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Original Research Article

Clinical Correlation betweenThyroid and Prolactin Hormone in Infertile Females

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Abstract: Hyperprolactinemia and Hypothyroidism adversely affects the fertility potential. The aim of our study was to assess the correlation between the Prolactin and Thyroid hormone levels amongst infertile females after excluding tubal and male factor. This hospital based descriptive study was conducted on 50 patients attending infertility clinic in Zenana Hospital, Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur from Jan 2015 to Jan 2016.Hyperprolactinemia was observed in 64% of the infertile cases in our study.In our study 27 female had hypothyroidism, out of which 74.07% had subclinical hypothyroidism and 25.93% had overt hypothyroidism.18%of patients had both Hypothyroidism &Hyperprolactinemia. 33.3% of hypothyroid females had hyperprolactinemia. 28.3% of hyperprolactinemic patients had hypothyroidism. Hence, measurement of both S.TSH and S.Prolactin levels should be done in infertility work up and treatment should be initiated accordingly to fulfill a woman's dream of motherhood.
Keywords: Hyperprolactinemia, Hypothyroidism, Infertility, Prolactin and TSH

INTRODUCTION

Hormonal disorders resulting from aberrant dysfunction of hypothalamus – pituitary – ovarian axis often lead to infertility.Prolactin within normal ranges can act as weak gonadotropin but at the same time suppress the secretion of GnRH.

Hyperprolactinemia adversely affects the fertility potential by impairing pulsatile secretion of GnRH and hence interfering with ovulation [1, 2].This disorder has been implicated in menstrual and ovulatory dysfunctions like amenorrhea, oligomenorrhea, anovulation, inadequate corpus luteal phase and galactorrhea [3, 4]. However many infertile women present with normal menses despite a raised serum prolactin.

The associations of hyperthyroidism or hypothyroidism with menstrual disturbances, anovulatory cycles, decreased fecundity and increased morbidity during pregnancy have been highlighted [1, 5, 6]. The increased prevalence of upper normal limit of serum TSH and raised anti-thyroperoxidase antibody titer indicate relatively more frequent occurrence of compensated thyroid function in infertile women than normal women of reproductive age group. Several studies emphasize that hypothyroidism cause's decreased negative feedback on hypothalamo-pituitary axis causing increased secretion of TRH which stimulates both thyrotrophs & lactotrophs thereby causing increased production of TSH & prolactin [7-9].

Morphological changes observed in the follicles in hypothyroidism can be a consequence of higher prolactin production that may block secretion and action of gonadotropins [10]. Adequate thyroid supplementation restores prolactin level as well and normalizes ovulatory function [11]. Even in the absence of hyperprolactinemia, hypothyroidism, itself may contribute to infertility since thyroid hormones may be necessary for the maximum production of both estradiol and progesterone [12].

Aim & Objectives

The aim of our study was to assess the clinical correlation between the Prolactin and Thyroid hormone levels amongst infertile females after excluding tubal and male factor.

MATERIAL & METHODS

This hospital based descripitive study was conductedon 50 patients attending infertility clinic in Zenana Hospital, Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur from Jan 2015 to Jan 2016.

A detailed history was taken, general physical and pelvic examination done. Investigation regarding infertility was done and those with male factor infertility, tubal pathology, congenital or acquired anomaly of genital tract and patient with previous thyroid disorder were excluded from the study.

Fasting venous blood were obtained on third day of menstrual cycle for estimation of serum prolactin levels and serum TSH, fT_3, fT_4 levels using immunoassay technique.
Normal range was taken as:–

- Serum Prolactin : 1.9 – 25 ng/ml
- S.TSH : 0.4 – 4.0 mIU/ml
- S.fT_3 : 1.8 – 4.2 ρg/ml
- S.fT_4 : 0.89 – 1.76 ηg/ml

OBSERVATION & DISCUSSION

As shown in Table no. 1 maximum no of cases (52%) belonged to 24 – 28 years age group. The mean age was 24.36±2.905 years.

Findings were in concurrence with AwasthiKumkum who concluded a study on 111 patients and maximum were in 24 – 28 years age group [13].

Out of 50 women 90 % were hindu and 10% were muslims.

Most of the cases (72%) belonged to middle class according to Kuppuswamy scale of socio-economic status.

Maximum no of cases (78%) had duration of infertility of 1 – 5 years. Mean duration was 3.7±2.67 years.

Awasthi K observed mean duration of infertility was 4.58 years [13].

This is more than the mean in our study and this indicates that women are now not waiting for too long to seek advice regarding infertility.

Menstrual abnormalities were observed in 48% of the cases. The majority of the cases presented with infrequent periods (40%).

The result of the study was concurrent with the observations of Choudhary [14] & Goswami [9]who had reported the menstrual abnormalities to be 44.6% of the total.

Awasthi K reported these abnormalities in nearly 57.6% of cases and infrequent periods in 50% of the cases [13].

Table1: Distribution of cases according to Socio-demographic profile and chief complains

S.no I	Age group (in years)	No. of cases	%
1.	19 – 23	20	40.00
2.	24 – 28	26	52.00
3.	29 – 33	4	8.00
	Mean age 24.36±2.905 years		
II.	Religion		
1.	Hindu	45	90.00
2.	Muslim	5	10.00
III.	Socio – Economic Status		
1.	Upper	6	12.00
2.	Middle	36	72.00
3.	Lower	8	16.00
IV.	Duration of infertility		
1.	1 – 5	39	78.00
2.	5 – 10	7	14.00
3.	10 – 15	4	8.00
V.	Menstrual disturbance		
1.	Regular period with average flow	26	52.00
2.	Infrequent periods	20	40.00
3.	Heavy menstrual flow	4	8.00

As shown in table no.2 Hyperprolactinemia was observed in 64% of the infertile cases in our study. 68.74% of hyperprolactinemic cases had S.Prolactin levels in range of 50 – 75 ng/ml. 15.63% cases of hyperprolactinemia had S.Prolactin above 75ng/ml but none had S.Prolactin>100ng/ml, therefore CT/MRI head was not indicated. The mean S.Prolactin in hyperprolactinemia was 59.06±12.98 ng/ml.

Thorner M Oobserved that 75% of cases with infertility had hyperprolactinemia [15].

Bohnet found hyperprolactinemia in 13.4% of infertile women while Scheithauer BW found it to be 81% [16, 17]. Significantly higher PRL levels were found in the controls by Triggianese P. [18], Binita G depicted hyperprolactinemia in 41% of infertile women and Avasthi K had depicted in 46% in their study, with mean S.Prolactin 76.33±55.97 ng/ml in hyperprolactinemic infertile females [9,13].

The mean S.Prolactin of all the infertile women was found to be 43.86±23.03ng/ml which was in agreement with observations made by Goswami B (47.73 ng/ml) and Turankar S (54.38ng/ml) emphasizing a higher occurrence of hyperprolactinemia in infertile women [9, 21]. 54% of the infertile women were hypothyroid and 46% were euthyroid.

Singh SK reported 57% incidence of hypothyroidism in infertile women and Awasthi K reported it as 27.27%, whileVerma I observed it as 23.9% [13, 19, 20].

Wide variations are observed in incidence of hypothyroid but it is an important cause of infertility.

70.37% of the hypothyroid women had S.TSH in the range of 5 – 10 mIU/ml , 25.93% had S.TSH ranging from from 10 – 20 mIU/ml while only 1 female out of 27 had S.TSH >20mIU/ml.

Mean S.TSH level in these hypothyroid women was 9.51±5.22mIU/ml.

Similar results were obtained by Turankar S where the infertile group had a mean S.TSH of 9.05±2.64 mIU/ml. [21]. Awasthi K observed mean S.TSH of 6.12±2.34mIU/ml in their study [13].

In our study 27 female had hypothyroidism, out of which 74.07% had subclinical hypothyroidism and 25.93% had overt hypothyroidism.

Females were classified as above so that we can distinguish easily between patients who are candidates for levothyroxine substitution (i.e overt hypothyroidism) and females who need further evaluation (i.e subclinical hypothyroidism for thyroid autoimmunity).

Surks found that data supporting associations of subclinical thyroid disease with symptoms of adverse clinical outcomes or benefits of treatment were few [22]. They concluded that consequences of subclinical thyroid disease (S.TSH 4.5 –10 mIU/ml) were minimal and recommended against routine treatment of cases with subclinical hypothyroidism. However, aggressive case finding is appropriate in pregnant women and others at high risk for thyroid dysfunction.

Khandelwal D stated that all patients with overt and subclinical hypothyroidism with S.TSH should be treated [23].They emphasized on the need to treat subclinical hypothyroidism of any magnitude in pregnant women and womenwho are contemplating pregnancy, to decrease the risk of pregnancy complications and impaired cognitive development of the offspring.

18% of patients had both Hypothyroidism & Hyperprolactinemia. 33.3% of hypothyroid females had hyperprolactinemia. 28.3% of hyperprolactinemic patients had hypothyroidism.

Goswami B observed 46.1% hypothyroid patients exhibiting hyperprolactinemia and Choudhary observed it to be 16.6% [9, 14].

A similar occurrence of 25.5% hyperprolactinemia patient had hypothyroidism was also reported by Awasthi [13].

Bispink L observed 37.8% of hypoyhroid infertile females had slightly elevated S.Prolactin levels [24]. After treatment with 50 – 150 µgm of l-thyroxine daily for 4 – 6 weeks. Elevated prolactin levels significantly decreased in 64% and 28.57% cases had pregnancy.

Mild hypothyroidism may cause ovarian insufficiency and assessment of thyroid function should be mandatory in infertile patients with elevated prolactin levels or chronic anovulation.

Table2: Distribution of cases according to level of serum Prolactin & Thyroid hormone

Sl. no	Serum Prolactin (ng/ml)	No of cases	%	Mean
1.	Normal (5 – 25)	18	36.00	
2.	Hyperprolactinemia (>25)	32	64.00	
a.	25 – 49.9	5	15.63	38.1±7.9ng/ml
b.	50 – 74.9	22	68.74	59.94±7.8ng/ml
c.	>75	5	15.63	76.17±0.94ng/ml
			Total	59.06±12.98ng/ml
II.	S.TSH (mIU/ml)			
1.	Normal (0.5 – 5)	23	46.00	
2.	Hypothyroidism (>5 – 30)	27	54.00	
a.	5 – 10	19	70.37	
b.	10 – 20	7	25.93	
c.	>20	1	3.70	
III.	Type of Hypothyroidism			
1.	Subclinical hypothyroidism	20	74.07	
2.	Overt hypothyroidism	7	25.93	
IV.	Association of Hyperprolactinemia with Hypothyroidism			
1.	Hyperprolactinemia only	23	46.00	
2.	Hypothyroidism only	18	36.00	
3.	Hyperprolactinemia with Hypothyroidism	9	18.00	

As shown in Table no .3Mean TSH in patient with subclinical hypothyroidism is 7.79±2.41mIU/ml and patients with hypothyroidism is have mean TSH level 14.41±7.88mIU/ml.

Table3: Distribution of cases According to the Thyroid status and hormone level

S.no	Thyroid Status	Mean S.TSH (mIU/ml)	Mean fT_3 (pg/ml)	Mean fT_4 (ng/ml)	Total
1.	Euthyroid	2.97±0.78	3.04±0.74	1.34±0.22	46% (23)
2.	Subclinical Hypothyroidism	7.79±2.41	3.03±0.77	1.34±0.19	40%(20)
3.	Overt Hypothyroidism	14.4±17.88	0.7±0.25	0.39±0.27	14% (7)

As shown in Table no. 4, 43.48% of women with hyperprolactinemia had menstrual disturbances; majority had infrequent periods (39.13%).

Godinjak observed menstrual disturbances in 40.33% of infertile women [25].

A significant association was found between menstrual irregularities and hyperprolactinemia ($P<0.05$), as was reported by Goswami [9].

The frequency of menstrual irregularities with hypothyroidism was found to be 55.56% much higher than that reported by Krassas GE (23.4%) and Kakuno Y (34.8%) [26-27].

24% cases had galactorrhoea and rest had no secretions from nipples. 39.13% of cases of hyperprolactinemia had galacorrhoea. All hyperprolacinemia patients don't exhibit galactorrhoea because breast milk production also requires estrogen and severe hyperprolactinemia often results in severe secondary hypogonadotrophichypogonadism and therefore, low circulating estrogen levels.

Occurrence of galactorrhoea was reported by Mishra et al to be 25% and Awasthi reported 9% [4, 13]. On comparing these studies it can be said that there is no consistent relation between galactorrhoea with infertility. The structural heterogenecity of prolactin also offers another possible explaination.

Table4: Distribution of cases according to Menstrual Disturbances & Galactorrhoea in Hyperprolactinemia and Hypothyroidism

Sl.no	Menstrual disturbances	Hyperprolactinemia	Hyperprolactinemia With Hypothyroidism	Hypothyroidism	Total
1.	Regular	56.52% (13)	55.56% (5)	44.44% (8)	52% (26)
2.	Infrequent periods	39.13% (9)	44.44% (7)	38.89% (20)	40% (20)
3.	Heavy menstrual disturbances	4.35% (1)	0	16.67% (4)	8% (4)
II.	Galactorrhoea				
1.	Present	39.13% (9)	22.22% (2)	5.56% (1)	24% (12)
2.	Absent	60.87% (14)	77.78% (7)	94.44% (17)	76% (38)

As shown in table no.5 it was found that galactorrhoea was associated with higher prolactin levels and this association was significant (P<0.05). But it was also seen that many infertile hyperprolactinemic females didn't have galactorrhoea. This suggests the importance of doing S.Prolactin in every infertile female with or without galactorrhoea [28-30].

The mean S.TSH level didn't show statistically significant difference.

Table5: Comparison of Mean Prolactin and Mean S.TSH Levels in presence or absence of galactorrhoea

Sl.no	Parameters	Galactorrhoea Present (n=12)	Galactorrhoea Absent (n =38)	P – value	Significance
1.	S. Prolactin	67.83 ±18.48	36.29 ±18.85	<0.05	Significant
2.	S.TSH	4.02 ±2.22	7.29 ± 5.45	>0.05	NS

CONCLUSION

After assessing the observations it may be concluded that hyperprolactinemia and hypothyroidism are important and widely prevalent causes of infertility and these may be coexistent or correlated. Subclinical hypothyroidism is also seen more commonly than overt hypothyroidism in infertile women and it warrants more investigations in such woman. Hence, measurement of both S.TSH and S.Prolactin levels should be done in infertility work up and treatment should be initiated accordingly to fulfill a woman's dream of motherhood.

REFERENCES

1. Williams C,GiannopoulosT,SherrifEA; Investigation of infertility with the emphasis on laboratory testing and with reference to radiological imaging. J ClinPathol, 2003;56:261–7.
2. Micinsk P, WielgusE; Abnormal ovarian reserve test reflects thyroid dysfunction. Pol JGyn Invest, 2006;9(1):30 – 4.
3. ZollnerU,Lanig K, Steck T; Assessment of endocrine status in patients undergoing in – vitro fertilization treatment. Is it necessary? Arch GynecolObstete, 2001;265(1):16 – 20.
4. Mishra R, Baveja R, Gupta V; Prolactin level in Infertility with menstrual irregularities.JObstet Gynecol India, 2002; 50: 40 – 3.
5. Cramer DW, Sluss PM, Powers RD; Serum Prolactin & TSH in an in vitro fertilization and thyroid function? J Assist ReprodGenet, 2003; 20(6): 210 – 5.
6. Poppe K, VelkeniersB; Thyroid disorders in infertile women.AnnEndocrinol (Paris), 2003; 64(1) :45 – 50.
7. Raber W, GesselA,NowothyP; Hyperprolactinemia in hypothyroidism ; clinical significance and impact of TSH normalization. Clin Endocrinol,2003; 58: 185 – 91.
8. Olivar AC, Chaffkin LM, Kates RJ, Allan TR; Is it necessary to obtain serum levels of thyroid stimulating hormone and prolactin in asymptomatic women with infertility? Conn Med, 2003; 67: 393 – 5.
9. GoswamiB, PatelS, ChatterjeeM; Correlation of prolactin and thyroid hormone concentration with menstrual patterns in infertile women. J of reproduction & infertility by Avicenna Research institute, 2009; 10(3):40.
10. Armada – Dias L, Carvalho JJ, Breitenbach MM; Is the infertility in hypothyroidism mainly due to ovarian or pituitary functional changes? Braz J MedBiolRes, 2001; 34(9): 1209 – 15.
11. Stoffer SS, McKeel DW Jr, Randall RV; Pituitary prolactin cell hyperplasia with autonomous

prolactin secretion and primary hypothyroidism. FertilSteril, 1981; 36(5) :682 – 5.
12. Wakim AN, Polizotto SL, Burholt DR; Influence of human granulosa cell steroidogenesis in vitro .J Assist ReprodGenet, 1995; 12(4) : 274 – 7.
13. AwasthiK; Hyperprolactinemiaand its correlation with hypothyroidism in infertile women.JObstetGynecolIndia, 2005; 56 :68 – 71.
14. Choudhary SD, GoswamiA; Hyperprolactinemia and reproductive disorders - a profile from North east. J Assoc Physicians India, 1995; 43(9): 617–8.
15. Thorner MO, BesserGM,Jones A; Bromocriptine treatment of female infertility: report of 13 pregnancies. Br Med J, 1975; 204(5998): 694 – 7.
16. Bohnet HG, Dalhen HG, Wuttke W; Hyperprolactinemicanovulatory syndrome. J ClinEndocrinolMetab, 1976; 42(1): 132– 43.
17. ScheithauerBW, Sano T, Kovacs KT; The pituitary gland in pregnancy: a clinicopathologic and immunohistochemical study of 69 cases. Mayo ClinProc, 1990; 65(4): 461 – 74.
18. Triggianese P, Perricone C, Perricorne R; Prolactin and Natural Killer cells: Evaluating the Neuroendocrine – immune axis in women with primary infertility & recurrent spontaneous abortion. Am J ReprodImmunol, 2015; 73(1): 56 – 65.
19. Singh SK, Agarwal JK; Thyroid dysfunction. J Assoc Physicians India, 1990; 38(7): 517.
20. Verma I, Sood R, JunejaS; Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility. Int J Appl Basic Med Res, 2012; 2(1): 17 – 9.
21. Turankar S, Sonoe K, Turankar A; Hyperprolactinemia and its comparison with hypothyroidism in primary infertile women. J ClinDiagn Res, 2013; 7(5): 794 – 6.
22. Surks MI, Ortiz E,Daniels GH; Subclinical thyroid disease : scientific review and guidelines for diagnosis and management. JAMA, 2004; 291 – 228.
23. KhandelwalD, TandonN; Overt and subclinical hypothyroidism : who to treat and how. Drugs, 2012; 72(1) : 17 – 38.
24. BispinkL,BrandleW, Lindner L; Preclinical hypothyroidism and disorders of ovarian function. GeburtshilfeFrauenheilkd, 1989; 49(10): 881 – 8.
25. Godinjak Z, Idrizbegovic E, Rama A; Correlation between hyperprolactinemia, MRI of hypophysis and clinical presentation in infertile patients. Med Arch, 2013; 67(1) : 22– 4.
26. Krassas GE, Pontikides N; Disturbances of menstruation in hypothyroidism. ClinEndocrinol (Oxf), 1999; 50(5): 655 – 9.
27. Kakuno Y, Amino N, KanohM; Menstrual disturbances in various thyroid diseases. Endocr J, 2010; 57(12): 1017 – 22.
28. Smith TP, Suliman AM; Groossvariability in the detection of prolactin in sera containing big prolactin (macroprolactin) by commercial immunoassays . J ClinEndocrinol Metab, 2002; 87 : 5410.
29. Ellis MJ, Reed MR, Livesey JH; Cross – reactivities of macroprolactin and big-prolactin in three commercial immunoassays for prolactin : a chromatographic analysis. Clin Biochem, 2007; 40: 1285.
30. Fahie – Wilson MN, John R, Ellis AR; Macroprolactin ; high molecular mass forms of circulating prolactin . Ann ClinBiochem, 2005; 42 :175.