ORIGINAL ARTICLE

Relationship of Cytological with Histopathological Examination of Palpable Thyroid Nodule

NAUSHEEN HENNA[1], SHAHZAD AHMED FAKHAR[2], NAVEED AKHTER[3], *MUHAMMAD MASOOD AFZAL[4], KHIZER AFTAB AHMAD KHAN[5], TAYYABA RASHID[6], FAROOZ AZIZ[7]*

ABSTRACT

Aims: To observe the relationship between cytopathological diagnosis (using Bethesda reporting system) and Histopathological examination and to find out the diagnostic accuracy of thyroid fine needle aspiration cytology (FNAC) as compared to gold standard i.e., histological examination.
Method: A retrospective data of 77 cases was collected having record of both FNAC and histopathological diagnosis (gold standard). The study recruited patients who were referred from outpatient department to Pathology department, Shalamar Institute of Health Sciences, Lahore, for FNAC of palpable thyroid nodule. The study included patients who underwent FNAC between Jan 2012-Dec 2016. The smears were evaluated and reported according to the standard Bethesda system. Statistical analysis was carried out using SPSS Vr 22.
Results: Total of 77 cases with both FNAC and histopathological examination of postsurgical specimen were included for statistical analysis. The correlation of FNAC with histological examination reveals sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of 85.7 %, 96.4%, 90%, 94.7% and 93.5% respectively. False positive rate was 2.6% and false negative rate was 3.9%.
Conclusion: It is concluded that FNAC is simple, rapid, reliable and very sensitive screening test. Cyto-histological diagnosis correlation is a quality assurance method as it allows to review and evaluate the false positive as well as false negative cases.
Key words: Thyroid, FNAC, Bethesda.

INTRODUCTION

A palpable thyroid nodule is a significant problem in population (4-7% of adult population) [1] but most of them are found to be non-neoplastic which do not need surgical intervention. The screening investigations are thyroid scan, ultrasonography and fine needle aspiration cytology (FNAC). In 1950s, FNAC of thyroidgland was first introduced in Scandinavian countries, which has been commonly practiced in United States in 1970s and then worldwide in the 1980s[2]. A palpable thyroid nodule is the main indication of FNAC, which has been considered to be rapid, minimally invasive and cost effective screening procedure. It is helpful for the patient and for the treating surgeon to plan appropriate management. Besides its many advantages, FNAC has certain limitations which have been related to sampling technique, pathologist skills of aspiration and interpretation of overlapping cytological features etc[3]. A pathologist and the surgeon should be fully aware of the limitations and pitfalls of FNA interpretation in order to manage the patient in the best possible way with the aim of reducing unnecessary avoidable surgeries[2]. The objectives of this study are to assess the relationship between cytopathological (using Bethesda reporting system)[4]and histopathological diagnosis, considering the histopathology examination as gold standard, and to determine the diagnostic accuracy of Thyroid FNAC.

[1]Assistant Professor, Shalamar Institute of Health Sciences, Lahore
[2]Assistant Professor, Fatima Memorial Hospital & Medical College, Lahore
[3]Associate Professor, Rai Medical College, Sargodha
[4,5,6]Demonstrator, Shalamar institute of Health Sciences, Lahore
[7]Professor and Head of Department of Pathology, Shalamar institute of Health Sciences, Lahore
Correspondence to Dr. Nausheed Henna
Email noshihenna2015@gmail.com, +923334399473

MATERIAL & METHODS

A retrospective data of 77 cases was collected having record of both FNAC and histopathological diagnosis (gold standard). This study included patients who were referred from outpatient department to Pathology Department, Shalamar Institute of Health Sciences, Lahore, for FNAC during the last 5 years (Jan 2012-Dec2016) for palpable thyroid nodule. Direct FNAC was carried out by palpation method and was performed by experts without using any anesthetic. Smears were fixed in 95% ethyl alcohol solution for half an hour and Hematoxylin and Eosin staining was done. The smears were examined and reported according to the

standard Bethesda system.[4]Cytology was reported by four consultant pathologist according to the departmental roster. Record of all patients, who underwent surgical intervention in the hospital, was also recovered and validated. Few patients with benign thyroid tumors underwent surgery due to large lesions causing discomfort or cosmetic defects. For surgical specimens, routine processing followed by Hematoxylin and eosin staining was performed. Collected data was analyzed using SPSS version 22.

RESULTS

A total of 77 cases were included in this study, who presented with palpable thyroid nodule to outpatient department for FNAC, for statistical analysis. Sixty nine (89.6%) out of 77 were female and 8 (10.4%) were male with Female: Male ratio of 8.6:1. Patients presented during 13-75 years of the age, with mean age of 38.2 ± 13 years. Maximum number of patients were from 31-40 years of age group (Table1). Laterality of the nodules is shown in figure 1 in terms of percentages.

Bethesda category I included 5 cases composed of 2 cyst fluid only, 5 colloid cysts and two hemorrhagic aspirates; category II comprised of 48 cases including 11 colloid goiter, 26 colloid nodule, 1 follicular nodule, 6 Hashimotos thyroiditis, 2 hyperplastic nodules; Category III included one case; category IV included 13 cases of follicular neoplasm, category V had two cases, one labelled as atypical cells and other as suspicious of papillary thyroid carcinoma, category VI included 4 cases (table 2).

Two cases of category Ishowed hemorrhagic aspirates on repeated attempts which was later on diagnosed as diffuse large B cell Non-Hodgkin's lymphoma (NHL) and other being nodular goiter on surgical specimen. One case in category II was reported as follicular nodule which later on diagnosed as Dyshormonogenetic goiter in a 13 year-old male patient on histological specimen. One case of category III was later on diagnosed as hyperplastic nodule on histology. Nine out of thirteen cases of category IV was diagnosed as follicular adenoma on postsurgical histopathological examination of specimen, two proved to be follicular carcinoma, one papillary microcarcinoma with follicular adenoma and Hashimoto's thyroiditis in surrounding tissue and one proved to be colloid nodule. In category V, one out of 2 cases (which was atypical on aspirate) was found to be hyperplastic nodule with surrounding multinodular goiter, whereasother was follicular variant of papillary carcinoma thyroid on postsurgical specimen (now named as noninvasive follicular thyroid neoplasm with papillary-like nuclear features" (NIFTP)). In category V, two cases were papillary carcinoma and two were diagnosed as medullary carcinoma thyroid (Table 2, Fig. 2).

For correlation analysis, suspicious and atypical cases of FNAC were included in neoplastic/suspicious group. After statistical analysis, Sensitivity was 85.71%, Specificity was 96.43%, false positive rate (FPR) was 2.6%, false negative rate (FNR) was 3.9%, Positive predictive value (PPV) was 90%, Negative predictive value (NPV) was 94.74% and Diagnostic accuracy was 93.51% (table 3).

Table 1: Frequency & percentage of patients in different age groups

Age range (years)	Frequency	%age
11-20	7	9.1
21-30	18	23.4
31-40	22	28.6
41-50	16	20.8
51-60	11	14.3
61-70	2	2.6
71-80	1	1.3

Fig. 1: Percentage of laterality of palpable thyroid nodule

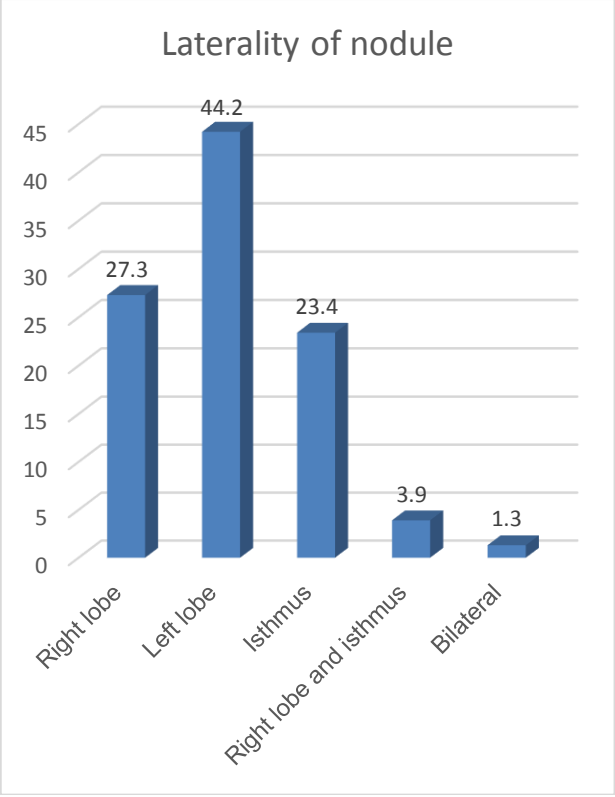


Table 2: Detailed Bethesda categories with corresponding histological diagnosis of each group.

Bethesda Category = n (%)	Cytological diagnosis	Histological diagnosis
I = 9 (11.7)	Hemorrhagic aspirate= 2	NHL: 1 Nodular Goiter: 1
	Colloid cyst= 5	Colloid cyst : 1 Hyperplastic nodule with degeneration: 1 MNG: 3
	Cyst fluid only: 2	Hyperplastic nodule: 1 Colloid cyst: 1
II =48 (62.3)	Colloid goiter: 26	MNG : 12 Follicular adenoma: 2 Hyperplastic nodule: 10 Colloid cyst: 2
	Hyperplastic nodule: 2	Hyperplastic nodule: 2
	Hashimoto: 6	Hashimotos: 6
	Follicular nodule: 1 Benign follicular lesion: 2 Colloid goiter: 11	Dyshormonogenetic goiter: 1 MNG: 1 Adenoma: 1 MNG: 8 Colloid nodule: 1 Hyperplastic nodule: 1 Papillary microcarcinoma with MNG: 1
III: 1 (1.3)	FLUS : 1	Hyperplastic nodule : 1
IV: 13(16.9)	Follicular neoplasm: 13	Follicular adenoma : 9 Follicular carcinoma: 2 Pap micro with adenoma: 1 Colloid nodule: 1
V: 2 (2.6)	Atypical cells : 1	MNG with hyperplastic nodule: 1
	Suspicious of PTH: 1	Follicular variant of papillary carcinoma: 1
VI: 4 (5.2)	Medullary CA: 2	Medullary CA: 2
	Papillary CA: 2	Papillary CA: 2

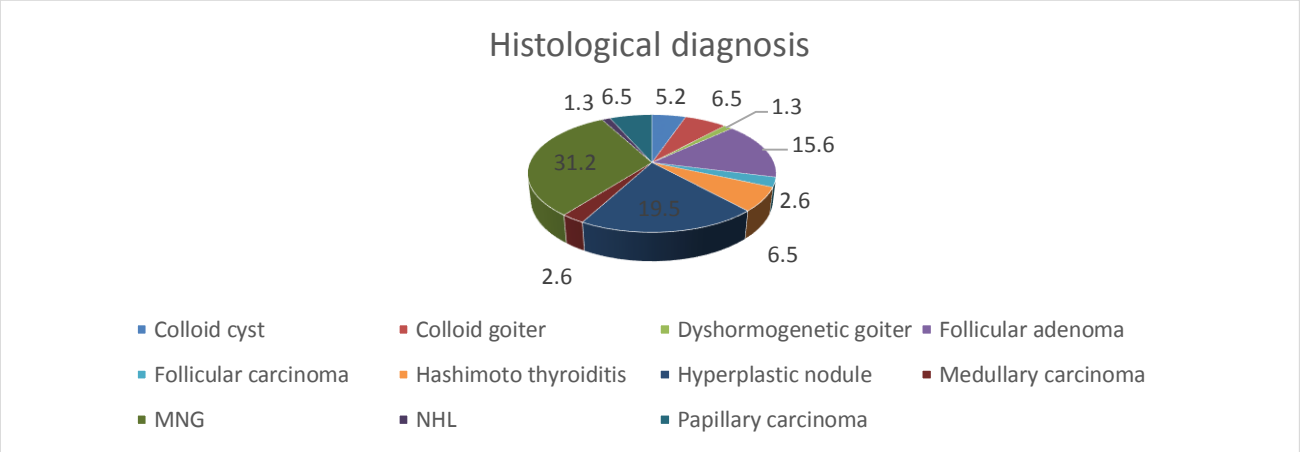
Table 3: Number & percentages of True positive (TP), False negative (FN), False positive (FP) and True negative (TN) in FNAC and histological diagnosis.

	FNAC neoplastic /Suspicious	**FNAC non-neoplastic**	**Total**
Histodiagnosis Neoplastic	18(TP)	3(FN)	21(27%)
Histodiagnosis non-neoplastic	2(FP)	54(TN)	56(73%)
Total n(%)	20 (26%)	57 (74%)	77

Table 4: Comparison of sensitivity, specificity, Positive predictive value (PPV), Negative predictive value (NPV) and diagnostic accuracy among various studies in comparison to the present study.

	Sensitivity	**Specificity**	**PPV**	**NPV**	**Accuracy**
Gupta et al. 2010 [6]	80	86.6	80	86.6	84
Basharat et al. 2011 [11]	80	97.7	80	97.7	96
Mamoon et al. 2013 [10]	85.7	73.3	50	94.2	76.2
Vasudev et al. 2014 [7]	96	66	66	96	90
Sharma C. 2015 [2]	89.5	98	84.6	98.6	97
Hajmanoochehri&Rakhi. 2015 [8]	95.2	68.4	83.3	86.6	85.14
Present study	85.7	96.4	90	94.8	93.5

Fig. 2: Pie chart shows the percentage of histological cases diagnosed in each group.



DISCUSSION

Published literature delineates that FNAC has an accuracy rate around 95% in the detection of thyroid malignancy. Nevertheless, like any other screening test, it has its limitations and diagnostic pitfalls[3]. Majority of palpable thyroid nodules are found to be non-neoplastic i.e., benign category as the published data showed[5]. Among benign category, colloid goiter is being the most common. Accurate assessment of FNAC helps the surgeon in selecting patients who need surgical intervention and in turn avoiding unnecessary surgeries. The Bethesda system for reporting of Thyroid cytology has been made to bridge the communication gap between pathologist and clinicians. This standard reporting system makes the cytology report clear and clinically relevant. Bethesda reporting system is followed in our institute.

Sukumaran et al in 2014[5] found Malignancy in 59.68%, suspicious of malignancy 4.03%, Follicular neoplasm 13.3%, Atypia of undetermined significance 4.43%, Benign in 12.5% and non-diagnostic/ unsatisfactory in 6.04%.

Gupta et al in 2010[6] reported FNAC results as colloid nodular goiter in 39(52%) cases, 12(16%) cases as follicular neoplasm, 9(12%) cases as papillary carcinoma, 6(8%) cases as hurthle cell lesions, 6(8%) cases as benign cystic lesions, and 3 (4%) cases to be suspected of malignancy. Vasudev et al. in 2014[7] reported benign cytology in 34.2%, 12 cases of suspicious cytologies were reported of which 2 cases were reported with a suspicion of Papillary Carcinoma and 10 cases (3.8%) with a suspicion of a Follicular lesion. Papillary Carcinoma was reported in 6 cases. Hajmanoochehri & Rabiee in 2015[8] reported distribution of the FNAC cases according to the Bethesda categories as benign and nonneoplastic cases 28.7%, 4% in the atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS) category, 26.7% were in the Follicular neoplasm or Suspicious of follicular neoplasm (FN/SFN) category, 15.8% were suspicious for malignancy and malignant cases of 24.8%, whereas, present study showed category I: 11.7%, II: 62.3%, III: 1.3%, IV:16.9, V: 2.6%.VI: 5.2%.

Literature search shows 3–18 % of thyroid FNAs reported as FLUS[5], however, its reporting rate at our institute remained 2%.Most published studies report a false negative rate and false positive rate in the range of 1–11%[1,2,5,8,9]. Our results were in concordance with the published data as FPR was 2.6% and FNR was 3.9%. However, we are also aware of the fact that true frequency of false negative results is very difficult to calculate because only few patient diagnosed as benign through FNAC undergo surgical intervention. Competent authorities are of opinion that false negative result should be kept under 5%[10] and so is the case in our study.

In thyroid gland diseases, literature shows the accuracy of FNAC to be 95%, sensitivity and specificity in the ranges of 79-90% and at 80-100% respectively[11]. Sensitivity varies between 56-100%, and specificity between 52-100%. A positive predictive value is reported to be 34–100%, whereas a negative predictive value is around 83–100%[2,].

The results of this study are in accordance with the literature (Table 4) as we found 85.7%, 96.4%, 90%, 94.8% and 93.5% as sensitivity, specificity, positive, predictive value, negative, predictive value and accuracy respectively.

CONCLUSION

This study concludes that FNAC is simple, rapid, reliable and very sensitive screening test. It should be kept as first line screening. FNAC effectively prevent unnecessary surgeries in benign cases which constitute the largest group among others. Cyto-histological diagnosis correlation is an excellent quality assurance method as it allows to review and evaluation of false positive and false negative cases.

REFERENCES

1. Gabalec F, Cap J, Ryska A, Vasatko T, CeeovaV. Benignfine-needle aspiration cytology of thyroid nodule: to repeat or not to repeat? European Journal of Endocrinology 2009; 161: 933-7.
2. Sharma C. Diagnostic accuracy of fine needle aspiration cytology of thyroid and evaluation of discordant cases. J Egyptian National Cancer Institute 2015; 27: 147-53.
3. Sinna EA and Ezzat N. Diagnostic accuracy of fine needle aspiration cytology in thyroid lesions. Journal of the Egyptian National Cancer Institute 2012; 24: 63–70.
4. Cibas ES, Ali SZ. The Bethesda System for Reporting Thyroid Cytopathology. *Am J ClinPathol*2009; 132: 658- 65.
5. Sukumaran R, Kattor J, Pillai RK, Ramadas PT, Nayak N, Somanathan T, George NA, Sebastian P. Fine Needle Aspiration Cytology of Thyroid Lesions and its Correlation with Histopathology in a Series of 248 Patients. Indian J SurgOncol 2014; 5(3): 237–241.
6. Gupta M, Gupta S, Gupta VB. Correlation of Fine Needle Aspiration Cytology with Histopathology in the Diagnosis of Solitary Thyroid Nodule. J Thyroid Research 2010; 1-5.
7. Vasudev V, Hemalatha AL, Rakhi B, Githanjali s. Efficacy and pitfalls of FNAC of thyroid lesions in children and adolescents. Journal of Clinical and Diagnostic Research 2014; 8(1): 35.
8. Hajmanoochehri F, Rabiee E. FNAC accuracy in diagnosis of thyroid neoplasms considering all diagnostic categories of the Bethesda reporting system: A single-institute experience. J Cytol 2015; 32: 238-43.
9. Basharat R, Bukhari MH, Saeed S, Hamid T. Comparison of Fine Needle Aspiration Cytology and thyroid scan in solitary thyroid nodule. Pathology Research International 2011; 1-9.
10. Mamoon N, Jamy R, Khan AH. Evaluation of fine needle aspiration cytology as a screening tool in thyroid lesions. JPMA 2013; 63 (9); 1120-23.
11. Anwar K, Khan IA, Zada B. The role of fine needle aspiration cytology in the management of solitary thyroid nodule. KUST Med J 2010; 2(2): 49-52.