pituitary's FSH and LH, all have a significant impact on a woman's fertility. An important component of the diagnosis of infertility is the evaluation of the hormones. The goal of the current study was to determine the relationship between the levels of progesterone hormone, estradiol, LH, FSH, thyroid hormone, and prolactin in infertile women. GnRH, one of the hormones required for ovulation, is inhibited by prolactin. Therefore, ovulation is impeded and consequently contributes to infertility when there is hyperprolactinemia. Additionally, LH and FSH discharges decrease when GnRH secretion declines. Consequently, gonadal steroidogenesis is hindered and gamete synthesis is not increased.[10]

In our study, 21 (14%) out of 150 had hypothyroidism. The mean value of TSH in our study was 7.47±1.82 µIU/ml which is more than the normal range, that is, 0.5-5 µIU/ml. In our study, the mean value of prolactin was 45.36±20.69 (6-30 ng/ml normal range).

There was significant positive correlation between TSH and prolactin (p value <0.05) in our study. Saxena et al also investigated TSH and PRL association in cases of infertility, and found a substantial positive link.[11] Turankar et al found a high incidence of hyperprolactinemia in infertile women and a positive correlation of 1:4 was found between hypothyroidism and hyperprolactinemia.[12]

Binita et al studied that the infertile women with hypothyroidism have showed significant high levels of PRL when compared to euthyroid patients.[13] The results of a study by Sharma et al among patients with subclinical hypothyroidism and primary hypothyroidism showed a positive correlation between TSH and PRL.[14]

The link between prolactin and TSH levels was statistically significant and exhibited a strong positive correlation (p<0.001). As a result, it is possible to propose hypothyroidism as a substitute marker for hyperprolactinemia. It is possible to hypothesize that such infertile women have a less sensitive hypothalamic-pituitary-thyroid axis and tissue hypothyroidism as a compensatory thyroid hormone profile.

In our study, half of the women (50%, 25/50) of the women had history of irregular menstrual cycles whereas Kumkum et al had reported the abnormality to be 57.6% in their study.[8] Thyroid dysfunction is one of major causes of reproductive disorders including menstrual irregularities, abnormal sexual development and infertility.

The mean value of FSH was 3.69±1.89 mIU/ml (normal range =2.5-10.2 mIU/ml). The mean value of LH was 11.73±11.15 mIU/ml (normal range =1.2-48 mIU/ml). The mean value of estrogen and progesterone is 86±47.18 pg/ml (normal range =15-350 pg/ml) on day 2 and 13.7±4.77 (normal range 2-25 ng/ml) on day 21 respectively.

In our study, there was significant positive correlation between FSH and LH (p value <0.05) i.e. with increase in FSH value there was increase in LH value and significant negative correlation of FSH with TSH and LH (p value <0.05).

Table 4 shows, significant negative correlation of TSH with FSH and LH (p value<0.05). There was insignificant negative correlation of TSH with estrogen (D2) and progesterone (D21) (p value>0.05). i.e. with increase in TSH value there was increase in prolactin value and with increment of TSH value there was decrement in FSH, LH, estrogen (D2) and progesterone (D21).

Prolactin antagonizes two hormones which are necessary for ovulation: The follicle stimulating hormone (FSH) and the gonadotropin releasing hormone (GnRH). When the prolactin level is high in the blood (hyper-prolactinaemia), the female will not ovulate and this will result in infertility.

This anovulation can also cause irregular menstrual cycles.[15]

Hyperprolactinemia causes infertility because prolactin inhibits the GnRH secretion. When the GnRH secretion is low, the FSH and LH secretions are also low and so they do not stimulate the gamete production and the gonadal steroid synthesis.[10]

Kumkum et al stated that amenorrhoea occurs in hypothyroidism due to hyperprolactinaemia, which results from a defect in the positive feedback of estrogen on LH, and because of the suppression of LH and FSH.[8] Kalsum et al in their study showed a substantial decrease in serum LH in follicular, ovulatory and luteal phase in hyperprolactinemic women experiencing primary and secondary infertility.[16] Significantly ($p<0.05$) decreased serum FSH levels were seen in ovulatory phase in women described with primary infertility. Similarly significant ($p<0.05$) decrease in serum FSH in luteal phase in hyperprolactinemic women reported with secondary infertility was observed.

Kalsum et al, in their study showed a significant decrease in serum LH in follicular, ovulatory and luteal phase in hyperprolactinemic women having primary and secondary infertility.[16] Significantly ($p<0.05$) low serum FSH levels were observed in ovulatory phase in women reported with primary infertility. Similarly significant ($p<0.05$) decrease in serum FSH in luteal phase in hyperprolactinemic women reported with secondary infertility was observed· Yamaguchi et al found decreased LH secretion in nocturnal hyperprolactinemic women.[17]

Santosh et al in case control study depicted that in groups of infertile women, they had a negative correlation with LH, FSH, and T3.[18]

LH and FSH both are negatively correlated with prolactin in our study. Mohan and, in their study of 70 women, found lower level of serum FSH in infertile women were when compared to control groups, difference being statistically significant ($p<0.001$).[19] Serum LH concentration was lower in the infertile group than in the control group ($p<0.001$).

Kalsum et al, in their study shows a significant decrease in serum LH in follicular, ovulatory and luteal phase in hyperprolactinemic women having primary and secondary infertility.[16] Significantly ($p<0.05$) low serum FSH levels were observed in ovulatory phase in women reported with primary infertility. Similarly significant ($p<0.05$) decrease in serum FSH in luteal phase in hyperprolactinemic women reported with secondary infertility was observed.

Yamaguchi et al found decreased LH secretion in nocturnal hyperprolactinemic women.[17]

Mc Neilly et al showed similar association between increased level of prolactin and a reduction in both LH and FSH during infertility in women with pathological hyperprolactinemia.[21]

CONCLUSION

TSH has strong positive co-relation between prolactin, FSH and LH indicating role in female infertility. Therefore, it is concluded that hyperprolactinemia with thyroid dysfunction may be a significant hormonal contributor to infertility in women. As a result, estimation of prolactin, T3, T4, and TSH regardless of her menstrual cycle at the time of initial consultation should be included in the workup for infertile women, especially those who have hyperprolactinaemia.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee with permission No. 80/MC/EC dated January 10, 2021

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