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Comparison of Fine Needle Aspiration Cytology with Histopathology in Assessment of Thyroid Nodules

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ABSTRACT

Objective: To determine the diagnostic accuracy of fine needle aspiration cytology (FNAC) in distinguishing benign nodules from malignant thyroid nodules, keeping histopathology as a gold standard.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Histopathology and Cytopathology, Armed Forces Institute of Pathology, Rawalpindi Pakistan, from Apr to Oct 2022.

Methodology: Fine needle aspiration cytology (FNAC) and histopathology reports of a total of 56 patients with thyroid nodules were analysed. Variables like the age of the patients and the qualitative variables like gender, benign or malignant thyroid nodules on FNAC and histopathology were measured and diagnostic accuracy was calculated. Concordance and discordance rates were also estimated by comparing histopathology and cytology reports.

Results: The results of our study were analysed in four groups. On cytology and histopathology, both concordant lesions with malignant and benign features displayed malignant and benign characteristics, respectively. Diagnostic accuracy of fine needle aspiration cytology (FNAC) in our study was 87.50%, with 72.72% sensitivity and 91.11% specificity. In our study, 87.5% (n=49) cases showed significant concordance between benign and malignant lesions, both on FNAC and histopathologic findings. The discordance rate between malignant and benign lesions were also reviewed. Discordant cases 12.5% (n=7) were mostly because of the sampling errors and artifacts in smears preparation and staining. A few discordan cases showed observer bias errors as well.

Conclusion: Fine needle aspiration cytology is a reliable predictor of malignancy and will help to reduce unnecessary radical thyroid surgeries in benign thyroid nodules.

Keywords: Concordance, Discordance, Thyroid Cytopathology, Thyroid Nodule.

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INTRODUCTION

Thyroid nodules are abnormal growths which are formed inside the gland. These nodules are distinct and show altered echogenicity on ultrasound scan.[1] Prevalence of clinically palpable thyroid nodules is 5.5% while on imaging prevalence varies from 20-76%.[2,3] In Pakistan, thyroid nodules are more common in females and prevalent in iodine deficient areas. There are many risk factors associated with the development of malignant thyroid nodules including age, gender, history of radiation exposure and family history of thyroid cancer.[4]

In evaluation of a thyroid nodule, multiple approaches are used like ultrasound, isotope scanning, fine needle aspiration cytology (FNAC) and histopathology.[5] However, FNAC is a single most sensitive, specific, and cost friendly method of choice, and as a screening tool.[6]

However, FNAC has some limitations including inadequate or hemorrhagic smears, sampling errors, faulty technique, drying artefacts, and worrisome architectural and histological alterations in thyroid nodules followed by fine needle aspiration cytology.

In one German study, sensitivity of FNAC was reported to be 60%, and also concluded that the diagnostic yield of FNAC could be improved by combining it with ultrasound findings.[7] An Egyptian study showed that the sensitivity was 57.89% and specificity was 88.10%.[8] In another study from Pakistan, FNAC showed a diagnostic accuracy of 63.9% while sensitivity and specificity were 82.3% and 64.3% respectively.[9] A study from Multan showed sensitivity of FNAC was 87% and specificity was 86.5%.[2] In another study overall sensitivity, and specificity of FNAC to diagnose a malignant lesion were 92% and 94.4% respectively.[10]

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The purpose of our research was to check the diagnostic accuracy of FNAC in our institute in differentiating a benign and malignant thyroid nodule, taking histopathology as a gold standard procedure.

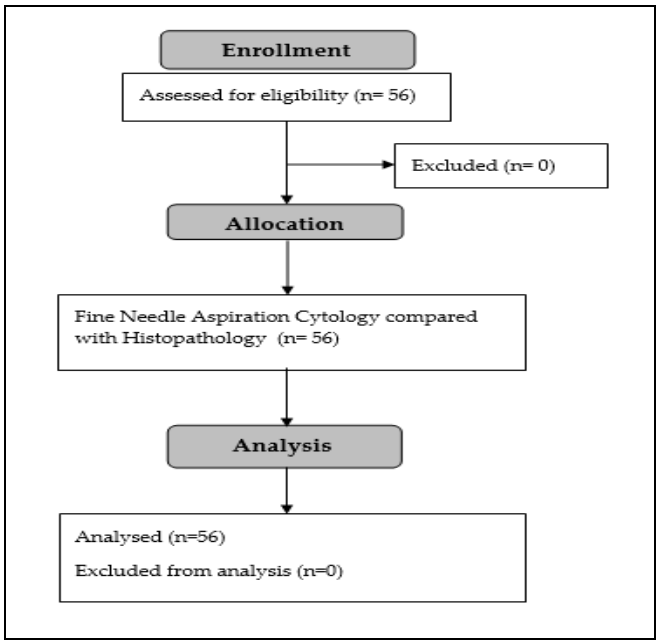
METHODOLOGY

This Quasi-experimental study was carried out in the department of Histopathology and Cytopathology, at Armed Forces Institute of Pathology, Rawalpindi Pakistan, from April to October 2022 after approval by institutional review board.

Inclusion Criteria: Patients of either gender with age ranging from 20-70 years of age presented with thyroid nodule, with FNAC (Bethesda System for Reporting Thyroid Cytopathology II–VI) and subsequent thyroidectomy specimen were included.

Exclusion Criteria: Patients with head and neck tumors other than thyroid were excluded.

Sample size was calculated using WHO calculator, taking into consideration the prevalence of thyroid nodule 5.5%.[11] This came to 56 patients with a clinically palpable thyroid nodule after taking informed consent and giving them a right to withdraw from the study at any time. Non-probability convenient sampling technique was employed for patient recruitment.



Demographic features like patient age, gender and cytological results were recorded. Fine needle aspiration cytology (FNAC) was performed with the help of a 25-gauge needle (5-10ml), Both wet fixed and air-dried smears were prepared. Wet fixed smears were fixed in an ideal fixative of 95% alcohol. The smears were stained with Papanicolaou, Hematoxylin and Eosin and Diff quick stains. Cytological results of thyroid lesions are categorized as per Bethesda System for Reporting Thyroid Cytopathology into 6 groups and their associated risk of malignancy is also listed in the Table-I.[12]

For histopathological analysis, after fixation of tissue in 10% buffered formalin, the tissue was processed in the Tissue Tek® tissue-processing equipment. After being embedded in paraffin wax, 5µm-thick sections were prepared on a semi-automated rotary microtome. These sections were mounted on charged glass slides and stained with haematoxylin and eosin dyes, which were then viewed under a light microscope. All cases were examined by expert histopathologists. FNAC results were compared with histopathological findings. All the data was entered into premeditated proforma which includes patient age, gender, FNAC results, histopathological results, and type of nodule. For this study, we divided cytological results into further into 2 main groups; Bethesda-II, which included benign thyroid nodule and Bethesda-III - Bethesda-VI, which included malignant nodules. These cytological results were compared with histopathological results.

Data was analyzed using Statistical Package for the social sciences (SPSS) version 23:00. Quantitative variables like age were calculated by using mean and standard deviation. Qualitative variables like gender, Bethesda System for Reporting Thyroid Cytopathology and histopathological analysis were presented using frequency and percentage.

Sensitivity of FNAC was calculated with the help of following analyzer TP/TP+FN. Specificity was calculated as TN/TN+FP. Diagnostic accuracy of FNAC was calculated as Sensitivity x Prevalence + Specificity x (1 – Prevalence).[13]

RESULTS

Out of the total 56 cases in this study, 46.4% (n=26) were males and 53.6% (n=30) were females. Overall, the mean age of patients was 40.0±9.0 years. On FNAC, 78.57% cases (n=44) were diagnosed as benign adenomatous colloid nodule. Out of 44 cases that were diagnosed benign, 93.18% (n=41) were true negative and concordant with histopathological diagnosis. However, 6.81% (n=3) cases were false negative or malignant discordant as they showed malignant features on histopathology. Out of these 3

cases, 33.33% (n=1) case was of follicular adenoma, 33.33% (n=1) case was of follicular thyroid carcinoma and other one 33.33% (n=1) was papillary thyroid carcinoma.

Table-I: FNAC showing Bethesda System for Reporting Thyroid Cytopathology and their associated Malignant Risk and Recommended Management

Bethesda Category	Diagnosis	Risk of Malignancy	Usual Management
I	Non-diagnostic	1-4%	Repeat FNAC with ultrasound guided
II	Benign	0-3%	Clinical follow up
III	Atypia of Undetermined significance AUS/Follicular lesion of undetermined significance (FLUS)	5-15%	Repeat FNAC
IV	Follicular neoplasm/Suspicious for follicular neoplasm	15-30%	Surgical lobectomy
V	Suspicious for malignant	60-75%	Near total thyroidectomy or surgical lobectomy
VI	Malignant	97-99%	Near total thyroidectomy

Table-II: Sensitivity, Specificity, Positive and Negative Predictive Values of Fine Needle Aspiration Cytology

Fine Needle Aspiration Cytology Findings	Histopathology Findings	
	Histopathological Positive	Histopathological Negative
Cytological Positive (n=12)	8(66.67%) (True Positive)	4(33.33%) (False Positive)
Cytological Negative (n=44)	3(6.82%) (False Negative)	41(93.18%) (True Negative)
Total(n=56)	11	45

*Sensitivity= TP/(TP+FN) = 8/ (8+3) * 100=72.72%*
*Specificity= TN/(TN+FP) = 41/ (41+4) * 100=91.11%*
*Positive Predictive Value= TP/(TP+FP) * 100= 8/ (8+4) = 66.67%*
*Negative Predictive Value= TN/(TN+FN) * 100=41/ (41+3) = 93.18%*
*Diagnostic Accuracy=(TP+TN)/All patients*100 = (8+41)/56=87.5%*

Twelve cases were diagnosed malignant as per Bethesda System for Reporting Thyroid Cytopathology, out of which 66.66% (n=8) were true positive, 25% (n=2) cases were reported Bethesda-III as per Bethesda reporting category which were later diagnosed as follicular adenoma and follicular thyroid carcinoma respectively. One case (12.5%) was reported as Bethesda-IV and later turned into follicular variant of papillary thyroid carcinoma and remaining 62.5% (n=5) were diagnosed as Bethesda-V and Bethesda-VI, out of which one turned into medullary thyroid carcinoma, and others turned into papillary thyroid carcinoma. Four out of 12 cases, 33.33% (n=4) were reported as false positive, one was reported as Bethesda-III and other 3 were reported as Bethesda-V. They were benign discordant and turned into benign on histopathology; one (25%) was Hashimoto thyroiditis and other 75% (n=3) cases were hyperplastic nodule. Most common neoplasm in thyroid on histopathology was papillary thyroid carcinoma and follicular thyroid carcinoma was the second one (Figure-1 and Figure-2).

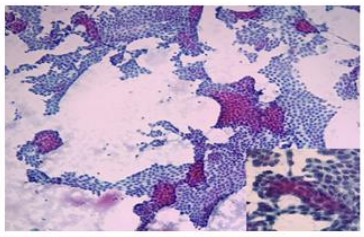


Figure-1A: Bethesda Category V showing papillary carcinoma features.

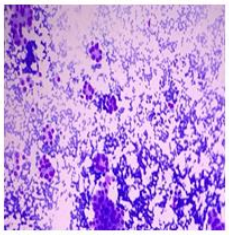


Figure-2A: Bethesda category II on 10X power

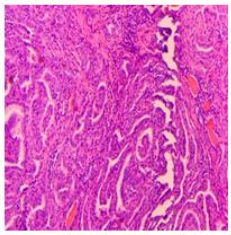


Figure-1B: Classical papillary thyroid carcinoma

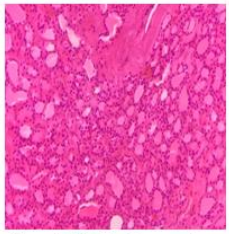


Figure-2B: Follicular neoplasm on 10X power

Cytological diagnosis achieved sensitivity of 72.73% and specificity of 91.11%, positive predictive value (PPV) of 66.67%, and negative predictive value (NPV) of 93.18%, false negative ratio (FNR) of 27 %, false positive ratio (FPR) of 8.8% and diagnostic accuracy of 87.50% was observed, as seen in Table-II.[14]

DISCUSSION

Thyroid nodules are not uncommon in our population with a prevalence of clinically palpable thyroid nodules as 4-7%. Between 85-89% of the lesions are benign, out of which adenomatous nodule or hyperplastic nodule is the most common lesion. It is named as thyroid follicular nodular disease by WHO classification in 2022.[15] Approximately 7-15% of thyroid nodules are malignant showing atypical features as shown in figures 2A and 2B.[16] Diagnostic approach of thyroid nodule is increased with the help of ultrasound, Isotope scan, FNAC and histopathology. FNAC is the most convenient, reliable, and economical test to categorize a thyroid lesion.[17] But the results can be improved when it is combined with an ultrasound scan. Bethesda System for Reporting Thyroid Cytopathology categorization of thyroid nodules.[18] In our study, as per inclusion criteria we included 56 patients with clinically palpable thyroid nodules. Among these 56 patients, female to male predominance is seen which

corresponds with the study done at CMH Multan, Pakistan.[2] Mean age of diagnosis is 40±9.0 years.

In multiple studies, specificity was more than 85% and sensitivity was more than 80% which are comparable to our study.[15-18] However, other studies showed that the diagnostic accuracy was less than 65%.[14] Our study showed sensitivity of 72%, specificity 91% and diagnostic accuracy of 87.50% which are comparable to previous studies conducted at different times during last 5 years.[9,15]

In the diagnosis of a frank malignant lesion, FNAC is very specific and sensitive diagnostic technique. It is important that patients with benign nodules on FNAC should have regular radiological and clinical follow-ups. Any lesion showing overlapping features must be discussed in intradepartmental meetings to prevent any error in the reporting. Further results could be improved by following the Bethesda System for Reporting Thyroid Cytopathology meticulously and improving the smears preparation.

LIMITATIONS OF STUDY

There were certain pitfalls in our study which could be due to the overlap of benign and malignant cytomorphological features especially Bethesda category III and IV. There were also some thyroidectomy specimens whose cytological smears were reported in other institutes. The last and most important factor is related to sampling technique and smear preparation: showing certain drying artefacts in smears preparation or in multinodular goitre needle, not probing all nodules, as a malignant nodule may be coexisting with a benign hyperplastic nodule. There are also certain limitations regarding categorizing a follicular lesion which gives a real challenge to a cytopathologist.

CONCLUSION

Our study findings concludes that fine needle aspiration cytology (FNAC) is an invaluable procedure which is minimally invasive for preoperative assessment of patients with a thyroid nodule. FNAC is a sensitive, specific, and accurate initial tool for the diagnostic evaluation of thyroid nodules.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AA & MA: Data acquisition, data analysis, critical review, approval of the final version to be published.

HD & HT : Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

UA, SH & NZ: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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