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Research Article

Hypothyroidism and hyperprolactinemia showed positive correlation in women with primary and secondary infertility

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ABSTRACT

Background: Hyperprolactinemia is a common problem which is encountered in reproductive disorder. Hyperprolactinemia is usually associated with menstrual and ovulatory disorders like amenorrhea, oligomenorrhea, anovulation, ovulatory cycle with short or inadequate luteal phase and galactorrhea. Hypothyroidism may also cause failure to ovulation in women of reproductive age group. This study has been conducted to correlate prolactin and thyroid stimulating hormone (TSH) levels in primary and secondary infertility.
Methods: The study comprises of 120 female subjects, which were divided into three groups-healthy control women (group 1), women with primary infertility (group 2) and secondary infertility (group 3). Fasting blood samples were collected between 7 AM to 8 AM. Hormones T3, T4, TSH and prolactin levels were estimated by enzyme linked fluorescent immunoassay (ELFA) method in all the study subjects.
Results: In the present study there was a positive correlation of hyperprolctinemia with hypothyroidism in both primary and secondary infertile women.
Conclusions: Hence it is recommended to screen serum prolactin levels along with thyroid hormones screening in women with infertility problems.

Keywords: Anovulation, Infertility, Prolactin, Hypothyroidism, Correlation

INTRODUCTION

Fertility in female is maintained by prevailing hormonal milieu, which is delicately balanced by hypothalamo-pituitary-thyroid-adrenogonadal axis. Thyroid hormones have profound effects on reproduction and pregnancy. Hypothyroidism can affect fertility due to anovulatory cycles, luteal phase defects, hyperprolactinemia and sex hormone imbalance.[1] Thyroid dysfunction is a condition known to reduce the likely hood of pregnancy and to adversely affect pregnancy outcome. Hyperprolactinemia is usually associated with menstrual and ovulatory disorders like amenorrhea, oligomenorrhea, anovulation, ovulatory cycles with short or inadequate luteal phase, and galactorrhea.[2]

In many infertility cases, the diagnosis is simply unexplained because a variety of reasons like lack of ovulation, mechanical stoppage and parental age etc.[3] Hyperprolactinaemia is most common hormonal disorder of hypothalamo-pituitary axis. There is close relationship between hypothalamic-pituitary-thyroid axis and hypothalamic-pituitary-ovarian axis.[4] Pathologic hyperprolactinaemia is generally applied for situation in which prolactin level increases because of some reasons other than physiologic causes. Subclinical hypothyroidism is defined by high TSH and normal thyroid hormones.[4,5]

Hyperprolactinemia is a common problem which is encountered in reproductive disorder.[6] Hypothyroidism is

one of the causes of ovulation dysfunction in women, resulting in infertility.[6] The ovulation can be affected by hormonal imbalance, thyroid disorders or chronic diseases such as diabetes.[7] Some women with galactorrhea and hyperprolactinemia might have primary hypothyroidism. This disease is characterized by low serum levels of thyroxine (T4) and decreased negative feedback on the hypothalaopituitary axis. The resulting increased secretion of thyrotropin releasing hormone (TRH) stimulates thyrotropes and lactotrophs, thereby increasing the levels of both TSH and prolactin.[8] Primary hypothyroidism is commonly associated with hyperprolactinemia due to the stimulatory effect of TRH on lactotrophs.[9] Women with hyperprolactinemia are often associated with hypothyroidism which is characterized by high serum TSH levels.[6] Aim of the present study was to find out the correlation between serum prolactin and thyroid hormone function in women with primary and secondary infertility.

METHODS

A total of 120 women aged between 23-39 years were recruited for the study, who are attending outpatient department of Gynecology and Obstetrics of Karpaga Vinayaga Institute of Medical Sciences, Madhuranthagam, Tamilnadu, India. Study subjects were divided into three groups- control women, women with primary infertility and women with secondary infertility. Each group consists of 40 women. All the women recruited for the study were age matched. Infertile women having tubular blockage, pelvic inflammatory disease, endometriosis, H/O hypophysis-hypothalamic disorders, liver, renal or cardiac diseases were not included in this study. Also those already had previous thyroid surgery or being on medications for thyroid disorders or hyperprolactinaemia in last 3 months; also cases where abnormality was found in husband's semen were excluded from study. Any congenital anomaly of urogenital tract or any obvious organic lesions were also excluded. Protocol for infertility work up in the women included: a detailed medical history, a gynecological examination, a hormonal profile (TSH, T3, T4, prolactin), screening for infectious diseases, hysterosalpingography.

The study was approved by the institutional ethics committee of Karpaga Vinayaga Institute of Medical Sciences and Research centre. An informed consent was obtained from all the participants. Blood samples were collected in fasting condition in between 7 AM to 8 AM. About 3 ml of blood is collected from the antecubital vein in plain tubes. Blood samples were centrifuged at 3500 rpm for 10 min to separate serum. Hormones T3, T4, TSH and prolactin levels were estimated by enzyme linked fluorescent immunoassay (ELFA) method. For adequate quality control both normal, abnormal reference control serum solutions and calibrators were run before analyzing test samples. Pearson correlation was used to find out the correlation between serum TSH and serum prolactin levels in primary and secondary infertile women.

For the statistical data analysis, descriptive statistics were used to show the characteristics of the infertile and fertile women. All the results were tabulated as mean and standard deviation. Unpaired student T test was used to find the significance between the different groups. Pearson correlation coefficient was used to see the correlation between infertility, prolactin and TSH levels. A two tailed, at minimum 95% confidence intervals and p-value <0.05 has been considered significant. All the data were analyzed using Statistical package for social science (SPSS) version 16.0 (IBM, Chicago, USA).

RESULTS

For the present study for total 120 women with age range of 23 to 29 years were recruited for analysis. The study subjects were divided into three groups: control women (normal reproductive function of the same age group), women with primary infertility and women with secondary infertility. The mean age of the control women was 26.27±3.5 years while for primary infertile women it was 27.80±3.8 and that of secondary infertile women was 28.40±2.5 years. There was no statistically significant difference in the mean age of control and cases when compared to each other (p-value >0.05).

Analysis of serum prolactin levels of infertile women reported that about 40% of primary infertile women and about 49% of secondary infertile women had higher serum prolactin levels while 84% of control women had normal prolactin levels. The mean serum prolactin levels in primary infertile women were 36.8±21.2 and that of secondary infertile women 44.9±21.1 ng/ml against the control women who had mean serum prolactin levels of 25.01±18.4 ng/ml (normal=2-25 ng/ml) and both groups are showing statistically significant difference against the healthy control women (p-value=0.0001) (Table 1,2). The mean serum PRL concentration was increased in infertile group as compared to the control group and it was found to be statistically highly significant (p value <0.001) (Table 1,2).

Table 1: Comparison of serum thyroid hormone levels in control women and women with primary infertility.

Parameter	Control women (n=40)	Primary Infertility (n=40)	p-value
T3 (ng/ml)	1.24±0.32	0.93±0.23	0.0001
T4 (ng/dl)	6.24±0.9	10.5±1.7	0.0001
TSH (µIU/L)	2.9±1.8	5.6±2.1	0.001
Prolactin (ng/ml)	25.01±18.4	36.8±21.2	0.009

The incidence of hypothyroidism (TSH > 57µIU /L) was about 60% in primary infertile women and about 50% in secondary infertile women.

The mean serum TSH level in the primary infertile group was 5.6±2.1 µIU /L, that of secondary infertile women group was 6.9±1.7 µIU/L and in control group it was 2.9±1.8 µIU/L (normal=0.28-6.28 µIU/L) which was having high significant difference when compared between the three groups (p <0.0001) (Table 1,2).

Table 2: Comparison of serum thyroid hormone levels in control women and women with secondary infertility.

Parameter	Control women (n=40)	Secondary infertility (n=40)	p-value
T3 (ng/ml)	1.24±0.32	0.86±0.28	0.0001
T4 (ng/dl)	6.24±0.9	11.52±1.7	0.0001
TSH (µIU/ml)	2.9±1.8	6.9±1.7	0.0001
Prolactin (ng/ml)	25.01±18.4	44.9±21.1	0.0001

Further on comparison of serum thyroid hormones and serum prolactin levels among primary infertile women and secondary infertile women revealed significant difference in serum TSH levels (p=0.003) only but not with the serum prolactin levels (p >0.09) (Table 3).

Table 3: Comparison of serum thyroid hormone levels in women with primary and secondary infertility.

Parameter	Primary infertility (n=40)	Secondary infertility (n=40)	p-value
T3 (ng/ml)	0.93±0.23	0.86±0.28	0.05
T4 (ng/dl)	10.5±1.7	11.52±1.7	0.009
TSH (µIU/ml)	5.6±2.1	6.9±1.7	0.003
Prolactin (ng/ml)	36.8±21.2	44.9±21.1	0.09

Table 4: Pearson correlation of serum TSH with prolactin in primary and secondary infertile women.

Parameter	Group	TSH	Prolactin
TSH	Primary infertile	1	0.51*
Prolactin	Secondary infertile	0.57*	1

*p <0.05

The Pearson's correlation coefficient was calculated for serum TSH and prolactin in primary and secondary infertile women. In primary infertile women correlation revealed the result indicated that serum prolactin levels were positively correlated with corresponding TSH levels (r=0.51, p <0.05) (Table 4, Figure 1).

In secondary infertile women serum prolactin levels also showed mild positive correlation with serum TSH levels (r=0.57, p <0.05) (Table 4, Figure 2). Hence, there was a strong association observed in primary and secondary infertile women with hyperprolactinemia and hypothyroidism.

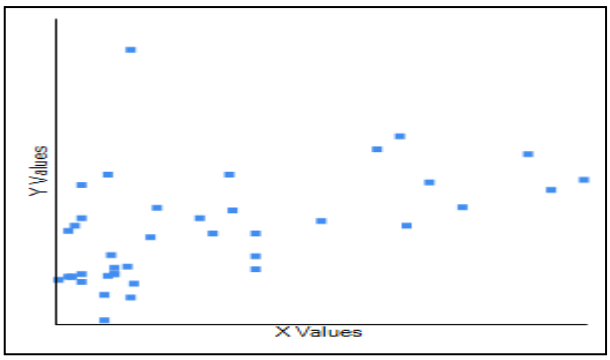

Figure 1: Correlation of serum prolactin and serum TSH levels in women with primary infertility.

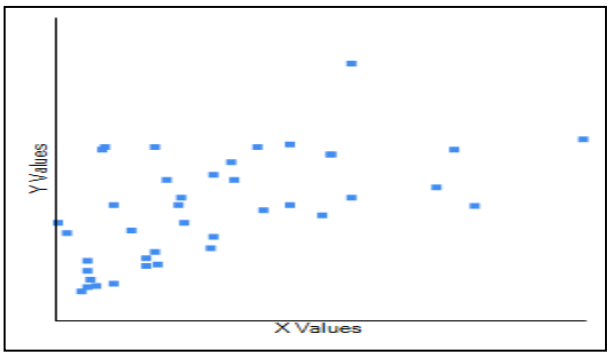

Figure 2: Correlation of serum prolactin and serum TSH levels in women with secondary infertility.

DISCUSSION

Thyroid hormones have profound effects on reproduction and pregnancy. In this study, some of the control women presented with hyperprolactinemia and hypothyroidism. This is in concordance with study of Goswamy B et al.[10] The prolactin levels were increased in infertile patients (49%) as compared to fertile controls (84%). About 60% of the infertile women had higher TSH levels when compared to fertile. A relative higher occurrence of hypothyroidism in infertile women when compared to control group reflects the tendency of infertile patients towards thyroid insufficiency or vice-versa. A higher occurrence of hyperprolactinemia (about 50%) was seen in infertile women. This higher propensity of hyperprolactinemia is in agreement with the findings of Kumkum et al who had depicted a prevalence of 46% in their study.[8] In our study, a significant negative correlation between serum TSH and serum prolactin levels in infertile women indicates that the rise in serum TSH level is accompanied with a lowering of serum Prolactin levels and vice-versa.

The final common pathway for TSH and prolactin secretion is the thyrotropin releasing hormone (TRH), which stimulates the secretion of both TSH and Prolactin. TRH is under negative feedback control of TSH through a short negative feedback loop, any increase in TSH will decrease the release of TRH which in turn will inhibit the secretion of prolactin and will also normalize the TSH

levels.[11] A prominent feature of the hormonal cascade is the negative feedback system operating when sufficiently high levels of the ultimate hormone have been secreted into the circulation.

Turankar et al, reported increased levels of prolactin and TSH in infertile women compared to the control group.[12] In a similar study Sharma et al, investigated prolactin and TSH levels in primary and secondary infertile women and determined galactorrhea in 15% of the subjects.[13] In addition, serum prolactin levels were measured as 79.40±56.59 ng/ml in hyperprolactinemic women; however, they reported no statistically significant difference in the levels of prolactin between the women with primary and secondary infertility. The cause of infertility and menstrual irregularities is said to be anovulation resulting from hyperprolactinemia. Raised levels of serum prolactin inhibit GnRH (gonadotropin releasing hormone) levels which are necessary for ovulation. The low GnRH levels causes decreased secretion of FSH and LH hormones, thus affecting gonadal steroid synthesis, resulting in infertility.[14] It is observed that the prevalence of hyperprolactinemia associated hypothyroidism which is characterized by high levels of serum TSH and low levels of thyroid hormones (T3 and T4) is high in infertile women as compared to normal fertile females.[6] Infertility due to hyperprolactinemia has been found to be associated with abnormal menstrual pattern as well as anovulatory cycles. Hyperprolactinemia is often the cause of amenorrhea occurring in hypothyroid patients. This hyperprolactinemia is said to be resulting from defective positive feedback of oestrogen on LH and FSH suppression. Ovulation is affected by impaired pulsatile secretion of GnRH because of hyperprolactinemia, thus ultimately resulting in menstrual and ovulatory dysfunctions.[10] Hyperprolactinemia is quite an important cause of infertility. Galactorrhea which is a typical clinical marker of hyperprolactinemia is not present in all the patients hence serum prolactin estimation is mandatory. Since there is increased TSH in infertile women as compared to controls emphasizes importance of estimation of thyroid hormones in infertility.

The incidence of hyperprolactinemia in our study is 46%. Mishra et al have reported an incidence of 20% in infertility with menstrual irregularities.[15] Our incidence of hyperprolactinemia is more, probably because the cases of tubal factor infertility were excluded. The mean prolactin level in hyperprolactinemic women in our study was 57.38±21.9 ng/ml whereas Mishra et al found it to be 128.28 ± 12.74ng/ml.[15] The incidence of hypothyroidism in hyperprolactinemic women is 24% (7/40). So, a positive correlation of 1:4 was found between hypothyroidism and hyperprolactinemia.

CONCLUSION

Screening of serum prolactin levels is mandatory in all infertile women especially those with oligomenorrhea and amenorrhea. As there was high incidence of hyperprolactinemia in women with galactorrhea and quite high in women with oligomenorrhea/anovulation, it is recommended that galactorrhea and measurement of serum prolactin levels are important screening procedures in primary and secondary infertile women. In this study, the relatively high prevalence of hypothyroidism in women with ovulatory dysfunction and oligomenorrhea emphasizes the importance of TSH screening in primary and secondary infertile women. Further, in this study we find a statistically significant difference between the three study groups in terms of serum TSH, T3, T4 and prolactin. There was a positive correlation of serum prolactin with serum TSH levels was observed in both primary and secondary infertile women.

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REFERENCES

1. Poppe K, Velkeniers B, Glinoer D. Thyroid disease and female reproduction. Clin Endocrinol. 2007;66(3):309-21.
2. Mishra R, Baveja R, Gupta V. Prolactin level in infertility with menstrual irregularities. J Obstet Gynecol India. 2002;52:40-43.
3. Kumar AN, Naidu JN, Stayanarayana U, Anitha M. Past, present and future of insulin gene and its related genes in relation to polycystic ovary syndrome. J Mol Genet Med.2014;8:107.
4. Frey KA, Patel KS. Initial evaluation and management of infertility by the primary care physicians. Mayo Clin Proc. 2004;79(11):1439-43.
5. Poppe K, Velkeniers B. Thyroid disorders in infertile women. Ann Endocrinol. 2003;64(1):45-50.
6. Valvekar U, Viswanathan S. Prevalence of hyperprolactinaemia and hypothyroidism in primary and secondary infertility women. Jour of Med Sci Tech. 2016;5(2);8-13.
7. Sultana A, Nadir S. Pituitary gonadotropic hormones in women with oligo/amenorrhea. J Ayub Med Coll Abbottabad. 2008;20(3):62-5.
8. Kumkum A, Jasmine K, Shweta G, Ajeshwar NP. Hyperprolactinaemia and correlation with hypothyroidism in infertile women. J Obstet Gynecol India. 2006;56(1):68-71.
9. Patel SS, Bamigboye. Hyperprolactinemia. J Obstet Gynecol. 2007;27(5):455-9.

10. Binita G, Suprava P, Mainak C, Koner BC, Alpana S. Correlation of prolactin and thyroid hormone concentration with menstrual patterns in Infertile women. J Reprod Infertil. 2009;10:207-12.
11. Freeman ME, Kanyiscka B, Lerant A, Nagy G. Prolactin: structure, function and regulation of secretion. Physiol Rev. 2000;80:1523-31.
12. Turankar S, Sonone K, Turankar A. Hyperprolactinaemia and its comparison with hypothyroidism in primary infertile women. J Clin Diagn Res. 2013;7(5):794-6.
13. Sharma N, Baliarsingh S, Kaushik GG. Biochemical association of hyperprolactinemia with hypothyroidism in infertile women. Clin Lab. 2012;58(7):805-10.
14. Poppe K, Velkeiners B. Thyroid and infertility. Verh K Acad Geneeskd Elg. 2002;64(6):389-99.
15. Mishra R, Baveja R, Gupta V. Prolactin levels in infertility with menstrual irregularities. J Obstet Gynecol India. 2002;52:40-3.

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