Study of the Levels of Thyroid Stimulating Hormone and Prolactin in Female Infertility

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ABSTRACT

Introduction: Infertility is defined as the failure of a couple to achieve conception (regardless of cause) after one year of unprotected and adequately timed intercourse. Measurement of prolactin and thyroid hormones, especially thyroid stimulating hormone (TSH), has been considered an important component of infertility work up in women. Dyslipidemia and other metabolic syndromes also play an important role in infertility.

Aims and Objectives: To study the levels of thyroid stimulating hormone(TSH) and prolactin(PRL), lipid profile and body mass index(BMI) in infertile women and apparently normal women.

Materials and Methods: A case control study was done at Government Kilpauk Medical College and Hospital and the serum levels of prolactin, total T3(TT3), total T4 (TT4), TSH, lipid profile and BMI were determined in 50 apparently healthy women, 50 infertile women in the age group of 16 to 35 years. The hormones were assayed using Enzyme Linked Immunosorbent Assay. Lipid profile was estimated by routine methods and BMI was calculated.

Results: There was a significant increase in mean serum prolactin levels of infertile groups when compared to control (40.61±14.48ng/dl vs 16.17±10.07 ng/dl) (p=0.001). Increased mean serum Triglyceride, increased BMI, and increased TT3 were observed in infertile group which was statistically not significant. The mean serum TSH, TT4, Total cholesterol(TC), high density lipoprotein(HDL) and age was not different in the infertile women compared to the controls.

Conclusion: Prolactin level was significantly increased in infertile women and estimation of prolactin may be included in the workup for infertile women.

Keywords: TSH, TT3, TT4, Infertility, Prolactin, Lipid profile.

INTRODUCTION:

Infertility is defined as the failure of a couple to achieve conception (regardless of cause) after one year of unprotected and adequately timed intercourse.¹ It could be primary i.e. when a couple has never conceived despite cohabitation and exposure to sexual activity over a period of two years or secondary infertility i.e. when a couple have achieved a pregnancy previously but regular unprotected sexual intercourse has not resulted in a second pregnancy.

Human infertility is a complex problem, which has numerous consequences depending on the society and cultural background, gender, lifestyle, sexual history, of the people it affects. Infertility is a global public health concern. This is partly due to its
complexity in etiology as well as difficulty in preventing, diagnosing and treating it. Although infertility is considered by some as primarily a woman's problem, men often contribute to and are also affected.

Multiple factors interplay in the reasons for female infertility. The consequences of childlessness in developing countries range from economic hardship, social stigmatization, violence and even denial of proper burial rites. Other consequences include psychological disturbances, social stigma and strain on relationships between husbands and wives.

The main causes of female infertility include ovulatory disorders, pelvic inflammatory disease (PID), endometriosis, polycystic ovarian syndrome, advanced age, environmental and occupational exposure to chemicals, congenital abnormalities and hormonal imbalance. Prolactin's primary function is to enhance breast development during pregnancy and to induce lactation. However, its secretion is pulsatile; it increases with sleep, stress, pregnancy, and chest wall stimulation or trauma. Hyperprolactinemia is defined as circulating prolactin levels above normal range, which occurs in conditions other than pregnancy and lactation, when physiological hyperprolactinemia occurs. Even in the absence of hyperprolactinaemia, hypothyroidism can contribute to infertility. This is because thyroid hormones are necessary for maximum production of both progesterone and estradiol. This is necessary for normal ovarian function and consequently, fertility.

Dyslipidemia and other metabolic syndromes also play an important role in infertility. In addition, weight loss causes a significant reduction in central fat deposits (11%) and serum luteinizing hormone levels with return of normal menstrual cycles in four out of five women. The age of menarche has been found to be correlated to risk factors for metabolic disease and this association worsened when obesity was present. So it was decided to include Lipid Profile and BMI along with hormonal factors in our study on infertility. Considering the clinical importance of hyperprolactinemia in ovulation disorders, sterility and menstruation disorders, this study was done for the determination of hyperprolactinemia, hypothyroidism, Lipid profile, BMI prevalence in infertile patients.

**MATERIALS AND METHODS:**

The Study consists of two groups and was carried out at Government Kilpauk Medical College and Hospital between September 2014 to February 2015. Group 1 consists of 50 apparently healthy women and Group 2 consists of 50 infertile women of age group 16 to 35 years.

**Inclusion criteria:**

Fifty apparently healthy women with proven fertility (who have had at least one child in the last 2 yrs were used as controls) (group-1). 50 women who were unable to conceive who were otherwise normal except for hormonal status after 1 year of unprotected sexual life (group-2).

**Exclusion criteria:**

Hypo and hyperthyroidism, Anatomical defects of reproductive tract, endometriosis, pelvic inflammatory disease (PID), other congenital disorders and other metabolic disorders like diabetes and hypertensive patients.

**Sample collection:**

Venous blood (5ml) was aseptically collected from the infertile and apparently healthy women by venepuncture and dispensed into clean plain tubes, allowed to clot, retracted and centrifuged at 5000 revolution per minute (rpm) for 5 min. The serum obtained was separated and frozen till used for prolactin, thyroid function assay (TSH, TT3 and TT4 assay) and lipid profile (Total cholesterol,
DISCUSSION:

The mean serum Prolactin concentration of the infertile women was significantly higher (p=0.001) than those of the controls. Increased mean serum Triglyceride(106.06±20.02mg/dl), increased BMI, and increased TT3 were observed in infertile group which was statistically not significant. In this study, Prolactin is significantly elevated in infertile women showing that the individual hormone is also enough to interfere with the functioning of the Hypo-thalamo-pituitary - ovarian (HPA) axis probably by acting on the granulosa cell receptors and inhibiting the process of folliculogenesis and thereby ovulation.\(^8,9\) This is because, the specific prolactin hormone receptors at the ovarian level may regulate the influence of estrogens as well as reproductive functions at the higher levels of the HPA axis thereby integrating the reciprocal relationship between these two major endocrine axis.\(^10\) These pathways may result in an abnormal feedback at the pituitary level and consequently infertility. However a higher occurrence of hyperprolactinemia (45%) was seen in the infertile group as compared to the controls in this study. This higher propensity of hyperprolactinemia is in agreement with the findings of Kumkum et al\(^11\) who had depicted a prevalence of 46% in their study. Choudhary and Goswami\(^12\) observed hyperprolactinemia in 16.6% and Singh et al in 57% of women with hypothyroidism.\(^13\) Hyperprolactinemia resulting from longstanding primary hypothyroidism has been implicated in ovulatory dysfunctions ranging from inadequate corpus luteal progesterone secretion when mildly elevated to oligomenorrhea or amenorrhea when circulating prolactin levels are high.\(^14\) Obesity is associated with cardiovascular disease, diabetes, osteoarthritis and malignancies such as colon and endometrial cancer, it is increasingly being recognized that this current obesity epidemic has

**Calculated Parameters:**

Body Mass Index (BMI): weight (in kg)/ sq. of height (in cm)

**Statistical analysis:**

Students “t” test was used to compare the level of the biochemical parameters analysed between the two groups.

**RESULTS:**

Table 1 shows the biochemical parameters of all the study subjects. There was a significant increase in the mean values of prolactin among the study groups compared to that of the control group.

**Table-1 : Biochemical Parameters of all the study subjects**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Parameters</th>
<th>Group – 1</th>
<th>Group – 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age (yrs)</td>
<td>25.04±8.84</td>
<td>25.88±5.43</td>
</tr>
<tr>
<td>2</td>
<td>Prolactin(nɡ/dl)</td>
<td>16.17±10.07</td>
<td>40.61±14.48*</td>
</tr>
<tr>
<td>3</td>
<td>TSH(mIU/ml)</td>
<td>2.11±1.72</td>
<td>2.62±1.57</td>
</tr>
<tr>
<td>4</td>
<td>TT3(nɡ/dl)</td>
<td>120.70±20.99</td>
<td>133.82±23.43</td>
</tr>
<tr>
<td>5</td>
<td>TT4(μɡ/dl)</td>
<td>8.78±1.60</td>
<td>8.75±1.63</td>
</tr>
<tr>
<td>6</td>
<td>Total Cholesterol (mg/dl)</td>
<td>176.68±15.55</td>
<td>180.08±30.45</td>
</tr>
<tr>
<td>7</td>
<td>HDL (mg/dl)</td>
<td>49.16±5.69</td>
<td>48.18±4.28</td>
</tr>
<tr>
<td>8</td>
<td>TGL (mg/dl)</td>
<td>90.06±18.63</td>
<td>106.06±20.02</td>
</tr>
<tr>
<td>9</td>
<td>BMI</td>
<td>22.60±4.97</td>
<td>26.16±4.85</td>
</tr>
</tbody>
</table>

* Statically significant (p<0.001)
also contributed to fertility problems. The mechanisms by which obesity causes or exacerbates subfertility are multifactorial. High BMI is associated with an increase in serum and follicular fluid leptin concentration and decrease in serum adiponectin levels.\textsuperscript{15,16} Leptin acting through the receptors on the theca and granulosa cells inhibits ovarian steroidogenesis. Obesity leads to menstrual abnormalities, chronic anovulation, subfertility and in the case of pregnancy to higher frequency of abortions, gestational diabetes and pre-eclampsia.

For these reasons, TSH, prolactin and lipid profile are commonly-ordered clinical tests in evaluating infertile women.

**CONCLUSION:**

Increased prolactin levels even without thyroid dysfunction and dyslipidemia may be a major contributory hormonal factor in infertility among infertile women. Estimation of prolactin, may be included in the workup for infertile women and this can be further confirmed if larger sample size is analysed especially focusing on prolactin.

**REFERENCES:**

