



THYROID STIMULATING HORMONE LEVELS IN SUSPECTED CASES OF THYROID MALIGNANCY

Biochemistry

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ABSTRACT

Introduction: Several studies have found elevated levels of thyroid stimulating hormone levels in subjects with suspected thyroid malignancy and measurement of serum TSH levels to be an independent predictor of malignancy in thyroid nodules. **Objectives of the study:** To measure the levels of TSH in suspected cases of thyroid malignancy. **Materials And Methods:** Detailed history and clinical examination was done in all the patients with suspected thyroid malignancies admitted to our hospital and were investigated as per the written proforma. After Informed consent thyroid profile and a FNAC was done in all cases. **Results:** A total of 58 subjects with the inclusion criteria and exclusion criteria protocol were enrolled in the study. Out of the 58 subjects, 16 were males, 42 were females in the age group of 38-50 years. We found elevated TSH (>5 mIU/L) in 14 subjects, 28 subjects had TSH levels between 1.60-4.99 and 16 subjects had TSH values between 0.34-1.59. 14 patients with TSH levels >5 mIU/L had malignancy. **Conclusion:** Our study concludes that the TSH levels can be used as independent 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:

The incidence of thyroid malignancies has increased three-fold over the past 3 decades and they account for 90% of endocrinal malignancies. 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.^{1,4} However not all these patients require surgery as only 5-6% of these are malignant. 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.⁵⁻⁹

High TSH levels have been associated with PTC pathogenesis in a mouse model.¹⁰ Suppression of TSH is currently recommended to manage differentiated thyroid cancer (DTC) patients, which has shown benefits to patient survival.¹¹ Thyroid hormones have also been suggested to have a tumor promoting effect on several cancers, including pancreatic, breast, ovarian, and prostate cancer.¹² However, findings of epidemiological studies linking TSH and thyroid hormones to the risk of thyroid cancer have been inconsistent.¹³ Most of the early studies reported an increased risk of thyroid cancer associated with elevated TSH levels¹³, several studies found no significant association¹⁴, and one reported a reduced risk.¹⁵ 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 objective of our study is to determine the levels of TSH in subjects with suspected cases of thyroid malignancies.

MATERIALS AND METHODS:

Source of data and Study design: A prospective study was conducted at Dept. of Biochemistry in collaboration with dept. of surgery, CCM Medical College and Hospital, Kachandur, Durg February 2018 to July 2019.

Inclusion Criteria:

- 1) Cases presenting with thyroid swellings clinically suspicious of malignancy including those with metastasis
- 2) Thyroid profile especially TSH levels measured before any medical intervention,
- 3) At least one FNAC done at the time of initial presentation
- 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 58 subjects with the inclusion criteria and exclusion criteria protocol were enrolled in the study. Out of the 58 subjects, 16 were males, 42 were females in the age group of 38-50 years. The mean age and SD in these subjects was 43.4211.07 years and 38.3512.09 years in males and females respectively (table 1). Subjects were further divide as per the duration of the disease. Majority of the subjects had duration of the disease as 1-5 years (table 2). Majority of the Subjects presented with the swelling followed by pain (table 3). 34 subjects presented with single nodular goitre and 20 had presented with multi nodular goitre (table 4). FNAC results in these subjects revealed colloidal goitre in 44, papillary carcinoma in 12 and follicular carcinoma in 2 subject. Post-operative specimen was subjected for histopathological examination which revealed colloidal goitre in 43, papillary carcinoma in 14 and follicular carcinoma in 1 patient. We found elevated TSH (>5 mIU/L) in 14 subjects, 28 subjects had TSH levels between 1.60-4.99 and 16 subjects had TSH values between 0.34-1.59. 14 patients with TSH levels >5 mIU/L had malignancy.

Table 1: Shows Gender wise distribution of the study subjects

Gender	Number of Subjects	Percentage
Males	16	27.58%
Females	42	72.41%
Total	58	100%

Table 2: Distribution of the subjects depending on the duration of the disease

Duration in years	Number of Subjects	Percentage
<1 year	10	17.24%
1-5 years	30	51.72%
>5 years	18	31.03%

Table 3: Distribution of the subjects depending on the clinical presentation

Duration in years	Number of Subjects
Swelling	56
Pain	10
Dysphagia	7
Dysphonia	7
Dyspnoea	9

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 autoimmune thyroid disease and thyroid cancer. An increased incidence of thyroid cancer is seen in patients with antibody evidence of Hashimoto's thyroiditis.¹⁴⁻¹⁸ 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.^{6,7,11}

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 relooked to confirm the diagnosis.

REFERENCES

- Khan A H, Majumder I. Serum creatinine and uric acid levels of hypothyroid patients. Bangladesh J Med Biochem. 3(2): 61-63 (2010)
- Iglesias P, Diez J J. Thyroid dysfunction and kidney disease. Eur J Endocrinol. 160: 503-15 (2009)
- Jameson J L, Weetman A.P. Disorders of the thyroid gland. In: Fauci A S, Longo D L, Kasper D L, et al. Harrison's principles of internal medicine. 18 ed. New York: McGraw Hill; 2008. p. 291
- Wedaatalla M A, Abdella A M. Assessment of plasma uric acid level among Sudanese female with thyroid dysfunction. Sudanese Journal of Public Health. 7(3): 89-92 (2012)
- Williams NS, Bulstrode CJK, O'Connell PR. The Thyroid and Parathyroids, Bailey & Love's Short Practice of Surgery, 25th ed. New York: Arnold;
- Boelaert K, Horacek J, Holder RL, et al., Serum thyrotropin concentration as a novel predictor of malignancy in thyroid nodules investigated by fine needle aspiration, J. Clin Endocrinol Metab, 2006; 91:4295-4301
- Haymart MR, Repplinger DJ, Levenson GE, et al, Higher TSH level in thyroid nodule patients is associated with greater risks of differentiated thyroid cancer and advanced tumor stage, J Clin Endocrinol Metab, 2008;93:809-14
- Gupta M et al, Correlation of Fine Needle Aspiration Cytology with Histopathology in the diagnosis of Solitary Thyroid Nodule, Journal of Thyroid Research, Feb 2010;
- Stergios A. Polyzos, Marina Kita, Zoe Efstathiadou et al, Serum thyrotropin concentration as a biochemical predictor of thyroid malignancy in patients presenting with thyroid nodules, J Cancer Res Clin Oncol. 2008; 134:953-96.
- Franco AT, Malaguamera R, Refetoff S, et al. Thyrotrophin receptor signaling dependence of Braf-induced thyroid tumor initiation in mice. Proceedings of the National Academy of Sciences of the United States of America. 2011;108(4):1615-20.
- Jonklaas J, Sarlis NJ, Litofsky D, et al. Outcomes of patients with differentiated thyroid carcinoma following initial therapy. Thyroid: official journal of the American Thyroid Association. 2006;16(12):1229-42. doi:10.1089/thy.2006.16.1229
- Moeller LC, Fuhrer D. Thyroid hormone, thyroid hormone receptors, and cancer: a clinical perspective. Endocr-Relat Cancer. 2013;20(2):R19-R29. doi:10.1530/Erc-12-0219
- Ye ZQ, Gu DN, Hu HY, Zhou YL, Hu XQ, Zhang XH. Hashimoto's Thyroiditis, microcalcification and raised thyrotropin levels within normal range are associated with thyroid cancer. World J Surg Oncol. 2013;11.
- Shi Y, Zou M, Farid NR 1993 Expression of thyrotropin receptor gene in thyroid carcinoma is associated with good prognosis. Clin Endocrinol (Oxf) 39:269-274
- Derwahl M, Broecker M, Kraiem Z 1998 Thyrotropin may not be the dominant growth

- factor in benign and malignant thyroid tumors. J Clin Endocrinol Metab 84:829-834
- Mazzaferri EL 2000 Thyroid cancer and Graves' disease: the controversy 10years later. Endocr Pract 6:221-225
- Jonklaas J, Sarlis NJ, Litofsky D, Ain KB, Bigos ST, Brierley JD, Cooper DS, Haugen BR, Ladenson PW, Magner J, Robbins J, Ross DS, Skarulis M, Maxon HR, Sherman SI 2006 Outcomes of patients with differentiated thyroid carcinoma following initial therapy. Thyroid 16:1229-124
- Braga M, Ringel MD, Cooper DS 2001 Sudden enlargement of local recurrent thyroid tumor after recombinant TSH administration. J Clin Endocrinol Metab 86:5148-515