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Prevalence of hyperprolactinaemia and hypothyroidism in primary and secondary infertility women

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Abstract

Prolactin secretion is controlled by hypothalamus which secretes prolactin inhibiting factor. Thyroid releasing factor (TRF), and thyroid stimulating hormone (TSH) have positive effect on prolactin secretion and can lead to galactorrhoea. Hyperprolactinaemia causes anovulation, amenorrhea, galactorrhoea, and reduced fecundity. With this background, the present study was planned to find out the prevalence of hyperprolactinaemia and hypothyroidism in women with infertility. Total 100 women patients of age range between 23 to 39 years were recruited for the study. Of the 100 women, 60 women were diagnosed as primary infertility and the remaining 40 were diagnosed as secondary infertility. Serum prolactin levels and thyroid stimulating hormone (TSH) levels were measured in all women. Patients were categorized based on their serum prolactin levels and TSH levels to find out the prevalence of hyperprolactinemia and hypothyroidism. The present study shows high prevalence of hyperprolactinemia and hypothyroidism in infertile women.

Keywords: Thyroid stimulating hormone, prolactin, hyperprolactinaemia, hypothyroidism, infertility, subclinical hypothyroidism.

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Introduction

Infertility has been defined as inability to conceive after one year of regular intercourse without contraception and accounts for one in six newly married couples [1]. It is primary if couple does not turn to be successful in achieving pregnancy, secondary if couple had achieved a pregnancy previously but are currently with conception difficulty. In many infertility cases, the diagnosis is simply unexplained because a variety of reasons like lack of ovulation, mechanical stoppage, sperm deficiencies and parental age etc [1]. Hyperprolactinaemia is most common hormonal disorder of hypothalamo-pituitary axis. There is close relationship between hypothalamic-pituitary-thyroid axis and hypothalamic-pituitary-ovarian axis [2]. 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 & normal thyroid hormones [2, 3].

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TSH, prolactin and growth hormone with FSH, LH acts synergistically in recruitment of new follicles. Even in absence of hyperprolactinaemia, thyroid dysfunction may contribute to infertility [4]. Thyroid hormone is essential for maximum production and balance of estradiol and progesterone and amplitude of LH pulses [3]. Abnormal levels not only causes galactorrhoea and amenorrhea, but also gonadal dysfunction and infertility. This indirectly suggest that both brain (impairing pulsatile secretion of GnRH), and pituitary might be targets for prolactin [5]. Morphological changes are observed in follicles in hypothyroidism can be a consequence of higher prolactin production, that may block both secretion and action of gonadotropins. Adequate thyroid supplementation restores prolactin levels as well and normalizes ovulatory function resulting in pregnancy.

As prolactin secretion is controlled by [6]:

1. Hypothalamus secretes prolactin inhibiting factor.
2. Vasoactive inhibitory peptide (VIP).
3. Thyroid releasing factor (TRF) has positive effect.
4. Thyroid stimulating factor (TSH) has positive effect and can lead to galactorrhoea.

Long-standing higher TSH levels due to Iodine deficiency probably resulted in hyperprolactinaemia causes anovulation, amenorrhea, galactorrhoea, reduced fecundity and increase in morbidity during pregnancy is noted by number of authors [7-9].

Materials and Method

100 women aged 23-39 years attending outpatient department of gynecology and obstetrics for the first time of Karpaga Vinayaga Institute of Medical Sciences, Madhuranthagam, Tamilnadu were recruited for the study. The study was carried out during the period of 1st May 2014 to 31st May 2015. Out of 100 women recruited for the study, 60 women were belonging to primary infertility category and remaining 40 women were of the secondary infertility category. Further, these women were also categorized on the basis of their serum prolactin levels and TSH (thyroid stimulating hormone) levels.

The study was approved by the institutional ethics committee and informed consent was obtained from all patients and controls. 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 TSH and prolactin levels were estimated by enzyme linked fluorescent immunoassay (ELFA) method using mini vidas kits. For adequate quality control both normal, abnormal reference control serum solutions and calibrators were run before analyzing test samples. All the results were tabulated as percentages.

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, FT4, FT3, prolactin), screening for infectious diseases and whenever indicated, hysterosalpingography and/or laparoscopy were enrolled after signing on informed consent.

Results

There were 100 patients recruited for the study out of total 100 women, 60 were of primary infertility and 40 patients were of secondary infertility. Mean age of the patients

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was 26±6.7. Both hypothyroidism and hyperthyroidism may result in menstrual disorders. Hypothyroidism is commonly associated with and such patients exhibit ovulatory dysfunction. Hence, assessment of serum TSH and Prolactin levels are mandatory in the work-up of all infertile women, especially those presenting with menstrual irregularities.

Table 1 shows different types of menstrual irregularities in relation to their serum prolactin levels. Out of 100 women 57 patients were having normal serum prolactin levels and remaining 43 patients presented with hyperprolactinemia. Table 2 shows range of serum prolactin levels in the women of study group includes primary and secondary infertile women. Normal range of serum prolactin level is 0 to 25ng/ml. Out of 60 primary infertile women, 31 patients presented with normal serum prolactin levels and out of 40 secondary infertile women, 26 patients only had normal serum prolactin levels. Table 3 shows range of serum TSH levels in women with primary and secondary infertility. 24 women with primary infertility and 19 women with secondary infertility had serum TSH levels less than 5mIU/ml. From table 4 it is evident that hyperprolactinemia is strongly associated with hypothyroidism. Table 5 shows serum TSH levels in infertile women with normal serum prolactin levels.

Following sub-clinical hypothyroidism symptoms were typically observed in infertile women:

-Dry skin – 10 %.
-Fatigue – 26 %.
-Cold intolerance – 5 %.
-Galactorrhoea - 7 %.
-Weight gain – 11 %.
-Muscle cramps – 3%.
-Hirsutism – 2%.
-Menstrual irregularities – 40%.

Hyperthyroidism - 3% in primary infertile women and 5% in secondary infertile women.
Hypothyroidism - 10% in primary infertile women and 8% in secondary infertile women.
Hyperprolactinaemia was depicted in 41% infertile women of both the groups.

Menstrual Pattern	**Normal prolactin**		**Hyperprolactinaemia**	
	No. of pts	**Percentage**	**No. of pts.**	**Percentage**
Amenorrhea	05	8.8	2	4.7
Oligo/Hypo menorrhea	25	43.9	21	48.8
Regular menses	21	36.8	18	41.8
Menorrhagia	06	10.5	2	4.7
Total	57	100	43	100

Table 1: Serum prolactin levels and menstrual pattern or irregularities

Serum prolactin in ng/ml	**Primary infertility**		**Secondary infertility**	
	No. of pts	**Percentage**	**No. of pts.**	**Percentage**
0 -25	31	51.66	26	65
26 – 50	17	28.33	05	12.5
51 – 100	07	11.6	07	17.5
101 – 150	03	05	01	2.5
151 – 200	02	3.33	01	2.5
Total	60	100	40	100

Table 2: Serum prolactin levels in the study group

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Serum TSH mIU/ml	Primary infertility		Secondary infertility	
	No. of pts	Percentage	No. of pts.	Percentage
<5	24	40	19	47.5
5 – 10	19	31.7	13	32.5
10 – 20	17	28.3	08	20
Total	60	100	40	100

Table 3: Serum TSH levels in all the study group women

Serum TSH mIU/ml	Primary infertility		Secondary infertility	
	No. of pts	Percentage	No. of pts.	Percentage
<5	22	75.8	10	71.4
5 – 10	06	20.7	01	7.2
10 – 20	01	3.5	01	7.2
> 20	00	0	02	14.2
Total	29	100	14	100

Table 4: Serum TSH levels in infertile women with hyperprolactinaemia

Serum TSH mIU/ml	Primary infertility		Secondary infertility	
	No. of pts	Percentage	No. of pts.	Percentage
<5	15	51.7	12	42.8
5 – 10	11	38	13	46.4
10 – 20	03	10.3	03	10.8
Total	29	100	28	100

Table 5: Serum TSH levels in infertile women with normal prolactin level

Discussion

Amenorrhea occurs in hypothyroidism due to hyper-prolactinemia resulting from a defect in the positive feedback of estrogen on LH. In this study few women show hypothyroidism symptoms with normal TSH and normal FT4**.** There is high occurrence of hypothyroidism which reflects tendency of infertility towards thyroid insufficiency or vice versa. High incidence of amenorrhea is seen in hyperprolactinaemia rather than in hypothyroidism. Prevalence of primary infertility was 75% and secondary was 25%. Hyperprolactinaemia was depicted in about 40% of infertile women.

Studies done by Haggerty et al [10], Papi et al [11] reported musculoskeletal and cardiovascular metabolic disorders in subclinical hypothyroidism similar to primary hypothyroidism. In the present study 70% of infertile women had ovulatory dysfunction, and 60% of them later became pregnant on thyroid replacement therapy. 2% women with infertility who presented without a history of ovulatory dysfunction had elevated TSH levels, and none became pregnant with treatment.

Majority of infertile women were euthyroid. However many infertile women present with normal menses despite a raised serum prolactin level. Prevalence in female with overt hypothyroidism was reported 39 to 57%, reported by Honbo et al [12] and Thomas R [13]. Bals-Pratsch et al [14] have proved the clinical importance of hyperprolactinaemia in ovulation disorders.

Prolactin is supposed to be important for maintenance of secretary activity of corpus luteum. The estimated incidence of hyperprolactinaemia in hypothyroidism has been reported from 0 to 40%. Staub JJ et al [14] say that thyroid never create a special symptom in people but most of sub-clinical hypothyroidism patients suffer from symptoms of this disease like fatigue, musculoskeletal symptoms and cold intolerance.

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Anovulatory cycles were reported by Rajan et al [15] as 31.4%, Mishra et al [5] as 51.4%, Binita Goswamy et al [16] as 58%. Kumkum [17] have noted anovulatory cycles were 49.5% and galactorrhoea in 9%. Oligo-ovulatory cycles were reported by Binita Goswamy et al [16] to be 82%, Kumkum [17] have reported 50%, Krasses et al [18] reported 23%.

Incidence of hypothyroidism in hyperprolactinaemia was 25.5%. There was high incidence of hyperprolactinaemia in infertile women, with positive correlation of 1:4 was found in hypothyroidism and hyperprolactinaemia. For the first time, Luboshitzky R. et al [19] an increase of serum prolactin was reported in woman with carpal tunnel syndrome and subclinical hypothyroidism.

Bahar A et al., [20] in their studies had shown that there was high prevalence of hyperprolactinaemia in sub-clinical hypothyroidism in female (21.7%) than male (11.3%). Perhaps estrogen in female may be the reason, because Meier et al [21] have found that women receiving estrogen before or after menopause have higher level of prolactin. In a study done by Binita et al [16] say that deranged prolactin levels were more in infertile patients (59.37%) as compared to fertile controls (40.63%).

Considering the clinical importance of hyperprolactinemia in sterility, several authors in their articles have highlighted the association of serum TSH and prolactin levels in infertile women. Menstrual disorders (mainly oligomenorrhoea), were reported by about 75% of the infertile women. In infertile patients with deranged TSH, 36% had higher TSH levels. A higher occurrence of hyperprolactinaemia (50%) was seen in infertile women.

Conclusion

The present study revealed a significant association between abnormal menstrual patterns, as well as anovulatory cycles with hyperprolactinemia in women with primary and secondary infertility. There was significant association between serum TSH and prolactin levels in infertile women both with normal or abnormal thyroid function (subclinical or overt, hypothyroidism or hyperthyroidism). Also there is high incidence in of hyperprolactinemia in infertile women with normal thyroid function.

References

1. 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.
2. Frey KA, Patel KS. Initial evaluation and management of infertility by the primary care physicians. Mayo Clin Proc. 2004; 79(11):1439-43.
3. Poppe K, Velkeniers B. Thyroid disorders in infertile women. Ann Endocrinol (Paris). 2003; 64(1):45-50.
4. 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 Reprod Genet. 2003; 20(6):210-215.
5. Mishra R, Baveja R, Gupta V. Prolactin levels in infertility with menstrual irregularities. J Obstet & Gynecol India. 2002; 52:40-43.
6. Raber W, Gessl A, Nowotny P, Vierhapper H. Hyperprolactinaemia in hypothyroidism: clinical significance and impact of TSH normalization. Clin Endocrinol. 2003; 58:185 –91.
7. Poppe K, Velkeniers B, Glinoer D. Thyroid disease and female reproduction. Clin Endocrinol (Oxf). 2007; 66(3): 309-21.
8. Mishra R, Baveja R, Gupta V. Prolactin levels in infertility with menstrual irregularities. J Obstet & Gynecol India. 2002; 52:40-43.
9. Staub JJ, Althaus BU, Engler H, et al. Spectrum of subclinical and overt hypothyroidism: effect on thyrotrophin, prolactin, and thyroid reserve, and metabolic

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impact on peripheral target tissues. Am J Med.1992; 92:631–642.
10. Haggerty JJ, Stern RA, Mason GA, et al. Subclinical hypothyroidism: a modifiable risk factor for depression? Am J Psychiatry. 1993; 150:508–510.
11. Papi G, Uberti ED, Bctterle C, et al. Subclinical hypothyroidism. Curr Opin Endocrinol. Diabetes Obes.2007; 14:197–208.
12. Honbo KS, Van Herle AJ, Kellett KA. Serum prolactin levels in untreated primary hypothyroidism. Am J Med. 1978; 64:782–787.
13. Thomas R, Reid RL. Thyroid disease and reproductive dysfunction: A review. Obstet Gynecol.1987; 70:789–798.
14. Bals-Pratsch M, De Geyter C, Muller T, et al. Episodic variations of prolactin, TSH, LH, melatonin and cortisol in infertile women with subclinical hypothyroidism. Hum Reprod. 1997; 12: 896–904.
15. Rajan P. Prolactin metabolism in Infertility. J Obstet Gynacol India. 1990; 40; 243-247.
16. 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; 10:207-212.
17. 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.
18. Krassas GE, Pontikides N, Kaltsas T, Papadopoulou P, Paunkovic J, Paunkovic N, et al. Disturbances of menstruation in hypothyroidism. Clin Endocrinol (Oxf) 1999; 50 (5):655–659.
19. Luboshitzky R, Aviv A, Herer P, Lavie L. Risk factors for cardiovascular disease in women with subclinical hypothyroidism. Thyroid. 2002; 12:421–425.
20. Bahar A, Akha O, Kashi Z, Vesgari Z. Hyperprolactinaemia in association with subclinical hypothyroidism. Caspian J of Internal Medicine, 2011; 2(2): 229-233.
21. Meier C, Christ-Crain M, Guglielmetti M, et al. Prolactin deregulation in women with subclinical hypothyroidism: effect of levothyroxine replacement therapy. Thyroid. 2003; 13:979–985.

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