Original article:

A STUDY ON SERUM PROLACTIN LEVEL AND ITS RELATIONSHIP WITH THYROID PROFILE IN INFERTILE WOMEN

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ABSTRACT

INTRODUCTION AND OBJECTIVE: Human infertility is a global health concern partly due to its complexity in etiology as well as difficulty in preventing, diagnosing and treating it. Clinical and experimental studies have suggested a close relationship between the Hypothalamus-pituitary-thyroid axis and Hypothalamic-pituitary-ovarian axis. Therefore this study was designed to determine the association of serum Prolactin and thyroid profile in infertile females.

MATERIALS AND METHODS: The study consisted of 40 diagnosed female infertile patients who availed health care facility at Obstetrics and Gynaecology of Gauhati Medical College and Hospital and 40 female fertile patients.Estimations of serum levels of Prolactin, TSH, TT3 and TT4 were done by BIO-RAD MICROPLATE READER VERSION 1.7. Statistical significance and correlation were done using unpaired student's "t" test and Pearson's correlation test.

RESULTS: A statistically significant increase was found in serum Prolactin and TSH of infertile female patients as compared with control groups ($p < 0.0001$ and $p < 0.01$ respectively). The serum Prolactin level showed significant positive correlation with serum TSH ($p < 0.01$) while serum prolactin level showed significant negative correlation with serum TT3 and TT4 ($p < 0.01$ and $p < 0.01$ respectively).

CONCLUSION: From the present study, it shows that thyroid disorders, especially hypothyroidism, may be an important hormonal factor along with hyperprolactinemia in the development of female infertility and may have therapeutic applications as correction of thyroid disorders may reverse the infertility.

KEY WORDS:

Infertility, Hyperprolactinemia, Hypothyroidism, serum prolactin, ovulation, infertile females.

INTRODUCTION:

Infertility is defined as the failure of a couple to achieve conception after one year of unprotected intercourse.[1] This condition may be further classified as Primary infertility, in which no previous pregnancy have occurred; and Secondary infertility, in which a prior pregnancy, although not necessarily a live birth, has occurred.[1] Although infertility is considered by some as primarily a woman's problem, men often contribute to and are also affected. [2] Infertility is a global health issue, varies across regions of the world affecting approximately 8-12% couples worldwide [3,4]. The WHO estimates that 60-80 million couples worldwide currently suffer from infertility.[5]

According to WHO, the national prevalence of primary and secondary infertility in India is 3% and 8% respectively[6,7].According to standard protocol, infertility evaluation usually identifies different causes, including male infertility (30%), female infertility (35%), the combination of both (20%) and finally unexplained or "idiopathic" infertility (15%).[8,9]

Prolactin, a 198-amino acid polypeptide secreted by the anterior pituitary lactotroph, is the primary trophic factor responsible for synthesis of milk by the breast.[1] Hyperprolactinaemia and Hypothyroidism are found to be closely inter-related. Measurement of Prolactin and thyroid hormones especially thyroid stimulating hormone (TSH) has been considered an important component of Infertility work up in women.[10]. Hypothyroidism or hyperthyroidism in females along with subclinical thyroid dysfunction have been found to be associated with anovulatory cycles, decreased fecundity and increased morbidity during pregnancy by number of authors.[11,12,13] Hyperprolactinemia which results from a longstanding primary hypothyroidism may result in ovulatory dysfunctions ranging from inadequate corpus luteal progesterone secretion to oligomennorhoea or ammenorhoea.[14] Amenorrhoea occurs in hypothyroidism due to hyperprolactinaemia, which results from a defect in the positive feedback of oestrogen on LH, and because of the suppression of LH and FSH.[15]

Thyroid dysfunction is implicated in a broad spectrum of reproductive disorders, ranging from abnormal sexual development to menstrual irregularities and infertility.[16,17] Hypothyroidism is associated with increased production of TRH, which stimulates pituitary to secrete TSH and Prolactin. Hyperprolactinemia adversely affects the fertility potential by impairing pulsatile secretion of GnRH and hence interfering with ovulation.[18,19] Even in the absence of hyperprolactinaemia, hypothyroidism may itself contribute to infertility. [20]

METHODS:

STUDY POPULATION: The study was conducted in the Department of Biochemistry, Gauhati medical college and hospital (GMCH) in collaboration with the Department of Obstetrics and Gynaecology, GMCH between August 2015 to July 2016. The study subjects were recruited from the out patient department(OPD) of Department of Obstetrics and Gynaecology of GMCH while the age matched control population were randomly drawn from the general population. The study consisted of a total of 80 participants. The study was conducted in two broad groups as follows:-

1. CASE- This group includes 40 female patients 20-40 years of age with either Primary or Secondary Infertility.
2. CONTROL- This group includes 40-age matched female patients without Infertility.

EXCLUSION CRITERIA:

All patients in this study had no history of tubal factors abnormalities, congenital anomaly of urogenital tract, history of thyroid disease or thyroid medications, previous thyroid surgery and husbands with male factor infertility.

SAMPLE COLLECTION AND ANALYSIS:

Taking all aseptic and antiseptic precautions, 5ml of blood was drawn from the median cubital vein. Estimations of Serum Prolactin, TSH, TT3 and TT4 were done by using BIO-RAD 680 ELISA microplate reader version 1.7. Fasting Plasma Glucose and Serum Creatinine were done using MERCK microlab 300 Semiautoanalyser.

ETHICS:

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This work has been sanctioned by the Instituitional Ethics Committee, Gauhati Medical College , vide letter no MCI/02/2015/116 dated 14th October 2015.

RESULTS:

BIOCHEMICAL PARAMETERS IN INFERTILE FEMALE PATIENTS:

A statistically significant increase was found in serum Prolactin and TSH of infertile female patients as compared with control groups ($p < 0.0001$ and $p < 0.01$ respectively) while serum TT3 and TT4 were significantly decreased ($p < 0.05$ and $p < 0.0001$ respectively) in the case group.

CORRELATION BETWEEN THE PARAMETRS:

The serum Prolactin level showed significant positive correlation with serum TSH ($p < 0.01$) while serum prolactin level showed significant negative correlation with both serum TT3 and TT4 ($p < 0.01$ and $p < 0.01$ respectively).

TABLES AND FIGURES:

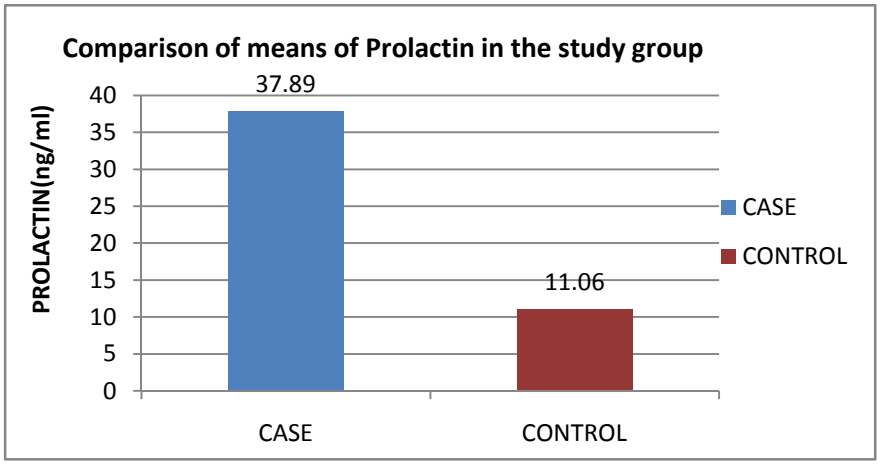
S.NO	PARAMETER	CASE (mean±SD)	CONTROL (mean±SD)	p-value
1.	PROLACTIN (ng/ml)	37.89 ± 25.24	11.06 ± 3.13	<0.0001***
2.	TSH (µIU /ml)	6.94 ± 5.93	4.04 ± 1.16	0.0033*
3.	TT3 (ng/ml)	0.67 ± 0.30	0.81 ± 0.17	0.0117*
4.	TT4 (µg/dl)	5.92 ± 2.18	8.03 ± 1.13	<0.0001***

Table 1.1 Shows Mean ± SD of various parameters in the case and control groups.

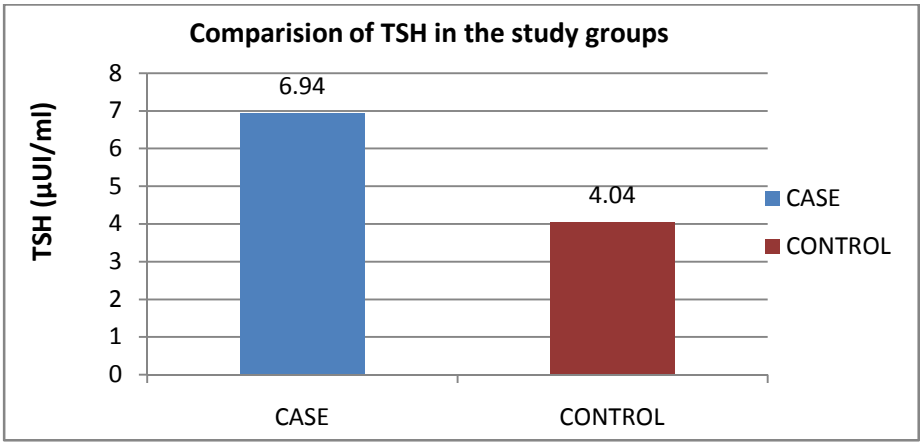
PARAMETERS	r value	P value
TSH	0.555	0.0002**
TT3	-0.42	0.008*
TT4	-0.48	0.002*

TABLE 1.2: CORRELATION OF PROLACTIN WITH OTHER BIOCHEMICAL PARAMETERS.

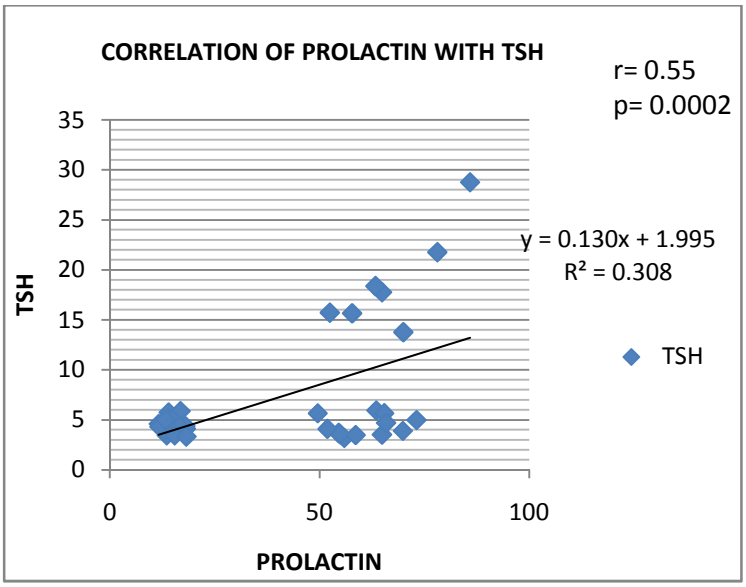
*Significant(P<0.05), **Very significant(P<0.001), ***extremely significant(P<0.0001).



Graph 1.1: Showing comparision of mean Prolactin in cases and controls.



Graph 1.2: showing comparision of mean TSH in cases and controls.



Pearson's Correlation coefficient (r) = 0.555

Coefficient of determination (r squared) = 0.308

The two-tailed P value is 0.0002, considered extremely significant.

Figure 1: showing correlation of Prolactin with TSH in Infertile patients.

DISCUSSION:

Measurement of Prolactin and thyroid hormones especially thyroid stimulating hormone (TSH) has been considered an important component of Infertility work up in women. Hyperprolactinemia also adversely affects the fertility potential by impairing pulsatile secretion of GnRH and hence interfering with ovulation.[21] The present study was conducted to estimate the serum levels of prolactin as well of thyroid profile, mainly TSH and to study the association between serum prolactin and serum TSH.

Majority of the infertile women had serum Prolactin within normal range. This is in concordance with study of Binita Goswamy et al[20] A statistically significant increase was found in serum Prolactin of infertile female patients as compared with control groups (p <0.0001).There was a higher occurrence of Hyperprolactinaemia (**47.5%**) in the case group. This higher propensity of hyperprolactinemia is in agreement with the findings of Kumkum et al [15]who had depicted a prevalence of 46% in their study. Binita Goswamy et al.[20] found the prevalence of 41% . A study conducted by Sharma Priyanka et al[22] found the occurrence of hyperprolactinaemia with a prevalence of 59.37% while Manjusha et al[23] found it to be 51%. This altered prolactin levels may contribute to the failure of conception and pregnancy as Prolactin is supposed to be important for the maintenance of secretory activity of the corpus luteum.[9]

A statistically significant increase was found in serum TSH of infertile female patients as compared with control groups (p <0.01). Majority of the infertile women had serum TSH within normal range. This is in concordance with study of Binita Goswamy et al[20] .Prevalence of Hypothyroidism in the reproductive age ranges from 2-4%.[24] In our study, the prevalence of hypothyroidism was 17.5%. Binita Goswamy et al [20] found the prevalence to be 8% while Sharma et al[26]found the prevalence to be 20%. Sharma Priyanka et al[23] found the prevalence to be at 36% while Manjusha D.Hivre et al[23] found to be 20%.

In our present study, the serum Prolactin level showed significant positive correlation with serum TSH (p <0.01). These findings are consistent with

with the findings of Binita Goswamy et al [20]and Iya Eze Bassey et al.[25]The infertile women with hypothyroidism had significantly higher mean Prolactin levels with a p value of <0.0001 than the cases with euthyroidism and controls. Similar observations were also made by Binita Goswamy et al [20], Iya Eze Bassey et al[25] and also by Manjusha D.Hivre et al[23] . Prolactin inhibits two hormones which are necessary for ovulation: the Follicle Stimulating Hormone (FSH) and the Gonadotropin Releasing Gormone (GnRH). When there are high levels of prolactin in the blood (hyperprolactinaemia), one will not ovulate and this will result in infertility. This anovulation can also cause irregular menstrual cycles [26].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. [27,28,29]

CONCLUSION:

The determination of serum levels of serum prolactin and TSH has been considered to be an important hormone profile work up for the female infertile patients.

From the present study, it seems that thyroid disorders, especially hypothyroidism, may be an important hormonal factor along with hyperprolactinemia in the development of female infertility and may have therapeutic applications as correction of thyroid disorders may reverse the infertility. A more elaborate study would have been desirable to precisely establish the impact of Prolactin and thyroid profile in infertile females but, due to paucity of time, resources and due to conduction of the study in a sole institution it was not implementable. However, we made a modest effort to fulfill the same through whatever resources available. Hence, it is hoped that the present study will encourage further studies on the present topic in a bigger way.

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