

Original Research Article

Evaluation of Bethesda system for reporting thyroid cytology with histopathological correlation

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ABSTRACT

Background: The Bethesda system of reporting thyroid cytopathology is a standardised system, improving communication between cytopathologists and clinicians, leading to more consistent management approaches. The aim of the research work was to study the utility of Bethesda system in reporting thyroid cytology with histopathological correlation of all the cases undergoing surgical resection.

Methods: We studied all the thyroid cytology cases received between November 2012 to April 2014, and classified them according to the Bethesda system. Histopathological correlation was done for all the cases which underwent surgical resection with evaluation of cyto-histological discrepancies.

Results: Out of 484 cases studied, 432(89.2%) were benign lesions, 20(4.1%) were malignant, 18 (3.7%) were Unsatisfactory/Nondiagnostic, 10(2%) were Follicular neoplasm/Suspicious for neoplasm, 3 (0.6%) were suspicious for malignancy, and 1(0.002%) case was reported as Atypia of undetermined significance. Out of the 54 cases available for histopathological follow-up, cyto-histological discrepancies were noted in 5 cases (9.2%). Statistical analysis of the present study showed that cytological analysis of thyroid lesions by Bethesda system has got high sensitivity (72.72%), high specificity (95.3%) with a positive predictive value of 80% and negative predictive value of 93.1% and a high accuracy (90.7%).

Conclusions: Reviewing the thyroid FNAs (fine needle aspirates) using Bethesda system allowed a more specific cytological diagnosis with better interlaboratory agreement. As evidenced by its high sensitivity and specificity, Bethesda system has proven to be a very effective guide for the clinical management of thyroid nodules.

Keywords: Bethesda, Cytology, Thyroid

INTRODUCTION

Fine needle aspiration (FNA) of the thyroid gland has proven to be an important and widely accepted, cost-effective, simple, safe, and accurate method for triaging patients with thyroid nodules.

Fine needle aspirations provide information that guides the management of patients with thyroid nodules by identifying patients who require surgical resection and patients who require no further interventions.¹

Thyroid cytopathology practice requires communication and collaboration among pathologists and primary clinicians, endocrinologists, radiologists, and surgeons, as well as correlation with surgical pathology interpretations. Therefore, consistent diagnostic terminology is imperative. While there are minimal difficulties in diagnosing most benign and overtly malignant lesions, diagnostic challenges arise when aspirate samples are quantitatively or qualitatively suboptimal to reliably exclude a neoplastic process. The management of these types of lesions has been further

complicated by the historic lack of universal terminology. Multiple organizations have proposed diagnostic guidelines for reporting thyroid FNA cytology results, including the Papanicolaou Society of Cytopathology Task Force and American Thyroid Association, although none have been necessarily universally accepted.¹

Throughout 2007, the National Cancer Institute (NCI), organized the NCI Thyroid Fine Needle Aspiration State-of-the-Science Conference. The current status of various aspects of thyroid FNA was discussed, including the following

- Indications and pre-FNA requirements,
- Training and credentialing for FNA,
- Technique,
- Reporting terminology and morphologic criteria,
- Ancillary studies, and
- Post-FNA testing and treatment.

Since the conference, there has been an initiative to publish an atlas and guidelines using a standardized nomenclature for the interpretation of thyroid FNAs, known as “The Bethesda System for Reporting Thyroid Cytopathology”.¹

The Bethesda System describes 6 diagnostic categories of lesions which have individual implied risks of malignancy that influence management paradigms. The present study was done to interpret the thyroid FNAC as per Bethesda system and to evaluate its efficacy by taking histologic findings as standard.

METHODS

Source of data

All the cases of thyroid lesions received in the cytology section of the department of pathology, KIMS, Hubli for FNAC; during the period of November 2012 to April 2014 (one and half year of prospective study).

Method of collection of data

In all the patients with thyroid lesions, clinical history, physical findings and probable diagnosis were noted. FNAC was performed by a pathologist either by conventional method of palpation or with sonological guidance using a 22 gauge needle. Direct smears were prepared and were either air dried and stained with Wright’s stain or fixed in alcohol and stained with ‘haematoxylin and eosin’.

Procedure of thyroid FNA

The FNA was done with a 22-23 gauge needle disposable needle attached to a 20ml plastic disposable syringe mounted on a handle (syringe holder) for single-hand grip. The patient was made to lie down in supine position

with neck hyper-extended. Extension of the neck was facilitated by avoiding a pillow under the head, and keeping under the neck to further extend the cervical spine and expose the gland more prominently. The patient was asked to refrain from swallowing during the procedure which takes about 5-20sec.²

The skin overlying the swelling was cleaned thoroughly with alcohol. The needle is inserted into the nodule and plunger is retracted to create a vacuum in the syringe. The needle is then moved back and forth and from side to side gently within the lesion, all the time maintaining the negative pressure in the syringe. The plunger was then released. The needle with syringe was then withdrawn from the thyroid. The needle was quickly detached from the syringe and the plunger was retracted to allow air to fill the syringe barrel. The needle was then re-attached to the syringe and the contents ejected on to a glass slide by pushing down the plunger.^{2,3} Direct smears were prepared and were either air dried and stained with Wright’s stain or fixed in alcohol and stained with ‘haematoxylin and eosin’.

Thyroid specimens received were fixed in 10% formalin for 12 to 24hrs after recording the gross morphological features. The specimens were routinely processed, embedded in paraffin wax and sections were cut at 3 to 6µm thickness. Sections were stained routinely with H and E stain. Special stains like Congo red were employed wherever indicated.

Inclusion criteria

Patients of all age groups and both sex, with palpable thyroid nodules who had come for FNAC.

Exclusion criteria

- Patients with skin infection at the site of aspiration,
- Patients with haemorrhagic diathesis,
- Critically ill or anxious patients,
- Non-cooperative patients.

Statistical analysis

- Sensitivity,
- Specificity,
- Positive predictive value and negative predictive value,
- Validity.

RESULTS

Total number of cases studied on FNAC were 484. Out of 484 cases, 432 (89.2%) were benign lesions, 20 (4.1%) were malignant, 18 (3.7%) were Unsatisfactory/Nondiagnostic, 10 (2%) were Follicular neoplasm/Suspicious for neoplasm, 3 (0.6%) were suspicious for malignancy, and 1 (0.002%) case was reported as Atypia of undetermined significance.

The maximum number of cases were in the age group of 21-40years. Out of the total 484 cases, 455 cases were females (94%) and 29 cases were males (6%).

Table 1: Cytological diagnosis as per the Bethesda system.

Cytological diagnosis	No. of cases	%
Unsatisfactory	18	3.7
Benign follicular lesion	432	89.25
Atypia of follicular lesion of undermined significance	1	0.002
Follicular neoplasm /suspicious for follicular neoplasm	10	2
Suspicious for malignancy	3	0.6
Malignant tumour	20	4.1
Total	484	100

Total number of benign follicular lesions were 432, out of which 276 were nodular goitre, 99 were Hashimoto thyroiditis, 35 were nodular goitre with secondary hyperplasia, 19 were primary hyperplasia and 3 were granulomatous thyroiditis.

Table 2: Cytological diagnosis of malignant lesions.

Diagnosis	Number of case(n=20)	%
Papillary carcinoma	15	75
Medullary carcinoma	4	20
Anaplastic carcinoma	1	5

Out of the 276 cases reported as nodular goiter and colloid goiter, follicular cells were arranged in clusters and singles in 230 (83.3%)cases and in honeycomb pattern in 46 (16.6%) cases. Hurthle cell change was noted in 90 (32.6%) cases and foamy macrophages were found in 112 (40.5%) cases. Colloid was moderate to abundant in 244 (88.4%) cases and it was scanty/absent in 32 (11.6%) cases.

Table 3: Comparison of percentage of distribution of fine needle aspiration diagnoses among published studies.^{20,22,29}

Diagnostic category	Present study	Yassa et al ⁸	Yang et al ⁹	Nayar & Ivanovic ¹⁰
Nondiagnostic/unsatisfactory	3.7	7	10.4	5
Benign	89.25	66	64.6	64
Aus/follicular lesion of undetermined significance	0.002	4	3.2	18
'Suspicious for follicular neoplasm'	2	9	11.6	6
Suspicious for malignancy	0.6	5	2.6	2
Malignant	4.1	5	7.6	5

Out of the 99 cases reported as Hashimoto thyroiditis, polymorphic population of lymphocytes were present in all cases, whereas lymphocytes infiltrating follicular cell clusters was found in 45 (45.5%) cases. Hurthle cell change was noted in 83 (83.8%) cases, anisonucleosis in 22 (22.2%) cases and multinucleated giant cells in 20(20.2%) cases. Colloid was scant in 72 (72.7%) cases and absent in 27 (27.2%) cases.

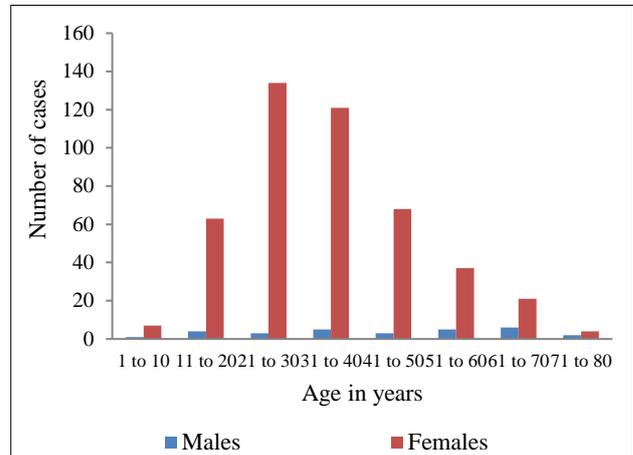


Figure 1: Graph showing age and sex distribution.

Out of the 20 malignant cases reported on cytology, 15 cases (75%) were papillary carcinoma, 4 cases (20%) were medullary carcinoma and 1 case was reported as anaplastic carcinoma.

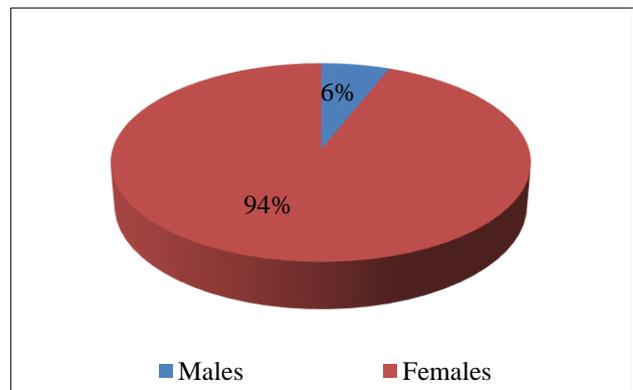


Figure 2: Pie diagram showing sex distribution.

Maximum number of papillary carcinoma cases i.e. 5 cases (33.3%) were in the age group of 20-29years, and 10 cases (66.6%) were reported in females. Male:Female ratio was 1:2. In all the 15 cases reported as papillary carcinoma, cellularity was observed to be moderate to marked. All the 15 cases showed papillary arrangement, and in 12 (80%)cases, cells were also arranged in monolayered sheets. Nuclei showed fine, powdery chromatin and intranuclear cytoplasmic inclusions in 13 (86.7%) cases. Nuclear grooves were observed in 8 (53.3%) cases. Colloid was scant in 13 (86.7%) cases and absent in 2 (13.3%) cases.



Figure 3: Papillary carcinoma: cut section showed solid, firm grey white areas with papillary excrescences along with brownish colloid filled areas in the periphery.

Histopathological follow-up was available in 54 cases, out of which 43 were reported as benign thyroid lesion, 8 cases were papillary carcinoma and 1 case each of medullary carcinoma, follicular adenoma and hurthle cell adenoma.



Figure 4: Medullary carcinoma: cut section showed grey to yellowish solid, firm and relatively well circumscribed area with brownish area in the periphery.

Cyto-histopathological correlation

Out of the 18 cases reported as ND/UNS, 2 cases were available for histopathological follow up, out of which 1 case was reported as papillary carcinoma and the other as nodular goiter. Out of 432 cases reported as benign, 41 cases were available for histopathological follow up, out of which 40 were benign and one case was reported as follicular adenoma.

There was one case of AUS/FLUS which on histopathological follow up was reported as follicular variant of papillary carcinoma. Out of the 10 cases

reported as FN/SFN, 1 case was available for follow up and was reported as hurthle cell adenoma. Out of the 3 cases reported as “suspicious for malignancy”, 2 cases were available for follow up, out of which 1 was reported as follicular variant of papillary carcinoma and the other as medullary carcinoma.

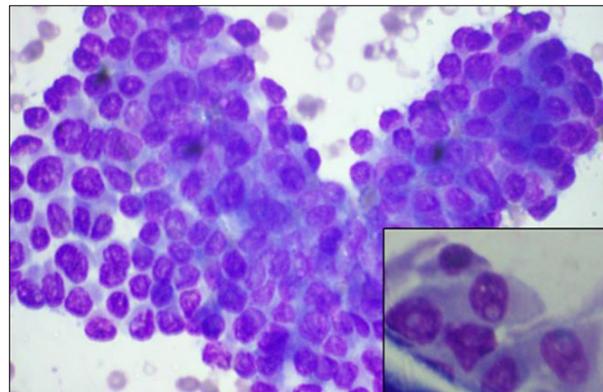


Figure 5: Papillary carcinoma: follicular cells arranged in papillary clusters; cells have moderate amount of cytoplasm with enlarged irregular nuclei some showing nuclear grooves. Inset: cells with INCI. (MGG, x40; Inset:MGG, x40).

Out of 20 malignant cases reported on cytology, 7 cases were available for histopathological follow up, out of which 5 were reported as papillary carcinoma and 2 were reported as nodular goiter.

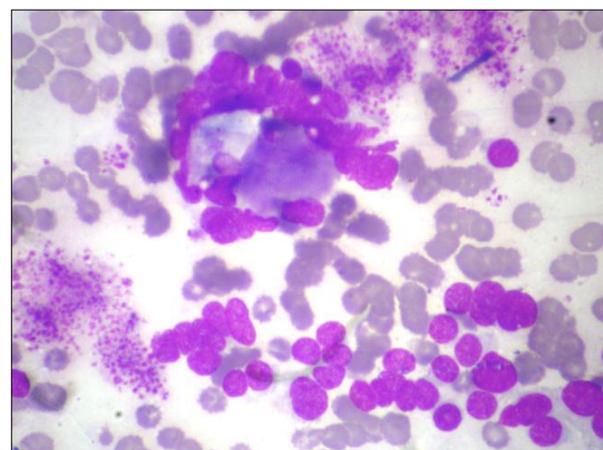


Figure 6: Suspicious for malignancy-medullary carcinoma: loose cluster of follicular cells with enlarged variably sized nuclei and inconspicuous nucleoli along with fragments of pink amorphous material (probably amyloid-shown by arrow). (MGG,x40).

Cyto-histological discrepancies were noted in 5 cases, amounting to 9.2%. Statistical analysis of the present study showed that cytological analysis of thyroid lesions by Bethesda system has got high sensitivity (72.72%), high specificity (95.3%) with a positive predictive value

of 80% and negative predictive value of 93.1% and a high accuracy (90.7%).

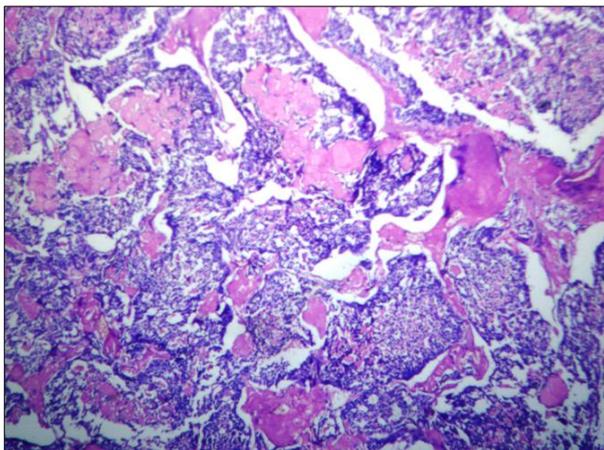


Figure 7: Medullary carcinoma-histopathology section: cells are arranged in nests separated by areas of amyloid. (H and E,x10).

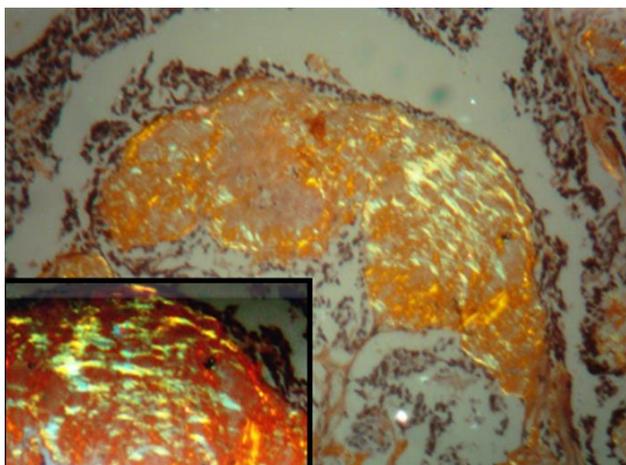


Figure 8: Medullary carcinoma-apple green birefringence under polarizing microscopy on Congo red stain (x10; Inset:x40)

DISCUSSION

FNAC is the first line diagnostic test for evaluating thyroid nodules. FNAC can effectively triage patients with neoplastic thyroid nodules as to who require surgery and who do not. However, due to the lack of a standardized system of reporting, pathologists have been using different terminologies and diagnostic criteria, thereby creating confusion among referring clinicians in the interpretation of the cytopathology report, ultimately hindering a definitive clinical management. Reviewing the thyroid FNAs with the Bethesda system allowed a more specific cytological diagnosis.⁴

In this study, an attempt was made to report the thyroid FNAs as per the Bethesda system and also to assess the efficacy by comparing with the histopathological

diagnosis wherever possible. Out of the 484 cases in the present study, 3.7% were unsatisfactory, 89.2% were benign follicular lesion, 0.002% were AUS/FLUS, 2% were FN/SFN, 0.6% were SFM, and 4% were malignant. We compared the results obtained in the present study with the studies of Yang et al, Yassa et al and Nayar and Ivanovic.⁵⁻⁷

The percentage of ND/UNS cases in the present study (3.7%) was in close comparison to that of Nayar and Ivanovic study (5%).⁷ Highest number of cases were under the benign category, and a similar observation was seen in all the above studies. The number of cases under AFLUS and SFM categories were much lower in our study than other studies. This can be attributed to the fact that in our institute, usually an ultrasound guided FNAC is performed for small nodules in order to obtain material from the exact pathological site. The percentage of malignant cases in the present study was 4.1% which was comparable to that of Yassa et al (5%) and Nayar and Ivanovic (5%).^{6,7}

In the present study, the age of presentation ranged from 3years to 78years. The median age in years in the present study was 40.8 which was similar to that obtained by Afroze et al.⁸ The M:F ratio was 1:15.6 in the present study which was in close comparison with that of Safirullah et al (1:12.6).⁹

In the present study, surgical follow up was available in 11.2% of cases, of which cyto-histological discrepancy was noted in 9.2%. In the study done by Yang et al, out of his 4073 FNA cases, 1052 patients (25.8%) had surgical follow up. The cyto-histological discrepancy in their study was 15.3%.⁵ Though the percentage of discrepancy was less in the present study, the available surgical follow-up cases were also proportionately less.

Female to male ratio for papillary carcinoma was 2:1 which was comparable with the study done by Srikande and Phadke.¹⁰ The cytological features which were observed in papillary carcinoma were compared with those observed in a study done by Tseng et al.¹¹ The percentage of cases which showed papillary structures, monolayered sheets and moderate cytoplasm were comparable with those observed in the study by Tseng et al.¹¹ Intranuclear cytoplasmic inclusions were observed in more cases (86.7%) in the present study than in that of Tseng et al.¹¹ None of the cases in the present study showed psammoma bodies whereas they were seen in 2.6% of cases in the study done by Tseng et al.¹¹

FNAC is a highly sensitive and specific method of evaluating thyroid nodules for malignancy. FNAC of thyroid nodule is reported to have sensitivity ranges from 65-98% and specificity of 72-100%. In the study done by Nggada et al, the sensitivity was 88.9% and specificity was 96%.¹² In the present study, sensitivity was 72.7% and specificity was 95.3% which is similar to the study done by Nggada et al.¹²

In the study done by Saddique M et al, positive predictive value was 81.8% and negative predictive value was 93.81%.¹³ In the present study, PPV was 80% and NPV was 93.1% which is very similar to that of Saddique M et al.¹³

CONCLUSION

The Bethesda system is a very useful standardised system of reporting thyroid cytopathology, improving communication between cytopathologists and clinicians, and interlaboratory agreement, leading to more consistent management approaches. As evidenced by its high sensitivity and specificity, Bethesda system has proven to be an effective guide for clinical management of thyroid nodules.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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