

Evaluation of Ultrasound Characteristics and Serum TSH Level in Predicting Malignancy among Patients Undergoing Thyroidectomy with FNAC-proven Diagnosis of Multinodular Goiter and Follicular Neoplasia: A Prospective Observational Study

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ABSTRACT

Background: Thyroid nodules are one of the most common diseases encountered in surgical practice. Predicting malignancy in patients with multinodular goiters (MNGs) becomes difficult due to the presence of multiple nodules. Targeting the nodule which might be malignant is of utmost importance. The task becomes difficult due to the presence of many different ultrasound scoring systems. This study aims to evaluate ultrasound characteristics and thyroid stimulating hormone (TSH) levels in predicting malignancy in patients with benign goiters and follicular neoplasia.

Materials and methods: Our study was a prospective observational study that was conducted between April 2021 and September 2022. Patients aged 18 years and above with fine needle aspiration cytology (FNAC) suggestive of MNGs and follicular neoplasia were included in the study. Analysis of the variables was done by using statistical analysis in a social science application.

Results: The final analysis was conducted on 106 patients who met the inclusion criteria. Ultrasound of the thyroid detected microcalcifications in 8.5% of patients, hypervascularity in 33%, solid components in 40.6%, and hypoechoic areas in 47.2% of the patients. The study showed that a TSH value of greater than 1.88 mIU/mL and solid components in ultrasonograph (USG) have high sensitivity and specificity in predicting malignancy.

Conclusion: This study shows that ultrasound characteristics of microcalcifications, hypervascularity, solid component, and TSH level greater than 1.88 mIU/mL are statistically significant and can be fairly used for predicting malignancy in benign goiter and follicular neoplasia. The presence of these features may warrant a surgical excision to confirm the diagnosis, even if the FNAC is reported as benign.

Keywords: Multinodular goiter, Follicular neoplasia, Fine needle aspiration cytology, Thyroid stimulating hormone level, Ultrasound of thyroid, Predictors of thyroid malignancy.

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INTRODUCTION

Thyroid nodules occur in about 8.5% of the general population, more commonly among women.¹ In 1 year, among a 100,000 population, the incidence of cancer of the thyroid is 8.7 and shows a climbing trend.² Malignancy in multinodular goiter (MNG) has an incidence of 5–10%. Children, male gender, adults with age <30 and above 60 years, and patients with prior radiation exposure are considered at high risk.³ Ultrasonography (USG) is considered a reliable diagnostic test in the initial stage of evaluating goiters. Nodules of thyroid detected during USG show highly diverse patterns, which makes it difficult to differentiate benign from malignant nodules. This necessitated the proposal of different scoring and reporting systems to classify nodules according to their risk of being malignant. A few such classifications include Thyroid Imaging Reporting and Data Systems (TIRADS), developed in 2009; modified TIRADS, developed in 2011; British U-system developed in 2014; and American Thyroid Association guidelines of 2015.⁴ American College of Radiology (ACR)—TIRADS tool of reporting put forth by the ACR is commonly used.⁵ The most reliable investigation to diagnose if a nodule is cancerous or not currently is fine needle aspiration cytology (FNAC).⁶ It has a limitation in

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MNG due to the presence of multiple nodules. MNG and solitary thyroid nodules have cancer incidences of 5–10% and 20–30%, respectively. Many FNACs can be avoided if nodules with a low risk of cancer are identified.⁷ Thyroid stimulating hormone (TSH) levels in the serum are a unique tool in predicting cancer in thyroid

nodules. The prevalence of malignancy is higher as the TSH level in serum increases. In this article, we have studied whether serum TSH concentration and ultrasound characteristics can predict malignancy in patients undergoing thyroidectomy with FNAC-proven diagnosis of MNGs and follicular neoplasia.

MATERIALS AND METHODS

Our study was a prospective observational study conducted at the teaching hospital of Kasturba Medical College, Manipal, General Surgery Department, from April 2021 to the end of September 2022. A total of 106 patients were recruited after obtaining consent with institutional ethical clearance. Patients with MNG and follicular neoplasia undergoing thyroidectomy and hemithyroidectomy with age above 18 years were enrolled. Those who had already been diagnosed with cancer of the thyroid were excluded. A detailed history was taken, and patients were examined. Appropriate investigations, that is, FNAC, USG characteristics, and TSH levels, which act as predictors of malignancy, were done preoperatively. Postoperative histopathological examination of the specimen was done. The predictors were compared with the results of histopathology (HPE) (malignant or benign). Analysis of statistics was done using the Statistical Package for the Social Sciences

application. Association among different variables predicting cancer was determined by using the Chi-squared test. Receiver operating characteristic (ROC) curve was used to detect accuracy of TSH level as a predictor of malignancy.

RESULTS

The final analysis was conducted on 106 patients who cleared the inclusion criteria. The study subjects were of a mean age of 45.9 years. In the study population, 47.2% of the study group were between the 40s and 60s. Among the study subjects, there were 13 males and 93 females. FNAC showed benign condition in 86.8% and follicular neoplasm in 13.2%. Ultrasound of the thyroid showed microcalcifications in 8.5% of patients, hypervascularity in 33% of patients, solid components in 40.6%, and hypoechoic areas in 47.2%. Intranodular vascularity was seen in all study participants, and none of the patients had infiltrative margins. The histopathological examination of the thyroidectomy specimen was reported as benign in 78.3% and malignant in 21.7% (Table 1). Of the 14 patients who were diagnosed with follicular neoplasm by preoperative FNAC, the postoperative histopathological examination of the thyroidectomy specimen was reported as malignancy in four cases. The rest of the cases were benign. The association between USG findings and biopsy reports for predicting malignancy was studied using the Chi-squared analysis, which showed that patients having microcalcifications, hypervascularity, and solid components were more likely to have thyroid malignancy (Table 2). Mean TSH levels and biopsy findings were compared by utilizing the Mann–Whitney *U* test, which showed that the higher the TSH level, the more the likelihood of malignancy, which was statistically significant. However, all patients had TSH levels within the normal physiological range (Table 3). TSH and solid components in USG have high sensitivity and specificity in predicting malignancy (Table 4). Even

Table 1: Histopathological examination of thyroidectomy specimen among study patients

Category	<i>n</i> = 106	%
Benign	83	78.3%
Papillary carcinoma	12	11.3%
Papillary microcarcinoma	6	5.7%
Follicular carcinoma	3	2.8%
Papillary carcinoma with follicular variant	2	1.9%

Table 2: Association between USG findings with biopsy findings for prediction of malignancy using Chi-squared test

Category	Malignant		Benign		<i>p</i> -value
	<i>n</i> = 23	%	<i>n</i> = 83	%	
Microcalcifications	6	26.1%	3	3.6%	0.001*
Hypervascularity	12	52.2%	23	27.7%	0.03*
Infiltrative margins	0	0.0%	0	0.0%	–
Hypoechoic areas	12	52.2%	38	45.8%	0.59
Intranodular vascularity (present)	23	100.0%	83	100.0%	–
Solid component	16	69.6%	27	32.5%	0.001*

**p*-values are statistically significant

Table 3: Comparison of mean TSH levels based on biopsy findings using the Mann–Whitney *U* test

Parameter	HPE	<i>n</i> = 106	Mean	Standard deviation	Mean difference	<i>p</i> -value
TSH	Benign	83	1.262	0.858	–0.872	<0.001*
	Malignant	23	2.134	0.966		

**p*-values are statistically significant

Table 4: Sensitivity, specificity, positive predictive value, and negative predictive value of significant predictors of malignancy in MNG patients

Variable	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
Microcalcifications	26.1%	96.4%	66.7%	82.5%	81.1%
Hypervascularity	52.2%	72.3%	34.3%	84.5%	67.9%
Solid component	69.6%	67.5%	37.2%	88.9%	67.9%
TSH levels	65.2%	80.7%	46.9%	89.2%	76.4%

Table 5: ROC curve analysis for TSH levels determining cutoff for predictors of malignancy in MNG patients

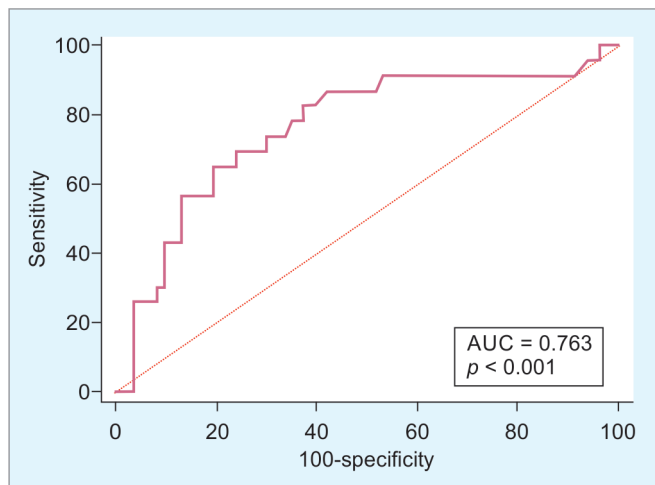
Variable	AUC	Standard error	95% confidence interval		p-value	Cutoff	Sn (%)	Sp (%)
			Lower	Upper				
TSH	0.763	0.059	0.670	0.840	<0.001*	>1.88	65.2	80.7

Sn, sensitivity; Sp, specificity; *p-values are statistically significant

Table 6: Comparison of USG results in our study with other studies in predicting malignancy

Variable	Rios et al., ⁸ n = 221	Yang et al., ¹⁰ n = 698	Yoon et al., ¹¹ n = 26	Chakravarthy et al., ⁹ n = 100	Our study, n = 106
Microcalcifications	<0.001*	Not compared	0.121	0.001*	0.001*
Solid component	Not compared	Not compared	Not compared	0.335	0.001*
Hypervascularity	Not compared	Not compared	Not compared	Not compared	0.03*
Hypoechoic areas	<0.001*	Not compared	Not compared	0.001*	0.59
Intranodular vascularity	<0.001*	<0.001*	Not compared	Not compared	–
Infiltrative margins	Not compared	Not compared	Not compared	Not compared	–

*p-values are statistically significant

**Fig. 1:** Receiver operating characteristic (ROC) curve—TSH level as a significant predictor of malignancy in MNG

though microcalcifications in USG have a specificity of 96.4%, it is not a good variable in predicting malignancy because sensitivity is low (26.1%). ROC curve analysis for TSH levels (mIU/L) determining the cutoff for predicting malignancy among MNG patients showed that TSH is a significant predictor of malignancy with area under ROC curve (AUC) of 0.763, a p-value of <0.001, and a cutoff value of >1.88 mIU/mL (Table 5) (Fig. 1).

DISCUSSION

In our study, out of 106 patients, 21.6% were malignant. Since the previous studies have taken into consideration only individual entities as predictors of malignancy in MNGs, this study, which correlates various aspects (TSH, USG, FNAC, and HPE), helps to understand and predict malignancy in benign goiters in a better way. In a prospective nonrandomized study conducted by Rios et al., microcalcifications, hypoechoic areas, and intranodular vascularity were found to be statistically significant in predicting malignancy, while variables such as solid component, hypervascularity, and infiltrative margins were not compared.⁸ As per a prospective observational study conducted by Chakravarthy et al., microcalcifications and hypoechoic areas are statistically

significant in predicting malignancy, while solid components are not significant, and variables such as hypervascularity, intranodular vascularity, and infiltrative margins were not studied.⁹ In our study, all of the above variables are compared, and microcalcifications, solid components, and hypervascularity were found to be statistically significant (Table 6).^{10,11} A retrospective study conducted by Lu et al. shows the mean TSH value in benign goiters to be 1.65 mIU/mL and in malignant goiters to be 2.22 mIU/mL with a p-value of 0.30. As per our study, the mean TSH level in benign goiters is 1.26 mIU/mL. The mean TSH level in goiters with malignancy is 2.134 mIU/mL with a value of $p < 0.001$, which shows statistical significance.

CONCLUSION

Our analysis shows that TSH level and ultrasound characteristics of microcalcifications, hypervascularity, and solid components are statistically significant and can be fairly used for predicting malignancy in MNG. The presence of these ultrasound characteristics with an elevated TSH level (>1.88 mIU/mL) might warrant surgery (total or hemithyroidectomy) as the possibility of malignancy is high. This might help in the early detection of thyroid malignancy.


LIMITATIONS

The sample size of our study is small. There might have been interrater differences in the reporting of ultrasound features since few of the ultrasound scans are done by postgraduates with less experience.

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