Eminence of Thyroid Stimulating Hormone (TSH) and Prolactin in Female Infertility in Tertiary Care Hospital of Himachal Pradesh

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ABSTRACT

Introduction: Fertility in females is asserted by the prevalent hormonal milieu, which is exquisitely stabilized by hypothalamo-pituitary-ovarian (HPO) axis. Thyroid dysfunctions are also known to impede the normal physiology of reproduction and pregnancy. The study was designed to evaluate the status of Thyroid stimulating hormone (TSH) and Prolactin in female infertility, and to ascertain the degree of association of TSH with prolactin in infertile females.

Material and Methods: The study recruited 50 infertile females who visited the Department of Biochemistry, Maharishi Markandeshwar Medical College and Hospital, Kumarhatti, Solan for hormonal evaluation. 50 age-matched healthy fertile females were enrolled in the control group. Blood samples were collected for analysis of TSH and Prolactin levels in both the groups.

Results: Among the study group, primary infertility was seen in 66% of the patients whereas 34% had secondary infertility. A greater part of the infertile females came out to be euthyroid (76%). A significant high serum level of prolactin was seen in infertile females as compared to the controls. A significant positive correlation was detected in infertile females making it obligatory to state that hypothyroidism was linked with hyperprolactinemia.

Conclusion: Normal operation of pituitary and thyroid are imperative for the normal physiology of reproduction. Our study elucidated an interrelation between dysfunctions of thyroid gland and pituitary gland. Hence their assessment becomes a requisite to explicate the etiopathogenesis of female infertility which will further assist in magnifying the aspect towards intriguing successful management guidelines.

Keywords: Thyroid stimulating hormone (TSH), Prolactin, Infertility, Hyperprolactinemia

INTRODUCTION

Human infertility is a crucial health issue globally, having varied impact on the life of a couple. Infertility is the failure to conceive even after one year of regular and unprotected intercourse[1]. In primary infertility, the couple has never conceived within the specified period; while in secondary infertility the couple has conceived previously but are unable to conceive currently[2]. Infertility evaluation recognizes various causes, including male infertility (30%), female infertility (35%), combination of both (20%) and idiopathic infertility (15%)[3].

Female factors resulting in infertility include ovulatory disorders, tubal factors and congenital abnormalities. Ovulatory dysfunction is caused by factors like polycystic ovarian disease and other hormonal imbalance.

Functionally intact hypothalamic-pituitary-ovarian axis regulates the physiology of reproduction in females[4]. Through the release of gonadotropin releasing hormones (GnRH), hypothalamus controls the pituitary gland which manages most other endocrine glands in human body. Thus aberrations in the chemical transmission from hypothalamus can influence pituitary gland, ovaries, thyroid, mammary gland and hence is a source of hormonal disparities. Hormonal imbalance hinder production of sufficient follicles required for the development of ovum, thereby resulting in anovulation[2].

Research explorations have proposed a close association between Hypothalamo-Pituitary-Ovarian (HPO) axis and Hypothalamo-Pituitary-Thyroid (HPT) axis. Reproductive potential may be modulated by specific thyroid hormone receptors at ovarian level. Furthermore, estrogens seem to assimilate the reciprocal relationship of these two prime endocrine axes through its impact at upper levels of HPT axis[5].

The entry of follicles into growing phase may be intensified by the collaborative action of pituitary hormones like TSH, Prolactin or growth hormone with FSH and LH. Besides this, maintenance of normal serum levels of both estradiol and progesterone requires thyroid hormones[6].

Thyroid dysfunction impedes various features of reproduction and pregnancy. Anovulation, reduced fecundity and raised morbidity during pregnancy have been found to be correlated with thyroid disorders[5,7]. Likewise, high prolactin levels affect fertility potential disrupting rhythmic production of GnRH and hence hindering ovulation[8]. The consequences are menstrual and ovulatory disorders such as amenorrhea,

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oligomenorrhea, anovulation, inadequate corpus luteal phase and galactorrhea[9].

Contemplating the aforementioned points, we planned a study to evaluate the status of thyroid stimulating hormone and prolactin levels in female infertility and to elucidate any association between the two hormones.

MATERIAL AND METHODS

The present case control study was conducted on 50 diagnosed female subjects of infertility referred to the Department of Biochemistry, Maharishi Markandeshwar Medical College and Hospital, Kumarhatti, Solan for hormonal analysis. Informed consent was obtained from all the subjects and Institutional ethical committee has approved the study. The inclusion criteria adopted for the selection of cases were diagnosis of infertility (both primary and secondary) and age between 20-40 years. Exclusion criteria included patients with tubal factors, cervical factors, pelvic inflammatory diseases or other infective sources, genetic factors including congenital anomalies of urogenital tract, male factor infertility, pre-existing thyroid disorder and hyperprolactinemia on treatment. 50 fertile age-matched female subjects were enrolled in the study as control subjects.

Biochemical analysis

Venous blood taken under aseptic conditions was allowed to clot. Serum was separated by centrifugation and analysis was performed on the clear serum. TSH and Prolactin were measured on CLIA Autoplex based on Chemiluminescence method. The normal range of serum TSH and prolactin were 0.28-6.82 µIU/ml and 1.2-19.0 ng/ml respectively.

STATISTICAL ANALYSIS

For the statistical data analysis, continuous variables were expressed as mean ± SD whereas discrete variables were expressed as percentage. Student t-test was applied for the comparison of means in the two groups. Differences were considered as significant if p value was <0.05. Pearson's correlation coefficient was calculated to deduce the correlation between TSH and prolactin in our study.

RESULTS

Among the study group, there was a predominance of primary infertility (66%) whereas secondary infertility was reported in 34% the infertile females (Table 1).

Majority of the women were found to be in the age group of 20-30 years in both the groups. It was noted that the mean age of the infertility females was lower than that of the controls but this difference was not statistically significant (Table 2).

It was heeded that a large proportion of infertile females (76%) were euthyroid having serum TSH values within the normal range. However, an aberration of the normal hormonal milieu was delineated in infertile females. The serum TSH concentration was revealed anomalous with elevated levels in 22% cases and reduced levels in 4% cases. Hyperprolactinemia was detected in 16% of the infertile females. When t-test was done, statistically significant higher prolactin (p= 0.0003) and TSH (p<0.00001) levels were found among patients of infertility when compared with control subjects as illustrated in Table 2. A statistically significant positive correlation was found between prolactin and TSH levels (r=0.7921, p<0.00001) among the infertile subjects (Figure 1).

Type of infertility	Number of cases	Percentage
Primary	33	66%
Secondary	17	34%

Table-1: Types of Infertility in the study group (n=50)

Parameter	Control (n=50)	Case (n=50)	P value
Age (years)	27.68 ± 3.80	28.6 ± 4.63	0.31557
TSH (µIU/ml)	2.05 ± 1.07	5.81 ± 4.75	<0.00001
Prolactin (ng/ml)	10.22 ± 5.40	14.9 ± 7.05	0.0003

Table-2: Parameters of the study and control group

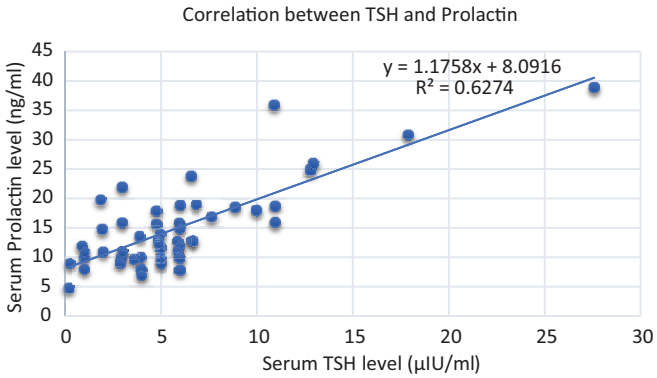

Figure-1: Scatter diagram showing correlation of TSH and prolactin in the study group

DISCUSSION

Thyroid dysfunction can incite important reproductive disorders. Thyroid receptors are exhibited by human oocytes and granulosa cells and hence aberrant secretion of hormones is linked with deferred onset of pubescence, menstrual disturbances, anovulatory cycles, infertility and early pregnancy loss [10].

Prolactin is an anterior pituitary hormone which has the foremost physiological action in lobuloalveolar growth of mammary gland during pregnancy and initiation and maintenance of lactation (lactogenesis). Raised prolactin levels can be physiological (pregnancy), pathological (hypothalamic-pituitary disease) or idiopathic in origin. Hyperprolactinemia restrains the pulsatile discharge of gonadotropin releasing hormone (GnRH) in hypothalamus. This negatively regulates the secretion of gonadotropins (Leutinizing hormone and Follicle-stimulating hormone) in the pituitary which in turn declines the production of estrogen and progesterone by the ovaries. This suppresses ovulation by decreasing normal follicular growth and development leading to atresia of the dominant follicle [11].

Hypothyroidism and hyperprolactinemia have a close association. In hypothyroidism, increased levels of Thyrotropin-releasing hormone (TRH) trigger both

thyrotrophs and lactotrophs, causing an elevation of both TSH and Prolactin. Disturbed folliculogenesis seen in hypothyroidism can be a result of raised prolactin production[12]. Sufficient thyroid supplementation can reinstall prolactin levels to optimal range and regularize ovulatory activity.

Our study comprised of 50 infertile women with the highest number of women in the age group of 20-30 years. Similar findings have also been illustrated by Mehra et al (n=100) with maximal infertile women in the age group of 28-32 years and Saxena et al (n=50) in 22-30 years [13,14]. Comparable findings have been mentioned by Biradar SM et al (n=50) with most infertile women in the age group of 24-28 years [15]. Identical to our study, in all the above researches, most females had primary infertility.

This research was aimed to assess the imbalance in thyroid and prolactin hormone levels in infertile females. On comparing the levels of prolactin and TSH in the cases and control group, the levels were significantly higher in infertile females as compared to the controls. A preponderance of euthyroidism (76%) and normal prolactin levels (84%) was elucidated on analysis of serum TSH and Prolactin levels in the infertile females. This is in accordance with the study of Binita Goswamy et al [16]. Our study revealed abnormal thyroid hormone levels in 24% of infertile females. Studies by Rehman et al (n=30, 33.3%) and by Keerthanaa and Hiremath (n=200, 25.5%) also depicted similar pattern of thyroid dysfunction in infertile women [17,18].

Our study ascertained a higher prevalence of hypothyroidism (22%) than hyperthyroidism (4%) among infertile females. Similar frequency of hypothyroidism has been detailed by Verma et al (n=394, 23.9%) [19], Keerthanaa and Hiremath (n=200, 23.5%) [18], Mehra et al (n=100,22%) [13]and Hivre MD et al (n=50, 20%) [20]. Hyperthyroidism was seen in 4% of our cases. Analogous observations were inferred by Binita et al (n=160, 5%) and Mehra et al (n=100, 1%) [16,13].

A prospective study by Vidyalakshmi determined 10% (n=100) prevalence of hyperprolactinemia in a group of infertile women. The statistics are congruent with our figures, where 16% showed increased prolactin levels [21]. The results of our study also correlate to those reported by Verma et al (n=394, 18.3%) [19].

We elucidated a significant positive correlation ($r=0.7921$, $p<0.00001$) between TSH and prolactin levels among infertile females. This is identical to the analysis of Mehra et al [13]. Research by Hivre MD et al and Binita et al proclaimed that hypothyroid infertile females depicted notable raised prolactin concentration as compared to the controls [20,16]. Likewise, Saxena et al also declared a strong positive association between serum TSH and prolactin levels in the childless women [14].

CONCLUSIONS

Our data uphold the postulation that infertile females have a surreptitious commotion in hypothalamo-pituitary-ovarian axis in contrast to their fertile equivalents. A positive association was deduced between serum prolactin and serum TSH level among the infertile females of the study group. Therefore, every infertile female should be scrutinized for TSH and prolactin levels besides other investigations, in order to open better prospects of conception for the infertile fraternity.

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