



## EVALUATION OF CLINICAL UTILITY OF TSH AS A BIOMARKER IN THE SUSPECTED CASES OF THYROID MALIGNANCY

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### ABSTRACT

**Introduction:** Thyroid malignancies account for 90% of endocrinal malignancies. The incidence of thyroid malignancies has increased three-fold over the past 3 decades. Many patients present to the surgical outpatient department with a thyroid nodule. A clinical examination is always the first step to assess a nodule. A thyroid profile is also essential. Recent studies have found levels of serum TSH to be an independent predictor of malignancy in thyroid nodules. This biomarker could be used as a screening test for malignancy.

**Objectives of the study:** To evaluate the utility of serum TSH estimation as a biochemical predictor of malignancy in suspicious thyroid nodules.

**Materials and Methods:** All patients were admitted and a detailed history and clinical examination was done and investigated as per the written proforma. Informed consent was taken and thyroid profile and a FNAC was done in all cases.

**Results:** A total of 44 subjects with the inclusion criteria and exclusion criteria protocol were enrolled in the study. Out of the 40 subjects, 6 were males, 38 were females. Most of the subjects belong to the age group of 41-50 years. We found elevated TSH (>5 mIU/L) in 5 subjects, 26 subjects had TSH levels between 1.60-4.99 and 13 subjects had TSH values between 0.34-1.59. Incidence of malignancy among the subjects with TSH levels >5mIU/L were 4.

**Conclusion:** TSH levels could be used as predictor in clinically suspect malignant thyroid swelling with a benign FNAC report. In such cases where TSH value is high, the FNAC can be relooked to confirm the diagnosis.

**KEYWORDS :** Thyroid stimulating hormone (TSH), fine needle aspiration cytology (FNAC), thyroid nodules and thyroid malignancy

### INTRODUCTION:

Thyroid disorders are most common endocrine disorders affecting Indian population, with the incidence of 42 million. The thyroid gland produces two related hormones, Thyroxin (T<sub>4</sub>) and triiodothyronine (T<sub>3</sub>), and these hormones play a critical role in cell differentiation during development and helps to maintain thermogenic and metabolic homeostasis (Fauci AS et al, 2008).<sup>1-4</sup> Thyroid malignancies account for 90% of endocrinal malignancies. The incidence of thyroid malignancies has increased three fold over the past 3 decades. Many patients present to the surgical outpatient department with a thyroid nodule. However not all these patients require surgery as only 5-6% of these are malignant. A clinical examination is always the first step to assess a nodule. A thyroid profile is also essential. This is accompanied by certain tests which increase the rate of detection. Fine needle aspiration cytology (FNAC) is the present gold standard and primary tool for assessing risk of malignancy. Other tests include ultrasonography, thyroid scintigraphy, CT scan and MRI. Recent studies have found levels of serum TSH to be an independent predictor of malignancy in thyroid nodules. This biomarker could be used as a screening test for malignancy.<sup>5-9</sup>

High TSH levels have been associated with PTC pathogenesis in a mouse model.<sup>10</sup> Suppression of TSH is currently recommended to manage differentiated thyroid cancer (DTC) patients, which has shown benefits to patient survival.<sup>11</sup> Thyroid hormones have also been suggested to have a tumor promoting effect on several cancers, including pancreatic, breast, ovarian, and prostate cancer.<sup>12</sup> However, findings of epidemiological studies linking TSH and thyroid hormones to the risk of thyroid cancer have been inconsistent.<sup>13</sup> Most of the early studies reported an increased risk of thyroid cancer associated with elevated TSH levels<sup>13</sup>, several studies found no significant association<sup>14</sup>, and one reported a reduced risk.<sup>15</sup> All studies that reported a positive association between TSH and thyroid cancer were cross-sectional or case-control studies.<sup>16</sup> Hence we have taken up this study utility of TSH as a biomarker in predicting malignancy and the common clinical presentation of thyroid malignancies.

**Objectives Of The Study:** The objectives of our study include,

- 1) To evaluate the utility of serum TSH estimation as a biochemical predictor of malignancy in suspicious thyroid nodules.

### MATERIALS AND METHODS:

**Source of data and Study design:** A prospective study was conducted at Dept. of Surgery, World College of Medical Sciences and Research,

from July 2019 to November 2019 with 6 months follow-up, Jhajjar, Haryana.

**Inclusion Criteria:** 1) Cases presenting with thyroid swellings clinically suspicious of malignancy including those with metastasis 2) At least one FNAC done at the time of initial presentation 3) Thyroid profile especially TSH levels measured before any medical intervention 4) All cases must be clinically and biochemically euthyroid.

**Exclusion Criteria:** Subjects with euthyroid state were excluded from the study.

**Sample collection and analysis:** Informed consent was taken and thyroid profile and a FNAC was done in all cases. All cases that gave consent for surgery were explained about risk and complications of surgery and anesthesia. Preoperatively investigations were sent according to protocol. A preoperative indirect laryngoscopy was done in all cases to check for the status of vocal cords. The type of surgery depended on the clinical diagnosis and FNAC report. Patients were followed up regularly over a minimum period of 6 months. Follow up was done at regular interval by clinical examination, serum thyroglobulin estimation, serum TSH levels and thyroid scan.

**Statistical Analysis:** Results on continuous measurements are presented on Mean ± SD and results on categorical measurements are presented in Number. Student t test has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters.

### RESULTS:

A total of 44 subjects with the inclusion criteria and exclusion criteria protocol were enrolled in the study. Out of the 40 subjects, 6 were males, 38 were females. Most of the subjects belong to the age group of 41-50 years. The mean age and SD in these subjects was 40.4212.07 years and in cases 36.3511.09 years (table 1 and table 2). Subjects were further divided as per the duration of the disease. Majority of the subjects had duration of the disease as 1-5 years (table 3). Majority of the Subjects presented with the swelling followed by pain (table 4). 24 subjects presented with single nodular goitre and 20 had presented with multi nodular goitre (table 5). FNAC results in these subjects revealed colloid goitre in 30, papillary carcinoma in 12 and follicular carcinoma in 2 subjects (table 6). Post-operative specimen was subjected for histopathological examination which revealed colloid

goitre in 29, papillary carcinoma in 13 and follicular carcinoma in 1 patient (table 6). TSH levels were evaluated in all the study subjects, we found elevated TSH (>5 mIU/L) in 5 subjects, 26 subjects had TSH levels between 1.60-4.99 and 13 subjects had TSH values between 0.34-1.59 (table 8). Incidence of malignancy among the subjects with TSH levels >5mIU/L were 4 (table 9).

**Table 1: Shows Gender wise distribution of the study subjects**

Gender	Number of Subjects	Percentage
Males	6	13.6%
Females	38	86.3%
Total	44	100%

**Table 2: Shows Age wise distribution of the study subjects**

Age group in years	Number of Subjects	Percentage
1-20 years	2	4.5%
21-30 years	11	25%
31-40 years	11	25%
41-50 years	14	31.8%
>50 years	6	13.6%

**Table 3: Distribution of the subjects depending on the duration of the disease**

Duration in years	Number of Subjects	Percentage
<1 year	4	9.09%
1-5 years	24	54.5%
>5 years	16	36.5%

**Table 4: Distribution of the subjects depending on the clinical presentation**

Duration in years	Number of Subjects
Swelling	44
Pain	8
Dysphagia	2
Dysphonia	2
Dyspnoea	2

**Table 5: Shows distribution of subjects depending on swelling presentation as Solitary/Multi Nodular Goitre**

Type of nodule	Number of Subjects	Percentage
Solitary Nodule Goitre	24	54.5%
Multi Nodular Goitre	20	45.4%

**Table 6: Shows distribution of subjects depending FNAC and Histopathology Reports**

	FNAC (no of subjects)	Histopathology (no of subjects)
Colloidal Goitre	30	29
Papillary Carcinoma	12	13
Follicular Carcinoma	2	1
Total	44	44

**Table 7: Shows study of TSH levels in the study subjects**

TSH levels in mIU/L	No of subjects	Percentage
0.3-1.59 mIU/L	13	29.5%
1.6-4.99 mIU/L	26	59.09%
>5 mIU/L	5	11.36%
Total	44	100%

**Table 8: Shows the Incidence of malignancy according to TSH levels in the study subjects**

TSH levels in mIU/L	No of subjects	No of patients with malignancy	Percentage
0.3-1.59 mIU/L	13	0	0%
1.6-4.99 mIU/L	26	10	38.4%
>5 mIU/L	5	4	80%

## DISCUSSION:

In our study, we found that Most of the subjects belong to the age group of 41-50 years. Females were affected more than males. FNAC results in these subjects revealed the common presentation of thyroid malignancy was papillary carcinoma of thyroid also with histopathology results postoperatively. Incidence of the malignancy was high with the increased TSH levels. TSH is a known thyroid growth factor. Well-differentiated thyroid cancers express TSH receptors. Although oncogenes and other growth factors are involved in thyroid cancer growth and development, it seems probable that TSH

can act as a cancer stimulus. This hypothesis is supported by improved survival in thyroid cancer patients treated with suppressive doses of levothyroxine and by cases of tumor growth post-T4 withdrawal or recombinant TSH.

Some studies have showed higher serum TSH levels associated with advanced stages of thyroid cancer. These findings suggest that TSH may play a central role in the development and /or progression of thyroid carcinomas. Supportive of the TSH receptor's role in cancer are the data on auto immune thyroid disease and thyroid cancer. An increased incidence of thyroid cancer is seen in patients with antibody evidence of Hashimoto's thyroiditis.<sup>17-21</sup> Our study findings were similar to the studies conducted in the past by Boelaert et al. (2006) Which concluded that, Serum TSH is independent predictor of malignancy in thyroid nodules. Risk of malignancy rises in parallel with serum TSH within normal range. Haymart et al. in their study also concluded that the Likelihood of thyroid cancer increases with higher TSH concentration. Higher serum TSH associated with advanced stage- differentiated thyroid cancer. Jonklaas et al. in their study also concluded that higher TSH concentrations are associated with diagnosis of thyroid cancer. Patients with thyroid cancer have lower serum total T3 concentrations.<sup>6,7,11</sup>

## CONCLUSION:

Our study strongly recommends that all the subjects with a thyroid swelling should undergo a thyroid function test. It is very important to pay special attention to the TSH values. TSH levels could be used as predictor in clinically suspect malignant thyroid swelling with a benign FNAC report. In such cases where TSH value is high, the FNAC can be re looked to confirm the diagnosis.

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