FINE NEEDLE ASPIRATION OF THYROID AS A SCREENING TEST- DIAGNOSTIC ACCURACY, DISCREPANCIES AND PITFALLS- STUDY OF 1175 PATIENTS IN A TERTIARY CARE CENTRE

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ABSTRACT

BACKGROUND

Fine needle aspiration cytology of thyroid plays a key role in the preoperative differentiation of benign from malignant nodules. The treatment decision is greatly influenced by the cytological diagnosis. The current study was done to assess the diagnostic accuracy, discrepancies and pitfalls when blind FNACs of thyroid is employed as a screening test and also to analyse the causes of diagnostic discrepancies so that improvement measures can be undertaken. Thyroid diseases are encountered very commonly in everyday clinical practice especially in females. However, a majority of the thyroid nodules are asymptomatic, and only 5 to 10% of the nodules turn out to be malignant after surgical excision.

METHODS

We analysed 1175 FNACs from our centre using descriptive study design. These were classified based on The Bethesda System of Reporting Thyroid Cytology (TBSRTC). 132 patients who underwent surgery from the 6 different categories were further analysed to study the diagnostic accuracy, discrepancies and pitfalls.

RESULTS

Sensitivity was 64.7%, specificity was 97.1% %, PPV was 78.5%, NPV was 94.4% and diagnostic accuracy was 92.6 %.

CONCLUSIONS

Blind FNAC has its own limitations**.** Image guided aspiration will be a better option to increase the yield of diagnostic material and for better targeting of the lesion. Ancillary techniques also can also be employed. After the introduction of the TBSRTC system of reporting for thyroid cytopathology, it is seen that there is a dramatic decrease in the rate of unwanted surgeries for thyroid lesions and among the surgically resected cases, malignancy rates have increased. The increased malignancy rates can be attributed to the careful selection of patients for surgery based on TBSRTC categories.

KEYWORDS

Thyroid Nodule, TBSRTC, Aspiration Cytology, Histopathology, Sensitivity, Specificity

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BACKGROUND

Thyroid diseases are encountered very commonly in everyday clinical practice especially in females. However, majority of the thyroid nodules are asymptomatic, and only 5 to 10% of the nodules turn out to be malignant after surgical excision.[1] FNAC is a cost effective, easy to apply method widely used as a screening test for all thyroid swellings of any age group in both sexes. Blind FNAC without any image guidance is still widely used as the primary diagnostic tool for any type of thyroid swelling. After the introduction of TBSRTC, the distinction between neoplastic and non-neoplastic conditions based on cytological findings is made clearer and this has helped the clinicians to avoid unwanted surgeries.[2]

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All patients in the suspicious categories and frankly malignant categories are usually taken for surgery. The decision for surgical treatment in the non-malignant TBSRTC categories is based on clinical suspicion, radiological findings and also due to cosmetic reasons. FNAC combined with TBSRTC as a screening test is at present considered to be the most accurate and preliminary diagnostic modality based on which clinical recommendation for surgical management is made possible. But it has certain limitations as well. There are certain grey zones in thyroid cytology which often leads to discrepancies between cytological and histopathological diagnosis. Overlapping cytomorphological features often lead to overdiagnosis or under diagnosis of malignancy.[3]

METHODS

The descriptive study was conducted on 1175 patients who underwent fine needle aspiration cytology as a screening test for thyroid lesions during the period of 2016-2018. Patients from all age groups and both sexes were included. Fine needle aspirations were done by the pathologist. Aspirated material was placed on glass slides and smears were prepared and immediately transferred to fixative.

TBSRTC Category	Number in Each Category	Percentage of Each Category
Category I	113	9.6
Category II	979	83.3
Category III	24	2.0
Category IV	16	1.4
Category V	22	1.9
Category VI	21	1.8
Total	**1175**	**100**

Table 1. Cytology Results as per TBSRTC Criteria

TBSRTC Category	No. of Surgery in Each Category	HPR Benign	HPR Malignant
I	10	9	1
II	108	102	6
III	3	2	1
IV	1	0	1
V	7	1	6
VI	3	0	3
Total	**132**	**114**	

Table 2. Results of Resected Specimens

TBSRTC Category	Total No.	Histological Types of Malignancy
I	1	PTC-classical
II	6	PTC classical (4),Follicular variant(2)
III	1	Follicular variant of PTC -multifocal
IV	1	Follicular Carcinoma
V	6	PTC - Classical (4) PTC - Follicular variant (1) PTC - Oncocytic variant (1)
VI	3	PTC - Classical (2) PTC - Oncocytic variant (1)

Table 3. Histological Types of Malignancy

		Histopathology		
		+ve	**-ve**	
Cytology	+ve	11	3	14
	-ve	6	102	108
		17	105	122
Observed Agreement			92.6%	
Expected Agreement			77.8%	
Cohen's Kappa			66.8%	
SE			10.7%	
95% CI			45.9% - 87.7%	

Table 4. Comparison of TBSRTC to HPR

After a period of fixation, these smears were stained by Papanicolaou's method. In each case two air dried smears were also prepared. These air-dried smears were stained with Giemsa stain. Evaluation was done by the Bethesda system of reporting thyroid cytopathology (TBSRTC)

Diagnostic category was given to each case based on the Bethesda system. These cases were followed up and cases which were operated in this hospital were analysed as to the diagnostic accuracy, discrepancies and the pitfalls in diagnosis. All discordant cases were reviewed and the possible causes for the discrepancy were analysed.

RESULTS

Out of the 1175 cases 113(9.6%) were categorised as TBSRTC I, 979(83.3%) as II, 24 (2%) as III, 16 (1.4%) as IV, 22 (1.9%) as V and 21(1.8%) as category VI. Cytodiagnosis as per TBSRTC criteria is shown in Table I. In the follow up of the 1175 FNACs done, the number of cases operated in our hospital was 132. Among these 18 patients were males and 114 were females with a male to female ratio of approximately 1:6 (male 13.6% and 86.4%). Age of the patients ranged from 18-76. Of these 132 patients 18 cases proved to be malignant by histopathology whereas the remaining 114 cases were benign. These patients belonged to the different TBSRTC categories mostly from those in the malignant or suspicious for malignant category as shown in Table 2. Patients from different categories who opted for surgery elsewhere were not included in this study due to difficulty in follow up.

132 patients belonging to different categories underwent surgery in this hospital. 10 cases from the non-diagnostic category were taken for surgery, 104 cases from category II, 6 cases from category III, 2 cases from category IV, 7 cases from category V and 3 cases from category VI. (Table-2).

Histological types of malignancy were papillary thyroid carcinoma (PTC) classical (11), PTC follicular variant (4), PTC oncocytic variant (2) and follicular carcinoma (1) as shown in Table 3.

For all statistical analysis non-diagnostic category was not considered. Category II was taken as cytologically benign. Category III, IV and V were taken as cytologically indeterminate category and category VI as cytological malignant. Of the 122 cases, 102 were true negative (83.6%), 11 were true positive (9%), 6 false negative (4.9%) and 3 false positive. (2.5%) as shown in Table 4. Sensitivity 64.7%, specificity 97.1% %, PPV 78.5%, NPV 94.4%%. Although the observed diagnostic accuracy (or agreement) was 92.6%, the expected agreement was 77.8%. The Cohen's Kappa was only 66.85 with 95% Confidence Interval (45.9% - 87.7%) as shown in Table 4.

DISCUSSION

Among the initial 1175 patients on whom aspiration was done a total of 113(9.6%) were classified as non-diagnostic. Various other studies have reported a wide range varying from 1.6 to 20 % in the non-diagnostic category.[4,5,6,7] Many of the cases in our study group were included in the non-diagnostic category because of the heavy blood contamination of the smears thereby obscuring the morphology of the cells by clotted blood. Thyroid gland being a highly vascular organ, the skill of the person doing the FNACs as well as the technician who prepare and stain the smears play a major role in procuring good quality smears. Technical expertise is of paramount importance so that a cellular aspirate is obtained wherever possible and optimal utilization of the material is made possible. Among the 122 cases taken for surgery 102 (83.6%) cases turned out to be true negative (Benign) on histopathology. Previous studies have reported a benign cytology diagnosis in 50% to 90% of the specimens (average, 70%).[8,9,10,11,12] Benign entities in our study included mostly multinodular goitre along with Hashimoto's' thyroiditis as proved by histopathological examination. Malignancy risk for category II as per the Bethesda system of reporting is expected to be 0-3%,[2] whereas in our case it was nearly 5% (False negative). Patients with benign cytology are usually asked to undergo surgical management only when other clinical risk factors are present. There are studies which reported still higher false negative rates reaching up to 14%.[13,14,15,16,17,18] Still other studies have reported false negative rates varying from 1.5 to 11.5%.[19,20,21] These data published in literature suggest that follow up of cytological benign cases at 6 months interval by repeated FNAC (As per the TBSRTC recommendation) may not be adequate in all cases.

A very important cause of a false negative diagnosis is follicular variant of papillary carcinoma where the cytodiagnosis has to be made solely on nuclear features which can often be subtle and focal. But in our study, among the false negative cases there were only two cases of follicular variant of papillary carcinoma while the remaining 4 cases were classical variants. We missed the diagnosis of malignancy because of the prominent cystic changes, paucity of nuclear

features and the absence of true papillary formations in the smears. False negative cytology diagnosis can also occur when the size of the target lesions are small. Reporting on suboptimal samples also contribute to false negative diagnosis. Image guided FNAC is a better option in such cases so that the lesion is not missed, and adequate material is obtained.

Positive cytology findings followed by a negative histopathology result can have serious implications and is the most important pitfall of thyroid cytopathology. The false-positive rate of FNAC results in thyroid cancer has been reported as 2-10%.[22,23,24] In our study, there were 3 (2.5%) such false positive results. Among this one case was categorised as suspicious of malignancy (Category V according to Bethesda system) based on the presence of papillary formations without nuclear features of malignancy and this case on histological examination showed cystic degeneration with areas of papillary hyperplasia. According to the Bethesda system, when one characteristic feature of papillary carcinoma alone is present in the smears it is reported as suspicious of malignancy and on resection only 60-75 % turn out to be malignant while the rest are benign. In the other 2 cases the smears were sparsely cellular and were labelled as category III based on nuclear atypia and the presence of hurthle cells. We advised repeat FNAC in these patients, but the clinicians opted for surgery and on histopathology proved to be Hashimoto's thyroiditis. It is a well-known fact that chronic thyroiditis of any type may mimic carcinoma thyroid in cytologic smears leading on to false positive diagnosis. This is due to the occurrence of cytological features of papillary carcinoma in these lesions. Studies show that prevalence of chronic thyroiditis is higher among patients with false positive FNA results than in those with confirmed papillary carcinoma.[25] The clinicians should also be aware of this and necessary patient counselling before surgery becomes important. The occurrence of papillary carcinoma in a case of Hashimoto's thyroiditis is not rare and, in such cases, the cytological diagnosis is often challenged by atypical cytological features and lymphocytic infiltration.[26]

In this study 11(9%) cases were true positive as evidenced from histopathology. Six of these patients were from category V, 3 from category VI and one each from category IV & III, The histological types of malignancy in these cases were as shown in Table 3. The only one case from category IV who underwent surgery here turned out to be Follicular carcinoma. There were no medullary carcinoma in our study group and the only case of anaplastic carcinoma diagnosed cytologically was treated without surgery.

The overall sensitivity of thyroid FNAC in this study is just 64.7%, specificity is 97.1%. This is comparable to the already reported results of 65-99% and 72-100% respectively.[27,22,23,24] We got a PPV 78.5%, NPV 94.4%%.The positive predictive value of a malignant FNA cytology result is 97-99% according to the Bethesda system whereas in our study the positive predictive value was only 78.5%. In our study we got a diagnostic accuracy of 92.6% whereas accuracy up to 97% has been reported in literature.[28] Preoperative diagnosis of thyroid nodules by blind FNAC, though widely used in most of the centres is not completely free of pitfalls. Even though the accuracy rate of FNA is high the reporting pathologist should be well aware of the pitfalls so as to avoid false positive/ negative diagnoses. There are certain cytomorphological features which may be seen in both benign and malignant conditions especially in papillary thyroid carcinoma leading to challenges in the diagnosis. Blind FNAC though used even now as a preliminary screening test in most of the institutions, the main limitations are related to lack of operator skill contributing to non-diagnostic aspirates, and non-availability of molecular techniques. Adequate sampling is very essential and for this aspirates should be obtained from multiple sites of the lesion or nodules. Rapid onsite evaluation of the material can help in assessing the adequacy. Wherever possible US guided FNAC can be done as it is the method of choice for selecting the nodules for the procedure[29,30]

CONCLUSIONS

After the introduction of the TBSRTC system of reporting for thyroid cytopathology, it is seen that there is a dramatic decrease in the rate of unwanted surgeries for thyroid lesions and among the surgically resected cases, malignancy rates have increased. The increased malignancy rates can be attributed to the careful selection of patients for surgery based on TBSRTC categories. Increasing incidence of thyroid cancer among our population is another reason. In the present study, malignancy rate was 13.6%. This is considerably higher and many of the studies during last one or two decades have shown an ever-increasing incidence of thyroid cancer worldwide. This increase has been related to increased detection of subclinical cases and is not considered as an increase of true occurrence of thyroid cancer.[31]

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