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Original Research Article

Hyperprolactinemia in patients with high TSH levels with both clinical and subclinical hypothyroidism

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ABSTRACT

Background: Hyperprolactinemia is the most common endocrine disorder involving hypothalamic–pituitary axis. This results from multiple causes such as medications, hypothyroidism, and pituitary disorders. Hyperprolactinemia and hypothyroidism are closely interrelated conditions. The present study aimed to estimate serum prolactin levels and determine the prevalence of hyperprolactinemia in newly diagnosed subclinical and clinical hypothyroid patients and correlation between TSH and prolactin levels in subclinical and clinical hypothyroid patients.

Materials and Methods: This study was conducted in the Department of Biochemistry, in collaboration with Department of Medicine, Department of Obstetrics and Gynecology, LATE BRKM Government Medical College, Jagdalpur, Chhattisgarh, India. Total of 138 patients presenting to Department of Medicine for various thyroid related problems were involved in this study. The newly diagnosed cases of primary hypothyroidism were included in this study. The demographic, physical and clinical history was taken from all the study subjects.

Results: In the present study, serum prolactin levels were significantly increased in subclinical (28.7 ± 6.4 ng/mL) and clinical hypothyroidism (15.02 ± 4.2ng/mL) compared to controls. Hyperprolactinemia was observed in 11 (22.9%) patients in subclinical hypothyroidism and 4 (8.3%) in clinical hypothyroid patients. In the subclinical hypothyroidism and clinical hypothyroidism, the serum TSH levels were (17.01 ± 8.2 μU/l, 7.3 ± 2.0 μU/l respectively) significantly increased than the controls. In the clinical hypothyroidism and subclinical hypothyroidism, the serum free T3 (fT3) levels were (5.6 ± 0.68 pmol/l, 2.54 ± 0.43 pmol/l respectively) significantly increased than the controls. In the clinical hypothyroidism and subclinical hypothyroidism, the serum total T3 (T3) levels were (1.27± 0.24 nmol/l, 0.59±0.12 nmol/l respectively) significantly increased than the controls.

Conclusion: The study results may conclude that, prolactin regulation is altered, in patients with clinical and subclinical hypothyroidism. Thyroid functions tests ought to be conducted in patients with hyperprolactinemia prior to performing further tests.

1. Introduction

Hyperprolactinemia is the most common endocrine disorder, occurs due to multiple causes like use of medications, thyroid disorders, and disorders of the pituitary. The Prolactin (PRL) secretion is inhibited by PRL inhibitor factor, released from hypothalamus. Dopamine antagonism, vasoactive inhibitory peptide (VIP) and thyroid-releasing hormone (TRH) enhances its secretion.[1] Hyperprolactinemia and hypothyroidism, closely interlinked conditions. The hyperprolactinemia prevalence in subclinical hypothyroidism (SCH) reported to be ranged from 0%–40% of hypothyroid patients. Pathologic hyperprolactinemia is a condition in which there

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is an increased prolactin levels other than physiological.[2,3]

However, TRH stimulates secretion of PRL and thyroid-stimulating hormone (TSH), causing elevated levels of PRL;[4,5] however, a increased hyperprolactinemia prevalence in hypothyroid is found in females compared to males due to estrogen requirement for this effect.[6]

Further, the elimination of prolactin from systemic circulation is compromised, which leads to increased prolactin concentrations.[7,8] Other reasons for high prolactin levels in hypothyroidism may be due to low sensitivity to the suppressant effect of dopamine on the synthesis of prolactin, and high prolactin synthesis through increased mRNA levels of PRL in the presence of lower thyroid hormone levels.[9]

Hyperprolactinemia in the premenopausal age group is associated with hypogonadism, galactorrhea, and amenorrhea; oligomenorrhea is associated with moderately increased PRL levels; short luteal phase, reduced libido, and infertility are observed in mild hyperprolactinemia. Osteopenia is associated with duration and severity of hypogonadism. Hyperprolactinemia in men is associated with impotence, low sperm production, infertility, reduced libido and gynecomastia.[1]

SCH characterized by elevated serum TSH levels with normal serum free thyroxine (fT4) and free T3 concentrations, linked with few or no sign and symptoms of hypothyroidism.[10]The common symptoms observed in hypothyroidism are dry skin, cold sensitivity, muscle cramps, fatigue, voice changes, menstrual irregularity, puffy eyes, and constipation. Decreased thyroid hormone concentrations were linked with increased PRL levels, which has been implicated in infertility.[11]

Therefore, present study aimed to measure serum prolactin levels and to assess the prevalence of hyperprolactinemia in newly diagnosed subclinical and clinical hypothyroid patients and correlation between TSH and prolactin levels in subclinical and clinical hypothyroid patients.

2. Materials and Methods

This present study was conducted in the Department of Biochemistry in collaboration with Department of Medicine, Department of Obstetrics and Gynecology, LATE BRKM Government Medical College, Jagdalpur, Chhattisgarh, India. Total of 138 patients presenting to Department of Medicine for various thyroid related problems were involved in this study.

The newly diagnosed cases of primary hypothyroidism were included in this study. The demographic, physical and clinical history was taken from all the study subjects. These patients were then segregated into two subclinical and clinical hypothyroidism according to their diagnosis. Similarly, forty-eight, age and sex matched healthy subjects were recruited as controls.

2.1. Exclusion criteria

The patients with history of hyperprolactinemia, lactating & pregnant women, liver disease, kidney disease, and the patients on antidepressants and estrogens or antipsychotics.

Under aseptic conditions, 4 ml fasting blood sample was collected from all the study subjects, centrifuged for 10 mins toobtain serum sample and preserved at –20^{o}C for further analysis. The serum levels of TSH, total and free thyroxine (T4 & fT4), total and free triiodothyronine (T3 & fT3) & prolactin (PRL) were measured by using chemiluminescence method with a fully automated Beckman Coulter Access 2 instrument.

2.2. Statistical analysis

The results were expressed in Mean±SD. Chi-Square test and one way ANOVA and Pearson correlation was applied. p-value <0.05 was considered as significant.

3. Results

Out of 138 patients, 42 patients who didn't meet with incorporation rules were avoided from study.

The clinical profile of the study subjects was shown in Table 1.

The mean age of the patients in subclinical hypothyroidism is 36.24 ± 8.02 years, in clinical hypothyroidism is 36.14 ± 7.06 years and in controls is 36.16 ± 7.1 years, which was statistically insignificant. In the present study, serum prolactin levels were significantly increased in subclinical (28.7 ± 6.4 ng/mL) and clinical hypothyroidism (15.02 ± 4.2ng/mL) compared to controls. Hyperprolactinemia was observed in 11 (22.9%) patients subclinical hypothyroidism and4 (8.3%) in clinical hypothyroid patients. In the subclinical hypothyroidism and clinical hypothyroidism, the serum TSH levels were (17.01 ± 8.2μU/l, 7.3 ± 2.0μU/l respectively) significantly increased than the controls. In the clinical hypothyroidism and subclinical hypothyroidism, the serum free T3 (fT3) levels were (5.6 ± 0.68pmol/l, 2.54 ± 0.43pmol/l respectively) significantly increased than the controls. In the clinical hypothyroidism and subclinical hypothyroidism, the serum total T3 (T3) levels were (1.27± 0.24nmol/l, 0.59±0.12nmol/l respectively) significantly increased than the controls. In the clinical hypothyroidism and subclinical hypothyroidism, the serum total T3 (T3) levels were (1.27± 0.24nmol/l, 0.59±0.12nmol/l respectively) significantly increased than the controls. In the clinical hypothyroidism and subclinical hypothyroidism, the serum free T4 (fT4) levels were (13.6 ± 4.2nmol/l, 5.6 ± 1.15nmol/l respectively) significantly decreased than the controls. In the clinical hypothyroidism and subclinical hypothyroidism, the serum total T4 (T4) levels were (79.01 ± 12.01nmol/l, 35.4 ± 8.2nmol/l respectively) significantly decreased than the controls.

Table 1: Comparison of biochemical parameters in different groups

Variables	Hypothyroidism		Controls(Mean ± SD) (n=42)	P value
	Subclinical(Mean ± SD) (n=36)	Clinical(Mean ± SD) (n=60)		
Female/Male	48/8	48/7	48/10	
Age (yrs)	36.24 ± 8.02	36.14 ± 7.06	36.16 ± 7.1	0.32
Biochemical parameters				
Serum Prolacctin(ng/mL)	28.7 ± 6.4	15.02 ± 4.2	7.03± 2.12	0.001
Hyperprolactinemia Female/male	11(22.9%) 8/3	4(8.3%) 3/1	0	0.012
SerumTSH (μU/l)	17.01 ± 8.2	7.3 ± 2.0	2.4 ± 0.7	0.001
SerumfT3 (pmol/l)	2.54 ± 0.43	5.6 ± 0.68	6.1 ± 1.2	0.001
SerumT3 (nmol/l)	0.59±0.12	1.27± 0.24	1.34±0.24	0.001
SerumfT4 (nmol/l)	5.6 ± 1.15	13.6 ± 4.2	14.3 ± 4.6	0.001
SerumT4 (nmol/l)	35.4 ± 8.2	79.01 ± 12.01	83.4 ± 14.3	0.001

Positive correlation was observed between serum TSH and PRL levels; however, the correlation was statistically non-significant, in patients with subclinical hypothyroidism, correlation of (r=0.11, p=0.45) was found, while in clinical hypothyroid patients it was (r=0.04, p=0.78).

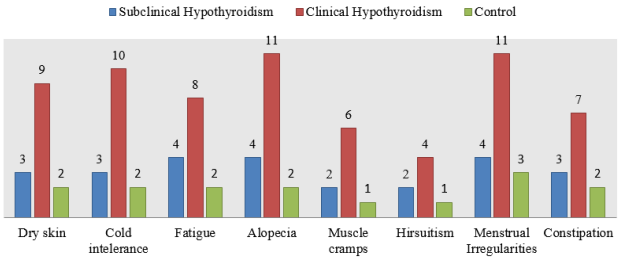

Fig. 1: Symptoms

In the present study, the symptoms were more in clinical hypothyroidism patients than the subclinical hypothyroidism. The symptoms such as alopecia and menstrual irregularities were observed in 11 cases each, cold intolerance in 10 cases, dry skin in 9 cases, fatigue in 8 cases, constipation in 7 cases and muscle cramps in 6 cases and others as shown in Figure 1.

4. Discussion

Hyperprolactinemia, one of the common endocrine disorder of hypothalamic–pituitary axis and usually seen in women.[12–14] In the present study, hyperprolactinemia prevalence in subclinical hypothyroidism is 11 (22.9%) patients and in clinical hypothyroidism is 4(8.3%) patients, suggesting that it is more prevalent in subclinical hypothyroidism than the clinical hypothyroidism.

Goel et al. in their study observed that PRL was increased in 21.3% subjects with overt hypothyroidism and 8% in subjects with SCH.[15] Bahar et al.in their study observed that the hyperprolactinemia prevalence was 22% in women with subclinical hypothyroidism (91 females had high PRL levels among 419 females).[16]

Hekimsoy et al. observed PRL elevation in 36% with overt hypothyroidism and 22% with subclinical hypothyroidism.[9] SamarjitKoner et al reported that the prevalence of hyperprolactinemia is 21% in all hypothyroid female patients, 23.0% in clinical or overt hypothyroid females, and 17.1% in SCH females, respectively.[17]

This higher propensity of hyperprolactinemia is in agreement with the findings of Kumkum A et al who had depicted a prevalence of 46% in their study.[18] In the present study, positive correlation was observed between serum TSH and PRL levels. In a study conducted by Hekimsoy et al on hypothyroid patients (overt and subclinical) found a positive correlation between TSH and PRL levels.[9] In a study by Alsultance, found a significant positive correlation between hypothyroidism and hyperprolactinemia.[19]

Kumkumet al. and Lal et al. observed a positive correlation between TSH and PRL.[18,20] In the present study, the symptoms were higher in clinical hypothyroidism patients than the SCH patients. The symptoms such as alopecia and menstrual irregularities were observed in 11 cases each, cold intolerance in 10 cases, dry skin in 9 cases, fatigue in 8 cases, constipation in 7 cases and muscle cramps in 6 cases etc. Alopecia was significantly more in women (14.4%) compared to men (1.6%), this observation was similar to the findings of Zltautkr, et al study, it was reported that hyperprolactinemia and hypothyroidism have roles in stimulating androgenic alopecia, this might be a probable reason for our female androgenic alopecia.[21] Hyperprolactinemia stimulates the production of androgen from adrenal and thyroxin effects on free and total testosterone with effect on thyroid binding globulin (TBG). So, co-existence of these two disorders can cause intensive alopecia.

In a study conducted by Goel et al. reported that significant difference between overt and subclinical hypothyroid patients for all hypothyroid symptoms (fatigue,

dryness of skin, cold intolerance, constipation, and weight gain) except alopecia and hirsutism. TRH caused hyperprolactinemia in hypothyroidism, perhaps there is some unknown etiology that causes hyperprolactinemia in these patients.

5. Conclusion

In conclusion, prolactin regulation is altered in clinical hypothyroidism patients and also in patients with subclinical hypothyroidism. Thyroid functions tests to be done in patients with hyperprolactinemia. Hyperprolactinemia causes reproduction disorders in women. Therefore, it is important to diagnose early and management of this disease.

6. Conflict of Interest

None.

7. Sources of Funding

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