

Review Article

Role of TSH in Predicting Malignant Thyroid Tumours

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Abstract

Background: Thyroid cancer, the most prevalent endocrine cancer is rising in number. Thyroid cancer can manifest mainly as dominant nodule or as a solitary nodule in a MNG. Researchers have observed thyroid nodules in 4-7% of the general population. It's very difficult to differentiate between benign and malignant thyroid swellings. There are several reliable indicators to identify thyroid nodules which are malignant. Recently, some studies have proposed a link between elevated Thyroid stimulating hormone levels, even within the normal range and the later identification of malignancy.

Aims and objective: to determine the predictive role of serum TSH in thyroid malignancies and to examine the association between serum TSH concentration and thyroid cancer.

Material and Methods: We included a total of 30 thyroid cancer cases in a retrospective investigation. We assessed serum TSH levels, pathology, age and sex. We analyzed the association between malignant thyroid tumours and serum TSH levels.

Result: The majority of thyroid malignancy patients in our study (16 out of 30) had serum TSH values which fall within the normal range but on the higher side.

Conclusion: Patients with higher serum TSH concentrations have an increased incidence of thyroid cancer which is attributed to the tropic impact of TSH on thyroid tissue, which promotes neoplasia and carcinogenesis. For patients with thyroid malignancies, the baseline blood TSH level can serve as a biochemical predictor of thyroid cancer. Upon diagnosis of thyroid cancer, a high serum TSH level could suggest a more aggressive and advanced stage of the disease. The terms thyroid gland, Thyroid-Stimulating Hormone (TSH) and cancer are pointing to a same direction.

Keywords: Carcinoma Thyroid; TSH; Serum Concentration

Introduction

The most prevalent endocrine tumours in the body are thyroid tumours. Both benign and malignant lesions originating from the thyroid gland are known as thyroid neoplasms. In India, the yearly incidence is 3.7 per 1 lakh people. Thyroid cancer accounts for fewer than one percent of all cancer cases. Women account for more than 75% of instances. Men make up less than 25% of cases, yet they are responsible for 45% of thyroid cancer deaths. A class of cancers known as thyroid malignancies has varying growth rates, therapeutic responses and histological responses. The majority of benign tumors, known as adenomas, originate from the glandular epithelium. They typically appear in middle age and are actual neoplasms. Women account for 80 percent of benign lesions [1,2]. Approximately 15 to 30 percent of surgically removed nodules have cancer in various stages. Malignancy is uncommon in children and is known to rise in frequency with age. Thyroid cancers originate from the epithelium, are well-differentiated and have a positive prognosis of 90 to 95 percent [3]. These cancers are often asymptomatic in their early stages, which can lead to delayed diagnosis. Regular screenings and awareness of risk factors are essential for early detection and improved outcomes in affected individuals.

TSH is secreted from the anterior pituitary; its secretion is inversely proportional to circulating thyroid hormones. Several studies have found that baseline serum TSH concentration can predict the malignancy of thyroid gland. K. Boelaert's in a study examined 1500 euthyroid participants undergoing fine-needle aspiration biopsy and presenting with thyroid enlargement. The results showed that the risk of getting thyroid malignancy as diagnosis was rising in proportion with rising value of serum TSH [4]. For the first time, Boelaert k, et al., found out that the blood TSH concentration, along with the patient's age, gender and the type of enlargement visible on clinical examination is an independent predictor of thyroid cancer. Patients with subclinical hyperthyroidism (TSH < 0.4 mIU/l) had the lower chance of malignancy, while those with subclinical hypothyroidism (TSH > 5.5 mIU/L) had the highest prevalence of thyroid cancer. Even for TSH levels within the normal range, further analysis revealed a markedly elevated chance for the existence of malignancy [5]. Many other studies have also confirmed these findings.

Haymart, et al., measured the preoperative serum TSH levels in 843 surgical patients. Those with a TSH of 5.0 mIU/l or more had around 55% chance of developing malignancy, around 16% chance when TSH was >0.06 mIU/l, a 25% chance when TSH was between 0.40 and 1.39 mIU/l and a 32% chance when TSH was between 1.40 and 4.99 mIU/l [6-21]. In a follow-up trial, Polyzos, et al., found that candidates with TSH 1.5-4.0 mIU/l had significantly higher adjusted odds ratios for the diagnosis of malignancy than those with lower serum TSH concentrations at presentation [20]. Last but not least, a study of 50 patients with normal thyroid hormone values having thyroidectomy for various etiologies revealed that subjects with serum TSH concentrations in the upper third of TSH values had a higher chance of having a cancer diagnosis than those whose serum TSH level was in the lower third. And also, those who later received a thyroid cancer diagnosis had lower blood levels of total T3. These combined results pointed towards the potential use of serum TSH levels as a diagnostic tool to classify the patient into high-risk categories. Haymart, et al., also suggested that the higher preoperative blood TSH concentrations is associated with both a higher incidence of differentiated thyroid carcinoma and a more advanced stage of the disease at diagnosis [21]. Compared to individuals with more localized disease (stage I and II), those with stage III and IV disease had significantly higher mean serum TSH levels. TNM classification and staging guided the staging process.

Additionally, Fiore, et al., support the observation that individuals with tumor stages T3-T4 have greater serum TSH levels than patients with tumor stages T1-T2 [22]. Also, considerably higher median serum TSH values are seen in those with positive lymph node metastasis than those without lymph node metastasis. Further evidence that TSH has a role in the etiology or development of thyroid cancer comes from this increasing likelihood of advanced disease. Age is one of the primary prognostic markers in most staging systems for well-differentiated thyroid tumors, which is unique among all malignancies. As people age, their serum TSH levels rise in iodine-repleted healthy adult populations, as evidenced by a cohort study [10]. Independent of age, additional analysis of this group demonstrated a correlation between greater blood TSH values and advanced-stage disease. A significant correlation was made between higher TSH levels and extrathyroidal extension, but not with other factors associated with a poor prognosis, like age (45 years), tumor size (4 cm) or the presence of distant metastases. These findings raise the intriguing topic of whether elevated blood TSH levels promote thyroid cancer invasion and thus support extrathyroidal disease spread [11].

Material and Methods

We conducted this retrospective study on participants who met the inclusion and exclusion criteria in the Kanyakumari Government Medical College Operation Theater registry from May 2023 to November 2024. Included were 30 thyroid cancer-operated patients who did not exhibit obvious thyroid dysfunction. We noted the demographics of these patients, the pathological information (preoperative FNAC) and the serum TSH concentration levels. We classified the cytological results as malignant, indeterminate, follicular, healthy cell and suggestive of papillary carcinoma. We advised thyroidectomies for patients with malignancy, indeterminate cytology and rapidly growing nodules. The final surgical pathology served as the basis for additional management.

We gathered demographic information such as age, sex, thyroid profile, FNAC results, stage and final surgical pathology report. The study excluded patients whose TSH levels were abnormal and those who were taking thyroxine supplements.

The study included all thyroid cancer cases that did not have obvious thyroid dysfunction. The study excluded patients with Graves disease, thyroid lymphomas, thyroiditis and secondary thyroid cancers.

Results

A maximum of 16 patients (53.33%) were in the >60 age group, while 12 patients (40%) were in the 31-60 age group. 17 patients (56.66%) with thyroid cancer were female. Table 1 shows that out of 30 thyroid malignancies, 7 (23.33%) had follicular carcinoma, 18 (60%) had papillary carcinoma, 4 (1.33%) had hurthle carcinoma and 1 (3.33%) had anaplastic carcinoma. Table 2 shows 16 patients with thyroid malignancy were having TSH in the upper range of normal level. The mean serum TSH concentrations for thyroid tumours in stages 1 and 2 were 2.71 mIU/L, whereas those in stages 3 and 4 were 3.56 mIU/L.

Carcinomas	Frequency	Percentage %
Follicular carcinoma	7	23.3
Papillary carcinoma	18	60
Hurthle cell carcinoma	4	13.3
Anaplastic carcinoma	1	3.3
Total	30	100

Table 1: Incidence of various types of carcinomas.

Serum TSH	Frequency	Percentage %
0.5-2	6	20
2-3.5	8	26.6
3-5.5	16	53.3

Table 2: Serum TSH concentrations.

Serum TSH	Papillary(n=18)	follicular(n=7)	Hurthle cell(n=4)	Anaplastic(n=1)
0.5-2	0	2	4	0
2-3.5	7	0	0	0
3-5.5	11	5	0	1

Table 3: Serum TSH in various types of thyroid carcinomas.

Stage	Mean serum TSH
Stage 1 and 2	2.71
Stage 3 and 4	3.56

Table 4: Serum TSH with stage of carcinoma.

Discussion

Several studies have linked elevated TSH levels, even within the normal range, to a later diagnosis of thyroid cancer in patients who arrive with thyroid nodules [14]. Furthermore, studies have linked elevated serum TSH levels to advanced stages of thyroid cancer. TSH, a known growth factor for thyroid nodules, can inhibit both the growth of existing nodules and the formation of new ones if exogenous thyroid hormone administration suppresses serum TSH levels. Studies that look back have also shown that TSH suppression is a useful way to tell if differentiated thyroid cancer will come back. It has also been known for a long time that treatment with suppressive dose of thyroxine can improve outcomes in this type of thyroid cancer. Prospective studies have linked strong TSH suppression, particularly in high-risk individuals, to a decrease in thyroid carcinoma-related death and relapse. Based on these results, it seems that TSH has a tropic effect on thyroid tissue, which encourages neoplasia and carcinogenesis [15]. This could potentially explain the association between higher serum TSH levels and an increased risk of cancer. These results imply that TSH might be crucial to the initiation and/or spread of thyroid cancers. It appears likely that TSH can function as a cancer stimulant, even though oncogenes and other growth factors have a role in the development and growth of thyroid cancer. The fact that thyroid cancer patients who received suppressive doses of levothyroxine lived longer and saw tumor growth after T4 removal or the addition of recombinant TSH supports this idea [16]. Studies have shown that TSH suppression, which is a known indicator of a person's chance of surviving differentiated thyroid cancer without relapse, has a growth-promoting effect on thyroid cancer, most likely through TSH receptors on tumor cells [17]. Researchers say that this trophic effect of TSH may help explain why the risk of getting a certain disease goes up when a person's serum TSH level is

in the upper half of the normal range or even higher than normal. Another hypothesis suggests that patients with lower TSH levels are becoming more autonomous, a phenomenon associated with a decreased incidence of cancer [18]. Studies have shown that the probability of diagnosing thyroid cancer rises from less than 10% for serum TSH concentrations at the lower end of the normal range to 25% if the same patient has a TSH concentration at the upper end of the normal range, assuming that serum TSH concentration is an independent predictor of thyroid cancer [19]. We examined the relationship between serum TSH concentration and thyroid cancer with the underlying idea that TSH, a known thyroid growth factor, may play a key role in the genesis and progression of thyroid cancer [7].

According to Judy Jin, et al., study, the age group under 30 has the highest incidence (32%). In our study, the age group over 60 years old exhibited a high frequency of 45.55% [12]. The age incidence in our study does not align with the findings of the previous study. According to the study by K. Boelaert, et al., patients who arrived with a single thyroid nodule had the highest incidence of thyroid cancer (n = 861, 10.8%), as opposed to those who presented with a diffuse or nodular goiter (n = 639, 4.2%) [13]. Another study by Polyzos, et al., found that patients with serum TSH concentrations in the upper tertile of the normal range had higher rates of malignancy [20]. Using binary logistic regression analysis, it was found that patients with serum TSH 1.5-4.0 mIU/L had a much higher chance of being diagnosed with cancer than those with either TSH 0.4-0.8 mIU/L or TSH 0.9-1.4 mIU/L. People whose blood TSH levels were between 3.5 and 5 mIU/l had the highest rate of malignant thyroid carcinoma in our study. That is, 16 out of 30 patients (53.33%) had a higher rate of cancer that is in people whose TSH levels were in the upper third of the normal range. The incidence of both papillary and follicular carcinomas was higher in individuals with blood TSH levels between 3.5 and 5 mIU/l or between 11 (61.11%) of 18 papillary carcinomas and 5 (71.42%) of 7 follicular carcinomas. In the study by M.R. Haymart, et al., 35 of 239 patients had stage 3 and 4 thyroid cancer with mean blood TSH levels of 4.9 mIU/l, while 204 of 239 patients had stage 1 and stage 2 thyroid cancer with mean serum TSH concentrations of 3.1 [21]. Of the 30 patients in our study, 17 had stage 1 and stage 2 with mean serum TSH concentrations of 2.71 mIU/l and 13 had stage 3 and stage 4 with mean serum TSH concentrations of 3.56 mIU/l. We compare our investigation's findings with those of the M.R. Haymart, et al., study [21].

In their study on the TSH level in metabolic syndrome, Jayalal JA, et al., recommended a mandatory thyroid function estimate for individuals with metabolic syndrome. In their research publication, Jayalal, et al., conducted a meta-analysis to predict malignancy in STN vs. MNG. According to it, the estimated risk of malignancy in thyroid nodules ranges from 7 to 15%, with a significant influence on the level of TSH [7,8].

Conclusion

The clinical presentation of thyroid cancers varies among many symptoms. The most typical appearance is that of a single thyroid nodule. None of the numerous predictors of thyroid cancer can definitively predict the nature of a thyroid nodule. In our study, which looked at how useful preoperative serum TSH levels are as a sign of cancer, we found a statistically significant link ($P < 0.01$) between higher TSH levels and malignant nodules. Those who presented with only cervical lymph node metastases and no initial thyroid enlargement, however, did not exhibit this association with elevated TSH levels. However, as all patients with a thyroid enlargement undergo a thyroid function test, it is crucial to pay careful attention to the TSH results. TSH levels can serve as a predictor when combined with a benign FNAC report and clinically suspected malignant thyroid enlargement. The FNAC can be re-examined to confirm the diagnosis in situations where the TSH value is elevated.

Conflict of Interest

The authors declare that there is no conflict of interest.

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