

Original Research Article

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Utility of pre-operative serum thyroid stimulating hormone in predicting thyroid malignancy

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ABSTRACT

Background: Thyroid cancer is the most common endocrine malignancy and its incidence continues to rise. Thyroid carcinoma in most cases presents clinically as a solitary nodule or as a dominant nodule within a multinodular thyroid gland. There are a number of well-established predictors of malignancy in thyroid nodules. More recently studies have suggested that higher concentration of TSH, even within the normal range are associated with subsequent diagnosis of thyroid cancer in patients with thyroid nodules and even higher serum TSH levels have been found associated with advanced stages of thyroid cancer. The objective of this study was to determine the serum thyroid stimulating hormone (TSH) concentration before surgery in different thyroid malignancies and to compare serum TSH concentration after surgery in thyroid malignancy

Methods: A hospital based observational study was conducted in a tertiary care hospital for a period of 2 year. 120 patients presenting with thyroid nodule without an overt thyroid dysfunction during the study period were included in the study. Chi-square was used as test of significance. Independent t test was the test of significance for quantitative data between two groups.

Results: Mean serum TSH was higher in thyroid malignancies and significant difference was observed between solitary and multinodular goitre. Mean serum TSH concentrations was significantly high in papillary carcinoma and advanced stages of carcinoma. Mean serum TSH was high in stage III and stage IV (5.17 ± 1.36 mIU/l) compared to stage I and II (4.03 ± 1.87 mIU/l).

Conclusions: The study concludes that TSH levels were high in thyroid malignancies arising from multinodular goitre, majority of thyroid malignancies had high levels of serum TSH concentrations and TSH was high with advanced stage of thyroid cancer

Keywords: Thyroid nodule, Thyroid malignancy, Thyroid stimulating hormone

INTRODUCTION

Thyroid neoplasm includes both benign and malignant tumour arising in the thyroid gland. In the India, thyroid cancer accounts for less than 1% of all malignancies (2% of women and 0.5% of men). Thyroid cancer is responsible for six deaths per 1 million persons annually. Although thyroid cancer accounts for less than 1% of all cancers, it is the commonest endocrine tumour that shows

a geographic variation in the incidence of tumour type and natural history.^{1,2}

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. Number of studies have suggested that higher concentrations of TSH, even within the normal

range, are associated with a subsequent diagnosis of thyroid cancer in patients presenting with thyroid nodules. Moreover, higher serum TSH levels have been found 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.

Although there is limited literature to suggest the role of TSH in predicting thyroid malignancies hence this study was undertaken with the following objectives to determine the serum thyroid stimulating hormone (TSH) concentration before surgery in different thyroid malignancies and to compare serum TSH concentration after surgery in thyroid malignancy.

METHODS

A prospective study was conducted in a tertiary care hospital for a period of 2 year. Patients presenting with thyroid nodule without an overt thyroid dysfunction to the centre during this period were included in the study. Subjects on thyroid hormone therapy, secondary malignancies in the thyroid (metastasis), thyroid lymphomas, thyroiditis and Grave's disease were excluded from the study. Sample size of 120 was obtained by using mean TSH among malignant thyroid lesions as 2.5 ± 0.3 mIU/L from the study by Megan Rist Haymart et al, at 5% absolute error using the formula $n = \frac{Z\alpha^2 SD^2}{d^2}$. 120 subjects who were diagnosed as thyroid malignancy by HPE were included in the study during the study period. These subjects were also followed up for a period of two years after the surgery to determine the TSH levels after surgical and medical treatment.

Demographic, pathological data (preoperative FNAC) and serum TSH concentration levels were recorded from these patients. Cytological results were classified into following categories: malignant, indeterminate, follicular neoplasm, Hurthle cell neoplasm and suspicious for papillary cancer. Thyroidectomy was recommended for patients with malignancy, indeterminate cytology and in patients with rapid increase in size of nodule. Additional management was based on the final surgical pathology. Demographic data obtained included patient's age and sex, FNA cytology results, nodule size, thyroid profile, final surgical pathology report and stage were determined. Patients in whom TSH levels were obtained while on thyroid hormone therapy were excluded from study. Serum TSH level was measured by a sensitive serum TSH assay by automated immune chemiluminescent assay.

Statistical Methods: Data was entered into data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Independent t test was the test of significance for quantitative data between two

groups. Analysis of variance was the test of the significance to find the mean difference in quantitative data between three or more groups. p value <0.05 was considered as statistically significant. Informed consent was obtained from all the subjects and Institutional ethical clearance was obtained prior to the start of the study.

RESULTS

In the study 120 subjects presenting with thyroid nodules and diagnosed as thyroid malignancies were included. Of them majority of them were females (72.5%) in the age group 26 to 40 years (44.2%). 83.3% had a solitary thyroid nodule and 16.7% had multinodular goitre. Majority of the lesions were diagnosed in HPE as follicular carcinoma (51.7%) and papillary carcinoma (46.7%). Majority of them had serum TSH in the range of 1.71-5.5 mIU/l (88.3%) (Table 1).

Mean TSH among subjects with Solitary thyroid nodule was 4.78 ± 2.1 mIU/l and among multi nodular goitre subjects was 5.87 ± 1.98 mIU/l. This observation between thyroid nodules was statistically significant. Hence proves that higher TSH levels were observed among multi nodular goitre than solitary thyroid nodule. Similarly, higher TSH levels were observed among subjects with papillary carcinoma, mean Serum TSH was high in Stage III and Stage IV compared to stage I and II. This difference was statistically significant (Table 2).

Table 1: Profile of subjects in the study.

		Frequency (n=120)	Percentage
Age	<25 years	09	7.5%
	26-40 years	53	44.2%
	41-60 years	48	40%
	>60	10	8.3%
Sex	Male	33	27.5%
	Female	87	72.5%
Preoperative diagnosis	Solitary thyroid nodule	100	83.3%
	Multinodular goitre	20	16.7%
Type of thyroid carcinoma	Follicular carcinoma	62	51.7%
	Papillary carcinoma	56	46.7%
	Hurthle carcinoma	2	1.7%
Serum TSH concentrations	0.91-1.70 mIU/l	02	1.7%
	1.71- 5.5 mIU/l	106	88.3%
	>5.51 mIU/l	12	10%

Table 2: Mean TSH comparison in different thyroid malignancies and stages during preoperative period.

		Serum TSH	P value
		Mean±SD	
Thyroid nodule	Solitary thyroid nodule (n=100)	4.78±2.1	0.001033*
	Multi nodular goitre (n=20)	5.87±1.98	
Histopathological diagnosis	Follicular carcinoma (n=62)	4.14±1.41	0.0008*
	Papillary carcinoma (n=56)	5.25±1.63	
	Hurthle carcinoma (n=2)	5.01±3.21	
Stage of tumor	Stage I and II (n=82)	4.03±1.87	0.001*
	Stage III and IV (n=38)	5.17±1.36	

Table 3: Mean TSH comparison in different thyroid malignancies and stages during postoperative period.

		Serum TSH	P value
		Post-operative at 3 months	
Thyroid nodule	Solitary thyroid nodule (n=99)	4.11±1.7	0.0001*
	Multi nodular goitre (n=18)	5.96±2.3	
Histopathological diagnosis	Follicular carcinoma (n= 61)	4.27±1.83	0.003*
	Papillary carcinoma (n=55)	5.45±1.88	
	Hurthle carcinoma (n=1)	5.63	
Stage of tumor	Stage I and II (n=82)	4.11±1.39	0.0001*
	Stage III and IV (n=35)	5.87±1.46	

During follow up 3 subjects had mortality. No significant difference was observed in mortality with respect to different types of thyroid malignancies. It was observed that after surgery mean TSH levels were not significantly reduced in all types of malignancy during follow up. Hence TSH can also act as a prognostic marker for thyroid malignancies (Table 3).

DISCUSSION

Thyroid cancer is the most common endocrine malignancy and its incidence continues to rise. Thyroid carcinoma, in most cases, presents clinically as a solitary nodule or as a dominant nodule within a multinodular thyroid gland.⁴ More recently, a number of studies have suggested that higher concentrations of TSH, even within the normal range, are associated with a subsequent diagnosis of thyroid cancer in patients presenting with thyroid nodules. Moreover, higher serum TSH levels have been found associated with advanced stages of thyroid cancer.⁶⁻⁸

These findings suggest that TSH may play a central role in the development and/or progression of thyroid carcinomas. 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.

It is documented that TSH has a trophic effect on thyroid cancer growth, which is most likely mediated by TSH receptors on tumor cells, and furthermore that TSH

suppression is an independent predictor of relapse-free survival from differentiated thyroid cancer. Studies have shown that the risk increases, associated with serum TSH concentrations in the upper half of the normal range, and even more strikingly in those whose TSH measurements were above normal, may at least in part be mediated by this trophic effect of TSH. An alternative explanation is that patients with lower TSH concentrations were developing autonomous function, which is itself associated with lower rates of malignancy.⁸⁻¹⁴

In the study proportion of thyroid malignancies was high in age group 26-40 year (44%), of them majority were solitary thyroid nodule (83.3%) and 16.7% multinodular goitre. Similarly, out of 120 patients 82 had Stage 1 and 2 with mean serum TSH concentrations of 4.03 mIU/L and 38 of 120 patients had stage 3 and 4 had mean serum TSH concentrations of 5.17 mIU/L.

Similar findings were observed in the below mentioned studies, in a study by Jonklaas J et al, the highest incidence of thyroid malignancy were seen in age group less than 30 year (32%).⁴ In the study by Boelaert K et al, the highest incidence of thyroid malignancy was seen patients presenting with solitary thyroid nodule (n = 861, 10.8%), compared with those who presented with a diffuse or nodular goiter (n = 639, 4.2%).⁶ In the study by Jonklaas J et al, the final histopathology report was Follicular carcinoma; 12 (9%), papillary carcinoma; 113 (87%) and Hurthle carcinoma; 5 (4%).⁴ Boelaert K et al, concluded that the risk of diagnosis of malignancy rose in parallel with the serum TSH at presentation, with significant

increases evident in patients with serum TSH greater than 0.9 mIU/liter, compared with those with lower TSH.⁶ In another study done by Polyzos et al, higher rates of malignancy were observed in patients with serum TSH concentration in upper tertile of normal range.⁸ Haymart MR et al, observed that 204 of 239 patients had stage 1 and 2 thyroid cancer with mean serum TSH concentrations of 3.1 mIU/L and 35 patients of 239 had stage 3 and 4 thyroid cancer with mean serum TSH concentration of 4.9 mIU/L.

Considering serum TSH concentration as an independent predictor of thyroid malignancy, studies have predicted probability of diagnosis of thyroid malignancy, increases from less than 10% for serum TSH concentrations at the lower end of the normal range up to 25% if the same patient has a TSH concentration at the upper end of the normal range.^{9,10}

During follow-up, it was also observed that TSH levels were not reduced significantly, were as increase in TSH levels were observed in all the malignant lesions. This suggests that TSH also plays an important role in postoperative prognosis in thyroid malignancies.

CONCLUSION

That TSH levels were higher in multinodular goitre than solitary thyroid nodule and higher TSH levels were observed in papillary carcinoma of thyroid than other tumors and TSH levels were high in advanced stages of thyroid malignancy.

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Ethical approval: The study was approved by the institutional ethics committee

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