DIAGNOSTIC ACCURACY OF FINE NEEDLE ASPIRATION CYTOLOGY IN DETECTION OF THYROID CARCINOMA IN PATIENTS WITH THYROID NODULES USING HISTOPATHOLOGY AS GOLD STANDARD

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ABSTRACT

Objective: To determine the diagnostic accuracy of fine needle aspiration cytology in detection of thyroid carcinoma in patients with thyroid nodules using histopathology as gold standard.

Study Design: Cross sectional validation study.

Place and Duration of Study: Department of Histopathology, Combined Military Hospital Multan, from Oct 2016 to Apr 2017.

Methodology: A total of 120 cases of thyroid lesions were included in the study. Data was analyzed using computer software SPSS 18. The quantitative variables like age, size of nodule, duration of the disease. Gender, marital status, use of iodine supplement in diet and thyroid carcinoma on fine needle aspiration cytology and histopathology were measured and diagnostic accuracy was also calculated.

Results: Out of 120 study cases, 28 (23.3%) were males while 92 (76.7%) were females. Mean age of our study cases was 42.31 ± 8.40 years. Mean disease duration was 8.34 ± 3.91 months that thyroid lesions were benign in 52 cases(43.4%), 20 cases were of suspicious for follicular neoplasm (16.6%). Histopathology documented thyroid carcinoma was present in 31 (25.8%) cases. Of these papillary carcinoma was seen in 25 cases (80.6%) and medullary carcinoma was seen in 6 cases (19.35%) Sensitivity of fine needle aspiration cytology was 87%, specificity was 86.51%, diagnostic accuracy was 86.66%, positive predictive value was 69.23% and negative predictive value was noted to be 95.06%.

Conclusion: Fine needle aspiration cytology is found to be a very accurate, sensitive and specific initial diagnostic modality in evaluating patients who presented with thyroid swellings. It is highly reliable, easy to perform, cost-effective and accurate tool in differentiating a malignant from benign lesion.

Keywords: FNAC, Thyroid carcinoma, Thyroid nodules.

INTRODUCTION

The thyroid gland is located antero-inferior to the larynx and consists of two lateral lobes connected by a thin isthmus[1]. Lesions of thyroid are common in our country and mostly involve women and in iodine deficient areas[2]. The risk of solitary thyroid nodule and thyroid carcinoma is high if there is history of exposure to ionizing radiation in childhood[2].

A solitary thyroid nodule is a benign encapsulated lesion, showing variable sized follicles[3]. The prevalence of thyroid nodules depends on how carefully one looks for them. Palpable nodules are found in 4% to 7% of adults, but the prevalence is much higher (20% to 70% adults) when non-palpable nodules are included[4].

A variety of tests are available to evaluate thyroid nodules, including radiological imaging, fine needle aspiration cytology (FNAC) and histopathology. In evaluating thyroid nodules, FNAC is the first-line diagnostic test, as it is a simple, rapid and cost effective test that can effectively distinguish between the non-neoplastic and neoplastic thyroidal lesions[5]. But the results are sometimes misleading[6].

Thyroid FNAC was introduced in Scandinavian countries in 1950s and became popular in the United States in 1970s and then worldwide in the 1980s. Today it remains the mainstay of diagnostic workup for thyroid pathologies.

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Thyroid FNAC is a safe and simple test that is considered as the test of first choice for the primary diagnosis and evaluation of patients with thyroid swelling. One of the major advantages is that FNAC can be done as an out-patient procedure. FNAC is relied upon to distinguish benign from neoplastic or malignant thyroid nodules and therefore has lead to a dramatic decrease in thyroid surgeries. Nevertheless, FNAC has some limitations like specimen inadequacy, sampling technique error and worrisome histologic alterations following fine needle aspiration of thyroid. Cytopathologist should be aware of these potential limitations and pitfalls of FNA interpretation[11].

In one study by Manoj Gupta and Bushan Gupta, FNAC results showed that 39 (52%) cases were of colloid nodular goiter, 12 (16%) follicular neoplasm, 9 (12%) papillary carcinoma, 6 (8%) hurtle cell lesions, 6 (8%) benign cystic lesions, and 3 (4%) were suspected of malignancy. Comparison of FNAC with histopathological findings was performed for the 45 benign cases. Histopathology revealed 39 cases as non-neoplastic lesions, 3 as papillary carcinoma and 3 as follicular adenoma. Sensitivity of FNAC has been reported to be 80% and specificity as 86.6%[7].

In another study by Bagga PK, Mahajan NC, 252 patients were selected. FNAC results were compared with that of histopathological diagnoses. FNAC results were found to be inadequate in 4 (1.6%), benign in 228 (90.5%), suspicious in 17 (6.7%), and malignant in three (1.2%). The histopathology of 32 cases that underwent surgery, revealed benign diagnoses in 25 and malignant in 6 cases, which included papillary carcinoma (50%), follicular carcinoma (33.3%), and medullary carcinoma (16.7%)[8].

In one study carried by Basharat at Mayo hospital Lahor, On FNAC 23 patients (46%) had benign lesion, 22 patients (44%) had indeterminate lesion and 5 patients (10%) had malignant lesions. On histopathology, 45 patients (90%) were confirmed to have benign lesions and 5 patients (10%), malignant lesions. After comparison of results of thyroid scan and FNAC with histopathology, the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of thyroid scan were 80%, 20%, 10%, 90% and 26%, respectively whereas those of FNAC were 80%, 97.7%, 80%, 97.7% and 96%, respectively[2].

Although data is available on this subject, but data shows wide variability. Sensitivity of FNAC thyroid varies from 72% to 90% and specificity varies from 80% to 97%. Keeping this in view, the purpose of my study is to resolve this issue by determining the diagnostic accuracy of FNAC in detection of thyroid carcinoma within thyroid nodules in our local population using histopathological examination as gold standard.

METHODOLOGY

This cross-sectional validation study was carried out at Department of Histopathology, Combined Military Hospital, Multan from 20th Oct 2016 to 20th April 2017, after the approval of ethical committee. Sample size was calculated using WHO sample size calculator with following parameters: Sensitivity of FNAC; 80%, margin of error for sensitivity; 15 %, specificity of FNAC; 86.6%, margin of error for specificity; 12%, prevalence of thyroid carcinoma; 16%, confidence level: 95%, anticipated population proportion: 4%, sample size: 120. A total of 120 patients with thyroid nodules of more than 02 months duration, were selected by non-probability, consecutive sampling technique, between 20-60 years of age, of both genders, after taking informed consent. Patients receiving chemotherapy or radiotherapy, already diagnosed cases of thyroid carcinoma on histopathology and patients with previous history of any type of thyroid surgery were not included in the study. A 10 gauge needle was used to perform FNAC by a histopathologist having an experience of three years. Smears were fixed in 95% alcohol solution, and staining was done using haematoxylin and eosin stains. Following FNAC, all the patients were subjected to surgery after pre-anesthesia assessment. Thyroidectomy specimens were evaluated by

histopathology. Specimens were processed in automated tissue processor and staining was carried out with haematoxylin and eosin stains. Comparison of FNAC with histopathological findings was done. All cases were examined by consultant histopathologist having an experience of more than five years. All the data was entered into the pre-designed proforma.

All the collected data was analyzed using computer software SPSS 18. The quantitative variables like age, size of nodule, duration of the disease was presented by calculating mean and standard deviation. The qualitative variables like gender, age groups, marital status, use of Iodine supplement in diet and thyroid carcinoma on FNAC and histopathology was presented by calculating frequency and percentages and diagnostic accuracy was also calculated.

Independent sample t-test was applied for effect modifiers like age, gender, size of nodule, marital status, use of Iodine intake, duration of disease for finding their significance level. Post stratification, chi square test was applied to see their effect on outcome. The *p*-value less than or equal to 0.05 was taken as significant.

RESULTS

Our study included a total of 120 patients meeting inclusion criteria of our study. Of these 120 study cases, 28 (23.3%) were males while 92 (76.7%) were females.

Mean age of our study cases was 42.31 ± 8.40 years (with minimum age of 30 years while maximum age of 60 years). Mean age of the male patients was 41.71 ± 5.46 years while that of female patients was 42.49 ± 9.12 years (*p*=0.671).

Table-I: Histopathology versus fine needle aspiration cytology with regards to gender, age groups, marital status, disease duration, size of nodule and iodine intake.

Variable (n=120)	Fine Needle Aspiration Cytology	Histopathology		*p*-value
		Positive	Negative	
Gender Male (n=28)	Positive (n= 12)	10 (TP)	02 (FP)	<0.001
	Negative (n= 16)	02 (FN)	14 (TN)	
Female (n=92)	Positive (n= 27)	17 (TP)	10 (FP)	<0.001
	Negative (n= 65)	02 (FN)	63 (TN)	
Age Groups Up to 45 Years (n= 83)	Positive (n= 22)	12 (TP)	10 (FP)	<0.001
	Negative (n= 61)	02 (FN)	59 (TN)	
45-60 Years (n=37)	Positive (n= 17)	15 (TP)	02 (FP)	<0.001
	Negative (n= 20)	02 (FN)	18 (TN)	
Marital Status Married (n=104)	Positive (n= 37)	25 (TP)	12 (FP)	<0.001
	Negative (n= 67)	04 (FN)	63 (TN)	
Unmarried (n= 16)	Positive (n= 02)	02 (TP)	00 (FP)	=0.008
	Negative (n= 14)	00 (FN)	14 (TN)	
Disease Duration Up to 6 months (n= 44)	Positive (n= 13)	11 (TP)	02 (FP)	<0.001
	Negative (n= 31)	04 (FN)	27 (TN)	
More than 6 months (n= 76)	Positive (n= 26)	16 (TP)	10 (FP)	<0.001
	Negative (n= 50)	00 (FN)	50 (TN)	
Size of Nodule Up to 10 cm (n= 54)	Positive (n= 15)	15 (TP)	00 (FP)	<0.001
	Negative (n= 39)	04 (FN)	35 (TN)	
More than 10 Cm (n= 66)	Positive (n= 24)	12 (TP)	12 (FP)	<0.001
	Negative (n= 42)	00 (FN)	42 (TN)	
Iodine Intake Yes (n= 08)	Positive (n= 06)	04 (TP)	02 (FP)	<0.001
	Negative (n= 02)	00 (FN)	02 (TN)	
No (n= 112)	Positive (n= 33)	23 (TP)	10 (FP)	<0.001
	Negative (n= 79)	04 (FN)	75 (TN)	

*TP=True positive, FP=False positive, FN=False negative, TN=True negative

Our study results have indicated that 83 (69.2%) were aged 30 to 45 years of age.

Of these 120 study cases 104 (86.7%) were married while 16 (13.3%) were un-married. Mean disease duration was 8.34 ± 3.91 months while 76 (63.3%) had disease duration more than 6 months and 66 (55%) had more than 10 cm size of nodule

Table-II: Cross tabulation of thyroid carcinoma on fine needle aspiration cytology with regards to histopathology.

Fine Needle Aspiration Cytology	Histopathology	
	Positive (n=31)	Negative (n=89)
Positive (n=39)	27 (TP)	12 (FP)
Negative (n=81)	04 (FN)	77 (TN)
Total	120	

with mean size of the nodules was 14.49 ± 4.04 cm. Only 8 (6.7%) of these patients were using iodine in their diet while remaining 93.3 % were not using iodine supplemented diet.

FNAC results revealed that thyroid carcinoma was present in 39 (32.5%) while histopathology documented thyroid carcinoma was

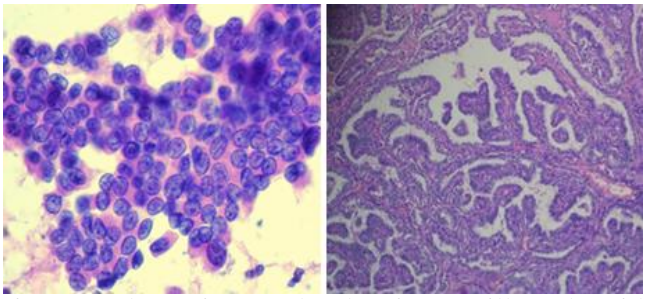

Figure-1: Photomicrographs showing papillary thyroid carcinoma on FNAC b. Histopathological view.

present in 31 (25.8%) of our study cases (fig-1).

Sensitivity of FNAC was 87%, specificity was 86.51%, diagnostic accuracy was 86.66%, positive predictive value was 69.23% and negative predictive value was noted to be 95.06% (fig-2).

Stratification was done with regards to gender, age groups, marital status, disease duration, size of nodule and iodine intake (table-I).

DISCUSSION

Nodular lesions of thyroid are quite common, having a prevalence of 4–7% of adult population. Majority are benign lesions whereas approximately 5-6.5% are malignant[17,18]. The distinction of benign lesions from malignant ones cannot be easily made on the clinical grounds alone. The patient with solitary thyroid nodule is evaluated by doing serum TSH to assess thyroid function and fine-needle aspiration cytology of the nodule, with or without ultrasound (US) guidance. As a result not only unnecessary surgery can be avoided by operating on only those patients with suspicion of carcinoma, but also possible injury of the recurrent laryngeal nerve, hypoparathyroidism, and thyroid hormone dependence in patients with benign thyroid nodules be avoided[9].

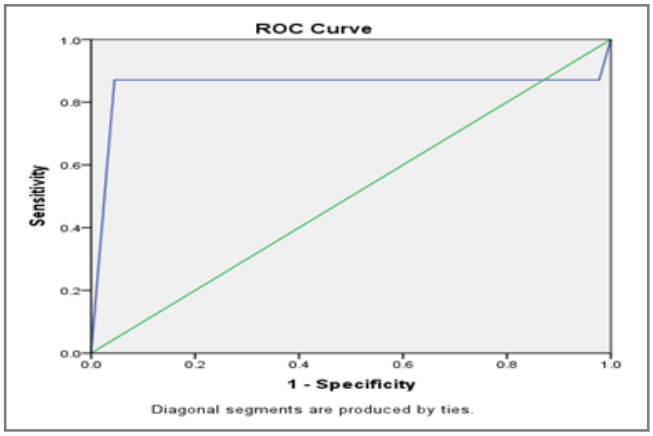

Figure-2: ROC curve showing true positive and true negative cases of thyroid carcinoma.

Many types of radiological tests are available for evaluation of thyroid lesions like ultra sonography, radionucleotide scanning and high resolution ultrasonography. However, FNAC, particularly augmented by ultrasound guidance is regarded as the most accurate and cost-effective procedure, especially for evaluation of the cystic nodules[1011].

Our study included a total of 120 patients meeting inclusion criteria of our study. Of these 120 study cases, 28 (23.3%) were male patients while 92 (76.7%) were female patients. Ciftci *et al*[12] also reported female gender predominance with 79.2% female patients undergoing thyroidectomy having multinodular benign goiter. Aurangzeb *et al*[13] from Peshawar reported female

to male ratio being 5:1 which is similar to that of our study results. Moosa *et al*[14] from Karachi also reported female gender predominating over male gender which are in compliance with that of our study results. Nadeem *et al*[15] from Raheem Yar Khan also reported female gender predominance with 70% female patients which is in concordance to our study results. Naqvi *et al*[16] from Sukkur reported 87% female patients which is similar to our study results.

Mean age in our study was 42.31 ± 8.40 years (with a minimum age of 30 years and maximum age of 60 years). Mean age of the male patients was 41.71 ± 5.46 years while that of female patients was 42.49 ± 9.12 years (p = 0.671). Our study results have indicated that 83 (69.2%) were aged 30 to 45 years of age. Ciftci *et al*[12] reported 41.5 ± 12.7 years mean age of the patients with benign multinodular goiter undergoing thyroidectomy. These results are close to our study results. Moosa *et al*[14] from Karachi reported 33.42 ± 12.4 years which is quite less than our findings. The reason for this difference is due to their inclusion criteria for age (17-45 years) while we included till 60 years of age. Nadeem *et al*[15] from Raheem Yar Khan also reported same results as that of our study results. Naqvi *et al*[16] also reported majority of patients belonging to 4th decade of life which is similar to our findings. Ahmad *et al*[17] from Peshawar reported 38 years mean age which is close to our findings.

Of these 120 study cases 104 (86.7%) were married while 16 (13.3%) were unmarried. Mean disease duration was 8.34 ± 3.91 months while 76 (63.3%) had disease duration more than 6 months and 66 (55%) had more than 10 cm size of nodule. Only 8 (6.7%) patients were using iodine in their diet while remaining 93.3% were not using iodine supplemented diet.

FNAC results revealed that thyroid carcinoma was present in 39 (32.5%) while histopathology documented thyroid carcinoma was present in 31 (25.8%) of our study cases.

Sensitivity of FNAC was 87%, specificity was 86.51%, diagnostic accuracy was 86.66%, positive predictive value was 69.23% and negative predictive value was noted to be 95.06% (table-II & III). In an Indian study[7], sensitivity of FNAC has been reported to be 80% and specificity as 86.6%, these findings are close to our study results. Sharma *et al*[11] from India also reported 89.5% sensitivity, 98% specificity, positive predictive value was 84.6% and negative predictive value was 98.6% while 97% diagnostic accuracy. These results are similar to that of our study results. Sinna *et al*[10] from Egypt also reported sensitivity as 92.8% while specificity as 94.8% and diagnostic accuracy was 93.6% which is in compliance with our study results.

CONCLUSION

Fine needle aspiration cytology (FNAC) is an accurate, sensitive and specific initial diagnostic modality in evaluating patients who presented with thyroid swellings. It is highly reliable, easy to perform, cost-effective and accurate tool in differentiating a malignant from benign lesion. It performs a significant role in better management of patients with thyroid swelling because it is a effective procedure in early detection of malignancy.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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