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UP TO WHAT EXTENT FNAC IS ACCURATE IN DETECTING MALIGNANCY IN SOLITARY THYROID NODULE?
(A comparison with post-operative histopathology findings)

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ABSTRACT:

INTRODUCTION: *Fine needle aspiration cytology has proved to be an excellent tool in the initial management of thyroid nodules. Numerous studies have shown its high sensitivity and specificity in diagnosing malignant tumors of the thyroid, especially papillary thyroid carcinoma. As with other diagnostic tests, its effectiveness is also dependent on the expertise of the operator performing the procedure and the adequacy of the specimen for interpretation of the cytomorphologic features*
AIMS & OBJECTIVES: *Aim of the study is to determine the accuracy of FNAC in detecting malignancy in management of solitary thyroid nodule*
METHODS: *A retrospective comparative study was conducted on 98 cases of solitary thyroid nodules who underwent for surgery between the years Aug 2003 and July 2008 in surgical unit I CHK. Five factors were analyzed when comparing the preoperative FNAC results with final histological findings: sensitivity, specificity, accuracy, positive and negative predictive values using 2×2 table.*
RESULTS: *The youngest patient in this study was 25 years old and the oldest patient was 65 years. The highest prevalence of a solitary nodule in our series was observed in the 4th decade of life i.e. in 41 patients (42.0%). Mean age of patients was 40.5 + 2.2 years. A total of 68 patients (69.4%) were females and 30 (30.6%) were males. There is a significant female preponderance of solitary nodule. Sensitivity was calculated 77.7%, specificity 98.9%, and accuracy 96.9% with a positive and negative predictive value of 87.5% and 97.8% respectively.*
CONCLUSION: *The above mentioned results suggest high specificity and sensitivity of FNAC done pre-operatively to investigate and differentiate benign from malignant lesions in cases of solitary thyroid nodules. . We recommend that preoperative FNAC should be performed routinely in all patients presenting with solitary thyroid lesion to rule out any malignant lesion so that unnecessary thyroid surgeries can be prevented. For only suspected carcinoma in 10%, surgery may be performed.*

KEY WORDS: Thyroid, solitary nodule, FNAC, malignancy, histopathology, accuracy

INTRODUCTION:
Solid nodules are the commonest form of solitary nodules, followed by cystic and mixed consistency on ultrasound examination. Discrete thyroid swellings are common and their importance lies in the malignant potential, particularly if they are cold on radio-isotope scan. In adult population thyroid nodules occur in 4-15% and are seen more frequently in women over the age of 60 years[1]. Many palpable thyroid nodules thought to be solitary are actually part of a multinodular thyroid gland. On radioisotope scanning, 85% of nodules are cold having 10- 25% chances of malignancy, whereas of the 5% nodules shown hot on scanning, 1% is malignant.[2]
Existing clinical investigative methods prove to be poor preoperative predictors of malignancy. Traditionally, any suspicious nodule of the thyroid gland is subjected to an ipsilateral hemithyroidectomy followed by intra-operative frozen section to determine the extent of subsequent surgery. This technique, however, is not infallible. False

positive diagnoses can lead to unnecessary resections and complications, false negative and indeterminate diagnosis can lead to incomplete resection and necessitate re-exploration and resection .[3]

The preoperative identification of malignancy in a thyroid nodule is difficult and often unreliable. Identification of malignant nodules preoperatively thus minimizes the indication for surgery in benign lesions. [4]

The preoperative histological evaluation is crucial in selecting patients for surgery and establishing the extent of the surgery. In the past these decisions were made according to thyroid scanning, but the specificity of this method is low, leading to a high rate of false-positive results, many cases of unnecessary surgical procedures, and a low incidence of malignancies found on final histological evaluation .[5]

Fine needle aspiration cytology has proved to be an excellent tool in the initial management of thyroid nodules. Numerous studies have shown its high sensitivity and specificity in diagnosing malignant tumors of the thyroid, especially papillary thyroid carcinoma. As with other diagnostic tests, its effectiveness is also dependent on the expertise of the operator performing the procedure and the adequacy of the specimen for interpretation of the cytomorphologic features.[6]

AIMS & OBJECTIVES:

To determine the accuracy of FNAC in detecting malignancy in solitary thyroid nodule.

PATIENTS AND METHODS:

A retrospective comparative analytical study was conducted on 98 cases of solitary nodules who underwent surgery in Surgical Unit-1 of Civil Hospital, Karachi between Aug 2003 to July 2008. The data was collected of all the patients from records of the patients. Only those cases were selected for the study in whom a complete history, physical examination, hormonal assay (serum TSH, T3 and T4) and radio-isotope (Tc99 scan) was done and their record was available. Similarly for assessment of the endocrine status of the thyroid gland biochemical assessment (thyroid function tests) was done in all patients and only euthyroid patients record were included in the study who presented with solitary thyroid nodule. Only euthyroid patients presenting with solitary thyroid nodule were included in this study. FNAC was performed preoperatively in all the patients and then the patients underwent for surgery. The specimen was taken and sent for histopathological evidence. In record of each patient , the results of FNAC and histopathology were available to assess the accuracy of FNAC by comparing procedures.

PROCEDURE:

All the FNAC's was performed without

TABLE 1:
AGE AND GENDER PREVALENCE

Age	Male	Female	Total (n=98)	Percentage
20-30	6	10	16	16.3%
31-40	14	27	41	41.9%
41-50	4	18	22	22.5%
51-60	5	9	14	14.2%
61-70	1	4	5	5.1%
Total	30 (30.6%)	68 (69.4%)	98 (100.0%)	100.0%

TABLE II:
COMPARISON OF FNAC VS. FINAL HISTOLOGICAL DIAGNOSIS

FNAC	Number of cases	Final Histopathological Diagnosis	
		MALIGNANT	BENIGN
POSITIVE	08	07 (True positive++)	01 (False positive)
NEGATIVE	90	02 (False negative)	88 (True negative++)
TOTAL	98	09	89

TP	07	FN	02
FP	01	TN	88

TABLE III:
SCREENING RESULT VALUES

Sensitivity TP/(TP+FN)	Specificity TN/(TN+FP)	Positive predictive value TP/(TP+FP)	Negative predictive value TN/(TN+FN)	Accuracy (TP+TN) / TP+FP+TN+FN
77.7%	98.9%	87.5%	97.8%	96.9%

TABLE IV:
GENDER AND AGE DISTRIBUTION OF CARCINOMA

	GENDER	AGE (Yrs)	HISTOPATHOLOGY	FNAC
01	Male	48	Papillary carcinoma	Positive
02	Male	45	Anaplastic carcinoma	Positive
03	Male	50	Follicular carcinoma	Negative
04	Male	55	Papillary carcinoma	Positive
05	Male	46	Papillary carcinoma	Positive
06	Female	43	Papillary carcinoma	Positive
07	Female	49	Papillary carcinoma	Positive
08	Female	52	Follicular carcinoma	Negative
09	Female	61	Papillary carcinoma	Positive

anesthesia, using a 21 gauge needle mounted on a syringe. The nodule was grasped by fingers and four to eight passes were made into the nodule while applying suction. Most of the specimens were embedded in hematoxylin eosin and the giemsa staining method was used when needed. Nodules less than 1cm in diameter were aspirated under ultrasound guidance. This procedure was done by two persons who were competent and experienced for the same. The accuracy rate of both persons was 97.2% (35/36) and 96.8% (60/62).

The type of surgery done on all the patients was dictated by fine needle aspiration results. Patients diagnosed with thyroid cancer underwent total thyroidectomy, whereas all the other cases of solitary nodules reported benign on FNAC, underwent Lobectomy with Ishthmusectomy. Patients with multinodular goiter with a dominant nodule and a benign FNAC result underwent sub-total thyroidectomy. All specimens were sent for histopathology.

DATA ANALYSIS:

The data collected was analysed through SPSS version 15.0. Analysis for FNAC reliability was done using 2 x 2 table and sensitivity, specificity, positive and negative predictive values and accuracy were calculated through comparison of the FNAC results with histopathological findings. Patients were then classified on the basis of their FNAC report as follows:

	Present	Absent
Positive	TP	FP
Negative	FN	TN

Parameters
Sensitivity TP/(TP+FN)
Specificity TN/(TN+FP)
Accuracy (TP+TN)/TP+FP+TN+FN
Positive predictive value TP/(TP+FP)
Negative predictive value TN/(TN+FN)

We divided the results of FNAC into 2 groups; Negative group consists of benign cysts, papillary adenoma, colloid nodule and thyroiditis with absence of atypical follicular cells. Positive group includes atypical follicular cells, suspicious papillary formation, Follicular adenoma and malignant cells.

RESULTS:

The youngest patient in our study was 25 years old and the oldest patient was 65 years. The highest prevalence of a solitary nodule in our series was observed in the 4th decade of life i.e. in 41 patients (42.0%). Mean age of patients was 40.5 +/- 2.2 years. A total of 68 patients (69.4%) were females and 30 (30.6%) were males. There is a significant female preponderance of solitary nodule in our series but males were dominant in malignancy group (males=5). [table1] [table 4]

FNAC ANALYSIS

FNAC was done in all the 98 cases. Three out of 98 were initially reported inconclusive because of hemorrhagic smears and were repeated. Ninety of these were benign, 8 were malignant. Of the 90 cases, which were reported as benign on FNAC, 88 cases (97.7%) were confirmed as benign on final histopathological diagnosis. The remaining 2 cases (false negative case = 2) histopathologically were follicular carcinoma of the thyroid.

FINAL HISTOPATHOLOGICAL DIAGNOSIS

Benign lesions were found in 88 cases (97.7%) the commonest being the Follicular adenomas with 40 cases (45.4%). Malignancy was found in 9 cases (10.2%). Papillary carcinoma was the commonest malignancy (6 cases). On histopathology following distribution of results were seen Follicular Adenoma 40(39.2%), Colloid nodule 10(9.7%), Hashimoto's thyroiditis 08(8.15%), Hyperplastic nodule 27(26.46%), Hurthle cell adenoma 4(4.0%), Papillary carcinoma 6 (6.8%), Follicular carcinoma 2 (2.2%) and Anaplastic carcinoma 1 (1.1%) respectively.

Out of 08 samples that were considered malignant on FNAC, only 07 (88.8%) turned out to be malignant on histopathology; 6 were papillary carcinoma, and 01 was anaplastic carcinoma and out of false positive group 01 was benign follicular adenoma. Of the 90 samples which were negative for malignancy on FNAC, two turned out to be follicular carcinoma, on histology (Table II) .

Analysis for FNAC reliability was done using 2x2 table; sensitivity 77.7%, specificity 98.9%, positive predictive value 87.5%, negative predictive value 97.8% and accuracy 96.9% were calculated (table III).

DISCUSSION:

The assessment of the patient presenting with solitary thyroid nodule includes three modalities of clinical examination, cytology and imaging investigations and the result of FNAC still remains as the only governing factor in the decision of surgical management[7]. Pre-operative Fine needle aspiration cytology has been well established as a diagnostic technique for selecting patients with thyroid nodules for surgical treatment, thereby reducing the number of unnecessary surgical procedures in cases of non-malignant tumors. Solitary thyroid nodule can be classified into benign and malignant nodule. Majority (90%) of thyroid nodules are benign and are classified as adenomas, colloid nodules, lymphocytic or granulomatous nodules, cysts, infectious nodules, hyperplastic nodules, thyroididtis, and congenital anomalies [2]. Follicular adenomas are more common and clinically present as a single nodule in most cases. Malignant thyroid nodules are classified as (i) Differentiated (papillary carcinoma, and follicular carcinoma), (ii) Undifferentiated (includes small cell, giant cell) , (iii) medullary carcinoma, and (iv) Miscellaneous (includes anaplastic, lymphoma, sarcoma, metastatic tumor) [2].

Preoperative fine-needle aspiration cytology (FNAC) of the nodules has currently become the most widely used technique to select patients for thyroidectomy. It is an accurate predictor of malignancy and significantly reduces surgery in benign conditions [3]. The cytological criteria on FNAC for papillary, medullary, and anaplastic carcinomas are well defined, whereas differentiation between follicular adenoma and follicular carcinoma is not reliable by FNAC alone as this distinction requires histological criteria, including capsular and vascular invasion [4,8]. Studies by Alexander Kessler & Mayo Clinic have shown the benefits of FNAC as a diagnostic method in the management of thyroid malignancy. A reduction in the rate of thyroid resections of thyroid gland (from 67% to 43%) was observed in suspected cases, and thus unnecessary operations were avoided [5, 9]. An increase in the rate of confirmed malignancy (from 14% to 25%) on final histology was also observed.

Prevalence of thyroid solitary nodule increases with age, occurring at a rate of 0-0.8% per year. It begins early in life and extends into the eighth decade. They are present in 5% persons at an average of 60 years. Its prevalence in females (6.4%) is more common than compared to males (1.5%) and this predisposition exists throughout all age groups[2]. In this study the male to female ratio was 1:2.2 with a female preponderance, the youngest patient of our series was 25 years old and the oldest patient was 65 years. The highest incidence of a solitary nodule in our series was observed in the 4th decade of life i.e. in 41 patients. Mean age of patients was 40.5 + 2.2 years.

In our study out of the 08 samples that

were considered malignant on FNAC preoperatively, 07 (88.8%) turned out to be malignant; 5 were papillary carcinoma, 1 was anaplastic, and 1 was follicular carcinoma, whereas the other one was reported as benign follicular adenoma. Of the 90 samples which were negative for malignancy on FNAC, only two were turned out to be follicular carcinoma on histology. The reported sensitivity of FNAC is between 79% and 98% according to most authors in reviewing the literature [5,8,10,11,12,13] , specificity ranges from 70% to 100% [5, 8,10,11,12,13], and false-positive and negative results in 5–25% of cases [5]. In our study overall sensitivity was calculated 77.7% and specificity was analyzed 98.9% which matches the above mentioned figures from different studies.

Accuracy of FNAC is estimated to be between 87% and 95% [5, 8,10,13,14,] and varies according to the histological evaluation. In cases of papillary carcinoma the accuracy is about 80% [5], due to the pathognomic features on histological specimen examination. In this study overall accuracy was 96.9%, and positive and negative predictive values were 87.5% and 97.8% respectively which again matches the searched literature [11, 13]. The accuracy of FNAC in cases of follicular carcinoma is lower and estimated to be between 10% and 40%, because identification of structural features of cell groups and the capsule of the nodule are essential for diagnosis [5, 15, 16] .

CONCLUSION:

The above mentioned results suggest high specificity and sensitivity of FNAC done pre-operatively to investigate and differentiate benign from malignant lesions in cases of solitary thyroid nodules. We recommend that preoperative FNAC should be performed routinely in all patients presenting with solitary thyroid lesion to rule out any malignant lesion, and select those patients who require excision of the lesion for subsequent histologic diagnosis. If FNAC proves to be either suspicious or malignant, surgery must be done. The optimal diagnostic strategy aims to avoid unnecessary surgery in patients with benign thyroid disease, while at the same time performing prompt surgical treatment of patients with thyroid carcinoma. According to the study results, FNAC accuracy was 96.9%, so only in those suspected cases of 3.1% or may be some more, thyroid surgery should be done to diagnose follicular carcinoma/ adenoma. However in more than 90% cases surgery may be avoided or delayed.

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