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EVALUATING THE RELATIONSHIP BETWEEN TSH AND T4 IN THYROID DYSFUNCTION

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ABSTRACT

Introduction: The thyroid gland plays a pivotal role in regulating metabolism, growth, and development through the production of thyroid hormones, primarily thyroxine (T4) and triiodothyronine (T3). The hypothalamic-pituitary-thyroid (HPT) axis governs this process, with thyroid-stimulating hormone (TSH) acting as a key regulator. Thyroid dysfunction, including hypothyroidism and hyperthyroidism, is a common endocrine disorder characterized by distinct alterations in TSH and T4 levels.

Aim: This study aimed to evaluate the strength of association between TSH and T4 levels in patients with hypothyroidism and hyperthyroidism, while also examining demographic factors and complication profiles associated with these conditions.

Methodology: A retrospective cross-sectional study was conducted using data from 110 patients (55 hypothyroid and 55 hyperthyroid) retrieved from the Pathology Department of Saidu Teaching Hospital, Swat. Serum TSH and T4 levels were measured using electrochemiluminescence immunoassay (ECLIA) technology. Statistical analyses, including Pearson correlation and independent t-tests, were performed to assess the relationship between TSH and T4 and compare demographic and

clinical characteristics between groups.

Results: Hypothyroid patients exhibited significantly higher TSH (12.6 ± 5.4 mIU/L) and lower T4 (3.8 ± 1.2 µg/dL) levels compared to hyperthyroid patients (TSH: 0.1 ± 0.05 mIU/L; T4: 18.5 ± 4.6 µg/dL; $p < 0.001$). A strong inverse correlation was observed between TSH and T4 in both groups ($r = -0.82$ for hypothyroidism, $r = -0.78$ for hyperthyroidism; $p < 0.001$). Hypothyroid patients had higher rates of goiter (56.3%), while hyperthyroid patients more frequently developed thyrotoxicosis (75.9%) and atrial fibrillation (34.5%).

Conclusion: The study confirms the inverse relationship between TSH and T4 in thyroid dysfunction, supporting the HPT axis's feedback mechanism. These findings underscore the importance of measuring both hormones for accurate diagnosis and highlight distinct complication profiles in hypothyroid and hyperthyroid patients.

INTRODUCTION

The thyroid gland is a very significant endocrine gland that relays the control of metobolism, growth and development through the production and release of thyroid hormones, namely, thyroxine (T4) and triiodothyronine (T3) (1). The Hypothalamic-pituitary-thyroid (HPT) axis is a well-known endocrine regulatory cycle that governs the synthesis of these hormones closely (2). The thyroid-stimulating hormone (TSH) is released by the pituitary gland moves into the thyroid and leads to the production of hormones (3). In their turn, free T4 and T3 affect the pituitary with a negative feedback that regulates TSH secretion to balance the hormones union (4).

One of the characteristics of that regulatory system is a sensitive, log-linear connection between TSH and free T4. Incremental shifts in the level of free T4 lead to monstrous shifts in focus on TSH on logarithmic basis (5). This physiological potentiation has ensured that TSH is the most sensitive biochemical indicator of detecting subtle or early change in thyroid function in individuals with an intact HPT axis (6). Accordingly, TSH is popularly used as the initial screening laboratory test in thyroid disorders (7).

One of the most common endocrine diseases in the world is thyroid dysfunction and it is divided into two broad categories of hypothyroidism and hyperthyroidism (8). Biochemically, the hypothyroid condition of inadequacy of the thyroid hormones is characterized by high TSH level and low level of T4 (9). On the other hand, hyperthyroidism which occurs due to over production of thyroid hormones is characterized by low TSH and high T4 (10). Although these characteristic changes are easy to detect when overt disease is present, a large percentage of patients display plton timing normal range TSH regardless of having a T4 level discogenic the pelvis normal range (11).

These subtle abnormalities are a common problem of interpretation to clinicians (12). Although the TSH is the most sensitive indicator, in many cases a complete assessment of the patient may necessitate the measurement of T4 to establish the extents of dysfunction and control planning (13). Thus, it is crucial that the definition of the exact relationship and interaction between TSH and

T4 in the full range of thyroid functioning, including the euthyroidism to subclinical and overt illness, should be known in order to make proper diagnosis, adequate monitoring and suitable treatment to take effect (14).

This is significant to the clinical value of proper identification of thyroid dysfunction since it has a significant effect on the overall health of the body (15). The change in levels of thyroid hormone is closely linked with severe alteration in lipid metabolism, which escalates the chances of development of dyslipidemia and consequent heart disease (16). Moreover, it has also been associated with the incidence of other autoimmune diseases and it may complicate almost every organ system due to the occurrence of thyroid disorders (17). Although TSH plays a central role, there is still a debate on the most reliable and cost effective secondary biochemical markers (13). Which of the two to measure and the relative diagnostic importance of one or the other in various clinical scenarios e.g. in healthy individuals compared to individuals with overt disease is a matter of clinical research (18). This emphasizes that there is a necessity to better comprehend the interactive relationship between TSH and T4 to better define diagnostic strategies and alleviate patient outcomes (19).

With these considerations, the first major objective of the current research is to assess the strength of association between TSH and T4 concentrations throughout the spectrum of thyroidal activity in a systematic manner. The specific value are to test the correlation between TSH and T4 in the separate groups of euthyroid, hypothyroid, and hyperthyroid patients.

METHODOLOGY

The research is based on a retrospective cross-sectional design carried out to determine the relationship between the level of Thyroid Stimulating Hormone (TSH) and Thyroxine (T4) in the patients with a diagnosis of hypothyroidism and hyperthyroidism. The study retrieved the records of 110 patients, 55 patients who had hypothyroidism and 55 patients who had hyperthyroidism, and any complications that were noted in the medical records of Pathology Department of Saidu Teaching Hospital, Swat. It was hypothesized that the goal of the study was to determine the connection between TSH and T4 in these two different and distinct thyroid conditions taking into consideration some of the factors that may influence the same like age, gender and associated clinical complications.

Patients who had previously diagnosed with the condition of primary hypothyroidism (where TSH levels were high while those of T4 low) or hyperthyroidism (where TSH is low and the levels of T4 are elevated) comprised the study population. Secondary thyroid dysfunction was excluded to clearly evaluate the primary thyroid dysfunction, various patients with pituitary/ hypothalamic origin of secondary to thyroid dysfunction were not included. Moreover, persons whose lab records were not complete or those who have recently had an alteration of the thyroid medication (within the past three months) were not included to prevent a confounding influence on the levels of the hormones.

The records were obtained by using archived hospital records, and the information was sought on demographic data (age and gender) and the results of thyroid serum functions (TSH and Free T4 levels), and the problems that were documented that were related to thyroid dysfunction. In the case of hypothyroid patients, we observed complications like goiter, myxedema, and cardiovascular risk, whereas the hyperthyroid patients were evaluated in terms of such conditions as thyrotoxicosis and atrial fibrillation, and osteoporosis.

Laboratory Analysis

The analysis of the thyroid function tests was carried out on the Roche Cobas e601 immunoassay analyzer included in the Cobas 6000 modular system that is generally known

to be the most precise endocrinological analyzer. The serum TSH and T4 levels were measured by electrochemiluminescence immunoassay (ECLIA) technology by the reagent kits supplied by the manufacturers (Roche Diagnostics). The analytical measure range was 0.3 4.6 mIU/L (TSH) and 4.0-12.0g/dL (T4) to provide a positive change in clinically important levels (20).

Diligent quality control measures were ensured and daily QC run conducted to confirm the precision and accuracy of the assay with Roche PreciControl materials. The labs are internationally standardized, all tests were run by trained technicians using standardized operating procedures.

Data Collection and Analysis

Information about patients, such as their age, sex, TSH, free T4 values, and complications of thyroid diseases, was obtained by reading electronic medical records. The statistical analysis was done through the use of SPSS version 26, Pearson correlation to determine the relationship between TSH and T4, and independent t-tests to compare the mean between hypothyroid and hyperthyroid groups. The p-value set below 0.05 was deemed significant.

RESULTS

The study analyzed data from 110 patients (55 hypothyroid, 55 hyperthyroid) to evaluate the relationship between TSH and T4 levels. Hypothyroid patients had significantly higher TSH (12.6 vs. 0.1 mIU/L) and lower T4 (3.8 vs. 18.5 µg/dL) than hyperthyroid patients ($p<0.001$). No significant age/gender differences existed between groups ($p>0.05$). Key findings are summarized below (see Table No 1).

Table 1: Demographic and Clinical Characteristics

Variable	Hypothyroidism (n=55)	Hyperthyroidism (n=55)	p-value
Age (years)	45.2 ± 12.8	42.7 ± 14.3	0.28
Gender (Female:Male)	40:15	38:17	0.72
TSH (mIU/L)	12.6 ± 5.4	0.1 ± 0.05	<0.001
T4 (µg/dL)	3.8 ± 1.2	18.5 ± 4.6	<0.001
Complications (%)	32 (58.2%)	29 (52.7%)	0.56

Values expressed as mean ± SD.

Complications included goiter (hypothyroid) and thyrotoxicosis (hyperthyroid).

Correlation between T4 and TSH

A strong inverse correlation ($r = -0.8$) was observed in both hypothyroid and hyperthyroid patients ($p<0.001$), consistent with the log-linear feedback mechanism of the HPT axis.

Table 2: Correlation Between TSH and T4 Levels

Group	Pearson's r	95% Confidence Interval	p-value
Hypothyroidism	-0.82	-0.89 to -0.71	<0.001
Hyperthyroidism	-0.78	-0.86 to -0.67	<0.001

Strong inverse correlation observed in both groups.

Complications wise distribution

Hypothyroid patients had higher rates of goiter (56.3% vs. 17.2%), while hyperthyroid patients more frequently developed thyrotoxicosis (75.9%) and atrial fibrillation (34.5%). These results confirm the diagnostic utility of TSH-T4 dynamics in differentiating thyroid disorders and highlight distinct complication profiles.

Table 3: Prevalence of Complications

Complication	Hypothyroidism (n=32)	Hyperthyroidism (n=29)
Goiter	18 (56.3%)	5 (17.2%)
Cardiovascular Risks	9 (28.1%)	12 (41.4%)
Thyrotoxicosis	—	22 (75.9%)
Atrial Fibrillation	2 (6.3%)	10 (34.5%)

Significant differences ($p<0.05$) in complication profiles between groups.

DISCUSSION

This paper focused on the analysis between TSH and T4 levels among patients with hypothyroidism and hyperthyroidism to show that there is a positive inverse correlation of these two hormones in both disorders. These findings validate the physiological tenet of feedback mechanism of the hypothalamic-pituitary-thyroid axis, one where in the presence of high levels of thyroid hormones, the secretion of TSH is inhibited and vice versa. A strong negative correlation of ($r = -0.8$) found in our study population was consistent with other studies by (4, 6) and this supports a universal interaction of endocrines which is used as the basis of thyroid function testing.

The demographic and biochemical profile of the groups of patients that we had demonstrated anticipated trends whereby hypothyroid patients had much higher amount of TSH and lower amount of T4 than hyperthyroid patients. Such results are in line with many studies that report the average hormonal patterns of these diseases (8, 10). Nevertheless, we have more clinically related findings in our study, as we investigate these hormonal relationships and complication profiles in a well characterized population of patients at a single institution, and expose patients to real-world clinical manifestations.

Where comparing our results with similar ones, we find some consistencies and some differences that one should discuss. In our study, the correlation between TSH and T4 was significantly stronger than in the study by (18), which may be attributed to differences in populations of the study and methods of investigation. The quality control that we employed in modern electro-chemiluminescence immunoassay technology could have added to the accuracy of our measurement and the resultant intensity of the correlations that we observed. Such methodological rigor enhances validity in our results and assists in the reliability of existing patterns of thyroid-testing protocols.

The patterns of complications that were noted in the studied groups showed significant clinical pictures. The incidence of goiter was found to be higher in hypothyroid patients whereas, thyrotoxicosis and atrial fibrillation were highly experienced by hyperthyroid patients. These data mostly confirm the published clinical manifestations of thyroid dysfunction and the particular frequencies we observed were slightly different than other published series (17, 21). As an example, we have a higher incidence of atrial fibrillation in

34.5% of patients with hyperthyroid compared to certain reports in the past which may be due to differences in patient population or different evaluation criteria.

A few elements of our study design probably affect the findings and their discussion. The design of the study as a retrospective one, despite achieving access to a very large population of patients, made the data more or less complete because it generated limitations. The absence of patients with recent changes in medications and secondary thyroid disorders assisted in the achievement of a more homogeneous study population but can restrict the translation of the finding to all patients having thyroid dysfunction. We also concentrate on overt thyroid disease and not subclinical thyroid disease and this gives us definite information involving known disease entities rather than less evident potential hormonal interactions present in situations wherein thyroid dysfunction is less vehemently apparent.

Our results have high clinical implications, the close relationship between TSH and T4, which is considered very weak yet significantly negative, confirms existing practices that prefer TSH as a main screening test of thyroid disorders (22). Nevertheless, our data also support the significance of both T4 measurements in patients with abnormal TSH-values in order to be able to characterize the extent of thyroid dysfunction. A key characteristic of the complication patterns we identified is that the monitoring of the individual patients should be condition specific and, among others, should focus on the cardiovascular complications to occur in cases of hyperthyroidism and structural alterations to the thyroid in cases of hypothyroidism.

Our research supports the current debate regarding the best test methods to be used on the thyroid. Although some authors have cast doubt on the need to measure T4 as part of routine practice because it only provides information not necessarily considered relevant (7), our results favor the importance of testing both TSH and T4 when there is established thyroid disease. Sophisticated immunoassay technologies satisfying the accuracy of our hormonal measurements also gives the modern day data in favor of the reliability of the methodologies of the contemporary measurements.

CONCLUSION

This study provides well-researched piece and reveals the validity of the inverse relationship existing between TSH and T4 in the case of thyroid dysfunction despite crucial clinical disparities in the pattern of complications between hypothyroid and hyperthyroid patients. These findings support the present guidelines of diagnosis and offer possible improvement points in clinical monitoring of patients. The research contributes to the increasing literature concerning the optimization of the diagnosis and treatment of thyroid disorders and eventually leads to better patient outcomes.

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