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Comparison of TIRADS [Thyroid imaging reporting and data system] with histopathology in assessment of thyroid nodules

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Abstract
Introduction: The thyroid gland is an endocrine organ, which acts perfectly in maintaining the normal growth and activity of human beings. Factors causing a disturbance in its auto-regulatory mechanism leads to various thyroid function disorders that may or may not result in thyroid nodules. Malignancy comprises of less than 10% of all thyroid nodules on the basis of already established Breast Imaging Reporting and Data System (BIRADS) for breast nodules a categorization system of ultrasound features in thyroid nodules-the Thyroid Imaging Reporting and Data System (TIRADS) is suggested.
Aims and Objectives: To assess validity of TIRADS in Indian population in differentiating thyroid nodules as benign and malignant taking histopathology as gold standard.
Methodology: A descriptive study was done at JSS Hospital over a period of 18 months for 82 patients presenting with clinically palpable thyroid nodules and results were drawn assuming 50 percent sensitivity of TIRADS grading in differentiating the lesion as benign and malignant with an alpha error of 5 percent and a precision of 15 percent. All demographic data was summarized as proportion, mean, standard deviation and sensitivity, specificity, positive predictive value, negative predictive value were measured with 95% confidence interval. The inferential statistics were obtained using Chi-square and Cramer's V tests.
Results: 42.7 per cent cases were present in TIRADS II, 34.1 per cent in TIRADS III, 9.8 per cent in TIRADS IV A, 4.9percent each in TIRADS 1V B and C, 3.7 per cent in TIRADS V. TIRADS grading when compared with histopathology was found to have a sensitivity of 82.35 percent, a specificity of 92.30 percent, positive predictive value of 73.68 percent and a negative predictive value of 95.24 percent.
Conclusion: TIRADS grading is a useful tool in pre operative evaluation and management, aids in deciding the timing of FNAC and when used along with it improves the diagnostic ability of a clinician in overall assessment of thyroid nodules.

Keywords: TIRADS, FNAC, BIRADS, USG thyroid, histopathology

Introduction

The thyroid gland is an endocrine organ, which acts perfectly in maintaining the normal growth and activity of human beings. The unique feature of this gland among all endocrine glands is that it is the first endocrine gland to appear in fetus. This being one of the largest endocrine glands (weighing about 25 g), a direct physical examination can be easily done because of its superficial location. The secretions from the gland are regulated by auto regulatory mechanisms. Factors causing a disturbance in its auto-regulatory mechanism leads to various thyroid function disorders that may or may not result in thyroid nodules. Thyroid nodules are very prevalent-they are found in approximately 8% adults by palpation, 41% by means of ultrasound and 50% in autopsy pathological examination [1]. Malignancy comprises of less than 10% of all thyroid nodules" [2]. However, since any nodule could be a carcinoma, the challenge lies in identifying the lesions that are malignant in a cost-effective, non-invasive manner while decreasing the medical, financial and emotional burden put on overwhelming excess in the patients with benign nodules. "On the basis of already established Breast Imaging Reporting and Data System (BIRADS) for breast nodules a categorization system of ultrasound features in thyroid nodules-the Thyroid Imaging Reporting and Data System (TIRADS) is suggested [3].
Classification has been proposed by Horvath *et al.* and modified by Kwak *et al.* [4, 5].
TIRADS 1: Normal Thyroid Gland
TIRADS 2: Benign Lesions

TIRADS 3: Probably Benign Lesions"
TIRADS 4: Suspicious Lesions (Subclassified as 4a, 4b and later 4c with increasing risk of malignancy)."
4a: one suspicious feature (5-10% risk of malignancy)
4b: two suspicious features (10-80% risk of malignancy)
4c: three/four suspicious features (10-80% risk of malignancy)
Suspicious sonographic features of malignancy: -

1. Solid component
2. Markedly hypoechoic nodule
3. Micro lobulations or irregular margins
4. Micro calcifications
5. Taller than wider shape

TIRADS 5: Probably Malignant Lesions (more that 80% risk of malignancy)
TIRADS 6: Biopsy Proven Malignancy
Before the appearance of high-resolution ultrasound, radionuclide scintigraphy was considered as the principle modality to assess the thyroid gland. Ultrasound is however more secure, non-ionizing and furthermore a lot less expensive option. C.T and M.R.I although less efficient than ultrasound, are also used in the work up of thyroid nodules usually for assessing the mediastinal extension of thyroid.

Objectives

Primary objective

1. To assess validity of TIRADS in Indian population in differentiating thyroid nodules as benign and malignant taking histopathology as gold standard.

Secondary objective

1. To assess TIRADS grading for clinically palpable thyroid nodules
2. To know histopathology findings for clinically palpable thyroid nodules
3. To compare TIRADS grading with histopathology findings

Methodology

a. Study Design: Descriptive Study
b. Study place: JSS Hospital Department of Surgery
c. Study Duration: Nov 2017 till April 2019
d. Sample size: Sample Size is considered as 82 assuming 50% sensitivity of TIRADS grading in differentiating benign and malignant lesion, precision of 15% and alpha error of 5%
e. Sampling technique and study population: Convenient sample. All consecutive cases coming to surgical department.
f. Inclusion criteria

1. All clinically palpable thyroid nodules
2. In a case of multinodular goitre the largest solid/suspicious nodule will be included for study.

g. Exclusion criteria

1. Toxic Nodular Goitre
2. Graves' Disease
3. Patients with bleeding diathesis
4. Patients unwilling for thyroidectomy
5. Patients not willing to be part of study

Study assessments of end points: Classify thyroid nodules as benign and malignant based on TIRADS scoring and histopathology respectively and comparing the results.

Statistical methods applied

Data analysis

All demographic data is summarized as proportion, mean, standard deviation and sensitivity, specificity, negative predictive value, positive predictive value are measured with 95% confidence interval. All the measurements are done using SPSS version 21 and EPI-Info version 7.

Descriptive statistics

The Descriptive procedure displays univariate summary statistics for several variables in a single table and calculates standardized values (z scores). Variables can be ordered by the size of their means (in ascending or descending order), alphabetically, or by the order in which the researcher specifies.

Descriptive statistics included

Mean,
Standard deviation,
Frequency and
Percent

Inferential statistics

Chi-square test

The Chi-Square Test procedure tabulates a variable into categories and computes a chi-square statistic. This goodness-of-fit test compares the observed and expected frequencies in each category to test either that all categories contain the same proportion of values or that each category contains a user-specified proportion of values.

Crosstabs (Cramer's V)

- The Crosstabs procedure forms two-way and multiway tables and provides a variety of tests and measures of association for two-way tables. The structure of the table and whether categories are ordered determine what test or measure to use. Cramer's V test was employed in the present study.

Results

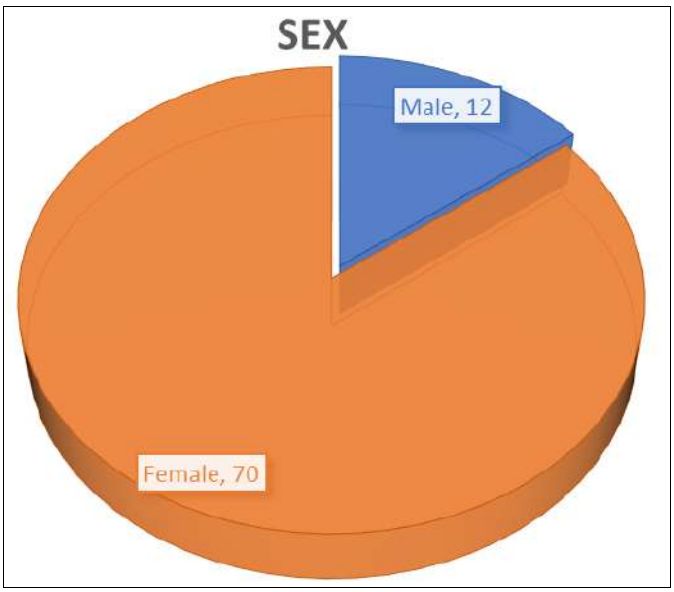

Fig 1: Sex Distribution

In our study out of 82 cases, no of females were 70 (85.4%) whereas 12 (14.6%) were male patients.

Table 1: TSH

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Euthyroid	73	89.0	89.0	89.0
	Hyperthyroid	4	4.9	4.9	93.9
	Hypothyroid	5	6.1	6.1	100.0
	Total	82	100.0	100.0	

89 percent patients were euthyroid, 4.9 percent were hyperthyroid and 6.1 percent were hypothyroid in the study

Table 2: TIRADS Grading

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	TIRADS II	35	42.7	42.7	42.7
	TIRADS III	28	34.1	34.1	76.8
	TIRADS IV A	8	9.8	9.8	86.6
	TIRADS IV B	4	4.9	4.9	91.5
	TIRADS IV C	4	4.9	4.9	96.3
	TIRADS V	3	3.7	3.7	100.0
	Total	82	100.0	100.0	

As per distribution of patients according to TIRADS grading 42.7 per cent were present in TIRADS II, 34.1 per cent in TIRADS III, 9.8 per cent in TIRADS IV A, 4.9percent each in TIRADS 1V B and C, 3.7 per cent in TIRADS V

Histopathology in different sex

On histopathology 8.3 percent males had colloid goiter, 25 percent had adenomatoid goiter, 8.3 percent had Hashimoto's Thyroiditis, 33.3 percent had papillary carcinoma and 25 percent had follicular carcinoma. 28.6 percent females had colloid goiter, 37.1 had adenomatoid goiter, 21.4 had hashimoto's thyroiditis, 10 percent had papillary carcinoma, 1.4 percent had follicular carcinoma and 1.4 percent had anaplastic carcinoma.

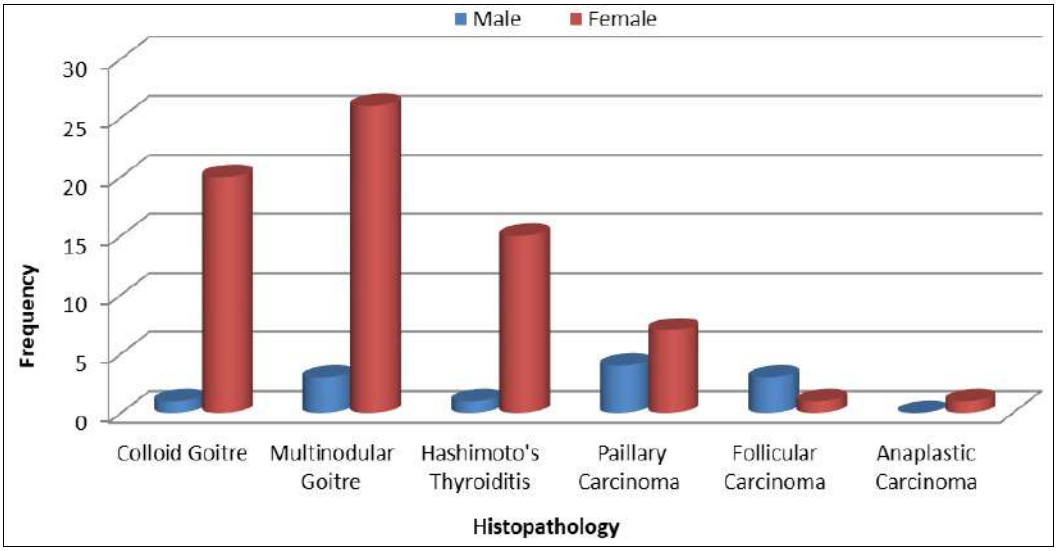

Fig 2: Histopathology in Different Sex

Benign VS Malignant in Different Sex

Table 3: Crosstab

			Sex		Total
			Male	Female	
Benign	Benign	Count	5	61	66
		% within Sex	41.7%	87.1%	80.5%
	Malignant	Count	7	9	16
		% within Sex	58.3%	12.9%	19.5%
Total		Count	12	70	82
		% within Sex	100.0%	100.0%	100.0%

In males 41.7 percent were found to have benign pathology whereas 58.3 had malignant nodules.

In females 87.1 percent had benign thyroid nodules whereas 12.9 percentage had malignancy

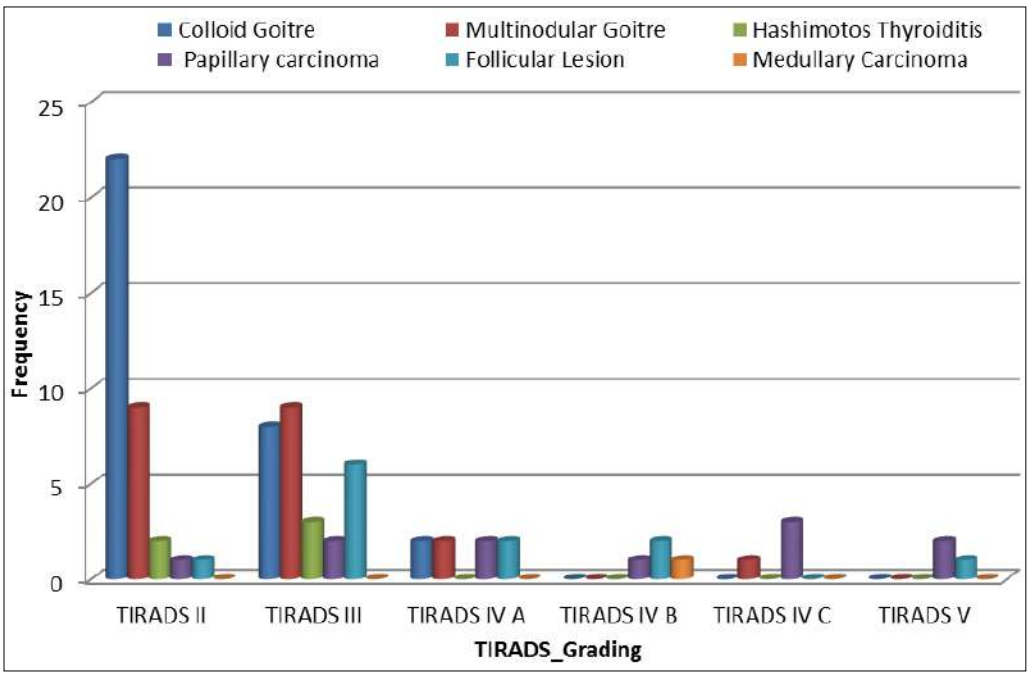

Fig 3: TIRADS vs FNAC

- On comparing TIRADS with FNAC- 68.8 percent cases of colloid goiter were graded as TIRADS II, 25 percent as TIRADS III, 6.2 per cent as TIRADS IV A.
- 42.9 percent cases of Multinodular Goitre were graded as TIRADS II and III each, 9.5 percent as TIRADS IV A and 4.8 percent as TIRADS IV C.
- 40 percent Hashimotos's Thyroiditis were graded as TIRADS II and 60 percent as TIRADS III.
- 27.3 percent cases of papillary carcinoma were TIRADS IV C, 18.2 percent as TIRADS V, TIRADS IV A and TIRADS III each.9.1 percent cases were graded as TIRADS IV B and TIRADS II each.
- 50 percent cases of follicular lesion on FNAC were graded as TIRADS III, 16.7 percent as TIRADS IVA and IV B each and 8.3 percent under TIRADS V and II each.
- 100 per cent cases of medullary carcinoma were graded as TIRADS IV B.

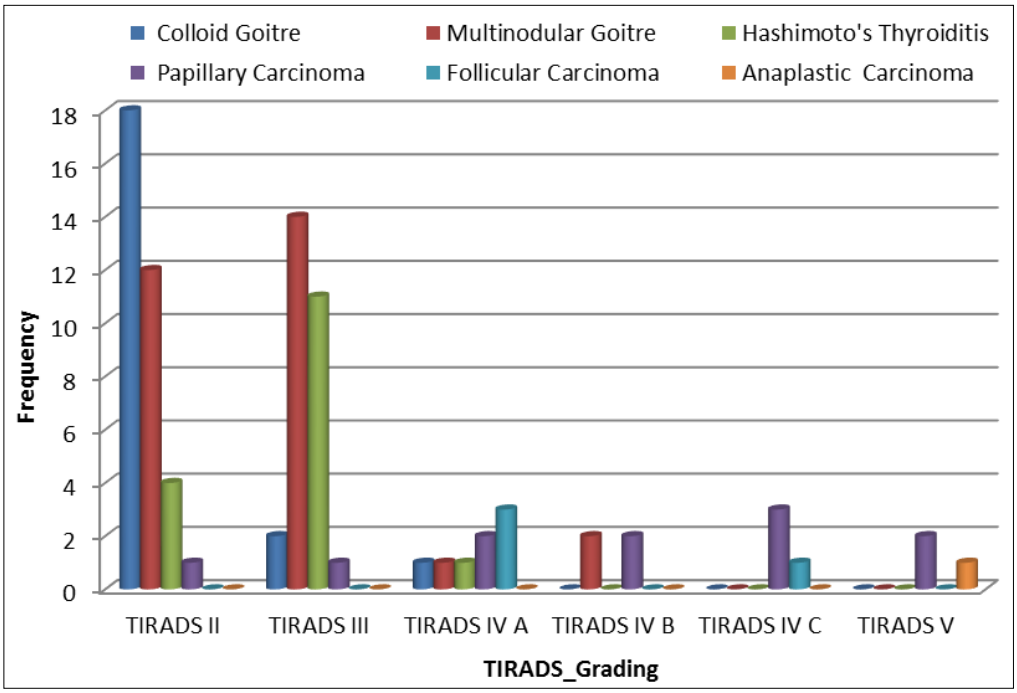

Fig 4: TIRADS vs Histopathology

- On comparing TIRADS with Histopathology- 18 (85.7 percent) cases of colloid goiter were graded as TIRADS II, 2 (9.5 percent) as TIRADS III, 1 (4.8 per cent) as TIRADS IV A.
- 12 (41.4 percent) cases of Multinodular Goitre were graded as TIRADS II and 14 (48.3 percent) cases as TIRADS III, 1 (3.4 percent) case as TIRADS IV A and 2 (6.9 percent) as TIRADS IV B.
- 4 (25 percent) cases of Hashimotos's Thyroiditis were graded as TIRADS II and 11 (68.8 percent) as TIRADS III

and 1 (6.2 percent) case as TIRADS IV A

- 3 (27.3 percent) cases of papillary carcinoma were TIRADS IV C, 2 (18.2 percent) as TIRADS V, TIRADS IV A and TIRADS IV B each and 1 (9.1 percent) case was graded as TIRADS II and TIRADS III each.
- 3 (75 percent) cases of follicular carcinoma on histopathology were graded as TIRADS IV A and 1 (25 percent) as TIRADS IVC
- 1 (100 per cent) case of anaplastic carcinoma was graded as TIRADS V

TIRADS in Benign vs Malignant

51.5 percent of all benign cases (66) on histopathology fell in to TIRADS II, 40.9 percent in TIRADS III whereas 4.5 percent in TIRADS IV A and 3 percent in TIRADS IV B.

31.2 percent of all malignant (16) cases fell in TIRADS IV A, 25 percent in TIRADS IV C, 18.8 percent in TIRADS V whereas 6.2 percent cases fell each into TIRADS II and III

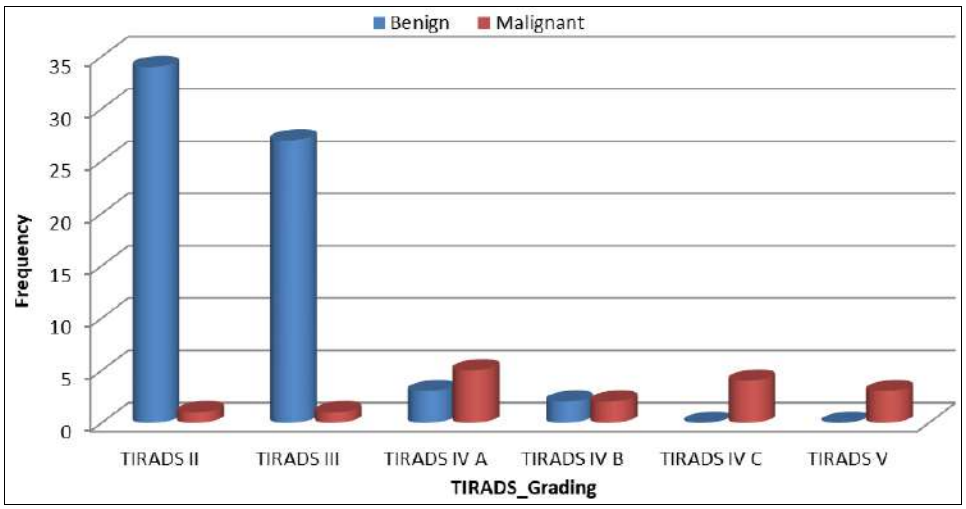

Fig 5: TIRADS in Benign Vs Malignant

Discussion

Thyroid ultrasound is an important imaging modality in the assessment of thyroid nodules both benign and malignant. No single feature on USG is sensitive enough to differentiate between benign lesion and a malignancy, hence a grading system as proposed by Horvath *et al*. Thyroid Imaging Reporting and Data System (TIRADS) is used to assess thyroid nodules.

Besides assessing the nodule USG also helps to differentiate a thyroid nodule from other cervical masses and is very useful in delineating the anatomy as opposed to radionuclide scan that provides limited anatomical information.

Various features noted on ultrasound thyroid are Solid/Cystic component, echogenicity of nodule, margins, lobulations, calcification and the shape of the thyroid nodule.

Rodney J Butch *et al.* in 1985 stated that that the major use of thyroid scanning has been to identify additional thyroid nodules when one of them is palpable [7].

In 1978 Brown M C *et al.* stated that ultrasound offers more accurate assessment of thyroid volume than either palpation or radionuclide scanning [8].

Nirad Mehta *et al.* in1994 stated that ultrasound of the thyroid is a reliable method for evaluation of solitary thyroid nodules when combined with FNAC [9].

However, no single feature on ultrasound thyroid has enough sensitivity or specificity to accurately tell that whether a nodule is benign or malignant. The documented results being variable owing to the low prevalence of malignancy in thyroid nodules

Pre-TIRADS scoring

In 2002 Papini *et al.* [10] were the first ones to report that hypoechoic nodules along with any other suspicious ultrasound feature need to undergo FNAC.

Brito *et al.* [11] studied the accuracy of ultrasound thyroid to predict malignancy in a systemic review and meta-analysis which comprised of more than 18000 nodules. According to their study taller than wide shape had maximum specificity after which followed internal calcification and infiltrating margins.

"In 2006 the SRU added that the selection of a nodule for FNAC in a multinodular thyroid should be based primarily on ultrasound characteristics rather than nodule size [12]"

In 2006 the American association of Clinical Endocrinologists (AACE) recommended that all hypoechoic thyroid nodules should undergo FNAC", with at least one additional suspicious feature on Ultrasound as described above.

In 2010 Ahn *et al.* [13] compared three sets of guidelines [Kim *et al*, AACE and SRU] and concluded- that AACE and Kim *et al.* are more accurate than SRU and recommended AACE guidelines where high specificity is required and Kim *et al.* for higher sensitivity

TIRADS

It was introduced first by Horvath *et al.* in 2009 [14]. 10 patterns of thyroid nodules on ultrasound were summarized into five categories of TIRADS.

Sine then several modifications have been made. Park *et al.* [15] suggested a TIRADS score based on multivariate logistic regression analysis and provided an equation for predicting the probability of malignancy in thyroid nodules on the basis of 12 ultrasound features.

Bonavita *et al.* [16] identified 4 particular benign thyroid patterns: cyst with colloid clot, spongiform configuration, giraffe pattern and diffuse hyperechogenicity which was 100 percent specific for thyroid nodule being benign. But this system relies on patterns rather than individual thyroid features.

Hambey *et al.* [17] suggested a scale for malignancy comprising 5 points in order to select nodules for biopsy which had following features: nodule echogenicity, calcification, internal content, nodule margin and shape, presence of hypoechoic halo and vascularity.

However, criterias for classification are not included in this system and is solely dependent on radiologist experience.

Recently Kwak *et al* [4, 5] used multivariate regression analysis and proposed a TIRADS score that looked at five risk features: microcalcifications, irregular margins, taller than wide shape, solidity and hypo echogenicity. This system is more accurate for stratification of risk and is convenient to use.

Our study included 82 patients with thyroid nodules which were predominantly female (70 females as opposed to 12 males). Out of all patients 73 were euthyroid, 4 were hyperthyroid and 5 hypothyroid. Amongst males 91.7 percent were euthyroid and 8.3 percent were hypothyroid whereas amongst females 88.6 percent were euthyroid, 5.7 percent were hyperthyroid and 5.7 percent were hypothyroid. Clinically 41 patients were found to have multinodular goiter, 16 with solitary nodule of thyroid, 13 with colloid goiter, 10 were suspicious of malignancy whereas 2 patients were suspected for autoimmune thyroiditis. FNAC was done for all the patients as routine work up and on FNAC 39 percent patients were reported to have colloid goitre, 25.6 percent with multinodular goitre, 14.6 percent with follicular lesion, 13.4 percent with papillary carcinoma, 6.1 percent with Hashimoto's thyroiditis while one case was reported to have medullary cancer.

Ultrasound Thyroid was done for all patients with TIRADS grading. Majority of the patients were in TIRADS II comprising 42.7 percent, TIRADS III was next comprising 34.7 percent, TIRADS IV A comprising 9.8 percent whereas TIRADS IV B and C comprised of 4.9 percent each and TIRADS V consisting of 3.7 percent of the cases. TIRADS II and III were taken as all benign whereas TIRADS IV and anything above as malignant. All these patients underwent surgery with majority undergoing total thyroidectomy i.e. 55 cases while 26 patients underwent hemithyroidectomy and isthmectomy was done for 1 case. Post-surgery all specimens were subjected to histopathology. On histopathology 21 cases (25.6 percent) had colloid goitre,29 cases (35.4 percent) had adenomatoid/nodular goitre, 16 cases (19.5 percent) had hashimoto's thyroiditis, 11 cases (13.4 percent) had papillary carcinoma, 4 (4.9 percent) had follicular carcinoma and one (1.2 percent) was found to have anaplastic carcinoma.

In males 41.7 percent were found to have benign pathology whereas 58.3 percent had malignant nodules. In females 87.1 percent had benign thyroid nodules whereas 12.9 percentage had malignancy. The sensitivity and specificity of TIRADS Grading was calculated taking histopathology as gold standard. In our study TIRADS grading was found to have a sensitivity of 82.35 percent, a specificity of 92.30 percent, positive predictive value of 73.68 percent and a negative predictive value of 95.24 percent.

A study conducted by Yashwanth A.S. [6] in Nitte University in 2015 reported the sensitivity being 94.87 percent, specificity 87.50 percent, positive predictive value as 95.1 percent and negative predictive value as 96.5 percent in a sample size of 55 patients with thyroid nodules.

From the results drawn from our study risk of malignancy increases from TIRADS IV A to TIRADS V. Majority of the cancers were found to be in TIRADS IV A, IV B and IV C, some were included in TIRADS V as well. Hence the ultrasound features if accurately classified according to TIRADS can point reliably towards the malignant potential of a thyroid nodule.

Conclusion

Ultrasound in evaluation of thyroid nodule is a safe, cost effective, comprehensive and repeatable noninvasive procedure. An ultrasound based TIRADS grading serves as an appropriate guide in classification of thyroid nodules.

Various conclusions drawn from our study are:

- Thyroid malignancies are more common in elder patients and have a pre disposition to male gender, although the nodules being more common in females
- TIRADS has a high sensitivity and specificity in identifying the thyroid nodule as benign or malignant where TIRADS II and III indicate benign nodules whereas TIRADS IV A and above point towards malignancy.
- TIRADS can be used to decide the timing of FNAC. In TIRADS II and III grades FNAC can be avoided and subjected only to suspicious features on Ultrasound whereas in TIRADS IV A or above it should be done mandatorily.
- In TIRADS II and III conservative surgical approach such as hemithyroidectomy can be planned when the pathology is limited to single lobe with a regular follow up.
- TIRADS grading when combined with FNAC serves as a better diagnostic tool in pre-operative evaluation and management of thyroid nodules.

Recommendation

TIRADS is recommended in line with BIRADS for the pre-operative diagnostic work up of clinically palpable thyroid nodules with fair amount of sensitivity and specificity.

Limitation

When used alone TIRADS has a lower sensitivity and specificity as compared to FNAC, hence should be used in conjugation with FNAC for appropriate results.

Summary

For those fulfilling the inclusion criteria patients details such as name, age, sex, IP number were tabulated along with relevant clinical diagnosis, thyroid function tests and USG of thyroid nodules with TIRADS grading as proposed by Horvath *et al*. and modified by Kwak *et al*. FNAC was done for all thyroid nodules included in the study.

Total thyroidectomy or hemithyroidectomy was done for majority of the cases with isthmectomy for one case of anaplastic carcinoma. All post op specimens were subjected to histopathology and once reported, the results were compared to TIRADS grading and conclusions drawn. Based on the results drawn a TIRADS grading on ultrasound thyroid is recommended for all clinically palpable nodules

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