



ROLE OF SERUM TSH IN PREDICTING MALIGNANCY OF THYROID SWELLINGS

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ABSTRACT

There are many methods to predict and diagnose malignancy in thyroid nodules, of which serum TSH is a novel method. The objective of this study is to evaluate the usefulness of serum TSH values as a predictor of malignancy in thyroid nodules. This prospective study involved 30 patients with thyroid swellings admitted in Maharajah's institute of medical sciences, Vizianagaram. Preoperative serum TSH values were correlated with final histopathology report.

Results: Mean preoperative TSH value in malignancy was higher compared to those with benign diseases. Incidence of malignancy increased with higher TSH values.

Conclusion: There is a definite relationship between higher TSH levels and malignancy. TSH levels could be used as predictor in clinically suspicious 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 swelling, Malignancy

INTRODUCTION

Thyroid malignancies account for 90% of endocrinal malignancies. The incidence of thyroid malignancies has increased three fold over the past 3 decades. The management of thyroid diseases has undergone a tremendous change over the ages, from the surgeries of the ancient times to the multidisciplinary approach of the modern era. A clinical examination is always the first step to assess a nodule. Fine needle aspiration cytology (FNAC) is the present gold standard and primary tool for assessing risk of malignancy [1]. 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 [2,3,4]. Although nodules are common, clinically detectable thyroid cancer is rare. Serum TSH is a well-established growth factor for thyroid nodules and suppression of TSH concentrations by administering exogenous thyroxine may interfere with growth of established nodules as well as formation of new nodules [5,6]. In the last few years, it has been reported that in patients with nodular thyroid diseases, the risk of thyroid malignancy increases with increasing concentrations of serum TSH, and even within normal ranges, higher TSH values are associated with a higher frequency and more advanced stage of thyroid cancer [7,8,9].

AIMS AND OBJECTIVES

The main objective of this study is to evaluate the utility of serum TSH estimation as a biochemical predictor of malignancy in suspicious thyroid nodules.

MATERIALS AND METHODS

This prospective study included 30 patients presenting with thyroid swellings at the department of general surgery, Maharaja's institute of medical sciences, Vizianagaram.

Inclusion Criteria

1. Patients whose thyroid profile especially TSH levels measured before any medical intervention.
2. Patients who underwent at least one FNAC done at the time of initial presentation.
3. Patients must be clinically and biochemically euthyroid.

Exclusion Criteria

1. Patients not in euthyroid state.
2. Patients who didn't undergo FNAC.

OBSERVATION AND RESULTS

30 cases were selected in the study, of which 6 were confirmed malignant by histopathology. Male to female ratio in our study is 1: 5, in malignant group the ratio was 1: 2. Out of 30 cases 18 presented as solitary nodule (STN) and 12 presented as Multi-Nodular Goiter (MNG).

The preoperative TSH levels were analyzed to check for any relationship between TSH levels and the likelihood of a thyroid nodule being malignant. At the same time a clinical study of those patients with confirmed thyroid malignancy was done. The observed results were subjected to statistical analysis.

Among the 18 patients with STN, 4 were proved to be malignant. Incidence of malignancy in STN is 22%. Among the 12 patients with MNG, 2 were proved to be malignant. Incidence of malignancy in MNG is 16.6%

Table 1: FNAC of the thyroid swellings

FNAC	No. of patients (n=30)	%
Colloid goiter	20	67
Papillary carcinoma	7	23
Benign cyst	2	7
Follicular neoplasm	1	3
Total	30	100

Table 2: Histopathological reports of the thyroid swellings

Histopathology	No. of patients (n=30)	%
Colloid goiter	24	80
Papillary carcinoma	5	17
Follicular carcinoma	1	3
Total	30	100

Table 3: Preoperative TSH values of thyroid swellings

TSH level (mU/L)	No. of patients (n=30)	%
0.40-1.39	10	33
1.40-4.99	18	60
>5	2	7
Total	30	100

Mean TSH value is 2.39 with standard deviation of 1.42

In HPE confirmed benign thyroid swellings the range was 0.43 - 4.42 and the mean was 1.80 with a SD of 1.03, 95% CI is 1.36 - 2.24.

In HPE confirmed malignant thyroid swellings the range was 1.72 - 5.28 and the mean was 3.71 with a SD of 1.22, 95% CI is 3.00 - 4.42.

In both the groups the p value was < 0.001 and statistically proved significant.

In 10 patients with serum TSH value 0.40 - 1.39 none had HPE proved malignancy, whereas in 18 patients with a value of serum TSH between 1.40 - 4.99 5 patients were proved malignant by HPE and in 2 patients with a value of > 5 1 patient was proved malignant by HPE. This indicates that higher the serum TSH value more is the chances of malignancy.

DISCUSSION

There are many predictors of malignancy in a thyroid nodule. A history of prior radiation exposure especially during childhood is known to be found in many cases of papillary carcinoma. Similarly, exposure to certain environmental risk factors such as excess dietary intake of iodine, retinol and vitamin E has shown to have an increased chance of malignancy.

In the presence of certain clinical signs and symptoms i.e. hard and fixed nodules, large nodules (>4cm) with presence of neck lymph nodes, rapid increase in size of thyroid nodules, associated hoarseness of voice, dysphagia, dyspnea and Horner's syndrome malignancy should always be suspected.

Serum TSH levels – a novel method in predicting malignancy. Many studies have shown a definite relation between preoperative serum TSH levels and thyroid malignancy. Furthermore, preoperative serum TSH concentrations are higher in patients with more aggressive tumors. Thus a baseline TSH would predict which nodules require a more aggressive approach and surgery.

Rationale behind choosing TSH levels as a predictor of Malignancy is that well-differentiated thyroid cancers express TSH receptors [10,11]. Although oncogenes and other growth factors are involved in thyroid cancer growth and development [12,13], 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 [14] and by cases of tumor growth post-T4 withdrawal or recombinant TSH [15]. Some studies have showed higher serum TSH levels associated with advanced stages of thyroid cancer.

The most common presenting symptom is a thyroid swelling. Majority presented with STN. Others presented as a dominant nodule of MNG. Incidence of malignancy in a solitary nodule of thyroid was higher (36%) than the incidence of malignancy in MNG (19%). In this series all were well differentiated carcinoma. Papillary carcinoma was the commonest histopathological type (93%) followed by follicular type (7%). This is consistent with literature and other studies.

In this study the mean preoperative TSH value was: $2.39 \pm 1.42 \text{ mU/L}$. All patients were euthyroid. The mean TSH value was significantly higher in malignancy than in benign disease i.e. $3.71 \pm 1.22 \text{ mU/L}$ vs. $1.80 \pm 1.03 \text{ mU/L}$. This is comparable to the results of Haymart [3] et al, Fiore et al [16] and Jonklaas et al [14].

On analysis of the preoperative TSH values it was observed that TSH level was an independent predictor of malignancy. Patients with values of $0.40\text{--}1.39 \text{ mU/L}$ had 0% chance of malignancy. Those with range of $1.40\text{--}4.99 \text{ mU/L}$ had 28% chance of malignancy whereas those with TSH levels $>5 \text{ mU/L}$ had 50% chance of malignancy.

According to Prasad C et al (2017)¹⁷ [n=240] higher TSH levels were associated with thyroid malignancy and the risk of malignancy rises in parallel with serum TSH. In the study by Zafonet al¹⁸ (2012) [n=386] TSH concentration was significantly higher in patients with differentiated thyroid cancer than in benign thyroid disease. In the study by Kim SS et al¹⁹ (2011) [n=554] preoperative TSH levels significantly higher in patients with differentiated thyroid cancer with extra thyroidal extension. In the study by Polyzos et al⁴ (2008) [n=565] frequency of thyroid malignancy increases with serum TSH. According to study by Boelaert et al² (2006) [n=1500] frequency of thyroid nodules increases with serum TSH, risk of malignancy increases with serum TSH concentrations within normal range.

CONCLUSION

Thyroid malignancies have a varied clinical presentation. Most commonly thyroid swellings presents as STN. In our study we evaluated the utility of preoperative serum TSH levels as a predictor of malignancy and it did show a statistically significant correlation ($P < 0.01$) between higher TSH levels and malignant nodules. However, as all patients with a thyroid swelling undergo a thyroid function test it is 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

- 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 EndocrinolMetab*, 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
- 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 ClinOncol*. 2008; 134:953-96
- Fiore E, Rago T, Provenzale MA, Scutari M, Ugolini C, Basolo F, et al. Lower levels of TSH are associated to a lower risk of papillary thyroid cancer in patients with thyroid nodular disease: thyroid autonomy may play a protective role. *EndocrRelat Cancer*. 2009;16(4):1251-60.
- Brewer C, Yeager N, Di Cristofano A. Thyroid-stimulating hormone initiated proliferative signals converge in vivo on the mTOR kinase without activating AKT. *Cancer Res*. 2007;67:8002-6.
- Rago T, Fiore E, Scutari M, Santini F, Di Coscio G, Romani R, Piaggi P, Ugolini C, Basolo F, Miccoli P, Pinchera A, Vitti P 2010 Male sex, single nodularity, and young age are associated with the risk of finding a papillary thyroid cancer on fine-needle aspiration cytology in a large series of patients with nodular thyroid disease. *Eur J Endocrinol* 162:763-770
- Boelaert K, Horacek J, Holder RL, Watkinson JC, Sheppard MC, Franklyn JA 2006 Serum thyrotropin concentration as a novel predictor of malignancy in thyroid nodules investigated by fine-needle aspiration. *J ClinEndocrinolMetab* 91:4295-4301
- Fiore E, Rago T, Provenzale MA, Scutari M, Ugolini C, Basolo F, Di Coscio G, Berti P, Grasso L, Elisei R, Pinchera A, Vitti P 2009 Lower levels of TSH are associated with a lower risk of papillary thyroid cancer in patients with thyroid nodular disease: thyroid autonomy may play a protective role. *EndocrRelat Cancer* 16:1251-1260.
- Stocker DJ, Burch HB 2003 Thyroid cancer yield in patients with Graves'disease. *Minerva Endocrinol* 28:205-212
- Shi Y, Zou M, Farid NR 1993 Expression of thyrotropin receptor gene in thyroid carcinoma is associated with good prognosis. *ClinEndocrinol (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 ClinEndocrinolMetab* 84:829-834
- Mazzaferri EL 2000 Thyroid cancer and Graves' disease: the controversy 10years later. *EndocrPract* 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 ClinEndocrinolMetab* 86:5148-515.
- Fiore E, Rago T, Provenzale MA, Lower levels of TSH are associated to a lower risk of papillary thyroid cancer in patients with thyroid nodular disease: thyroid autonomy may play a protective role. *Endocrine-Related Cancer* 16:1251-1260.
- Prasad C, Kumar S, Kumar TY. Comparative study on association between serum TSH concentration and Thyroid cancer. *IntSurg J* 2017;4:2800-5.
- Zafon C, Obiols G, Baena JA, Castellví J, Dalama B, Mesa J 2012 Preoperative thyrotropin serum concentrations gradually increase from benign thyroid nodules to papillary thyroid microcarcinomas, then to papillary thyroid cancers of larger size. *J Thyroid Res* 2012:530721
- Kim SS, Lee BJ, Lee JC, Song SH, Kim BH, Son SM, Kim IJ, Kim YK, Kang YH 2011 Preoperative serum thyroid stimulating hormone levels in well-differentiated thyroid carcinoma is a predictive factor for lateral lymph node metastasis as well as extrathyroidal extension in Korean patients: a single-center experience. *Endocrine* 39:259-265.