

RELATIONSHIP BETWEEN SERUM THYROID STIMULATING HORMONE LEVELS AND TUMOUR PATHOLOGY IN PATIENTS WITH THYROID SWELLINGS

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ABSTRACT: INTRODUCTION: Thyroid diseases are, arguably, among the commonest endocrine disorders worldwide. The National Goitre Control Programme in India has shown that India has the world's highest goitre belt in the Himalayan & Sub-Himalayan region with a prevalence of 29%. It seems probable that thyroid stimulating hormone (TSH) can act as a cancer stimulus. This study was devised to analyse the levels of TSH in patients with thyroid swellings and to determine the correlation between the TSH level and nature of thyroid swelling, if any. **MATERIALS AND METHODS:** All patients who presented to our OPD with evidence of a thyroid swelling from July 2012 to June 2013 were included in the study. Estimation of T₃, T₄, and TSH, USG of the thyroid region, FNAC from the swelling and Histopathological examination of surgical specimen (When applicable) were done. Data was analysed by commercially available statistical software packages. **RESULTS:** 45 patients were included in the study. Preoperative TSH values were compared with the final histopathological diagnosis. The mean TSH value was 1.86 ± 0.91 mIU/l for benign lesions and 2.39 ± 0.90 mIU/l for malignant lesions. **CONCLUSION:** TSH levels in patients with thyroid nodules may be used as diagnostic adjuncts for the identification of high-risk patients, who require further investigation and/or surgical intervention.

KEYWORDS: Thyroid Stimulating Hormone, Thyroid Neoplasms, Papillary Thyroid Carcinoma.

INTRODUCTION: Thyroid diseases are, arguably, among the commonest endocrine disorders worldwide. India also is no exception to this worldwide trend. According to a projection from various studies on thyroid, it has been estimated that about 42 million people in India suffer from thyroid diseases.^[1] The National Goitre Control Programme in India has shown that India has the world's highest goitre belt in the Himalayan & Sub-Himalayan region with a prevalence of 29%.^[2] Thyroid diseases are different from other diseases in terms of their ease of diagnosis, accessibility of medical treatment & the relative visibility that even a small swelling of the thyroid offers to the treating physician. Goitre has been treated in innumerable ways since the ancient times & as such a vast amount of data has been accumulated on the outcome of the diseases.

Thyroid malignancy is a rare condition seen in only 10% of clinically apparent solitary thyroid nodules. On investigation, many apparently solitary thyroid nodules will be shown to be part of a multi-nodular goitre. European Thyroid Cancer Taskforce opined that the risk of malignancies is similar among hypo-functioning single nodules and multi-nodular goiter.^[3] There is a female preponderance of approximately 3:1.^[4] Aetiologically the most common cause is exposure to ionizing

radiation in childhood. Medullary carcinoma of thyroid often has a genetic basis & is associated with MEN Syndrome.^[5]

Although oncogenes and other growth factors are involved in thyroid cancer growth and development, it seems probable that thyroid stimulating hormone (TSH) can act as a cancer stimulus.^[6] Higher TSH value in patients with thyroid nodules is associated with greater risk of differentiated thyroid carcinoma. This hypothesis is supported by improved survival in thyroid cancer patients treated with suppressive doses of levothyroxine.^[7]

Limited information is available regarding the correlation of level of TSH with thyroid neoplasm in North Bengal population. Hence, this study was devised to analyse the levels of TSH in patients with thyroid swellings and to determine the correlation between the TSH level and nature of thyroid swelling, if any.

Ethics: Appropriate clearance was taken from the Institutional Ethical Committee prior to initiation of the study.

MATERIALS AND METHODS: All patients who presented to our OPD with evidence of a thyroid swelling from July 2012 to June 2013 were included in the study. After documentation of a detailed history, a general and locoregional examination was done. After clinical assessment, each patient was advised estimation of T₃, T₄, and TSH by Enzyme-linked Immunosorbent Assay (ELISA) to know the exact thyroid function status.

All patients were subjected to an Ultrasonographic examination of the thyroid region and a Fine Needle Aspiration Cytology (FNAC) from the swelling. Surgery was planned for patients based on the preoperative test results. Those who required medical management were referred to the Endocrinology Department for further management.

After surgery, all specimens were sent to the Department of Pathology for histopathological examination. All the histopathologically confirmed cases were sincerely followed by evidence-based interventions according to internationally accepted clinical protocols. Data was analysed by commercially available statistical software packages.

RESULTS: 45 patients were included in the study. There was a definite female predominance (female: male = 6.5:1) with a majority of the patients in the fourth decade of life (42.2%). (Table 1)

FNAC reports were obtained using the Bethesda Classification system. (Table 2) Majority of the patients were Bethesda II (68.9%) which included Colloid goitre, Grave's Disease and Thyroiditis. 8.9% of the patients were Bethesda IV where because of a follicular nature of the neoplasm, FNAC could not exclude malignancy. 22.2% of the patients were Bethesda VI wherein 90% (9 out of 10 patients) were diagnosed to have papillary carcinoma and 10% (1 out of 10 patients) had medullary carcinoma.

Table 3 illustrates the comparison between USG findings and the FNAC impression. Out of the 25 cases which were determined as colloid goitre on USG, FNAC diagnosed 3 as follicular neoplasms and 4 as Papillary Carcinoma. However, out of the 6 cases diagnosed as a malignancy on USG, 5 were confirmed to be so on FNAC (4 Papillary Carcinoma, 1 Medullary Carcinoma) and 1 was determined as Follicular neoplasm, which on histopathological examination (HPE) turned out to be follicular carcinoma.

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Preoperative TSH values were compared with the final histopathological diagnosis. (Table 4) The mean TSH value was 1.86 ± 0.91 mIU/l for benign lesions and 2.39 ± 0.90 mIU/l for malignant lesions. Thus, TSH values were higher for malignant cases and this was statistically significant (p value = 0.048).

DISCUSSION: Thyroid diseases are commonly encountered in day to day practice and comprise one of the most common endocrine disorders worldwide. India is no exception and it has been projected that about 42 million people suffer from thyroid diseases in the country.^[1] The National Goitre Control Programme in India has shown that India has the world's highest goitre belt in the Himalayan & Sub-Himalayan region with a prevalence of 29%.^[2]

Only 10% of clinically apparent solitary thyroid nodules are eventually diagnosed as thyroid malignancies. On investigation, many apparently solitary thyroid nodules will be shown to be part of a multinodular goitre. European Thyroid Cancer Taskforce opined that the risk of malignancies is similar among hypofunctioning single nodules and multinodular goiter.^[3]

Medical literature reports a female preponderance of approximately 3:1 but in our study, we obtained a female preponderance of 6.5:1.^[4]

FNAC results yielded a diagnosis of malignancy in 22.2% of our cases which was considerably different from other studies which showed a range of 5% – 7.6% [8]. USG findings were compared with FNAC impressions as medical literature reports that FNAC has a better sensitivity and specificity than USG [9]. USG seemed to detect malignancy cases better than benign cases.

It has been postulated that oncogenes and other growth factors are responsible for growth and development in thyroid cancer, it seems probable that thyroid stimulating hormone (TSH) can act as a cancer stimulus.^[6] Preoperative TSH values were compared with the final histopathological diagnosis. The mean TSH value was 1.86 ± 0.91 mIU/l for benign lesions and 2.39 ± 0.90 mIU/l for malignant lesions. Thus, TSH values were higher for malignant cases and this was statistically significant (p value = 0.048). Medical literature states that having a high TSH level within the normal range is an independent risk factor for Differentiated Thyroid Cancer, and may contribute to the initiation of thyroid carcinogenesis. TSH levels in patients with thyroid nodules may be used as diagnostic adjuncts for the identification of high-risk patients, who require further investigation and/or surgical intervention.^[10]

CONCLUSION: A variety of diagnostic modalities exist for the detection of thyroid malignancy. However, each modality has its own advantages and disadvantages. As per our study and other available medical literature, elevated TSH levels may also be used in conjunction with other investigations for diagnosis of malignancy in thyroid swellings.

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Age (in years)	Female	Male	Total
0-9	0 (0%)	0 (0%)	0 (0%)
10-19	2 (4.4%)	0 (0%)	2 (4.4%)
20-29	6 (13.3%)	1 (2.2%)	7 (15.6%)
30-39	16 (35.6%)	3 (6.7%)	19 (42.2%)
40-49	8 (17.8%)	2 (4.4%)	10 (22.2%)
50-59	4 (8.9%)	0 (0.0%)	4 (8.9%)
60-70	3 (6.7%)	0 (0.0%)	3 (6.7%)
Total	39 (86.7%)	6 (13.3%)	45 (100.0%)

Table 1: Distribution of patients according to age and sex

FNAC (Bethesda classification & impression)	Female	Male	Total
II	27 (60.0%)	4 (8.9%)	31 (68.9%)
Colloid Goitre	18 (40.0%)	3 (6.7%)	21 (46.7%)
Grave's Disease	2 (4.4%)	(0.0%)	2 (4.4%)
Thyroiditis	7 (15.6%)	1 (2.2%)	8 (17.8%)
IV	4 (8.9%)	(0.0%)	4 (8.9%)
Follicular neoplasm	4 (8.9%)	(0.0%)	4 (8.9%)

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VI	8 (17.8%)	2 (4.4%)	10 (22.2%)
Medullary Carcinoma	1 (2.2%)	(0.0%)	1 (2.2%)
Papillary Carcinoma	7 (15.6%)	2 (4.4%)	9 (20.0%)
Total	39 (86.7%)	6 (13.3%)	45 (100.0%)

Table 2: Distribution of patients according to FNAC report

		FNAC Impression						
		Colloid Goitre	Follicular neoplasm	Grave's Disease	Medullary Carcinoma	Papillary Carcinoma	Thyroiditis	Total
USG impression	Colloid Goitre	18	3	0	0	4	0	25
	Cyst	2	0	0	0	1	0	3
	Grave's Disease	0	0	2	0	0	0	2
	Malignancy	0	1	0	1	4	0	6
	Thyroiditis	1	0	0	0	0	8	9
	Total	21	4	2	1	9	8	45

Table 3: comparison between FNAC impression and USG impression

		No. of patients	TSH (mIU/l)	
			Mean \pm SD	Range
Final Diagnosis	Colloid Goitre	18	1.93 \pm 0.76	0.22 - 3.40
	Follicular Adenoma	5	1.70 \pm 0.97	0.28 - 2.90
	Non-operated benign lesions	10	1.80 \pm 1.19	0.08 - 3.20
	Papillary Carcinoma	9	2.44 \pm 0.89	0.28 - 3.20
	Follicular Carcinoma	2	2.85 \pm 0.10	2.78 - 2.92
	Medullary Carcinoma	1	0.98 \pm NA	0.98 - 0.98
	Total	45	2.00 \pm 0.93	0.08 - 3.40

Table 4: Comparison between mean TSH value and Histopathological diagnosis

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