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Original Research Paper

status of thyroid, TSH and prolactin hormones in primary infertile

Medical Science

KEYWORDS : primary infertility; thyroid; prolactin

*** Dr. Priyanka Soni** — MSc Medical Biochemistry, Jawahar Lal Nehru Medical College Ajmer, * Corresponding author

Dr. G. G. Kaushik — MD, Senior Professor Dept. of Biochemistry, Jawahar Lal Nehru Medical College Ajmer

ABSTRACT

Aim *- To assess the levels of prolactin, thyroid Hormones (T3 and T4), and TSH in primary infertile women and compare it with control in Indian population and to find out the correlation of prolactin and TSH levels.*

Method *- The study included 100 females diagnosed as primary infertile were compared with 50 age matched fertile females. The activities Prolactin, T3, T4, TSH were evaluated in primary infertile cases and compared with normal healthy fertile females. Thyroid and prolactin hormone correlation also assessed.*

Results *- We found greater prevalence of hyperprolactinemia and hypothyroidism in infertile women as compared to the control group and a significant positive correlation between TSH and Prolactin levels in subjects enrolled in the study was observed. Hypothyroidism was also significantly more common in patient having hyperprolactinemia.*

Conclusion *- Thyroid and prolactin hormones play significant role in female fertility and both are interrelated to each other.*

Introduction:

Successful pregnancy results from an interaction between myriad physiological processes in both men and women. Any disruption to this interactive system, whether in a man or woman can result in an inability to have a biological child called infertility.[1] Primary infertility is the term used to describe women that has never been able to conceive after a minimum of 1 year of attempting to do so.[2]

The World Health Organization (WHO) estimates that 60 to 80 million couples worldwide currently suffer from infertility. Data extrapolated from WHO by the Indian Council of Medical Research (ICMR) suggested that approximately 13– 19 million couples are likely to be infertile in India at any given time (ICMR and NAMS 2005).[3]According to the 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%). [4, 5]

Endocrines play central role in maintaining fertility. There is a known association of hyperthyroidism and hypothyroidism with menstrual disturbances and decreased fecundity. Therefore assessment of thyroid dysfunction has been considered as an important component of infertility work up in women.[6]

Measurement of prolactin is usually included in the differential work up for female patients who present with amenorrhea, oligomenorrhoea, galactorrhea or infertility or for male patients who present with sexual dysfunction. However, its secretion is pulsatile; it increases with sleep, stress, pregnancy, and chest wall stimulation or trauma.[7] Hyperprolactinemia is defined as circulating prolactin levels above normal range, which occurs in conditions other than pregnancy and lactation, when physiological hyperprolactinemia occurs. [8]

The relationships between thyroid hormones, TSH, prolactin, and female infertility are multiple and complex. Thyrotropin-releasing hormone (TRH) is a potent stimulus of prolactin and the association between hypothyroidism and hyperprolactinemia is well appreciated. Hyperprolactinemia, because of a variety of causes, can reduce pulsatile GnRH secretion and interfere with ovulation. Even in the absence of hyperprolactinemia, hypothyroidism may contribute to infertility since thyroid hormone may be necessary for maximum production of both estradiol and progesterone.[9]

So, the aim of the study was to evaluate the levels of prolactin, thyroid Hormones (T_3 and T_4), and TSH in primary infertile women in Indian population and to find out the correlation of prolactin and TSH levels.

Material and method:

A cross-sectional hospital based study has been carried out in the R.I.A.laboratory, Department of Biochemistry, in collaboration with Department of Gynecology, in J L N Medical College and Group of Hospitals, Ajmer. Ethical consideration was taken from the research review board & ethical committee of the institution. An informed written consent was obtained from all the participants prior to participation in the study.

A consecutive sample of 100 patients attended to outpatient department of gynecology, having a diagnosis of primary infertility was included. It was compared with 50 age matched healthy fertile females.

Inclusion criteria:

- Age 18-40 years
- Diagnosed as primary infertility
- Duration of marriage >1 year

Exclusion criteria:

Infertile women having pelvic pathology, like- fibroid Uterus, tubular blockage, pelvic inflammatory disease, endometriosis on diagnostic laparoscopy or hysteroscopy and with genital TB (PCR-positive).

Patients who were already on treatment for thyroid disorders or hyperprolactinemia.

Male factor abnormalities were also excluded from the study.

Blood samples were collected by venipuncture by aseptic technique and samples with signs of hemolysis were discarded. The serums separated from the samples were analyzed for following biochemical parameters viz serum T_3, T_4 and TSH and Prolactin.

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Serum T_3, T_4 and TSH levels were estimated on a I-125 Gamma counter, Model number IC-4702, using the RIA kits supplied by Bhabha Atomic Research Centre Trombay ,Mumbai. Serum Prolactin levels were estimated by Prolactin ACCUBIND ELISA KIT on Bio-rad model 680 and washer PW 40.

Ranges for T_3 (triiodothyronine):
1)Hypothyroid: <0.7ng/ml
2)Euthyroid(normal): 0.7-2.0 ng/ml
3)Hyperthyroid: >2.0 ng/ml
Ranges for T_4(thyroxine):
1)Hypothyroid: <5.5 µg/dl
2)Euthyroid(normal): 5.5-13.5 µg/dl
3)Hyperthyroid: >13.5µg/dl
Ranges for TSH:
1)Hypothyroid: >5nIU/ml
2)Euthyroid(normal): 0.17-4.05 nIU/ml
3)Hyperthyroid: <0.15 nIU/ml
Normal Range for Serum Prolactin= 1.2-19.5 ng/ml

Statistical analysis:
Data were analyzed using the Statistical Package of Social Sciences (SPSS) version 19.0. The groups were compared on sociodemographic and different clinical variables using independent samples t-test and chi-square test as appropriate. Descriptive statistics were expressed as mean and frequency as appropriate. Pearson correlation was applied to find out the correlation among variables. The level of significance was set at *p* value < 0.05.

Results:
TABLE 1- Comparison of cases and controls on different variables using t test and chi square test.

	Groups		*p* value
Cases (N=100)	Healthy control (N=50)		
Mean value(SD)	Mean value(SD)		
Age	26.61(5.59)	25.02(4.36)	0.08
Years of marriage	5.46(3.12)	4.7(2.48)	0.14
T_3 (ng/ml)	1.04(0.59)	0.84(0.32)	0.02
T_4 (µg/dl)	7.69(3.4)	6.52(2.25)	0.02
TSH (µIU/ml)	3.71(3.56)	5.07(4.13)	0.03
Prolactin (ng/ml)	38.3(41.29)	16.12(16.79)	0.00
	N(%)	N(%)	*p* value
Hypothyroidism Yes	33(33%)	8(16%)	0.028
NO	67(67%)	42(84%)	
Hyperprolactinemia Yes	52(52%)	8(16%)	0.000
NO	48(48%)	42(84%)	

In our study we found that hyperprolactinemia was significantly more common in the primary infertile patient group as shown in table 1. It was found that out of 100 primary infertile cases, 52 had hyperprolactinemia and in healthy fertile controls out of 50 fertile women, 8 had hyperprolactinemia, on Chi Square Test the p value was 0.000 which is statistically significant($p<0.05$). The mean values were also statistically significantly higher in primary infertile patient group. The mean serum Prolactin level in cases was found as 38.295±41.2962ng/ml while in controls as 16.122±16.7935ng/ml, for which the p value was to be statistically significant ($p<0.05$). Similarly hypothyroidism was also significantly more common in the primary infertile patient group (table 1), it was found that out of 100 primary infertile cases, 33 were found to be suffering from hypothyroidism and in healthy fertile controls out of 50 fertile women, 8 were having hypothyroidism, upon Chi Square Test the p value was 0.028 which is statistically significant ($p<0.05$).

We found that serum TSH and prolactin levels are significantly and positively correlated to each other on pearson's correlation test, where the r value (correlation coefficient) was 0.802 and *p* value was 0.000.

TABLE 2- Comparison of normoprolactinemic and hyperprolactinemic groups on different variables using t test and chi square test.

Normoprolactinemic (N=48)	Groups Hyperprolactinemic(N=52)		*p* value
Mean value(SD)	Mean value(SD)		
Age	26.54(6.11)	28.06(4.65)	0.163
Prolactin (ng/ml)	9.5(3.8)	64.87(41.38)	0.000
T_3 (ng/ml)	1.32(0.68)	0.78(0.35)	0.000
T_4 (µg/dl)	9.38(3.79)	6.06(1.91)	0.000
TSH (µIU/ml)	2.95(3.31)	5.37(3.41)	0.000
	Normoprolactinemic (N=48) n	Hyperprolactinemic(N=52) n	*p* value
Hypothyroidism YES	10	23	0.000
NO	38	29	

We further divided 100 cases into 2 groups as normoprolactinemic and hyperprolactinemic having 48 and 52 patients respectively in each group and then compared both groups on different parameters as shown in table 2. Hypothyroidism was significantly more common in hyperprolactinemic group. The mean values of T3, T4 and TSH were also differed significantly between the groups, denoting correlation of hypothyroidism with hyperprolactinemia.

Discussion:
In this study we have found that the thyroid and prolactin hormones have significant role in female infertility. As shown in results, hypothyroidism and hyperprolactinemia was more common in the infertile patient group. We also found positive correlation between hyperprolactinemia and hypothyroidism which shows interplay of these hormones in many patients of infertility.

The incidence of hyperprolactinemia in our study was 52% in infertile women and in control group it was only 16%, showing a significant role of prolactin hormone in female infertility. The mean serum prolactin level in infertile women was 38.3±41.29 ng/ml. Similarly Neha Sharma and Dr. G.G. Kaushik reported that out of the one hundred infertile women studied, sixty (60%) had primary infertility and forty women (40%) had secondary infertility. The incidence

of hyperprolactinemia was 46%. They concluded that a high incidence of hyperprolactinemia was found in infertile women and a positive correlation was found between hyperprolactinemia and hypothyroidism.[10] Similar to our study Kumkum et al. conducted a study to find out the incidence of hyperprolactinemia in female infertility among 112 women with infertility and they found incidence of 46 %.[11] Similarly Mishra et al., have reported an incidence of 20% in infertility with menstrual irregularities.[12] Our incidence of hyperprolactinemia is more, probably because the cases of tubal factor infertility were excluded.

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 (a condition which is called hyperprolactinaemia), one will not ovulate and this will result in infertility. This anovulation can also cause irregular menstrual cycles. Hyperprolactinaemia 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.[11]

Another finding of our study was that incidence of hypothyroidism was significantly greater in female infertile women than the control group. As mentioned in results incidence of hypothyroidism in infertile group was 33% versus 16% in control group. Similar to our findings D. Mohana Priya et al., found incidence of 53.7% of hypothyroidism in infertile females.[13] Our results were consistent with Verma *et al.*,[14] Biradar *et al.*,[15] and Rijal *et al.*, [16]. In these studies most of the population belonged to primary infertility.

In our study on comparison of hyperprolactinaemic and normoprolactinaemic groups we found that among the cases out of 100 primary infertile women 48 were found to normoprolactinemic and 52 as hyperprolactinaemic. The incidence of hypothyroidism in normoprolactinaemic women was found to be 20.8%(i.e.10 out of 48)while the incidence of hypothyroidism in hyperprolactinaemic women was 44.2%(i.e.23 out of 52) .The p value being 0.013($p<0.05$) which is statistically significant. Similar findings were reported by Poppe and Velkeniers , they observed that in hyperprolactinaemic patients without any sign of pituitary dysfunction, there are normally reduced levels of thyroid hormones.[17] The mean serum TSH concentration of the hyperprolactinaemic infertile women was 5.36±3.41 μIU/ml as shown in table 2 which is significantly higher ($p<0.05$) than those of the normoprolactinemic infertile women. A significant positive correlation between TSH and prolactin levels in subjects enrolled in the study ($r = 0.802$, $p<0.05$) was observed. Our findings were consistent with Sharma et al.,[10] Turankar,et al.,[18] Kumkum et al.,[11] and Goswami, et al.,[9]. Kumkum et al., stated that 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. It also mentioned that the prevalence of ovulatory dysfunction was one of the causes of female infertility.

Studies have shown that for normal sexual function, thyroid secretion of T_3, T_4 needs to be approximately normal. Evidence from experimental and clinical studies have suggested a close relationship between the hypothalamic – pituitary – ovarian axis (HPO) and the hypothalamic – pituitary – thyroid axis (HPT)[19]. This is because, the specific thyroid hormone receptors at the ovarian level may regulate the influence of estrogens as well as reproductive function at higher levels of the HPT axis thereby integrating the reciprocal relationship between these two major endocrine axes [20]. In hypothyroidism, increased TRH production leads to hyperprolactinemia and altered GnRH pulsatile secretion. This leads to a delay in LH response and inadequate corpus luteum leading to abnormal follicular development and ovulation. At the cellular level, thyroid hormones synergize with FSH mediated LH/HCG receptor to exert direct stimulatory effects on granulose cell function e.g. progesterone production. Altering the peripheral metabolism of estrogen and decreasing SHBG production is another pathway by which hypothyroidism may impact on fertility. These pathways may result in an abnormal feedback at the pituitary level and consequently infertility [17]. The relatively higher occurrence of deranged TSH values in the hyperprolactinaemic infertile women when compared to the normoprolactinemic infertile women and control group in this study reflects the tendency of hyperprolactinaemic infertile women towards thyroid insufficiency or the vice versa.

Conclusion:

This study concluded that both thyroid and prolactin hormones play significant role in female fertility and both are interrelated to each other. Patients with hyperprolactinemia have high chances of having thyroid dysfunction also. Every patient having primary infertility should have undergone assessment of thyroid hormones and prolactin hormone.

References:

1. Agarwal A, Shyam SR Allamaneni. Role of free radicals in female reproductive diseases & assisted reproduction. Reprod Biomed Online 2004; 9(3): 338-47.
2. Fraser D, and Loso R, (1999) update on progesterone therapy J. Reprod. Med Reprod. Med 44; 139 – 232.
3. Indian Council for Medical Research (ICMR) and National Academy of Medical Sciences (NAMS). National Guidelines for Accreditation, Supervision and Regulation of ART clinics in India. New Delhi: Ministry of Health and Family Welfare, Government of India; 2005.
4. Evaluation and Management of the infertile couple. 2008(accessed on 08 Feb, 2012) http://www.glowm.com/?p=glowm.cml/sectionview&articleid=320.
5. Hendershot GE, Mosher WD, Pratt WF. Infertility and age: An unresolved issue. Fam Plann Perspect 1982; 14:287.
6. Cramer DW, Sluss PM, Powers RD et al. Serum prolactin and TSH in an in vitro fertilization population: is there a link between fertilization and thyroid function? J Assist ReprodGenet 2003; 20: 210-5.
7. LA Nilsson, C Roepstorff, B Kiens, H Billig, C Ling. Prolactin suppresses malonyl-CoA concentration in human adipose tissue. Horm Metab Res. 2009;41(10):747–51.
8. S Bernichtein, P Touraine, V Goffin. New concepts in prolactin biology. J Endocrinol. 2010;206:1–11.
9. B Goswami, S Patel, M Chatterjee, BC Koner, A Saxena. Correlation of prolactin and thyroid hormone concentration with menstrual patterns in infertile women. J Reprod Infertil. 2009;10(3):207–12.
10. Sharma Neha, Dr. Kaushik .G.G, Baliarsingh, Biochemical association of hyperprolactinemia with hypothyroidism in infertile women. Clin Lab 2012;58 (7-8):805-10.
11. Avasthi Kumkum, Kaur Jasmine , Gupta Shweta, Narang Pal Ajeshwar. Hyperprolactinema and its correlation with hypothyroidism in infertile women. J Obstet Gynecol India. 2006 ;56: 68-71.
12. Mishra R, Baveja R, Gupta V et al.,. Prolactin level in infertility with menstrual irregularities. J Obstet Gynecol India 2002;52:40-3.
13. Priya, D. M., Akhtar, N., & Ahmad, J. (2015). Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility. *Indian journal of endocrinology and metabolism*, *19*(4), 504.
14. Verma I, Sood R, Juneja S, Kaur S. Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroid-

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ism on infertility. Int J Appl Basic Med Res. 2012;2:17–9.

15. Biradar SM, Poornima RT, Sonagra AD, Murthy DS. Thyroid dysfunction in infertile women. Int J Pharma Bio Sci. 2012;2:53–8.
16. Rijal B, Shrestha R, Jha B. Association of thyroid dysfunction among infertile women visiting infertility center of Om Hospital, Kathmandu, Nepal. Nepal Med Coll J. 2011;13:247–9.
17. K Poppe, B Velkeniers, D Glinoer. Review: Thyroid disease and female reproduction. Clin Endocrinol (Oxf) 2007;66(3):309–21.
18. S Turankar, K Sonone, A Turankar. Hyperprolactinaemia and its Comparision with Hypothyroidism in Primary Infertile Women. J Clin Diagn Res. 2013;7(5):794–96.
19. Doufas AG, Mastorakos G. The hypothalamic-pituitary-thyroid axis and the female reproductive system. *Ann N Y Acad Sci*. 2000;900:65-76.
20. S Saha. The female reproductive system and the hypothalamic-pituitarythyroid axis. [Internet].2012.Available from http://www.pharmaceuticalintelligence.com/2012/12/11/the-female-reproductive-systemand-the-hypothalamic-pituitary-thyroid-axis.