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Comparative study of Serum PRL, LH, FSH in overt and subclinical hypothyroid females in reproductive age group

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Abstract: *Hypothyroidism is associated with an increase in the levels of thyroid releasing hormone (TRH) which in turn stimulates secretion of thyroid stimulating hormone (TSH) and prolactin (PRL). PRL inhibits the synthesis and secretion of gonadotropins(FSH & LH). Abnormal menstrual patterns are commonly observed in overt hypothyroidism.[1] Studies considering an association between overt hypothyroidism and female reproductive hormones are not adequate particularly in eastern India. Therefore, present study is aimed to evaluate the relationship between overt and subclinical hypothyroidism and female reproductive hormones. Subjects were randomly selected having high TSH level.They were categorized into subclinical and overt hypothyroid. Results were analysed by using Graph pad prism 5, comparison was done using independent group t test and correlation was determined by Pearson's correlation coefficient. Result showed that with overt hypothyroidism PRL increased and FSH & LH decreased significantly whereas in subclinical hypothyroidism PRL increased but FSH and LH are not significantly decreased. Most of the patients presented with oligomenorrhea .*

Key words : *FSH, hypothyroid, LH, oligomenorrhoea, PRL.*

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I. Introduction

The thyroid hormones affect function of almost all the organs in the body and plays a major role in the homeostasis of many body functions like reproduction. Thyroid dysfunction is a common endocrine disorder.The prevalence of hypothyroidism in developed world is about 4-5%[(2)]. Prevalence of subclinical hypothyroid in developed world is 4-15% ([2)] Among all cities, Kolkata recorded the highest prevalence (21.67%) while others showed comparable rates ranging from 8.88% (Hyderabad) to 11.07% (Delhi).

Both hyperthyroidism and hypothyroidism may result in menstrual disturbances. Numerous researchers have shown abnormal menstrual patterns. Most showed that 50 to 70% of hypothyroid female patients had menstrual abnormalities and an increased serum prolactin in women with subclinical hypothyroidism [[3,4]]. The most common manifestation of hypothyroidism is oligomenorrhea. Severe hypothyroidism is commonly associated with failure of ovulation. Ovulation and conception can occur in mild hypothyroidism.

The relationship of thyroid dysfunction, PRL and serum gonadotropins at a time has not been done in eastern India .Hence we will conduct a study of serum gonadotropins and PRL in hypothyroid females, both overt and subclinical.

II. Materials and Methods

2.1 Study population : Reproductive age group patients (15 to 49 years) who had no history of other diseases, only diagnosed as primary hypothyroidism were included in the study. Primary hypothyroidism was diagnosed on the basis of low serum thyroxin (T_4) and elevated TSH levels. A detailed menstrual history was obtained. Subjects were divided into overt & subclinical hypothyroid according to their serum TSH and T_4 level.

2.2 Inclusion Criteria:

1) Newly diagnosed primary hypothyroid patients.
2) Females of reproductive age group.(15 to 49 years)

2.3 Exclusion Criteria :

- Patients already taking thyroxin
- Patients getting treatment for infertility
- Patients taking antidepressants**,** antipsychotics
- Pregnancy & lactation

- Liver & kidney diseases.

2.4 Method:

provided written informed consent**.**.Diagnosis was based on history, lab reports, inclusion& exclusion criteria.A detailed menstrual & fertility history of the selected hypothyroid females were taken. After exclusion of other significant causes, serum PRL, FSH & LH levels were estimated.

Subclinical hypothyroidism was diagnosed when TSH levels were elevated but thyroxin (T_4) were within normal range. In **overt hypothyroidism**, TSH levels were high and T_4 levels were low. TSH usually increases when T_4 and T_3 levels drop.Serum T_4, TSH and serum gonadotropins (FSH and LH) were estimated by ELISA method. The test was done preferably within first 5 days of menstrual cycle as the levels of gonadotropins are lowest in this phase of cycle and thereby the interpretations are more sensitive in postmenstrual phase. Some patients could not come again for the test within first 5 days of menstruation as they lived in rural area far away from hospital.

	Normal range
T_4	5-13mIU /l
TSH	0.4- 5.5µIU/mL
PRL	1.2-19.5 ng/ml
FSH	3-12 mIU/ml
LH	0.5-10.5 mIU/ml

2.5 **Statistical analysis** were done with Graph Pad Prism5.Data were analyzed by unpaired t test. A p-value <0.05 was considered statistically significant. Pearson's correlation coefficient was calculated to determine the relationship.

III. Results

In our study 25 subclinical and overt hypothyroidism patients were taken in each group. In subclinical hypothyroidism group oligomenorrhoea (64%) was the dominant menstrual dysfunction, followed by normal menstruation (28%).Only 8% had menorrhagia in our study. In overt hypothyroidism group again it was oligomenorrhoea (80%) which was the principal menstrual abnormality followed by normal menstruation (12%). The percentage of females with menorrhagia was 8%.(table :1).Unique feature of our study was none of our married subjects had history of infertility,8% were unmarried in our study group.

Table 1: Menstrual status of the study group

	normal	**oligomenorrhea**	**menorrhagia**
subclinical	**28%**	**64%**	**8%**
overt	**12%**	**80%**	**8%**

Table 2 Hormonal status in whole study group

	TSH	**T4**	**PRL**	**FSH**	**LH**
subclinical	**7.94±1.18**	**11.56 ± 3.19**	**18.96±8.177**	**8.35±11.18**	**4.84±12.24**
overt	**16.9±10.12**	**1.78 ± 2.07**	**28.74±11.27**	**5.73±12.15**	**0.84±6.53**

Table 3.Comparison of TSH & PRL between subclinical & overt hypothyroid patients

	TSH(Mean ±SD)	PRL (Mean ±SD)	P value
Subclinical hypothyroid (25)	7.94±1.18	18.96 ± 8.177	0.0001***
Overt hypothyroid (25)	16.99±10.12	28.74±11.273	0.0003***

Table 4.Comparison of TSH &FSH between subclinical & overt hypothyroid patients

	TSH (Mean ±SD)	FSH (Mean ±SD)	P value
Subclinical hypothyroid (25)	7.94 ±1.18	8.35± 11.18	0.856
Overt hypothyroid (25)	16.99 ±10.12	5.73± 11.273	0.0008***

Table 5 Comparison of TSH &LH between subclinical & overt hypothyroid patients

	TSH (Mean ±SD)	LH (Mean ±SD)	P value
Subclinical hypothyroid (25)	7.94±1.18	4.84± 12.24	0.213
Overt hypothyroid (25)	16.99 ±10.12	0.84 ± 6.5	0.0001***

Table 6. Correlation of TSH, PRL, FSH, LH in subclinical hypothyroid

	TSH&PRL	TSH& FSH	TSH & LH
No.of XY pairs	25	25	25
spearman r	-0.08769	0.2169	0.5769
95% confidence	0.3384	-0.2069 to 0.574	-0.3562 -.4527
Is correlation significant	ns	ns	ns

Table 7. Correlation of TSH, PRL, FSH, LH in clinical hypothyroid

	TSH&PRL	TSH& FSH	TSH & LH
No.of XY pairs	25	25	25
spearman r	-0.5432	-0.6341	-0.5350
95% confidence	0.1765-.7775	-0.8270-0..3076	-0.7729- 0.1653
Is correlation significant	**yes**	**yes**	**yes**

Figures showing pattern of correlation in subclinical & overt hypothyroid

Fig :2a Overt hypothyroid Fig:3a subclinical hypothyroid

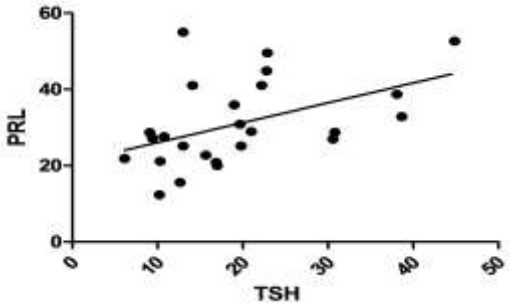


Fig:2b

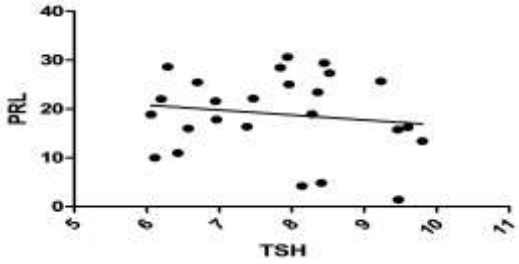
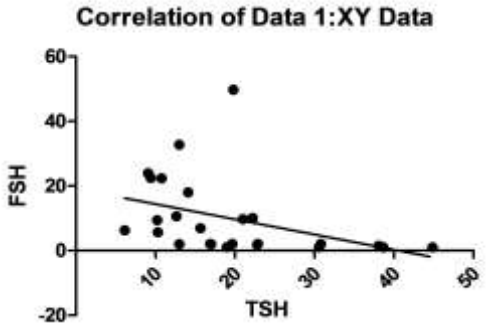


fig 3b



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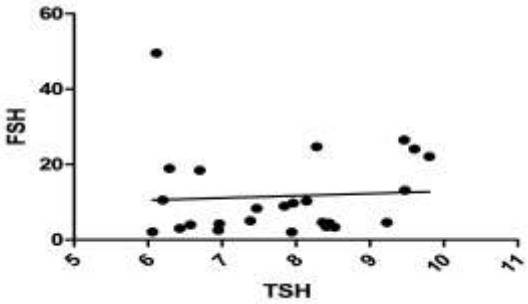

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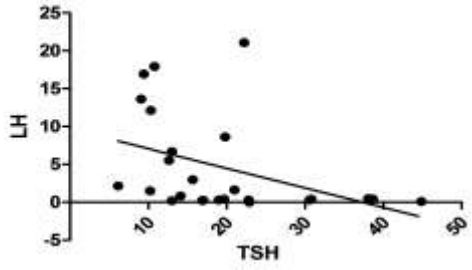

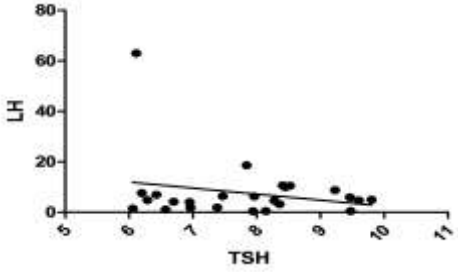

IV. Discussion

Hyperprolactinemia is commonly associated with hypothyroidism. It may develop due to a compensatory increase in the discharge of central hypothalamic thyrotropin-releasing hormone, which results in stimulation of prolactin (PRL) secretion. Prolactin elimination from the systemic circulation is reduced in patients with primary hypothyroidism, which contributes to increased prolactin concentrations [4,5,6,7].

Hyperprolactinemia of variable magnitude (39% to 57%) has been reported in overt hypothyroidism in several studies; but research on the prevalence and extent of hyperprolactinemia in subclinical hypothyroidism are few and has different results [4,5,6,7].

Raber et al[10],Meier et al[11]., in their study on subclinical hypothyroidism reported the prevalence of hyperprolactinemia. Meier[11] noticed prolactin levels returned to normal in whom L-thyroxin was supplemented, while PRL levels remained high in those who received placebo. In our study we observed significant rise of serum PRL in both, overt ($p<0.0003$) & subclinical cases. ($p<0.0001$) (table:3) .

Parul Goel et al[8] observed PRL elevation in 16 patients (21.33 %) with overt hypothyroidism, and in six patients (8%) with subclinical hypothyroidism. We found abnormally high PRL in 20% patients with overt hypothyroid,& 5% in subclinical hypothyroid along with high TSH. All these patients showed oligomenorrhea.(table:1). A higher incidence of amenorrhea could be linked to hyperprolactinemia that was seen in the majority of patients with hypothyroidism.

Neema Acharya et al[9] ,in their study found no significant correlation between TSH & PRL in subclinical cases, Similar findings have been observed by us.(fig 3a),but there is significant positive correlation in clinical hypothyroid in our study.(fig 2a)

PRL inhibits gonadotropins. Neema Acharya et al[9] observed low serum FSH and LH levels in both groups with menorrhagia and infertility. In our study FSH & LH levels were low normal, significntly decreased in overt hypothyroidism. In 2 overt patients we found abnormal rise in FSH and LH which may be due to occult ovarian failure. Similar observation was seen by Neema Acharya et al[9]. In overt hypothyroidism, we found that TSH negatively correlated with FSH & LH (fig: 2b,2c), but no such correlation in subclinical hypothyroid (fig:3b,3c). In abnormal high FSH,LH. polycystic ovarian disease should be excluded.

Binita Goswami's[12] study proposed amenorrhoea occurs in hypothyroidism due to hyperprolactinaemia which results from a defect in the positive feedback of oestrogen on LH, and because of LH and FSH suppression. Serum FSH & LH levels, usually low when estimated in the initial 5 days of menstrual cycles. Very low gonadotropin along with TSH should exclude pituitary failure.

V. Conclusion

The existence of hypothyroidism and menstrual irregularities can be explained partly by raised PRL. The increase in the incidence of hyperprolactinemia even in patients with subclinical hypothyroidism emphasizes the significance of prolactin screening in all hypothyroid cases.[8] All hyperprolactinaemia patients should undergo thyroid function tests.

Elevated gonadotropins in some patients may be explained that they were in proliferative phase, they couldn't come in 5th day of cycle.Large sample size & other lab parameters (eg: fT_4,fT_3) also be included in further studies.

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