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EVALUATION OF THYROID NODULES ON HIGH RESOLUTION ULTRASOUND AND COLOUR DOPPLER WITH TIRADS CLASSIFICATION AND ITS CORRELATION WITH FINE NEEDLE ASPIRATION CYTOLOGY FINDINGS

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ABSTRACT

Background: Thyroid gland is superficially located endocrine gland. Thyroid gland is affected by various pathologies starting from diffuse enlargement including nodular lesions, thyroiditis, and malignancies. USG is a non invasive, easily available and low cost investigating modality and is most common and the most useful to detect its pathology. The study was conducted with the objective to evaluate the gray scale features and colour doppler findings of thyroid nodules with thyroid imaging reporting and data system (TIRADS), to characterize the thyroid nodules into benign and malignant; to compare gray scale, colour doppler, and thyroid imaging reporting and data system (TIRADS) findings with fine needle aspiration cytology (FNAC) findings by the use of the bethesda system for reporting thyroid cytopathology (TBSRTC). We will also like to determine sensitivity, specificity and risk of malignancy in concluding benign and malignant lesions on high-resolution ultrasound, colour doppler and thyroid imaging reporting and data system findings. **Method:** This was a prospective study done on 100 patients that referred to the Department of Radiodiagnosis, Gauhati Medical College and Hospital, Guwahati, Assam from 1st of August, 2019 to 31st of July, 2020. All the patients with palpable thyroid nodules with or without symptoms were studied under gray scale, colour Doppler USG and then FNAC was performed. **Results:** Majority of the patients were females in the age group of 21-30 years and mean age of our study was 33.94. USG was found to be useful to differentiate benign thyroid nodules from malignant thyroid nodules. The cases were correlated with FNAC findings. It was found that there was significant correlation between the ultrasound features and FNAC results. The risk stratification for malignancy under TIRADS was also found to have significant correlation with FNAC results. **Conclusion:** USG is useful to rule out malignant lesions. However, with the addition of both USG and FNAC to rule out the malignant etiology in thyroid nodules then it will play a better role in management of patients.

KEYWORDS: USG, Colour Doppler, FNAC, TIRADS, Thyroid.

INTRODUCTION

The thyroid is a bilobed structure located within the lower neck and is draped anteriorly around the trachea.[1] The left and right lobes are located immediately to the left and right of the trachea respectively, and are connected anteriorly by a thin rim of thyroid tissue known as the isthmus. The internal carotid arteries and internal jugular veins are located posterolateral to the thyroid lobes, whereas the strap muscles of the neck are located anteriorly.[2] The mature thyroid gland is an H- or U-shaped endocrine organ located in the base of the neck.[3]

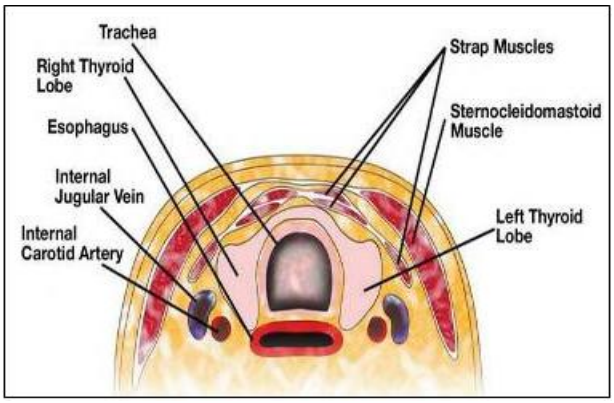

Figure 1.1: Drawing illustrates the cross-sectional anatomy of the thyroid and adjacent soft tissue structures. (Ref-The Thyroid: Review of Imaging

Features and Biopsy Techniques with Radiologic-Pathologic Correlation- Radio Graphics 2014).

As the thyroid gland is superficially located so, high resolution real-time gray scale and colour doppler sonography can demonstrate normal thyroid anatomy and pathologic conditions with remarkable clarity. As a result, ultrasound plays an increasingly important role in the diagnostic evaluation of thyroid disease, although it is only one of several diagnostic methods currently available. To use ultrasound effectively and economically, it is important to understand its current capabilities and limitations.[4]

Nodules in the thyroid are very common and their prevalence rates are largely dependent on the identification method. By just palpation, the prevalence rate ranges from 4 to 7%, whereas by using the imaging modalities such as the high-resolution ultrasonogram, it ranges from 20 to 76% in the adult population.[5] The nodules discovered with radiographic studies are called thyroid incidentalomas.[6] The majority of the nodules are clinically occult but readily detected by high-resolution Ultrasonography (USG).[4],[7],[8]

Thyroid cancer is rare and accounts for < 1% of all malignant neoplasms. It has a good long-term prognosis after surgical excision. The high prevalence of thyroid nodules in the general population calls for a clear strategy to identify patients in whom surgical excision is genuinely indicated as opposed to those who can be managed conservatively.[9]

The correlation between imaging methods and the prevalence reported at surgery and autopsy ranges between 50 and 65%.[10]

With American Thyroid Association and its current management guidelines state that diagnostic USG should be performed in all patients with thyroid nodules and fine needle aspiration (FNA) in potentially malignant nodules. Various features seen on USG, such as irregular margins, hypoechogenicity, absence of a surrounding halo, calcifications, and solid internal composition, have been investigated as predictors of malignancy.[11]

The purpose of this study is to evaluate the thyroid nodules using gray scale USG with colour doppler and also with the help of thyroid imaging reporting and data system (TIRADS) and to correlate the characteristics of benign and malignant nodules with the fine needle aspiration cytology (FNAC) by the use of the bethesda system for reporting thyroid cytopathology (TBSRTC). In our study we also evaluated the risk of malignancy associated with each TIRADS score.

AIMS AND OBJECTIVES

1. To evaluate the gray scale features and colour doppler findings of thyroid nodules with thyroid imaging reporting and data system (TIRADS).
2. To characterize the thyroid nodules into benign and malignant based on gray scale, colour doppler and thyroid imaging reporting and data system (TIRADS) findings.
3. To compare gray scale, colour doppler, and thyroid imaging reporting and data system (TIRADS) findings with fine needle aspiration cytology (FNAC) findings by the use of the bethesda system for reporting thyroid cytopathology (TBSRTC).
4. To determine sensitivity, specificity and risk of malignancy in concluding benign and malignant lesions on high-resolution ultrasound, colour doppler and thyroid imaging reporting and data system findings.

METHODS

The data for the study is collected from patients referred to the Department of Radiodiagnosis, Gauhati Medical College and Hospital, Guwahati, Assam.

Study Period: The study was performed during the period from 1st of August, 2019 to 31st of July, 2020 for a duration of twelve months. Written and informed consent was obtained from the subjects before initiating the study.

Study Design: Hospital-based prospective study with due approval of the Institutional ethical committee, Gauhati Medical College and Hospital (GMCH).

Sampling Procedure: Purposive sampling.

Sample Size: A total of 100 patients. The study population is a mixture of the male and female population.

This study is a hospital-based prospective study carried out on 100 patients visiting the ENT OPD, Gauhati Medical College and Hospital (GMCH) and referred to the Department of Radiodiagnosis, Gauhati Medical College and Hospital (GMCH) for a period of the 12-months duration.

Case Selection: Patients attending ENT OPD and referring to the Department of Radiodiagnosis, Gauhati Medical College and Hospital (GMCH) with patients with palpable thyroid nodules, without any symptoms and patients with palpable thyroid nodules, associated with symptoms were chosen as cases for our study. Complete clinical history of the patients was taken.

Patient Preparation: After taking a detailed history of the cases, the procedure of ultrasonography of thyroid was explained to the patient. The patients who need fine needle aspiration cytology (FNAC) was decided and was explained to the patient and due consent was taken.

Inclusion Criteria: Patients with symptoms of a swelling in the anterior aspect of the neck were chosen for the study if they have met the following criteria.

- Patients with palpable thyroid nodules, without any symptoms.
- Patients with palpable thyroid nodules, associated with symptoms.

EXCLUSION CRITERIA

- Neck swelling other than thyroid.
- Children below 12 years.
- Previously diagnosed cases of benign disease or thyroid malignancies.
- Non co-operative patients or patients who don't give consent for the fine needle aspiration cytology.
- Critically ill or anxious patients.
- Patients with bleeding diathesis.
- Patients with skin infection at the site of aspiration.
- Lost for follow up.

RESULTS

Ultrasound characteristics of the nodules.

Sl. No.	Characteristics of nodules	No. of Patients	Percentage
1	Composition		
	Cystic	4	4
	Spongiform	2	2
	Mixed	80	80
	Solid	14	14
2	Echogenicity		
	Anechoic	6	6
	Hyperechoic /Isoechoic	87	87
	Hypoechoic	5	5
	Very hypoechoic	2	2
3	Halo		
	Thin complete halo	11	11
	Thick incomplete halo	3	3
4	Margin		
	Well defined/Smooth	93	93
	Ill-defined	3	3
	Lobulated/Irregular	3	3
	Extra thyroidal	1	1
	extension		
5	Calcification		
	None/ Large comet-tail artifacts	82	82
	Macrocalcification	11	11
	Peripheral/rim calcification	2	2
	Punctate echogenic foci	5	5
6	Doppler		
	Peripheral flow pattern	10	10
	Both together (peripheral and internal flow)	63	63
	No significant vascularity	27	27
	Thyroid inferno (PSV > 70cm/s)	0	0
7	Shape		
	Wider than tall	97	97
	Taller than wide	3	3
8	Others		
	Vascular encasement	1	1
	Cervical lymphadenopathy	3	3

Risk of Malignancy In Each Tirads Category

Bethesda I		Bethesda II	Bethesda III	Bethesda IV	Bethesda V	Bethesda VI	Total
TR I	4	2	--	-	-	-	6
TR II	5	54	2	-	1	-	62
TR III	1	19	2	1	-	-	23
TR IV	-	1	-	2	1	1	5
TR V	-	-	-	1	1	2	4
Total	10	76	4	4	3	3	100

Sensitivity, Specificity, Ppv And Npv

Tirads Classification	Fnac Results		Total
	Positive for Malignancy	Negative for Malignancy	
Positive For Malignancy			
Count	8	1	9
% of Total	8%	1%	9%
Negative For Malignancy			
Count	2	89	91
% of Total	2%	89%	91%
Total			
Count	10	90	100
% of Total	10%	90%	100%

Sensitivity= 80%, Specificity= 98.8% Accuracy = 97%
PPV = 88.8% NPV = 97.8%

Risk of Malignancy In Each Different Tirads Category

TIRADS	Risk of malignancy
TR 1	0%
TR 2	0%
TR 3	4.3%
TR 4	83.3%
TR 5	100%

Comparison of Our Study with Other Studies

	Our study	Gokulakrishnan Periakaruppan et al.[12]	Eleonora Horvathet al.[10]	Moifo et al.[13]	Kwak et al.[14]
TIRADS 1	0%	0%	0%	0%	0%
TIRADS 2	0%	0%	0%	0%	0%
TIRADS 3	4.3%	2.2%	1.79%	2.2%	1.7%
TIRADS 4	83.3%	38.5%	76.13%	5.9%-57.9%	3.3 %–72.4%
TIRADS 5	100%	77.8%	98.85%	100%	87.5%

Comparative statistical values on tirads –fnac correlation

Author (year)	Sensitivity % age	Specificity % age	PPV %age	NPV %age
Eleonora Horvath et al.[10]	99.6	74.35	82.1	99.4
R. M. Singaporewalla et al.[15]	70.6	90.4	60	93.8
Ashraf M Abdelkader et al.[16]	76.9	91.3	71.4	76.4
Gokulakrishnan Periakaruppan et al.[12]	92.3	94.15	54.54	99.38
Present Study (2020)	80	98.8	88.8	97.8

DISCUSSION

The present series of the study consisted of 100 cases who presented, predominantly with thyroid swelling. Certain points related to the subject are considered in the discussion.

1. In the study conducted by us, out of 100 patients, the majorities (85%) were female and the rest (15%) were male. Thyroid nodules are found to be 5.6 times more common in females than males. In a study done by Mazzaferri et al.[17] they concluded that thyroid nodules are 4 times more common in women than men.
2. The mean age of thyroid nodules in our study was 33.94. There were total of 10 cases (10%) diagnosed as malignant nodules on FNAC.
3. The majority of the nodules we assessed were categorized under TIRADS II (62%) and TIRADS III (23%). Followed by TIRADS I (6%), TIRADS IV (5%), and lastly only a few of the nodules were categorized under TIRADS V (4%). Gokulakrishnan Periakaruppan et al.[12] studied among 184 patients and they concluded that, out of the 184 nodules, 117 were categorized under TIRADS 2, 45 were classified under TIRADS 3, 13 were classified under TIRADS 4, and 9 were classified under TIRADS 5.
4. Out of the 100 patients in our study, all 100 underwent FNAC, 3 underwent FNAC of cervical lymphadenopathy along with FNAC of the thyroid nodule. Maximum of the nodules were diagnosed as Bethesda II (76%), followed by Bethesda I (10%), Bethesda III (4%), Bethesda IV (4%), Bethesda V (3%) and Bethesda VI (3%).
5. The final diagnoses of the nodules were made with the help of the Bethesda system for reporting thyroid cytopathology. Majority of the nodules were diagnosed as a colloid nodule (43%), followed by

Multinodular goiter (34%), adenomatoid nodule (13%), papillary carcinoma (5%), follicular neoplasm (3%), Hurthle cell carcinoma (1%) and anaplastic carcinoma (1%). In a study conducted by Baby Manoj PP et al. (18) out of the 25 patients, nodules of 4 patients(16%) were malignant, 13 patients(48%) were benign, and 8 patients(36%) were indeterminate on HRUSG. Pathologically, 20 (80%) were benign and 5 (20%) were malignant. All the four pathologically proved malignant nodules were correctly diagnosed as malignant nodules by HRUSG. Out of the 13 benign nodules, 1 proved to be malignant on pathology as papillary carcinoma. The most common benign pathology in our study was benign colloid goiter seen in 60% cases. Follicular adenoma was seen in 12% and thyroiditis in 8% of patients.

6. We categorized 6 cases (6%) in TIRADS I. Among 6 cases (6%), 4 cases (4%) were finally categorized in Bethesda I in the FNAC examination and the remaining 2 cases (2%) were came out to be Bethesda II. All 6 cases (6%) were finally diagnosed as benign nodules.
7. In our study, 62 cases (62%) were categorized in TIRADS II. Among 62 cases, 5 cases (5%) came out to be Bethesda I in FNAC, 54 cases (54%) as Bethesda II, 2 cases (2%) as Bethesda III and 1 case (1%) came out as Bethesda V. Among 62 cases (62%) in TIRADS II are considered benign and on FNAC among 62 cases (62%), 61 cases (61%) came as benign, however, 1 case (1%) came out as suspicious for malignancy.
8. Among 23 cases (23%), we categorized under TIRADS III. Out of 23 cases (23%), 1 case (1%) came out as Bethesda I, 19 cases (19%) came out as Bethesda II, 2 cases (2%) came out as Bethesda III and only 1 case (1%) came out as Bethesda IV. We considered all cases to be benign on USG however, on FNAC, one case (1%) came out as suspicious for follicular neoplasm.
9. Out of 100 cases in our study, we found 5 cases (5%) to be categorized under TIRADS IV. Out of the 5 cases (5%), 2 cases (2%) came out as Bethesda IV on FNAC, 1 case (1%) as Bethesda V, 1 case (1%) as Bethesda VI and 1 case (1%) came out to be Bethesda II. Under TIRADS IV we considered all 5 cases (5%) to be malignant nodules, however on FNAC 1 case (1%) came out as benign.
10. Out of 100 cases in our study, we categorized 4 cases (4%) under TIRADS V. On FNAC, 1 of the case (1%) came out to be Bethesda IV, 1 case (1 %) to be Bethesda V and 2 cases (2%) to be Bethesda VI. All cases suspected to be malignant on TIRADS, came out as malignant on FNAC.
11. From our study, on the correlation of the thyroid nodules based on USG and FNAC results, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were found to be 80%, 98.8%, 88.8%, 97.8%, and 97% respectively.
12. The receiver operating characteristic (ROC) curve for TIRADS data considering FNAC as was evaluated, the curve was found in the upper left quadrant. The accuracy of the correlation of the study is evaluated with the area under the curve. The area under the curve was found to be 0.988 which is suggestive of a very good correlation between TIRADS and FNAC results. In the study conducted by Gokulakrishnan Periakaruppan et al.[12] the area under the curve was0.932 in the ROC curve, which indicated that the results are very good.
13. Upon the use of the chi-square test to correlate the findings of TIRADS and FNAC, the chi-square statistic is 68.3896. The p- value is < 0.00001. (Significant at $p < .05$). A significant association was noticed in our study between TIRADS and Bethesda system for reporting thyroid Cytopathology (TBSRTC). The Cohen's kappa coefficient value in our study found to be 0.83 which signifies almost perfect agreement between US diagnosis and FNAC diagnosis.
14. The risk of malignancy in our study in TIRADS I, TIRADS II, TIRADS III, TIRADS IV, and TIRADS V were 0%, 0%, 4.3%, 83.3%, and 100 %. The risk of malignancy was highest found in TIRADS V however there is no risk of malignancy found in TIRADS I and TIRADS II.

ILLUSTRATIONS (FIGURES)

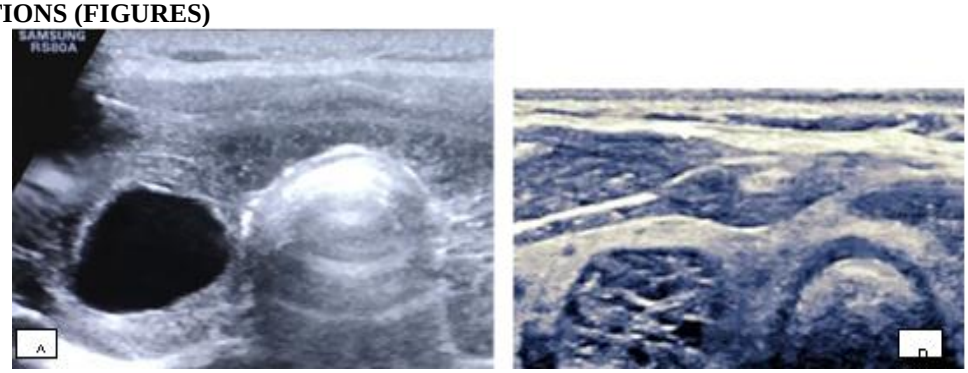

Figure I: Image A, US image demonstrating a well defined (score 0), cystic (score 0), wider than tall (score 0) nodule in right lobe of thyroid without any calcification/comet tail artefact representing TIRADS I nodule (Total score of 0).

Image B, US image demonstrating a well defined (score 0), spongiform (score 0), wider than tall (score 0) nodule in right lobe of thyroid without any calcification/comet tail artefact representing TIRADS I nodule (Total score of 0).

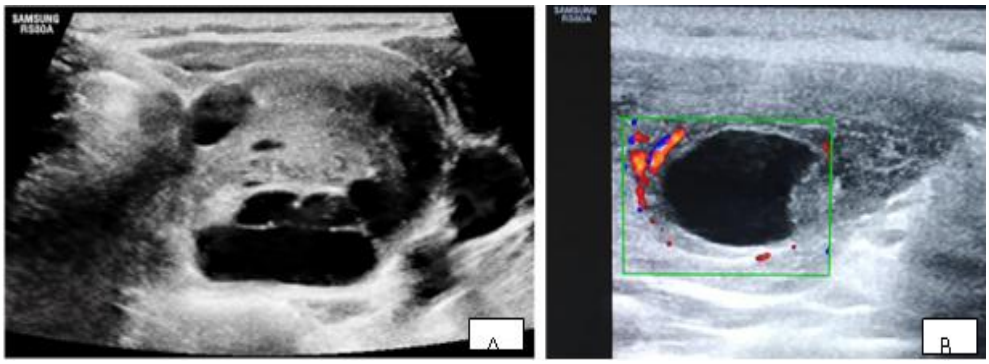

Figure II: Image A, US image demonstrating a well defined (score 0), mixed solid cystic (score 1) with hyperechoic/ isoechoic mural component (score 1), wider than tall (score 0) nodule in left lobe of thyroid without any calcification/comet tail artefact representing TIRADS II nodule (Total score of 2).
Image B, US image demonstrating a well defined (score 0), mixed solid cystic (score1) with small hyperechoic/ isoechoic mural component (score 1), wider than tall (score 0) nodule in left lobe of thyroid without any calcification/comet tail artefact representing TIRADS II nodule (Total score of 2). There is peripheral vascularity seen on colour doppler study.

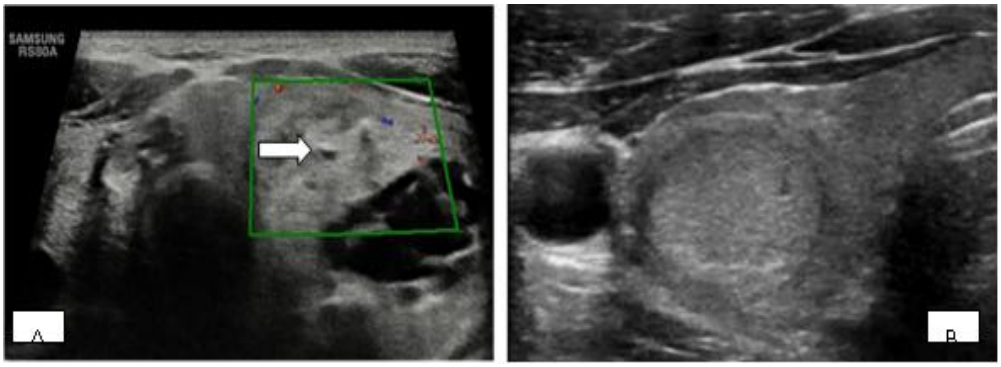

Figure III: Image A, US image demonstrating multiple nodules in both lobes of thyroid. The nodule of the left lobe (arrow) is well defined (score 0), mixed solid cystic (score 1) with hyperechoic/ isoechoic mural component (score 1), wider than tall (score 0) with areas of macrocalcification (score 1) representing TIRADS III nodule (Total score of 3). There is minimal internal vascularity seen within the nodule.
Image B, US image demonstrating a well defined (score 0), solid (score 2), hyperechoic/ isoechoic (score 1), wider than tall (score 0) nodule in right lobe of thyroid without any calcification/comet tail artefact (score 0) representing TIRADS III nodule (Total score of 3).

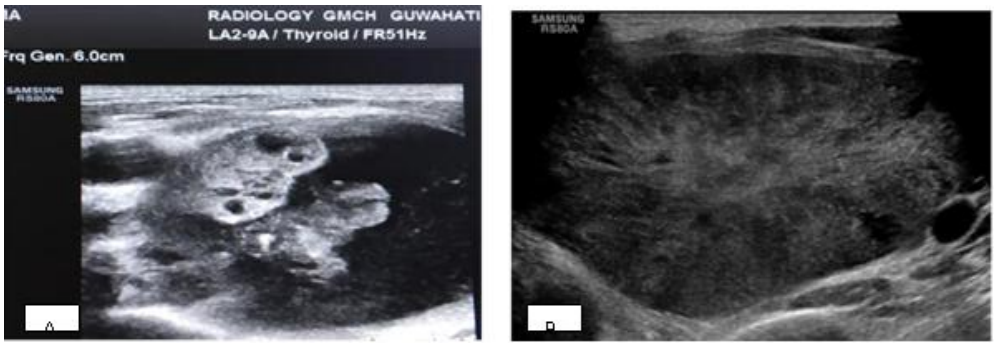

Figure IV: Image A, US image demonstrating a well defined (score 0), mixed solid cystic (score 1) with hyperechoic/ isoechoic mural component (score 1), wider than tall (score 0) nodule in right lobe of thyroid with areas of punctate echogenic foci (score 3) representing TIRADS IV nodule (Total score of 5).
Image B, US image demonstrating a well defined (score 0), solid (score 2), hypoechoic (score 2), wider than tall (score 0) nodule in left lobe of thyroid without any calcification/comet tail artefact (score 0) representing TIRADS IV nodule (Total score of 4).

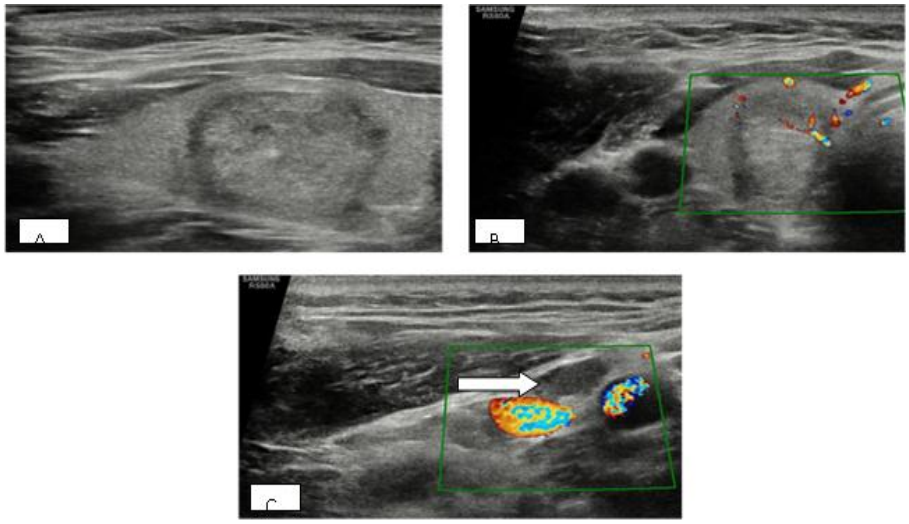

Figure V: Image A, US image demonstrating a well defined (score 0), solid (score 2), hyperechoic/ isoechoic (score 1), taller than wide (score 3) nodule in right lobe of thyroid with areas of punctate echogenic foci (score 3) representing TIRADS V nodule (arrow) (Total score of 9). Image B, US image of the same patient demonstrating both peripheral and internal vascularity on colour doppler study.Image C, US image of the same patient demonstrating prominent ipsilateral cervical lymph node (arrow).

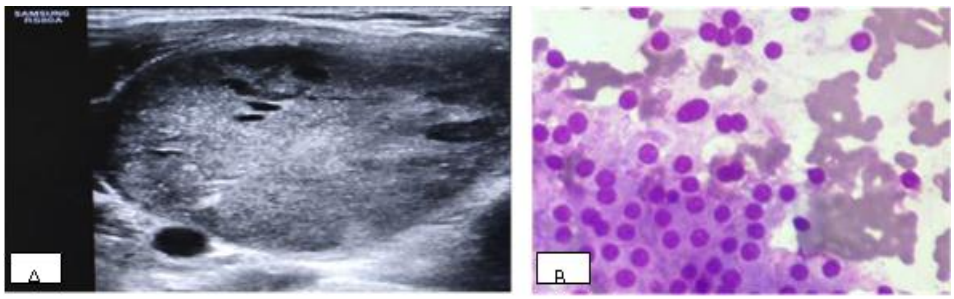

Figure VI: Image A, US image demonstrating a colloid nodule in left lobe of thyroid.Image B, Corresponding cytopathology image showing scattered bits of colloid and normal follicular cells suggesting colloid nodule.

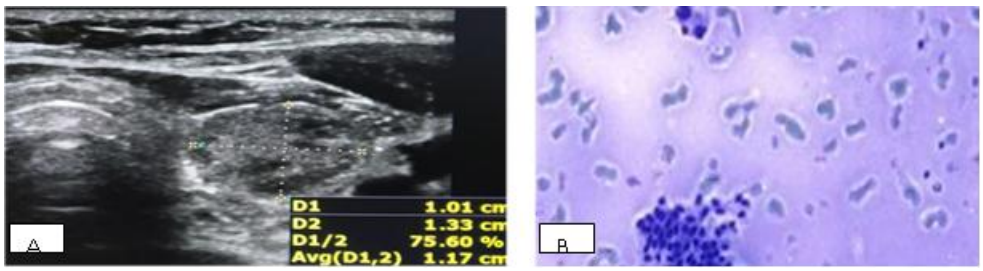

Figure VII: Image A, US image demonstrating an adenomatoid nodule in right lobe of thyroid. Image B, Corresponding cytopathology image showing evenly spaced honeycomb arrangement of follicular cells representing macrofollicles. Features are suggestive of adenomatoid thyroid nodule.

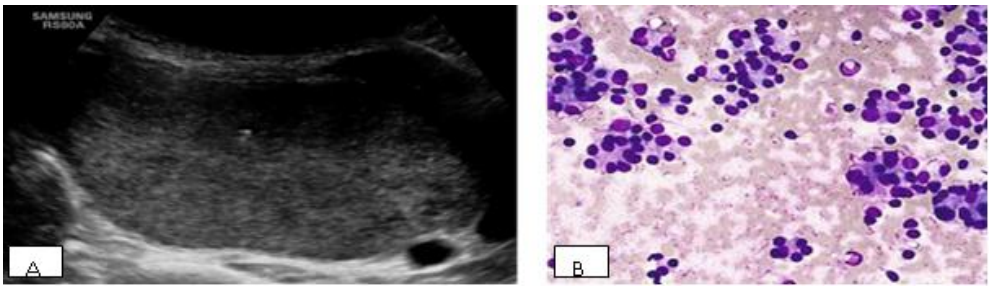

Figure VIII: Image A, US image demonstrating a nodule in left lobe of thyroid proven to be follicular neoplasm. Image B, Corresponding cytopathology image showing many uniform sizes, repetitive microfollicles with nuclear pleomorphism suggestive of follicular neoplasm.

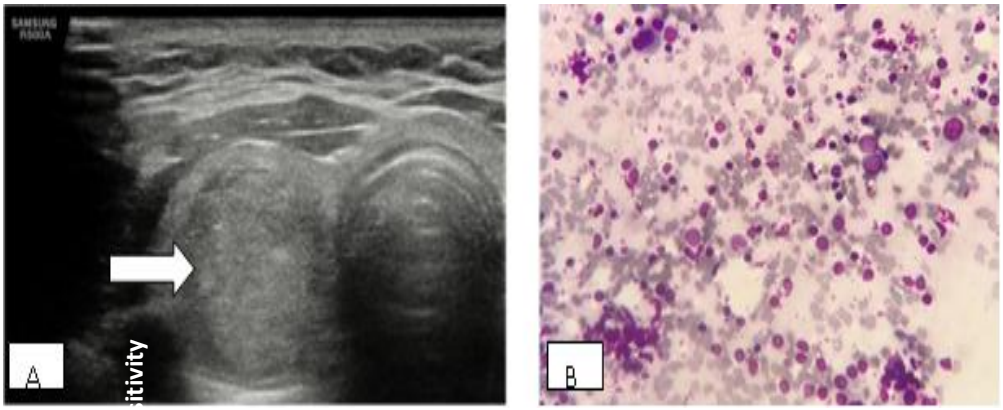

Figure IX: Image A, US image demonstrating a nodule in right lobe of thyroid (arrow) proven to be papillary carcinoma.Image B, Corresponding cytopathology image showing papilla and intranuclear cytoplasmic inclusions suggestive of papillary carcinoma.

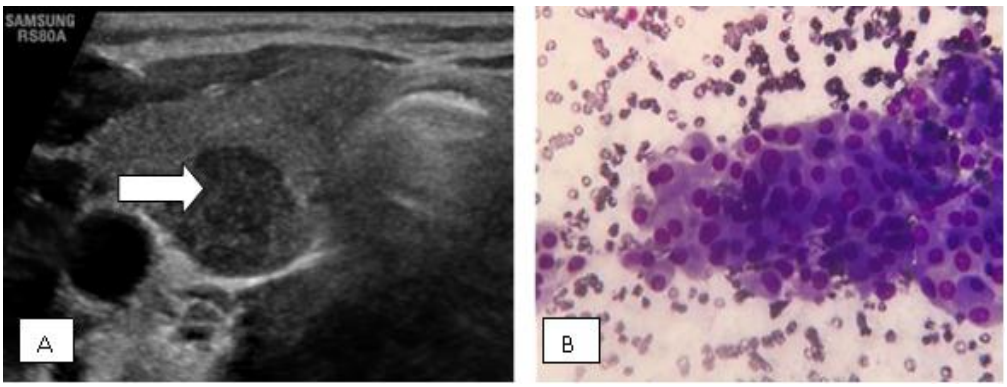

Figure X: Image A, US image demonstrating a nodule in right lobe of thyroid (arrow) proven to be Hurthle cell carcinoma. Image B, Corresponding cytopathology image showing hurthle cell groups with nuclear budding in the centre of hurthle cell group.

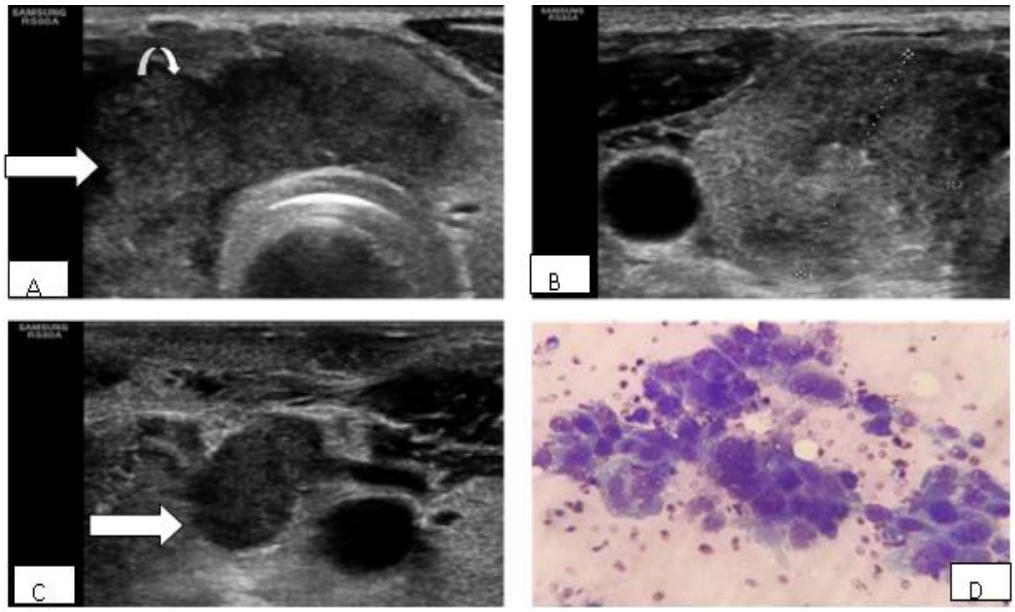

Figure XI: Image A, B: US images demonstrating a nodule in right lobe and isthmus of thyroid (solid arrow) with invasion to the adjacent structure (curved arrow) proven to be anaplastic carcinoma. Image C, US image of the same patient showing ipsilateral enlarged cervical lymph node (arrow). Image D, Corresponding cytopathology image showing highly pleomorphic large cells arranged diffusely with round to oval nuclei, coarse chromatin and moderate to abundant cytoplasm in the background of inflammatory cells suggesting anaplastic carcinoma.

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