Section: Pathology

Original Research Article

A COMPARATIVE STUDY OF THE BETHESDA SYSTEM OF REPORTING THYROID FNAC WITH HISTOPATHOLOGICAL ANALYSIS OF LESIONS REQUIRING SURGICAL MANAGEMENT

Asra Fatima[1], Tahniyat Ara[2], Zeenath Begum[1], Zainab Zohra[3], Mandakini B Tengali[4]

[1]Flat FG7 Asian Life Style Apartment Beside Asian Mall, Kalaburagi, Karnataka, India
[2]Akbar Bagh, Near KNZ Hall, Kalaburagi, Karnataka, India
[3]Bank colony, Kalaburagi, Karnataka, India
[4]Department of Pathology, Faculty of Medical sciences, Khaja Banda Nawaz University, Kalaburagi, Karnataka, India.

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Corresponding Author:
Dr. Zeenath Begum,
Email: drzeenta@gmail.com

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Abstract

Background: Fine needle aspiration cytology (FNAC) is an efficient, cost effective and safe out-patient procedure in diagnosis of thyroid nodules. With the advent of Bethesda system of reporting thyroid FNAC, the procedure has obtained even more standardization, reproducibility, predictive value and all in all, greater clinical significance. Aim: The aim of this study was to assess the effectiveness of FNAC thyroid reported under Bethesda guidelines by comparing the preoperative cytological diagnoses with the postoperative histopathological diagnoses. **Materials and Methods:** In this study, FNAC of 100 patients of clinically palpable and non palpable thyroid swelling were evaluated and classified according to the Bethesda system. 56 patients of this group underwent surgical management and histopathological diagnosis was obtained in them. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of FNAC reported under Bethesda system were obtained by comparing the cytological and histopathological diagnoses. **Result:** Total 100 cases were studied, that include84(84%) benign, 2(2%)AUS/ FLUS, 5(5%) FN, 4(4%) SM and 5(5%) of malignant categories. 56 cases were available for follow-up histopathology. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of FNAC came out to be 81.8 %,88.3 %, 64% ,95 % and 87% respectively. **Conclusion:** In our study, FNAC reported under Bethesda system came out to be a highly efficient tool in diagnosis of thyroid nodules. However, addition of more advanced methods like immunocytochemistry and molecular techniques can further increase this efficacy especially in the groups diagnosed as Atypia of undetermined significance/Follicular lesion of undetermined significance, Follicular neoplasm/Suspected for follicular neoplasm and Suspected for malignancy.

INTRODUCTION

Thyroid nodule is a discrete lesion in the thyroid gland that is radiologically distinct from the surrounding parenchyma. Thyroid nodules are common; their prevalence in general population is high, the percentage vary depending on the mode of discovery: 2-6% (palpation), 19-35 % (ultrasound) and 8-65% (autopsy data).[1]

Fine needle aspiration cytology (FNAC) of thyroid is the initial screening test of thyroid nodules and is utilized as a preoperative diagnostic technique which is safe, simple, and cost effective for triaging patients with thyroid nodules. The Bethesda system classifies thyroid FNA into six categories ,each category is linked to a malignancy risk & has a recommended clinical management.[2] The third edition of the Bethesda Thyroid Reporting System refined and updated the use of molecular and other ancillary tests.[3] The aim of the study is to assess the productivity of FNAC in thyroid lesions presented as thyroid nodules by Bethesda categorization and compare the results of Bethesda category IV, V and VI with histopathological study.

Objective of the study:

- To study the thyroid cytology and to categorized diseases based on Bethesda system
- To correlate the cytological findings with histopathology of cases managed surgically.

Type of study: Retrospective observational study.

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Inclusion Criteria
All palpable Thyroid lesion of various age group and lesions of thyroid identified in USG.
Exclusion Criteria
Ectopic thyroid lesion. Category I of Bethesda is also excluded as the cases were referred again under USG guidance.
Inclusion Criteria for Histopathology: All the thyroid specimens received in the department of pathology which were managed as per Bethesda categorization and also few samples with high clinical suspicious of malignancy irrespective of Bethesda category.
Exclusion Criteria for Histopathology: Samples of thyroid specimens without cytology reports as per Bethesda are excluded. Thyroglossal cysts are excluded.

MATERIALS AND METHODS

The present study was carried out after the ethical clearance, the study was done from November 2021 till January 2023, a fifteen months study in Khaja Banda Nawaz teaching and general hospital and Faculty of medical sciences Khaja Banda Nawaz university. Fine needle aspiration cytology of all the palpable thyroid masses which was carried out and categorized as per Bethesda during above said period are studied and Bethesda cases which were managed surgically their histopathology was studied to asses reproducibility of Bethesda system of cytology. Partial and hemithyroidectomy samples, also biopsy in case of cytological reporting as AUS, received in the department of pathology are processed and slides were stained with H&E are observed under a microscope and correlated with cytological findings for the reproducibility of the Bethesda categorization. [Table 1].

RESULTS

Total 100 cases were studied, the data included 84(84%) benign, 2(2%)AUS/ FLUS, 5(5%) FN, 4(4%) SM and 5 (5%) of malignant categories [Table 2]. Out of 100 cases, 56 cases were available for follow-up histopathology. We compared the original FNA diagnosis of these 56 cases with that of histopathological examination and calculated the risk of malignancy for each category [Table 3 and 4]. Out of 40 category II cases,38 were reported as benign lesions and 2 were found to be reported as papillary carcinoma thyroid giving a malignancy risk of 2.3%. Out of 2 cases of AUS/FLUS, 1(one) was found to be atypical parathyroid adenoma and another 1 (one) was found to be medullary carcinoma of thyroid giving a malignancy risk of 50%. Out of 5 cases of FN, 2 cases were reported as follicular adenoma, 1(one) case was of hyalinising trabecular adenoma and 2 were found to be Hurthle cell carcinoma giving a risk of malignancy40%. Out of 4 cases of Suspicious For Malignancy, 4 were found to be malignant (2 were papillary and 2 were medullary carcinoma). Out of 5 cases of category VI, 2 were turned out as follicular adenoma, 2 were found to be follicular variant of papillary carcinoma and 1 was anaplastic carcinoma.
The female to male ratio was 7.3:1 [Figure 4]. Majority of lesions were in 31-40 years of age group [Figure 3]. The median age is 37 years. Distribution of lesions in female and male patients in different age group and comparative study with other series is shown in table.[5]
Statistical analysis was performed using SPSS software version Microsoft Office Excel 2007.
The diagnostic values (sensitivity, specificity, positive predictive value, negative predictive value, and accuracy) and risk of malignancy for FNAs using the Bethesda system were calculated for cases with surgical follow-up. FNA smears interpreted as nondiagnostic were excluded. True negative cases were defined as nodules with benign FNA cytology and surgical pathology. Follicular neoplasm/suspicious for follicular neoplasm, suspicious for malignancy, and malignant cases confirmed to be malignant upon final histology were considered true positive. Nodules with cytological results of FN/SFN or suspicious for malignancy or malignant diagnosed as benign on surgical excision were interpreted as false positive. False negative samples included cases with benign cytology that were found to be malignant upon histopathology.

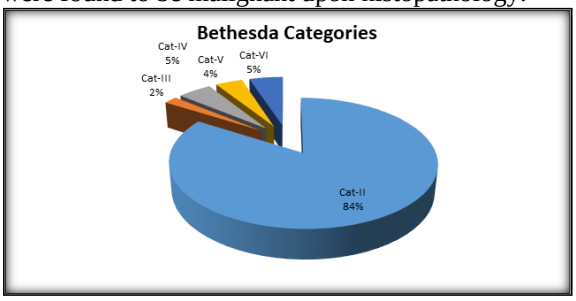

Figure 1: Showing distribution of cases according to Bethesda system

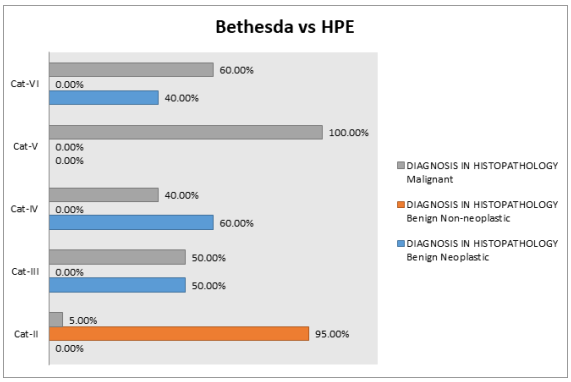

Figure 2: Showing Cytological-Histopathological correlation of thyroid lesion.

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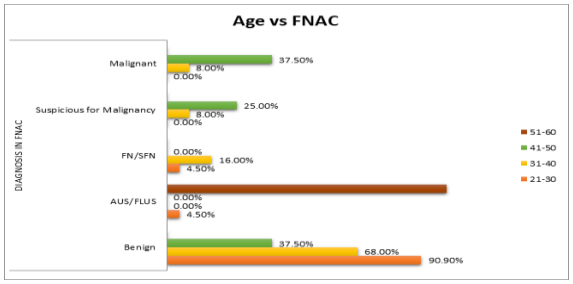

Figure 3: Showing age distribution of thyroid lesions according to Bethesda system

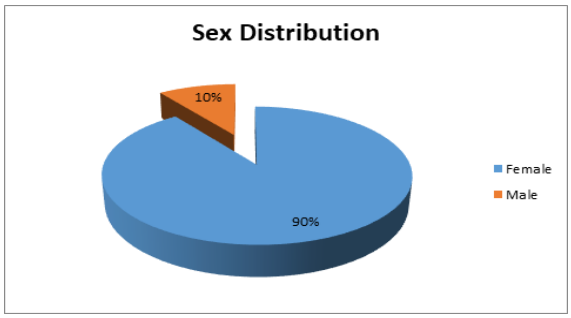

Figure 4: Showing sex distribution of thyroid lesions.

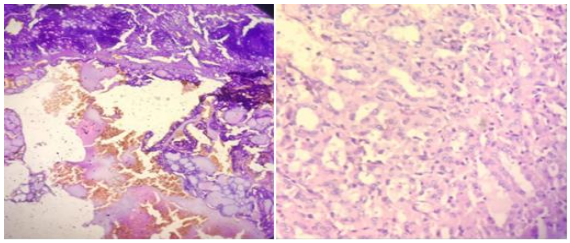

Figure 5: Multinodular goiter(4X,H&E) Fig: Papillary carcinoma Thyroid.(10X,H&E)

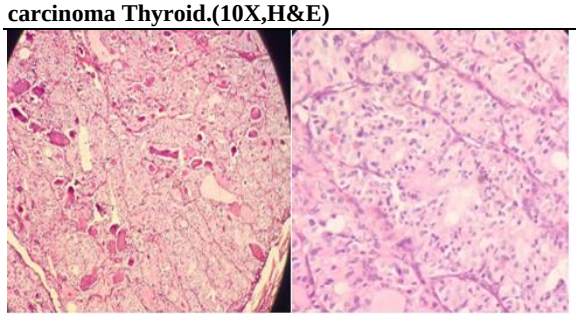

Figure 6: Hyalinizing trabecular adenoma,10X(H&E) Hyalinizing trabecular adenoma 40X(H&E)

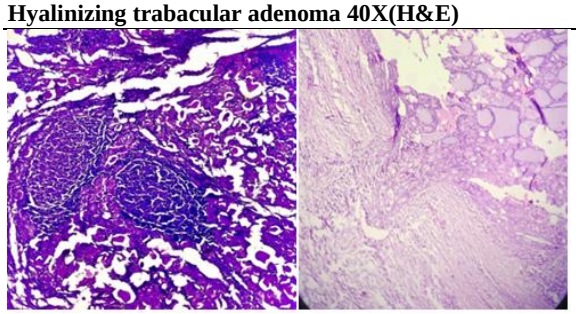

Figure 7: Hahimoto thyroiditis(10X,H&E) Figure: Papillary Carcinoma with capsular invasion.

Table 1: The 2023 Bethesda System for Reporting Thyroid Cytopathology: Implied Risk of Malignancy with Expected Ranges Based on Follow-Up of Surgically Resected Nodules with Recommended Clinical Management.

Diagnostic Category	Risk of Malignancy average (%) and range	Usual management
Non diagnostic or Unsatisfactory Cyst fluid only Virtually acellular specimen Other(obscuring blood,clotting artifact)	13(5-20)	Repeat FNA with ultrasound guidance
Benign Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule etc.) Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context. Consistent with granulomatous (subacute) thyroiditis. Others	4(2-7)	Clinical and sonographic follow-up
III. Atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS)- AUS-nuclear atypia:AUS- others	22(13-30)	Repeat FNA,molecular testing,diagnostic lobectomy,or surveillance
IV . Follicular neoplasm(FN) -Specify if Hurthle cell/oncocytic type	30(23-34)	Molecular testing,diagnostic lobectomy
V. Suspicious for malignancy(SFM) - Suspicious for papillary carcinoma - Suspicious for medullary carcinoma - Suspicious for metastatic carcinoma - Suspiciou for lymphoma	74(67-83)	Molecular testing, lobectomy or near total thyroidectomy
VI. Malignant	97(97-100)	lobectomy or near total thyroidectomy

Table 2: Distribution of cases according to Bethesda system

Bethesda category	FNAC diagnosis with subcategories	No of cases	Total no of cases &(%)
CATEGORY-II (Benign)	Nodular colloid goitre Colloid cyst Adenomatoid nodule Hashimotos thyroiditis	36 18 2 28	84(84%)

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CATEGORY-III (AUS/FLUS)	AUS	2	2(2%)
CATEGORY-IV (FN/SFN)	Follicular neoplasm Hurthle cell neoplasm	3 2	5(5%)
CATEGORY-V (Suspicious for malignancy)	Suspicious for papillary carcinoma Suspicious for medullary carcinoma	2 2	4(4%)
CATEGORY-VI (Malignant)	Papillary carcinoma thyroid Medullary carcinoma thyroid Anaplastic ca rcinoma thyroid	2 2 1	5(5%)

*ND/UNS-non-diagnostic/unsatisfactory; AUS/FLUS-Atypia of undetermined significance/Follicular lesion of undetermined significance; SFM-Suspicious for malignancy

*chi-square statistic=400.00,p-value less than 0.001(Highly significant association).

Table 3: Cytohistological correlation with assessment of risk of malignancy

Bethesda category	No. Of cases (100)	Cases that underwent surgery (56)	Histopathology diagnosis (56)			
			Benign non-neoplastic	Benign Neoplastic	Malignant	Risk of malignancy
Cat- II	84	40	Nodular colloid goitre(22) Hashimotos thyroiditis (16)	-	Papillary carcinoma (2)	2.3%
Cat- III	2	2	-	Atypical parathyroid adenoma (1)	Medullary carcinoma thyroid(1)	50%
Cat- IV	5	5		Follicular adenoma (2) Hyalinising trabecular adenoma (1)	Hurthle cell carcinoma (2)	40%
Cat- V	4	4			Papillary carcinoma (2) Medullary carcinoma (2)	100%
Cat- VI	5	5		Follicular adenoma (2)	Anaplastic carcinoma (1) Follicular variant of Papillary carcinoma (2)	60%

Table 4: Cytological-Histopathological correlation of thyroid lesion.

Bethesda Grading	Diagnosis in histopathology			Total
	Benign Neoplastic	Benign non-neoplastic	Malignant	
Cat-II	0	38	2	40
	0.0%	95.0%	5.0%	100.0%
Cat-III	1	0	1	2
	50.0%	0.0%	50.0%	100.0%
Cat-IV	3	0	2	5
	60.0%	0.0%	40.0%	100.0%
Cat-V	0	0	4	4
	0.0%	0.0%	100.0%	100.0%
Cat-VI	2	0	3	5
	40.0%	0.0%	60.0%	100.0%
Total	6	38	12	56
	10.7%	67.9%	21.4%	100.0%

*chi-square statistic = 59.733, p-value<0.001 (Highly significant association)

Table 5: Age and sex distribution of thyroid lesion (based on fine-needle aspiration cytology according to Bethesda system)

Age range (years)	Total no of patients (100)	Gender M/f	ALL FNAs (N=100)				
			Bethesda II	Bethesda III	Bethesda IV	Bethesda V	Bethesda VI
10-20	2	0/2	2	-	-	-	-
21-30	37	0/37	35	1	1	-	-
31-40	45	4/41	37	-	4	2	2
41-50	7	4/3	3	-	-	2	2
51-60	4	0/4	3	1	-	-	-
61-70	5	2/3	4	-	-	-	1
Total	100	10/90	84	2	5	4	5

Table 6: Comparison of percentages of distribution of fine needle aspiration diagnosis with other studies

Diagnostic category	Present study	Jo et al	Yassa et al	Nayar and Ivanovic	Payal M et al	Shagutta et al
Benign	84	59	66	64	80	77.6

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AUS/FLUS	2	3.4	4	18	4.9	0.8
SFN	5	9.7	9	6	2.2	4
SFM	4	2.3	9	2	3.6	2.4
Malignant	5	7	5	5	2.2	3.6

Table 7: Comparison of percentages of risk of malignancy of present study with other studies

Diagnostic category	Present study	Jo et al	Yassa et al	Nayar and Ivanovic	Payal M et al	Shagutta et al
Benign	2.3	11	0.3	2	13	3.1
AUS/FLUS	50	17	24	6	100	50
SFN	40	25.4	28	14	25	20
SFM	100	70	60	53	50	80
Malignant	60	98.1	97	97	100	100

Table 8: Comparison of percentages of sensitivity, specificity, diagnostic accuracy, positive and negative predictive value of present study with other studies

Study	No of cases	Sensitivity	Specificity	Accuracy	positive predictive value	Negative predictive value
Al Sayer et al	70	86%	93%	92%	80%	96%
Bouvet et al	78	93.5%	75%	79.6%	85.3%	88.2%
AF Roze et al	170	61.9%	99.3%	94.5%	92.8%	94.7%
Ko et al	207	78.4%	98.2%	84.4%	99%	66.3%
Cusick et al	283	76%	58%	69%	72%	64%
Muratli et al	126	87.1%	64.6%	77.3%	76.1%	79.5%
Present study	100	81.8%	88.3%	87%	64%	95%

Statistical analysis showed the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of FNAC to be 81.8 %,88.3 %, 64% 95 % and 87% respectively. [Table 8]

DISCUSSION

Thyroid malignancies constitute 1% of all cancers and are responsible for 0.5% of all cancer related deaths worldwide.[4] The six-tired Bethesda system provides standardized nomenclature for reporting thyroid FNA smears .The advantage of this systematic approach is that each of the six Bethesda categories has implied risk of malignancy which helps the clinicians to plan appropriate therapy necessary for the patient.[5] We compared the results in our study with Jo et al., Chang et al., kapila et al., Yassa et al., Payal M et al and Nayar and Ivanovic.[6] The distribution of cases as per six-tier Bethesda system is different from other studies, with the percentage of cases in benign category being higher, the excision is due to cosmetic purpose and even to detect incidental malignancies.[7] [Table 6] The percentage of AUS/FLUS category is lower as compared to other studies. As per the guidelines of the Bethesda system, only aspirates with features of atypia, microfollicles and focal occurrence of Hurthle cell that could not be categorized as benign, SFN, SFM and malignancy were described as AUS/FLUS.[6] In our study the distribution of AUS is 2% that did not exceed the target 7%. The recommended management for AUS/FLUS is clinical correlation and repeat FNAC at an appropriate interval thus reducing the incidence of surgery.[6] The risk of malignancy for different categories in our study correlated well with the risks mentioned in the Bethesda system and with studies of Jo et al, Yassa et al and Nayar and Ivanovic and differences with the studies of Payal M et al and Shagutta et al. [Table 7] We have compared the sensitivity, specificity, diagnostic accuracy, positive and negative predictive value of present study with other studies.[Table 8]

CONCLUSION

Examining thyroid fine needle aspirations (FNAs) using the Bethesda system for reporting has facilitated accurate cytological diagnosis. This system establishes a uniform and reproducible approach to reporting thyroid cytology, resulting in enhanced clinical relevance and heightened predictive value. The diagnostic utility is contingent upon factors such as the nature of the disease, the cytopathologist's experience, and a comprehensive awareness of specific limitations.

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