Original Article

Thyroid Cytology Evaluation Based on the Bethesda System with Clinico-Morphological Correlation

Dimple Mehrotra*, Anita A.M., Sainath K. Andola and Anuradha G. Patil

Department of Pathology, M.R. Medical College, Kalaburagi, Karnataka, India

Keywords: *Thyroid, Cytology, TBSRTC, Histopathology, Accuracy*

ABSTRACT

Background: FNAC of Thyroid gland is a widely accepted and accurate method for evaluation of thyroid nodules. In the past, terminology of reporting of Thyroid FNACs varied markedly, which made it difficult for the clinicians to interpret the reports and decide the management protocol. To cater to this issue, The Bethesda System of Reporting Thyroid Cytology was proposed with six diagnostic categories and appropriate management protocol for each category. This study was undertaken to categorize FNAC of Thyroid lesions according to the Bethesda System of Reporting Thyroid Cytology (TBSRTC) and to correlate with Histopathology wherever feasible.

Methods: The present study includes 175 Thyroid FNAC cases studied over a 3-year period (August 2012- July 2015). These cases were categorized according to TBSRTC and the cytological diagnosis was correlated with histopathology wherever it was available. The Sensitivity, Specificity, Positive Predictive value (PPV), Negative Predictive value (NPV) and Accuracy was also calculated.

Result: A total of 175 Thyroid FNAC cases were collected over 3 years. The mean age was 36.18 years and the male to female ratio was 1:9.3. Percentage of cases in Category I to VI according to the Bethesda system of reporting Thyroid cytology were 4.57%, 68.58%, 5.72%, 17.14%, 1.14% and 2.85% respectively. Histopathological details were available in 19.42% of the cases. The sensitivity, specificity, PPV, NPV and accuracy were 69.23%, 89.47%, 81.81%, 80.95% and 81.25% respectively.

Conclusion: The findings of the present study were consistent with other studies that used TBSRTC.

***Corresponding author:**
Dr. Dimple Mehrotra, A-32, Nanda Marg, Adarsh Nagar, Delhi 110033, INDIA
Phone: +91 -9900415163, 9810139357
Email: drdimplemehrotra@gmail.com

Introduction

Thyroid cytology has been regarded as the first line diagnostic procedure for assessment of thyroid lesions. Cytological reporting formats used in the past ranged from histology-equivalent categories to categories like equivocal, inconclusive, indeterminate, atypical, suspicious, uncertain, malignancy suspicious, possibly neoplastic, possibly malignant and probably malignant to report thyroid aspirates that fell between benign and malignant diagnostic categories. These made it difficult for clinicians to interpret the reports. [1]

To address terminology related issues, the National Cancer Institute (NCI) hosted the NCI Thyroid FNA State of the Science Conference and proposed the Bethesda System for Reporting Thyroid Cytopathology. This was a standardized system with six general diagnostic categories and clear categorical nomenclature including malignancy risks. [2]

This study was undertaken to classify thyroid lesions based on the Bethesda system of reporting Thyroid Cytology, which would help in planning prognostic and therapeutic approaches. The cytological diagnosis was also correlated with histopathology wherever available.

Materials And Methods

The present study was conducted in the Department of Pathology, Basaveshwar Teaching and General Hospital attached to M.R. Medical College, Kalaburagi, Karnataka, after taking approval from the Institutional Ethics Committee. The study includes 1 year retrospective (August 2012 to July 2013) and 2 years prospective (August 2013 to July 2015). All the patients with clinically diagnosed Thyroid lesions referred for Thyroid FNAC were included in the study. Neck swellings other than thyroid swellings and patients having known Bleeding diathesis were excluded. Both non aspiration and aspiration techniques were followed depending on the nature of the thyroid swelling. In special cases such as when the lesions were difficult to localize, Ultrasonography-guided FNAC was done after taking informed consent from the patient for FNAC. Slides were prepared by smearing the aspirate and stained with May Grunwald Giemsa (MGG) and Haematoxylin and Eosin (H&E). In doubtful cases, such as those where malignancy was suspected clinically and studying the nuclear details was important, wet smears were prepared and stained with Papanicolaou stain (PAP). Slides for wet smears were fixed in 95% ethyl alcohol, while the others were air dried. Stained smears were studied under light microscopy.

The cases in which surgical intervention was decided upon by the surgeon based on the thyroid cytology report were closely followed. The post-operative specimen was received in 10% formalin in fresh state and allowed to fix for 24 hours. Detailed gross examination was done and bits were given. Paraffin embedded H&E stained sections were obtained and studied under light microscopy.

Cytological diagnosis was correlated with the histopathology and the efficacy of FNAC was estimated by using the methodology of Galen and Gambino [3] as follows:-

$$\text{Sensitivity} = \frac{TP}{Tp + FN} X100$$

$$\text{Specificity} = \frac{TN}{TN + FP} X100$$

$$\text{Positive Predictive Value (PPV)} = \frac{TP}{TP + FP} X100$$

$$\text{Negative Predictive Value (NPV)} = \frac{TN}{TN + FN} X100$$

$$\text{Accuracy/ Efficacy} = \frac{TP + TN}{TP + FP + TN + FN} X100$$

[TP = True Positive, FP = False Positive, TN = True Negative, FN = False Negative]

The statistical values are interdependent statistical concepts indicating the accuracy of results.

Results

In the present study, 175 cases of thyroid FNAC were received. These were categorized according to the Bethesda system of reporting thyroid cytology into 6 categories. Majority of the cases were received in the period of August 2014 to July 2015 (38.28%). Age of the patients ranged from 5 to 85yrs with the mean age of 36.29years. Maximum number of cases was seen in the age group of 21-30years (29.14%). There was a female preponderance with male to female ratio being 1: 9.3. The most common complaint was painless swelling in front of neck which was seen in all the patients who presented with thyroid swellings and the other presenting complaints are shown in Table1. In majority of the cases the duration of the thyroid swelling was in the range of 0-3 months (38.8%). The right lobe of thyroid was involved in majority of the cases (34.8%). Size of the swelling: ranged from 2x1cms to 12x7cms. The nature of the swelling was firm in most of the cases (44%).

In majority of the cases direct unguided FNAC was performed (95%). The ratio between Direct: USG guided

was 19:1. In majority of the cases the aspiration technique of FNAC was employed (71%). The ratio between Aspiration: Non Aspiration was 2.4: 1. Amount of aspirate ranged from 0.5ml to 10 ml**.** In majority of the cases the aspirate was hemorrhagic (62%). The ratio between hemorrhagic: dark brown was 1.6: 1.These 175 cases were reported according to The Bethesda System of Reporting Thyroid Cytology.

Category I –Non Diagnostic or Unsatisfactory included 8/175 cases (4.57%). Out of which in 5 cases only cyst fluid was aspirated and in 3 the aspirate was hemorrhagic and acellular.

Category II – Benign included 120/175 cases (68.57%). Majority of the cases in Category II were Benign Follicular Nodule (Colloid nodule/ Adenomatoid nodule) accounting for 91/120 cases (75.8%). This was followed by Hashimoto/ Lymphocytic thyroiditis with 26/120 (21.6%) and finally Granulomatous thyroiditis with 3/120 (2.6%).

Histopathological details were available in 21/91 cases of Benign Follicular Nodule, out of which positive correlation was found in 18 cases.

Category III- Atypia of Undetermined Significance (AUS) Or Follicular Lesion of Undetermined Significance (FLUS) included 10/175 cases (5.7%).

Category IV- Follicular Neoplasm (FN) or Suspicious for a Follicular Neoplasm (SFN) included 30/175 cases (17.14%). In this category, 2 cases were reported as Hurthle cell neoplasm. Histopathological details were available in 11/30 cases, out of which positive correlation was found in 9 cases.

Category V- Suspicious For Malignancy (SFM) included 2/175 cases (1.14%). Resected Surgical specimen was received in 1 case in which the histopathological findings favoured a diagnosis of Follicular Adenoma.

Category VI- Malignant included 5/175 cases (2.86 %). Out of the 5 cases, 2 cases were diagnosed as Papillary carcinoma and the remaining 3 cases as Anaplastic carcinoma.

Resected Surgical specimen was received in 1 case the cytological and histopathological findings of which correlated with a diagnosis of Papillary carcinoma.

The final categorization of these 175 cases according to TBSRTC and the cytohistopathological correlation in 34 cases which underwent surgery is shown in Table 2.

Cytological features of each of these Bethesda categories are shown in Fig.1. The gross and microscopic features of some of the cases are shown in Fig.2.

Statistical Analysis of the above data reveals that the number of True Positive (TP), True Negative (TN), False Positive (FP) and False Negative (FN) was 11 (32%), 18 (53%), 2 (6%) and 3 (9%) respectively. On applying Chi-square Test, The two-sided P value was 0.0002, which is considered extremely significant. The row/column association was statistically significant. Chi-square statistic (with Yates correction) was 13.622 and Degree of freedom was 1. The Accuracy of Thyroid FNAC in correctly diagnosing malignancy was 85.29%. Hence, the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of Thyroid FNAC in detecting malignancy were 78.57%, 90%, 84.62%, 85.71% and 85.29% respectively.

Discussion

FNAC has an extremely important role in the evaluation of thyroid nodules or swellings. The present study was undertaken to categorize Thyroid FNAC cases according to the Bethesda system of reporting Thyroid cytology so as to improve communication between the pathologist and surgeon in deciding the treatment modality for the patients and avoid unnecessary surgeries. The FNAC diagnosis of these cases was also correlated with Thyroid Function Tests and Histopathology wherever feasible. Thereby, providing data for the statistical analysis in these cases i.e., sensitivity, specificity, positive predictive value, negative predictive value and accuracy of Thyroid FNAC in detecting malignancy.

The mean age in the present study was 36.29 years, which correlates well with the study conducted by Naz et al [4] where the mean age at presentation was 39.7 years as shown in Table 3.

The Male: Female ratio in the present study was 1: 9.3, which correlates well with the study conducted by Richmond et al [5] who reported a Male: Female ratio of 1:6.1 as shown in Table 4.

In the present study, all of the cases presented with a swelling in front of the neck followed by dysphagia, pain and tenderness over the swelling, whereas, in the study conducted by Richmond et al [5] the majority of cases presented with dysphagia followed by enlarging nodule and hoarseness.

In the present study, majority of the cases were in Category II followed by Category IV which correlates well with the studies conducted by Yang et al [6], Yassa et al [7] and Joshi et al [8] as shown in Table 5.

The accuracy in the present study was 85.29% , which is comparable to the accuracy reported by Ko et al [9] and Kessler et al [10] as, 84.4% and 87% respectively as shown in Table 6.

Table 1: Clinical Features

Complaints	Number Of Cases
Swelling infront of the Neck	175
Dyspnoea	2
Change of Voice	3
Dysphagia / Difficulty in swallowing	13
Weight Gain	2
Weight Loss	2
Palpitation and Anxiety	3
Pain and Tenderness on palpation	9
Weakness	2
Tremors	3
Fever	5
Referred pain- Ear, Shoulder	3
Exophthalmos	1
Polymenorrhoea	1
Cold intolerance	5
Sweating	2
Numbness in hands and feet	1

Table 2: TBSRTC Category wise distribution of cases and their Cytohistopathological correlation.

Bethesda Category	No. of cases in the category	No. of cases in which HP available	FNAC diagnosis	Histopathological diagnosis	
I	8	0	-	-	
II	120	21	BFN	13	CG
				5	MNG
				3	FA
III	10	0	-	-	
IV	30	11	FN	9	FA
				1	HT
				1	MNG
V	2	1	SFM	FA	
VI	5	1	PC	PC	

Table 3: Comparison of the Mean age of presentation.

Study	Year	Mean Age (In Years)
Singh et al [11]	2011	57.5
Muratli et al [12]	2014	51.24
Naz et al [4]	2014	39.7
Richmond et al [5]	2014	55
Present Study	2015	36.29

Table 4: Comparison of Male: Female ratio.

Study	Year	Male:Female
Singh et al [11]	2011	1: 4.7
Muratli et al [12]	2014	1: 4.8
Naz et al [4]	2014	1: 3.6
Richmond et al [5]	2014	1: 6.1
Present study	2015	1: 9.3

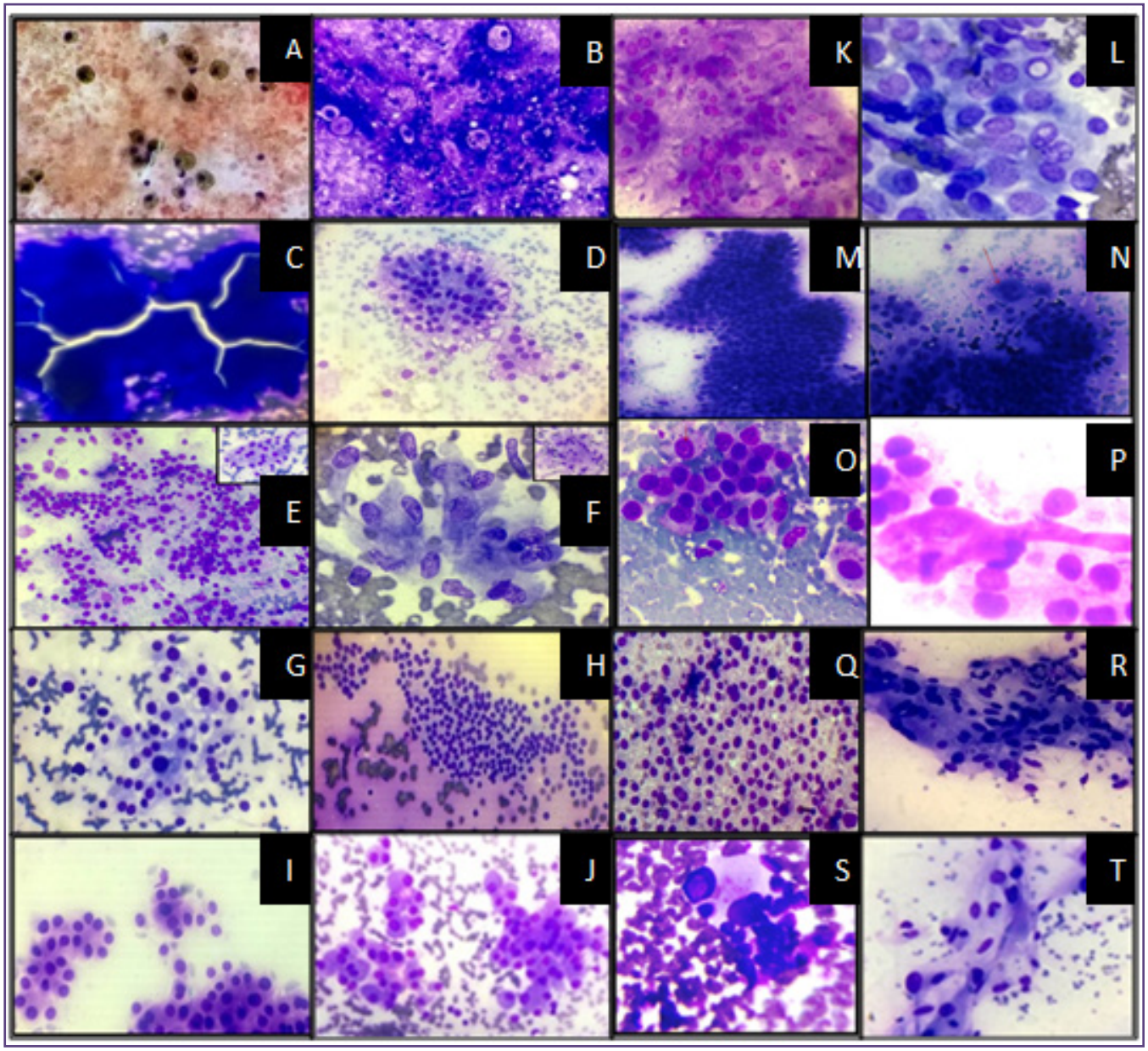

Fig. 1-A) Category I- Cyst macrophages only- [H&E; 400X], B) Category II- Cyst macrophages and hemosiderin laden macrophages in a colloid background-[MGG; 400X], C) Mirror cracking appearance of dense colloid- [MGG; 400X], D) Fire Flare appearance-[MGG; 400X] , E) Hashimoto/Lymphocytic thyroiditis- Lymphocytes impingeing onto follicular cells -[MGG; 100 X]. Inset-Askanazy cells -[MGG; 400X], F) Granulomatous Thyroiditis- Epithelioid cells- [MGG; 1000X], Inset-Granuloma, G) Category III-Some follicular cells show nuclear enlargement, often with prominent nucleoli [MGG; 400X], H) to J)=Category IV-H)-Microfollicles with follicular cells showing small uniform nuclei- [MGG; 100X], I)Same case of Category IV showing Follicular cells with hyperchromasia and some enlarged nuclei-[MGG; 400X], J) Hurthle cells showing abundant eosinophilic granular cytoplasm-[MGG; 400X], K) Category V- Follicular cells showing nuclear enlargement, macronucleoli, anisonucleosis and nuclear pallor- Suspicious for Papillary carcinoma [MGG; 400X], L) to P)-Category VI- Papillary carcinoma- L)FNAC-Intranuclear cytoplasmic pseudoinclusions, [MGG;1000X], M)Cells arranged in papillary fronds [MGG; 400X], N) Arrow- Multinucleated giant cell [MGG; 400X], O) Arrow- Nuclear Clearing[MGG; 1000X], P) Chewing –gum colloid [H&E;1000X], Q) to T) Category VI-Anaplastic carcinoma-Q)- Follicular cells showing anisonucleosis, pleomorphism and multinucleation [MGG; 400X], R) Nuclear enlargement, prominent nucleoli and spindle cells [MGG; 1000X], S) Intranuclear cytoplasmic pseudoinclusions [MGG; 1000X], T) Prominent nucleoli and spindle cells.

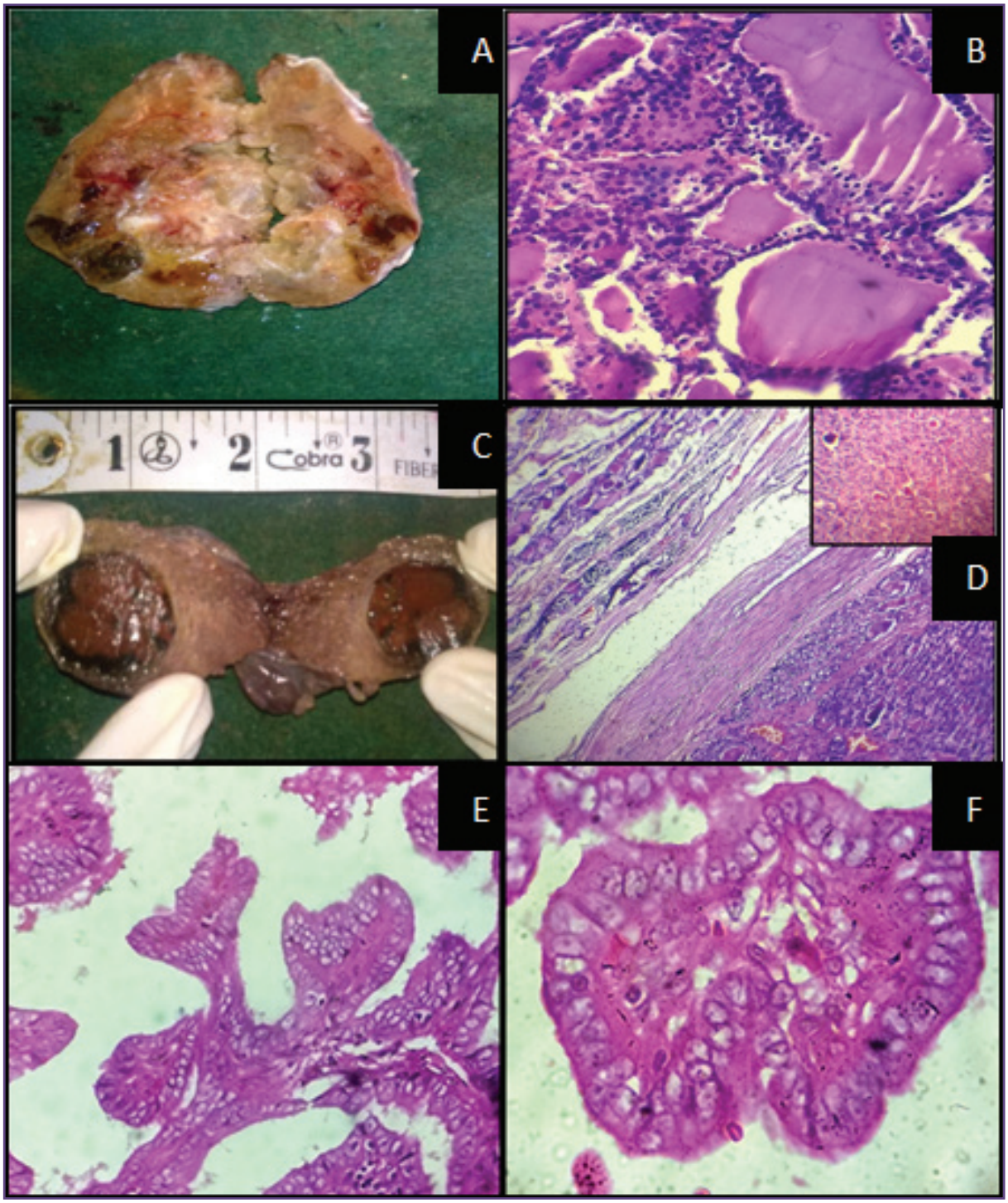

Fig.2- A) & B)-Colloid goitre-A) Hemithyroidectomy specimen- cut section reveals multiple honey colored colloid filled nodules B) Same case showing variable sized thyroid follicles showing marked hyperplasia of lining epithelium-[H&E; 400X], C)&D)- Follicular adenoma-C) Lobectomy specimen- Cut section shows a well circumscribed, capsulated, solitary nodule, D) Same case showing a well defined capsule [H&E; 100X]. Inset-Microfollicular(fetal) pattern [H&E; 400X], E)&F)- Papillary carcinoma- E) Branching papillae with central fibrovascular core and stratified lining of cuboidal cells, F) Optically clear Orphan Annie eye nuclei.

Table 5: Comparison of the distribution of cases according to TBSRTC .

S.No.	STUDY	YEAR	CAT I	CAT II	CAT III	CAT IV	CAT V	CAT VI
1	Yang et al [6]	2007	10.4	64.6	3.2	11.6	2.6	7.6
2	Yassa et al [7]	2007	7	66	4	9	9	5
3	Theoharis et al [13]	2009	11.1	73.8	3	5.5	1.3	5.2
4	Nayar et al [14]	2009	5.3	64.2	17.8	5.9	1.9	4.9
5	Marchevsky et al [15]	2010	12.9	71.6	9.8	1.5	2.3	2
6	Jo et al [16]	2010	18.6	59	3.4	9.7	2.3	7
7	Renshaw et al [17]	2010	23.6	54	7.7	8.6	1.8	4.2
8	VanderLaan et al [18]	2011	12.5	62.7	10.9	4.2	4.5	5.2
9	Kim et al [19]	2011	1.8	58.3	16.3	1.2	6.2	16.2
10	Krane et al [20]	2011	13.9	66.9	10	2	3.2	3.9
11	Singh et al [11]	2011	13.2	41.3	3.7	5.6	3.9	4.5
12	Mondal et al [21]	2013	1.2	87.5	1	4.2	1.4	4.7
13	Muratli et al [12]	2014	10.8	59.5	8.7	0.6	2.8	17.6
14	Naz et al [4]	2014	4.7	76.3	12.7	2.1	3.4	0.8
15	Mehra et al [22]	2015	7.2	80	4.9	2.2	3.6	2.2
16	Mamtha et al [23]	2015	10.84	60	12.5	3.34	4.16	9.16
17	Joshi et al [8]	2015	0	65.5	7.3	14.5	4.5	8.2
18	Melo- Uribe et al [24]	2015	4.08	23.47	2.04	16.84	37.24	16.33
19	Present Study	2015	4.57	68.58	5.72	17.14	1.14	2.85

Table 6: Comparison of the statistical analysis.

Study	Year	No.of cases	Sensitivity	Specificity	PPV	NPV	Accuracy
Al Sayer et al [25]	1985	70	86	93	80	96	92
Cusiok et al [26]	1990	283	76	58	72	64	69
Bouvet et al [27]	1992	78	93.5	75	85.3	88.2	79.6
Afroze et al [28]	2002	170	61.9	99.31	92.86	94.74	94.58
Ko et al [9]	2003	207	78.4	98.2	99	66.3	84.4
Al Hureibi et al [29]	2003	196	38	89.9	66.7	73.2	72
Kessler et al [10]	2005	170	79	98.5	98.7	76.6	87
Mahar et al [30]	2006	125	98	70	91	93	91
Haberal et al [31]	2009	260	92.6	91.6	83.5	96.5	91.9
Muratli et al [12]	2014	126	87.1	64.6	76.1	79.5	77.3
Present study	2015	175	78.57	90.00	84.62	85.71	85.29

Conclusion

This study was undertaken to classify the thyroid lesions based on The Bethesda system of reporting Thyroid Cytology and provide data that would help in planning the therapeutic approach in patients with thyroid swellings. The cytomorphological analysis was done to assess the diagnostic accuracy of cytology in diagnosis of thyroid lesions.

Acknowledgements

None

Funding

None

Competing Interests

None Declared

References

1. Cibas ES, Ali SZ. The Bethesda System for Reporting Thyroid Cytopathology. Am J Clin Pathol 2009; 132: 658-665.
2. Wang HH. Reporting thyroid fine-needle aspiration: Literature review and a proposal. Diagnostic Cytopathology 2006; 34(1): 67–76.
3. Parikh R, Mathai A, Parikh S, Chandra SG, Thomas R. Understanding and using sensitivity, specificity and predictive values. Indian Journal of Ophthalmology. 2008; 56(1):45-50.
4. Naz S, Hashmi AA, Khurshid A, Faridi N, Edhi MM, Kamal A, Khan M. Diagnostic accuracy of Bethesda system for reporting thyroid cytopathology: an institutional Perspective. International Archives of Medicine 2014; 7: 46-50.
5. Richmond BK, Judhan R, Chong B, Uber At, Aburahma Z, Mangano W, Stephanie Thompson. False-negative Results with the Bethesda System of Reporting Thyroid Cytopathology: Predictors of Malignancy in Thyroid Nodules Classified as Benign by Cytopathologic Evaluation. Am Surg. 2014; 80(8): 811–816.
6. Yang J, Schnadig V, Logrono R, et al. Fine-needle aspiration of thyroid nodules: a study of 4703 patients with histologic and clinical correlations. Cancer. 2007; 5: 306-315.
7. Yassa L, Cibas ES, Benson CB, et al. Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. Cancer. 2007; 6: 508-516.
8. Joshi D, Jesalpura NS. Comparison between Bethesda System and Conventional System in Thyroid Cytopathology. IJSR. 2015; 4(9): 78-80.
9. Ko HM, Jhu IK, Yang SH, Lee JH, Nam JH, Juhng SW, et al. Clinicopathologic analysis of fine needle aspiration cytology of the thyroid. A review of 1,613 cases and correlation with histopathologic diagnoses. Acta Cytol. 2003; 47: 727–732.
10. Kessler A, Gavriel H, Zahav S, Vaiman M, Shlamkovitch N, Segal S, et al. Accuracy and consistency of fine-needle aspiration biopsy in the diagnosis and management of solitary thyroid nodules. Isr Med Assoc J. 2005; 7: 371–373.
11. Singh RS, Wang HH. Eliminating the "atypia of undetermined significance/follicular lesion of undetermined significance" category from the bethesda system for reporting thyroid cytopathology. Am J Clin Pathol. 2011; 136:896–902.
12. Muratli A, Erdogan N, Sevim S, Unal I, Akyuz S. Diagnostic efficacy and importance of fine needle aspiration cytology of thyroid nodules. Journal of Cytology. 2014; 31:73-77.
13. Theoharis CG, Schofield KM, Hammers L, et al. The Bethesda thyroid fine-needle aspiration classification system:year 1 at an academic institution. Thyroid. 2009; 19: 1215-1223.
14. Nayar R, Ivanovic M. The indeterminate thyroid fine needle aspiration: experience from an academic center using terminology similar to that proposed in the 2007 National Cancer Institute Thyroid Fine Needle Aspiration State of the Science Conference. Cancer Cytopathol. 2009; 11(7):195 -202.
15. Marchevsky AM, Walts AE, Bose S, et al. Evidence-based evaluation of the risks of malignancy predicted by thyroid fine needle aspiration biopsies. Diagn Cytopathol. 2010;38:252–259
16. Jo VY, Stelow EB, Dustin SM, Hanley KZ. Malignancy Risk for Fine Needle Aspiration of Thyroid Lesions According to The Bethesda System for Reporting Thyroid Cytopathology. Am J Clin Pathol. 2010; 134: 450- 456.
17. Renshaw AA. Should "atypical follicular cells" in thyroid fine-needle aspirates be subclassified? Cancer Cytopathol.2010; 118: 186-189.
18. VanderLaan PA, Marqusee E, Krane JF,. Clinical Outcome for Atypia of Undetermined Significance in Thyroid Fine-Needle Aspirations .Should Repeated FNA Be the Preferred Initial Approach?. Am J Clin Pathol 2011;135:770-775
19. Kim SK, Hwang TS, Yoo YB, et al. Surgical results of thyroid nodules according to a management guideline based on the BRAFV600E mutation status. J Clin Endocrinol Metab.2011; 96:658-664.
20. Krane JF, VanderLaan PA, Faquin WC, et al. The atypia of undetermined significance/follicular lesion of undetermined significance: malignant ratio: a proposed performance measure for reporting in The Bethesda System for Thyroid Cytopathology. Cancer Cytopathol. 2012; 120(2):111-116.
21. Mondal SK, Sinha S, Basak B, Roy DN, Sinha SK. The Bethesda system for reporting thyroid fine needle aspirates: A cytologic study with histologic follow up. Journal of Cytology.2013; 30(2): 94-99.
22. Mehra P, Verma AK. Thyroid Cytopathology Reporting by the Bethesda System:A Two-Year Prospective Study in an Academic Institution. Pathology Research International.2015, 1-11.

23. Mamatha M, Sekhar SC, et al.. A comparative study between conventional system and the Bethesda system applied for reporting thyroid cytopathology. International Archives of Integrated Medicine. 2015; 2(3): 87-95.
24. Melo-Uribe MA, Sanabria A, Romero-Rojas A, et al. The Bethesda system for reporting thyroid cytopathology in Colombia: Correlation with histopathological diagnoses in oncology and non-oncology institutions. Journal of Cytology. 2015; 32(1):12-16.
25. Al-Sayer HM, Krukowski ZH, Williams VM, Matheson NA. Fine needle aspiration cytology in isolated thyroid swellings: A prospective two year evaluation. Br Med J (Clin Res Ed) 1985; 290: 1490–1492.
26. Cusick EL, MacIntosh CA, Krukowski ZH, Williams VM, Ewen SW, Matheson NA. Management of isolated thyroid swellings: A prospective six year study of fine needle aspiration cytology in diagnosis. BMJ.1990; 301: 318–321.
27. Bouvet M, Feldman JI, Gill GN, Dillmann WH, Nahum AM, Russack V, et al. Surgical management of the thyroid nodule: Patient selection based on the results of fine-needle aspiration cytology. Laryngoscope.1992; 102:1353–1356.
28. Afroze N, Kayani N, Hasan SH. Role of fine needle aspiration cytology in the diagnosis of palpable thyroid lesions. Indian J Pathol Microbiol. 2002; 45: 241–246.
29. Al-Hureibi KA, Al-Hureibi AA, Abdulmughni YA, Aulaqi SM, Salman MS, Al-Zooba EM. The diagnostic value of fine needle aspiration cytology in thyroid swellings in a university hospital, Yemen. Saudi Med J. 2003; 24: 499–503.
30. Mahar SA, Husain A, Islam N. Fine needle aspiration cytology of thyroid nodule: Diagnostic accuracy and pitfalls. J Ayub Med Coll Abbottabad. 2006; 18: 26–29.
31. Haberal AN, Toru S, Ozen O, Arat Z, Bilezikçi B. Diagnostic pitfalls in the evaluation of fine needle aspiration cytology of the thyroid: Correlation with histopathology in 260 cases. Cytopathology.2009; 20: 103–108.