

Fine needle aspiration cytology as the primary diagnostic tool in thyroid enlargement

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Abstract

Background: In the preoperative decision-making of the thyroid swellings, fine needle aspiration cytology (FNAC) is becoming an ever more vital tool. **Objectives:** To compare the advantage of preoperative FNAC of thyroid swellings with postoperative histopathology to reach a consensus protocol as a simple procedure for diagnosis and optimal management of thyroid swellings. **Materials and Methods:** A prospective study of preoperative FNAC was carried out on 178 incidental thyroid swellings attending a tertiary care centre in Kishanganj, Bihar. Evidence-based surgical interventions were done, irrespective of FNAC findings and diagnosis was confirmed by histopathological examination (HPE) postoperatively in all the cases. **Results:** In the FNAC, preponderance of the cases (75.84%) was colloid goitre followed by granulomatous thyroiditis; follicular carcinoma was noted in 7.30 percent and anaplastic carcinoma in 3.37 percent of cases. Histopathological examination showed colloid goitre predominantly (76.97%), followed by follicular carcinoma (8.99%). The overall prevalence of malignancy was 11.24 percent diagnosed by HPE and 9.55 percent by FNAC. In our FNAC series sensitivity of was 90 percent while specificity was 100 percent; accuracy was 98.88 percent. Predictive value of a positive test and negative tests was 100 percent and 98.75 percent respectively. **Conclusion:** The study highlights that FNAC should be treated as a first-line diagnostic test for thyroid swellings to guide the management though this is not a substitute for HPE as a need to improve primary healthcare in India.

Key words: Fine needle aspiration cytology, histopathology, thyroid swelling

INTRODUCTION

Fine needle aspiration cytology (FNAC) is now accepted as a cost-effective, minimally invasive, low-complication non-operative diagnosis for most of the thyroid lesions and is highly successful in triaging patients with solitary thyroid nodule (STN) into operative and non-operative groups. The location of the target lesion, careful searching for malignant cells and repeat FNAC are the key to successful diagnosis to plan a proper surgical management in thyroid mass.^[1-5] Thyroid nodules that should be considered for FNAC include any firm, palpable, solitary nodule or

nodule associated with worrisome clinical features. FNAC should also be performed on nodules with suspicious ultrasonographic features; dominant or atypical nodules in multinodular goiter; complex or recurrent cystic nodules; or any nodule associated with palpable or ultrasonographically abnormal cervical lymph nodes; it should be performed on any abnormal-appearing or palpable cervical lymph nodes.^[6] The distinction of the benign and malignant thyroid nodules is fundamental, as malignancy necessitates surgery, while strict patient follow-up is necessary in the case of a benign mass. FNAC is considered to be the “gold standard” in the selection of patients for surgery.^[7] Any solitary or dominant thyroid nodule larger than 1 cm should have cytology done as smaller nodules carry a very low risk of morbidity. FNAC is the most cost-effective invasive preoperative investigation, whose simplicity and safety justify its use for “selective” surgery and is considered the “gold standard” in the management of thyroid nodules.^[8,9] FNAC is usually performed without local anesthesia and the patient does not require any previous preparation. In medical centers with longstanding experience, diagnostic

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(adequate) biopsies obtained from solid nodules range from 90–97%.^[10,11] It has been reported that, although FNA is guided by palpation (conventional or non-ultrasonographic palpation-guided FNA) in 87% of cases in North America and Europe, the US-FNA is becoming increasingly popular. During this procedure, US guidance is used instead of palpation, which seems to enhance the value of the FNA diagnostic accuracy.^[12,13] Clinically significant complications after FNA have hardly ever been reported.^[14,15]

Though thyroid swellings are very common incidental findings in this part of the country very little work has been reported. In the present study, cases with thyroid swellings were evaluated with FNAC as the first line of important diagnostic test to correlate the preoperative diagnostic workup with FNAC along the clinical findings with that of postoperative pathological findings. The aims and objectives of the study were:

1. To study the advantage of FNAC as a simple procedure for the diagnosis of thyroid swelling and to utilize it on the patient's first visit to the hospital
2. To compare the preoperative FNAC with postoperative histopathology and to determine the sensitivity and specificity of this test.

MATERIALS AND METHODS

This was a prospective study on 178 subjects with incidental thyroid swelling attending the otorhinolaryngology (ENT) outpatient department (OPD) at a tertiary care teaching hospital in Kishanganj Bihar during January 2007 to December 2009. The main outcome measures were to correlate the preoperative diagnostic workup with FNAC along the clinical findings with that of postoperative pathological findings.

Data collection procedure

The institutional ethical committee approved the study. All the caregivers of the patients were explained about the purpose of the study and were assured strict confidentiality. Written informed consents were taken from each of them prior to the study. The participants were also given the options to withdraw from the study whenever they wished. Counseling was also done regarding possibility of iatrogenic hoarseness of voice particularly to those who by their profession had to depend on their voice.

The principal investigator thoroughly examined all cases by detailed history, family history, residence, food habits and drug intake with special emphasis on onset, duration and rate of growth and particularly any irradiation in the head and neck area in the recent or distant past. In female patients, an enquiry was made about reproductive health too. This was followed by general and system-based

otorhinolaryngological assessment. Routinely, thyroid status was determined by estimation of T₃, T₄ and Thyroid Stimulating Hormone (TSH) by Enzyme linked Immunosorbent Assay (ELISA) method in all patients to know the exact thyroid function status. FNAC was done in all the cases as an OPD procedure with other non-invasive procedures, viz. X-Ray chest PA, and ultrasonography as and when required. We have not done isotope scan in our study as the facility is not available here. After clinical assessment, each of the participants was routinely investigated with standard preoperative procedure for general anesthesia. Following admission, the patient was prepared to euthyroid state wherever necessary and surgical interventions were done in all cases. During operation all operative findings were recorded including macroscopic finding, visualization and isolation of parathyroid glands and recurrent laryngeal nerve, and status of draining lymph nodes. All specimens were sent to the Department of Pathology of the institute in a 10% buffered formal saline with correct labeling for histopathological study. In the postoperative period all the patients were followed for any immediate or delayed complication. Indirect laryngoscopy was done to see the vocal cord movement and their position routinely before discharge. Then patients were followed up on an OPD basis after six weeks, 12 weeks and 24 weeks to note the condition of the scar, any discharge or persistence of swelling. All the histopathologically confirmed cases were followed by evidence-based interventions. Information on thyroid swellings was disseminated in health education sessions to complement the findings of the study.

Procedure followed in fine needle aspiration cytology

We followed the standard procedure like our forerunners in this field.^[16-19] Procedure was explained to the patient for his/her cooperation and they were asked to refrain from swallowing. No anesthetic drug was used as it was a minimally painful procedure. In the supine position with the neck moderately extended with a pillow under the shoulder blades, the skin over the swelling was cleaned. The swelling was fixed in between left thumb and index finger and a disposable plastic 10 ml syringe fitted in a 22-gauge disposable needle was held in the right hand. In most of the cases 22-23-gauge needle was used (around 0.7 mm) which was 25–50 mm in length.

The needle was inserted in a near vertical direction with the plunger of the syringe in resting position. After checking the position of the needle in the predetermined site the plunger was retracted up to a negative volume of 10 ml. To obtain the greatest possible yield, the needle was moved back and forth within the lesion in different directions with the negative pressure maintained in different directions. The function of this negative pressure was not to tear cells from the tissue but merely to hold the tissue against

the sharp cutting edge of the needle. The softer tissue components protruded over the edge, were cut or scraped off and accumulated in the lumen as the needle advanced through the tissue to obtain a reasonable sample to reduce false negative diagnoses. In solitary masses the first needle pass was made to test whether the lesion was cystic or not. Aspiration was stopped if any material was found to appear in the hub of the needle or in the syringe. When the aspiration was complete the plunger was released to eliminate negative pressure before the needle was withdrawn. Detaching the needle from the syringe, the plunger was withdrawn to allow 2-3 ml of air in the syringe and the needle was reattached and then the material was blown out onto a clean dry slide by pushing the plunger, keeping the needle tip touching the already numbered slide. With the help of another slide the material was spread and air dried. Any cystic fluid thus withdrawn from the swelling was mixed with anticoagulant, centrifuged and the deposit was studied microscopically after spreading. AgNOR counting and staining with May Grunewald Giemsa (MGG) stain in fine needle aspiration smears was done.

$$\text{Specificity: } \frac{\text{TN} \times 100}{\text{TN} + \text{FP}} = 100\%$$

$$\text{Sensitivity: } \frac{\text{TP} \times 100}{\text{TP} + \text{FN}} = 90\%$$

$$\text{Accuracy: } \frac{\text{TP} + \text{TN} \times 100}{\text{TP} + \text{TN} + \text{FP} + \text{FN}} = 98.88\%$$

$$\text{Percentage of false-positive: } \frac{\text{FP} \times 100}{\text{FP} + \text{TN}} = 0\%$$

$$\text{Percentage of false-negative: } \frac{\text{FN} \times 100}{\text{FN} + \text{TP}} = 10\%$$

$$\text{Predictive value of a positive test: } \frac{\text{TP} \times 100}{\text{TP} + \text{FP}} = 100\%$$

$$\text{Predictive value of negative test: } \frac{\text{TN} \times 100}{\text{TN} + \text{FN}} = 98.75\%$$

Statistical analysis used

The collected data was thoroughly cleaned and entered into MS-Excel spreadsheets, and analysis was carried out. The procedures involved were transcription, preliminary data inspection, content analysis, and interpretation. Percentages were used in this study to analyze epidemiological variables.

RESULTS

The majority of the participants belonged to the age group of 21-40 years; the highest incidence of thyroid swelling in our study was found in the fourth decade (40.45%) followed by third decade (35.39%). Females outnumbered males with a ratio of 4:1 [Table 1].

FNAC was done in all 178 cases in our study on an OPD basis. The majority of the cases (75.84%) were diagnosed as colloid goitre followed by granulomatous thyroiditis. Follicular carcinoma was seen in 7.30 percent and anaplastic carcinoma in 3.37 percent of cases. Following operative procedures, the sample was subjected to histopathological examination (HPE). HPE showed the majority of the cases (76.97%) to have colloid goitre, followed by follicular carcinoma (8.99%) [Table 2].

The overall prevalence of malignancy in our study was 11.24 percent diagnosed by HPE and 9.55 percent by FNAC. Among females, 9.22 percent cases were diagnosed as malignant by FNAC whereas 9.93 percent were malignant as per HPE; among males 10.81 percent cases were malignant as per FNAC and 16.22 percent were malignant as per HPE. The malignancy rate was more in men (16.22%) as compared to women (9.93%) in our series [Table 3].

‘True-positive’ (TP) and ‘True-negative’ (TN) cases are those which are diagnosed correctly as malignant and benign respectively. ‘False-positive’ (FP) cases consist of those cases which are benign but wrongly diagnosed as malignant. ‘False-negative’ (FN) refers to those cases

Table 1: Age-sex distribution of the study population

Demographic parameters	No. of cases	Percentage
Age group	n = 178	
0-10	7	3.93
11-20	13	7.30
21-30	63	35.39
31-40	72	40.45
41-50	17	9.55
51-60	6	3.38
Sex	n = 178	
Females	141	79.21
Males	37	20.79

Table 2: Thyroid swelling by fine needle aspiration cytology and histopathology

Diagnosis of thyroid swelling		No. of cases	Percentage
Colloid goitre	FNAC	135	75.84
	HPE	129	76.97
Granulomatous thyroiditis	FNAC	13	7.30
	HPE	15	8.43
Follicular adenoma	FNAC	11	6.18
	HPE	13	7.30
Follicular carcinoma	FNAC	13	7.30
	HPE	14	8.99
Anaplastic carcinoma	FNAC	6	3.37
	HPE	7	3.93
Total	FNAC	178	100
	HPE	178	100

Table 3: Sex distribution of prevalence of malignancy as per fine needle aspiration cytology and histological examination

Sex		Total	Benign (%)	Malignant (%)
Female	FNAC	141	128 (90.78)	13 (9.22)
	HPE		127 (90.07)	14 (9.93)
Male	FNAC	37	32 (86.49)	5 (13.51)
	HPE		31(83.78)	6 (16.22)
Total	FNAC	178	161(90.45)	17 (9.55)
	HPE		158 (88.76)	20 (11.24)

Table 5: Predictive value for negative result of FNAC as reported

Author	No. of FNAC	Diagnostic accuracy (%)	False-negative	Predictive value for negative result
Frale, 1976	20	95	5	95
Gershengorn <i>et al.</i> , 1977	33	89	3	97
Rossen <i>et al.</i> , 1983	153	83	1	99

which are malignant but are diagnosed as benign. Based on study findings, the usefulness of FNAC in case of thyroid swelling can be measured. Sensitivity of FNAC was 90 percent while specificity was 100 percent; accuracy was noted to be 98.88 percent. Predictive value of a positive test and negative tests was 100 percent and 98.75 percent respectively [Table 4].

DISCUSSION

In our study the majority of the cases (76.97%) were found to have colloid goiter, followed by follicular carcinoma (8.99%); papillary carcinoma was not found. We had a diagnostic accuracy of 98.31 percent with a predictive value for negative test of 98.75%. Because of these reasons FNAC has been an important tool with growing popularity. FNAC was done in all cases on an OPD basis. The accuracy of the test was 79.7 percent and the incidence of false-negative turned out to be 3.3 percent.

The accuracy, percentage of false-positive, and the predictive value for negative result of FNAC as reported by the workers^[20-22] in this field are as follows [Tables 5 and 6]:

In our series, histopathology of resected thyroid specimens yielded a malignancy rate of 11.24% (20 cases out of 178 in the study). Comparable reports from other workers^[23-29] in this field all over the world showed thyroid malignancy as below.

Thus we have re-evaluated the scope of FNAC in thyroid

Table 4: Correlation of fine needle aspiration cytology and histopathological examination in detecting the malignant nature of the thyroid swelling

FNAC diagnosis	Histopathological diagnosis		
	Malignant	Benign	Total
Positive	18 (TP)	0 (FP)	18
Negative	2 (FN)	158 (TN)	160
Total	20	158	178

Table 6: Percentage incidence as reported

Authors	Year	Incidence (%)
Schlessinger <i>et al.</i>	1938	8
Kendal and Condon	1969	11-20
Kapur <i>et al.</i>	1982	11
Bhansali	1982	9
Ng Eh <i>et al.</i>	1992	18.4-26.2
Adwork J. A.	1995	15
Abu Eshy <i>et al.</i>	1995	15.2

swelling and utilized its value in guiding the surgical management. In our study the specificity was 100%; the sensitivity was 90% as compared with 64.3% sensitivity reported by others.^[30]

In 1995, Agarwal *et al.*, in the Tata Memorial Hospital, Mumbai, evaluated thyroid nodules in 100 cases. FNAC demonstrated an accuracy of 90.9%, a sensitivity of 76.5%, and a specificity of 95.9%. False-positive 2%, false-negative 4%; positive and negative predictive value was 86.7% and 92.2%. They resumed FNAC as an adjunct to clinical judgment and not to replace it.^[31] In 1980, Ghosal, Pal and Mazumdar reported that accuracy rate of FNAC was 93%.^[32] In 1995, Mandreker *et al.*, in Goa Medical College favored the use of FNAC in thyroid lesions, especially solitary thyroid nodules.^[33] Gardner *et al.*, reviewed the histological findings of 56 thyroid lobectomies in comparison to FNAC observed that abundant colloid, regular spacing, and large follicles are helpful in distinguishing macro follicular and mixed lesions from micro follicular ones, which have a higher malignant potential.^[34]

Based on novel pattern analysis in the interpretation of a solitary thyroid nodule, the study at Salem showed a sensitivity of 66.7% and specificity of 98.9%. The positive predictive value and negative predictive value were 88.9% and 96% respectively and the overall diagnostic accuracy was 95.4%. The study demonstrated the feasibility and applicability of pattern analysis in diagnosing thyroid lesions by FNAC.^[35] The study from Queen Elizabeth II Health Sciences Centre, Canada concluded that the introduction of a reporting template increased the diagnostic precision of thyroid FNAC reporting without impacting the overall

diagnostic categorization or cytohistologic concordance.^[36] FNAC is a common investigation in the diagnosis of superficial lumps though its success depends on the skill of the person performing the procedure.^[37]

To augment compliance all pertinent investigations in our study population were done in the OPD to reduce the length of stay in the hospital and that helped in better patient compliance. Since there is no fool proof noninvasive test to predict a thyroid carcinoma, the resection of even non-neoplastic thyroid gland was undertaken followed by histopathological examination along with the simple, sensitive and cost-effective AgNOR staining and quantification..

We had several limitations. It could have been better if we had done US and computed tomography (CT)-guided FNAC that have a higher probability of higher accuracy along with any wet stain (H and E, Pap stain).

The basic requirements of the accomplishment of FNAC depend on the diagnostic criteria, immediate interpretation, surgical competence, optimum preparation to arrive at a definitive diagnosis. Research is needed on the optimization and standardization of diagnostic criteria for the progress of patient management practice based on diagnostic schema.

To sum up, FNAC of thyroid nodules has become one of the most useful, safe, accurate, relatively simple, inexpensive, less time-consuming OPD procedures, virtually painless, highly patient-compliant with highly accurate dependable tool in the diagnosis of thyroid pathology.

FNAC is not a substitute for conventional surgical histopathology, it is regarded as an extremely valuable complement in diagnosis and it is becoming just as indispensable. The study highlights that FNAC should be treated as a first-line diagnostic test for thyroid swellings to guide the management though it is not a substitute for histopathological examination as a need to improve primary healthcare in India.

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