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CYTOMORPHOLOGICAL SPECTRUM OF THYROID NODULES DIAGNOSED BY FINE-NEEDLE ASPIRATION CYTOLOGY IN A TERTIARY CARE CENTER

Original Article

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ABSTRACT

Background: Fine-needle aspiration cytology (FNAC) is a safe, reliable, and non-invasive diagnostic procedure for thyroid lesions, effectively reducing unnecessary surgical biopsies. This outpatient procedure enables rapid and accurate evaluation of thyroid nodules.

Objective: This study aimed to analyze the cytological spectrum of thyroid lesions and evaluate the diagnostic efficacy of FNAC using the Bethesda classification system.

Materials and Methods: A cross-sectional study was conducted over one month at the Pathology Department of King Edward Medical University/Mayo Hospital, Lahore, involving 82 patients with thyroid nodules. FNAC was performed using 22–24-gauge needles, with samples processed per standard fixation and staining protocols.

Statistical Analysis: Data was analyzed using SPSS version 23. Qualitative variables (e.g., lesion type) were reported as frequencies and percentages, while quantitative variables (e.g., age) were expressed as mean ± SD.

Results: Of 82 aspirates, distribution by Bethesda categories was: non-diagnostic (ND) 16 (19.5%), benign (BN) 36 (43.9%), follicular neoplasm (FN) 13 (15.8%), atypia of undetermined significance (FLUS) 10 (12.2%), suspicious for malignancy (SM) 5 (6.1%), and malignant 2 (2.4%). Thyroid lesions predominated in women (69%) compared to men (31%), with the highest incidence in patients aged 30–40 years.

Conclusion: The Bethesda system standardized FNAC reporting, identifying higher malignancy risks in FLUS, FN, and SM categories. FNAC proved to be a safe, timely, and first-line diagnostic tool for thyroid nodules.

Keywords: FNAC, thyroid nodule, Bethesda classification, diagnostic evaluation, cytology.

INTRODUCTION

Thyroid nodules are a common clinical finding, with approximately 85–90% being benign (Haugen et al., 2016). These nodules vary significantly in size, ranging from 0.5 millimeters to 8.8 centimeters, though the average diameter typically falls between 1.0 and 1.9 cm (Gharib et al., 2016). Their prevalence in the adult population is estimated at 4–7%, with a higher incidence in women (5%) compared to men (1%) (Dean & Gharib, 2018). While most nodules are harmless, about 3–10% may harbor malignancy, depending on factors such as age, genetic predisposition, and other risk factors (Haugen et al., 2016). Thyroid lesions can be classified as neoplastic (benign or malignant) or non-neoplastic (non-cancerous pathological changes), with variations in metastatic patterns observed between developed and developing nations due to geographical and racial influences (Kitahara & Sosa, 2016).

Accurate diagnosis remains crucial, as conventional clinical and radiographic features lack sufficient specificity and sensitivity for routine use (Gharib et al., 2016). Fine Needle Aspiration Cytology (FNAC) has emerged as the gold standard for evaluating thyroid nodules due to its rapid, cost-effective, safe, and reliable nature (Cibas & Ali, 2017). This minimally invasive technique allows for the diagnosis of both neoplastic and non-neoplastic lesions without scarring, reducing the need for surgical biopsies (Haugen et al., 2016). FNAC is particularly valuable in assessing superficial and deep-seated lesions, including lymphadenopathy, while minimizing patient trauma and healthcare costs (Cibas & Ali, 2017).

To standardize reporting, the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was introduced, categorizing FNAC findings into six diagnostic groups: non-diagnostic, benign, atypia of undetermined significance (AUS), follicular neoplasm/suspicious for follicular neoplasm, suspicious for malignancy, and malignant (Cibas & Ali, 2017). This system helps clinicians estimate malignancy risk and guide appropriate treatment strategies (Haugen et al., 2016). Given its critical role in thyroid nodule evaluation, FNAC, supported by the Bethesda classification, remains indispensable in modern diagnostic practice (Gharib et al., 2016).

MATERIALS AND METHODS

Study Design and Ethical Considerations

This cross-sectional diagnostic study was conducted after obtaining ethical approval from the Institutional Review Board (IRB) of King Edward Medical University, Lahore. Comprehensive pre-research planning was undertaken, including determination of sample size, research design, development of a standardized proforma, and establishment of inclusion/exclusion criteria. The study protocol was thoroughly reviewed by the Department of Pathology at King Edward Medical University to ensure methodological rigor and ethical compliance.

Study Setting and Duration

The investigation was carried out at the Pathology Department of King Edward Medical University/Mayo Hospital, Lahore, over a period of one month following approval of the research synopsis. This tertiary care setting was selected due to its high patient volume and established cytopathology services.

Sample Size Determination and Sampling Technique

The sample size was calculated using the formula for prevalence studies:

$$n = \frac{Z^2_{1-\alpha/2} . p.q}{d^2}$$

where:

$Z_{1-\alpha/2} = 1.96$ (corresponding to 95% confidence level)

p = anticipated prevalence of benign lesions (83.31%)

q = 1 - p (16.69%)

d = desired precision (8%)

This calculation yielded a required sample size of 82 patients. Non-probability convenience sampling was employed for patient selection.

Inclusion and Exclusion Criteria

The study included:

Patients presenting both neoplastic and non-neoplastic thyroid lesions

FNAC specimens demonstrating moderate to high cellularity on preliminary assessment

Exclusion criteria comprised:

Hemorrhagic specimens compromising cytological evaluation

Samples with inadequate cellularity for definitive diagnosis

Patients with bleeding disorders or anticoagulant therapy

METHODOLOGICAL PROCEDURES

Clinical Evaluation:

All participants underwent comprehensive clinical assessments including detailed history taking and thorough physical examination of the thyroid gland, with documentation of nodule characteristics.

FNAC Technique:

Procedures were performed using aseptic technique with 23–24-gauge needles attached to 10ml syringes

Multiple passes were made through different areas of each nodule to ensure representative sampling

Both conventional palpation-guided and ultrasound-guided aspirations were employed as clinically indicated

Sample Processing:

Aspirated material was immediately processed

For fluid specimens, centrifugation was performed at 2000 rpm for 5 minutes

Sediment was used to prepare 3-4 smears per patient using standard techniques

Slide Preparation and Staining:

Two slides were immediately fixed in 95% ethanol for:

Hematoxylin and Eosin (H&E) staining

Giemsa staining

Two additional slides were air-dried for rapid assessment

Special stains were applied when indicated

Cytopathological Evaluation:

All slides were examined by at least two experienced cytopathologists

Cellularity was graded as high, moderate, or low

Morphological features were systematically evaluated

Final diagnoses were categorized according to the Bethesda System for Reporting Thyroid Cytopathology

Data Collection and Analysis
Data were collected using a standardized proforma capturing:

Demographic variables (age, gender)

Clinical findings

Cytomorphological characteristics

Final diagnostic categorization

Statistical analysis was performed using SPSS version 23:

Continuous variables (e.g., age) were expressed as mean ± standard deviation

Categorical variables (e.g., diagnostic categories) were presented as frequencies and percentages

Interobserver variability was assessed using kappa statistics

Diagnostic accuracy measures were calculated where applicable

Quality Assurance Measures
To ensure study quality:

All FNAC procedures were performed by trained personnel

Standard operating procedures were strictly followed

Double-blind slide review was conducted for equivocal cases

Regular calibration sessions were held among pathologists

Internal validity checks were performed on all data entries

This comprehensive methodology was designed to provide reliable data on the cytological spectrum of thyroid lesions while rigorously evaluating the diagnostic utility of FNAC in our clinical setting. The standardized approach facilitated comparison with existing literature while accounting for local epidemiological factors.

RESULTS

There were 82 cases, including 25 men (31 per cent) and 57 women (69 per cent). A ratio of 1:2.5 indicates most women.

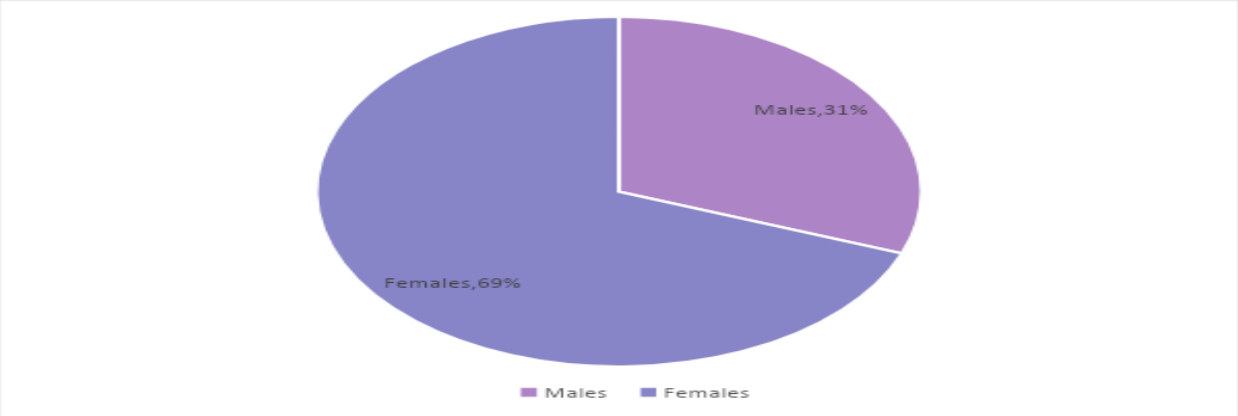

Figure 01: *Frequency of Male and Females*

The oldest patient observed was 70 years old, while the youngest patient was 18 years old. The maximum number of patients lay between the ages 30-55years with a mean age of 42.5 years.

Table 01: Age-wise distribution of cases in the study group

Age (Years)	No. of cases	Percentage%
0-10	00	00%
11-20	5	6.1%
21-30	13	15.8%
31-40	17	20.7%
41-50	27	32.9%
51-60	30	36.5%
61-70	**8**	**9.7%**

Table 02: Histopathological examination finding the wise distribution of cases

S. No.	HOPE	No. of cases	Percentage
1	Bethesda Category 1 (Non-Diagnostic or Unsatisfactory)	16	19.5%
2	Bethesda Category 2 (Benign colloid goiter)	36	43.9%
3	Bethesda Category 3 (Follicular Lesion of Undetermined Significance)	10	12.2%
4	Bethesda Category 4 (Follicular Neoplasm)	13	15.8%
5	Bethesda Category 5 (Highly Suspicious for Malignancy)	05	6.2%
6	Bethesda Category 6 (Suggestive of Papillary Thyroid Carcinoma)	02	2.4%
	Total cases	**82**	**100%**

TBSRTC was used to classify 82 different types of thyroid lesions. More than half of the aspirations were classified as non-diagnostic, benign, follicular neoplasm, FLUS, or highly suspected of malignancy. The remaining aspirates were classified as malignant, non-follicular neoplasm or FLUS (2.3 per cent). The distribution of sexes and ages was analyzed. Women were more likely than men to suffer from thyroid disease, and those in their third or fourth decade were the most likely to be impacted. There are 69% females and 31% males in the population.

Table 2 lists the many types of thyroid lesions that fall into each of the several classifications. In our research, the female to male ratio was 2.5:1. An 18-year-old female with a simple colloid goiter was the youngest case. A female thyroid cancer patient, 70 years old, was the oldest. According to the study, the most prevalent thyroid lesion was simple colloid goiter, most common in the 3rd to the fourth decade. Papillary carcinoma was the most common kind of thyroid cancer, occurring most frequently in people in their sixties and seventies.

Table: 03 TBSRTC: Implied risk of malignancy and recommended clinical management

Diagnostic category	Risk of malignancy (%)	Usual management
Non-diagnostic or unsatisfactory	1–4	Repeat FNA with ultrasound guidance
Benign	0–3	Clinical follow-up
Atypia of undetermined significance or follicular lesion of undetermined significance	5–15	Repeat FNA
Follicular neoplasm or suspicious for follicular neoplasm	15–30	Surgical lobectomy
Suspicious for malignancy	60–75	Near-total thyroidectomy or surgical lobectomy
Malignant	**97–99**	**Near-total thyroidectomy**

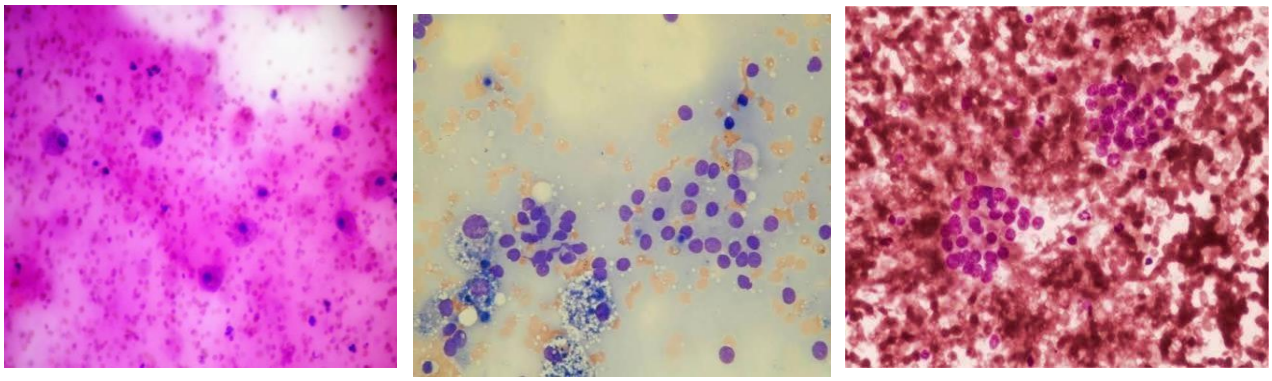

Figure 02: *Category 1: Non-Diagnostic or Unsatisfactory (Cyst fluid only), Category 2: Benign (Colloid Goiter), Category 3: Follicular lesion of undetermined significance*

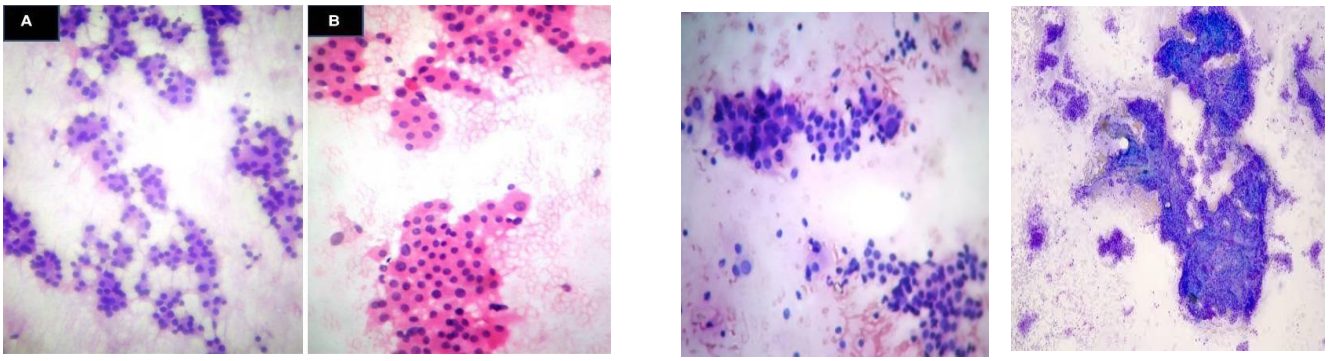

Figure 03: *Category 4: Follicular Neoplasm or Suspicious for F.N, Category 5: Suspicious for Malignancy, Category 6: Thyroid Papillary Carcinoma*

Table 05: Comparison to other studies Microfollicular with the scanty colloid in the background

Lesions	Parikh et al	Uma et al.	Bhatta et al	Our study
Non diagnostic / Unsatisfactory (Category 1)	19	22	-	16
Benign (Colloid Goiter) (Category 2)	207	381	77	36
Follicular Lesion of uncertainty Significance (FLUS) (Category 3)	08	14	03	10
Follicular Neoplasm (Category 4	-	-	-	13
Highly Suspicious for Malignancy (Category 5)	06	17	10	05
Suspicious for papillary thyroid carcinoma (Category 6)	03	05	07	02
Total Cases	**240**	**434**	**90**	**82**

Table 06: Summary of Results

Study variables	Results
Age (Mean ± SD) years	±42.5
Gender% (M: F)	31% (1):69% (2.5)
Histopathological diagnosis (benign: malignant)	**91:09**

DISCUSSION

Fine-needle aspiration cytology

(FNAC) is a widely used, minimally invasive, and cost-effective diagnostic tool for evaluating thyroid nodules, particularly in resource-limited settings where surgical intervention may not be feasible for all patients due to financial constraints and limited healthcare access (Bongiovanni et al., 2012). Despite its advantages, the interpretation of thyroid FNAC results can be challenging due to variability in cytological findings (Cibas & Ali, 2017). To address this issue, The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was developed following a consensus meeting involving cytopathologists, endocrinologists, surgical pathologists, radiologists, and surgeons (Ali & Cibas, 2018). This six-tiered classification system standardizes reporting, improves communication between clinicians and cytologists, and provides estimated malignancy risks for each diagnostic category, thereby aiding clinical decision-making (Haugen et al., 2016).

In our study, thyroid FNAC results were classified according to the Bethesda system, revealing the following distribution: non-diagnostic (19.5%), benign (43.9%), follicular lesion of undetermined significance (12.2%), follicular neoplasm (15.8%), suspicious for malignancy (6.2%), and malignant (2.4%) (Parikh et al., 2013). Consistent with previous studies, the benign category (Bethesda II) was the most prevalent, primarily comprising colloid goiter and thyroid cysts (Uma et al., 2015). Additionally, follicular neoplasms (Bethesda IV) and papillary thyroid carcinoma (Bethesda VI) were identified, aligning with established malignancy risks for each Bethesda category (Bhatta et al., 2018). Our findings demonstrated a high proportion of non-neoplastic (benign) lesions (87%), which correlate

with studies by Parikh et al. (2013), Uma et al. (2015), and Bhatta et al. (2018), reinforcing the observation that most thyroid nodules evaluated by FNAC are benign. This further supports the role of FNAC in reducing unnecessary surgeries, particularly in low-resource settings where surgical options may be limited (Gharib et al., 2016).

Our study analyzed various cytomorphological patterns of thyroid nodules, demonstrating the efficacy of FNAC in diagnosis and subsequent treatment planning (Cibas & Ali, 2017). The implementation of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) has significantly improved standardization in thyroid FNAC reporting (Ali & Cibas, 2018). This six-tiered classification system provides critical clarity, particularly for indeterminate categories such as follicular lesion of undetermined significance (FLUS), follicular neoplasm (FN), and suspicious for malignancy (SM), which carry higher malignancy risks (Haugen et al., 2016). Patients falling into these categories require close clinical monitoring, with surgical intervention remaining a viable option for definitive diagnosis and management (Gharib et al., 2016).

However, while the Bethesda system enhances diagnostic precision, further prospective studies with larger case series are needed to strengthen the cyto-histopathological correlation of these categories (Bongiovanni et al., 2012). Such research would refine risk stratification and improve clinical decision-making, particularly for indeterminate lesions (Ali & Cibas, 2018).

CONCLUSION

FNAC remains the gold standard for initial evaluation of thyroid nodules, offering an optimal balance between diagnostic accuracy, cost-effectiveness, and minimal invasiveness. The Bethesda system has revolutionized thyroid cytopathology reporting, enabling better risk stratification and management. Nevertheless, ongoing research, particularly in indeterminate categories, is essential to optimize diagnostic accuracy and patient outcomes. In resource-limited settings, FNAC proves indispensable, reducing unnecessary surgeries and ensuring efficient use of healthcare resources. Future studies should focus on refining indeterminate classifications to further enhance the clinical utility of thyroid FNAC.

AUTHOR CONTRIBUTION

Author	Contribution
Muhammad Umair Naseer	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Muhammad Bilal	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Sara Sonum	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Muhammad Kaleem	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Hiba Akram	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Yasha Altaf	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Amir Rafeeq	Contributed to study concept and Data collection Has given Final Approval of the version to be published

Sania Saher	Writing - Review & Editing, Assistance with Data Curation
Safdar Ali*	Writing - Review & Editing, Assistance with Data Curation

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