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A Clinical Study on Distribution of Malignant Lesions on FNAC in a Study Population Attending a Teaching Hospital in North India

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Abstract

Aim: *the present study is undertaken to evaluate the distribution of malignant lesions on FNAC in Nothern Indian population.*

Introduction: *Clinical examination, although very accurate in most cases of thyroid lesion, is inadequate in some areas especially, in staging of thyroid malignancies and in detecting the multi-nodularity of the gland.*

Material And Methods: *The study was conducted in a teaching hospital for a period of 1 year. It was a prospective hospital based Study. In each case, a brief clinical history and examination was carried out. Patient were explained about whole of the procedure & the consent for the procedure was taken in all patients. FNAC of thyroid gland was done both free guided and ultrasonic- guided and the results were correlated statistically*

Observation*: Out of total 139 patients, 87 patients were benign; 19 were male and 68 were female. The malignant lesions were 39; 8 were male and 31 were female. The most common neoplastic lesion by ultrasound guided FNAC was Papillary carcinoma accounting for 32, 3 cases of Medullary carcinoma, 1 Anaplastic carcinoma, 2 cases of Hurthle's carcinoma and 1 Lymphoma. In Free hand FNAC, 36 out of 139 patients were cytologically diagnosed as neoplastic cases were diagnosed. Two cases of papillary carcinoma and one case of medullary carcinoma were not picked up in Free hand FNAC and was diagnosed in USG Guided FNAC, which yielded representative material for cytological study. Comparison of neoplastic lesions results both by USG guided FNAC and Free Hand FNAC in 38 patients shows difference of 2 cases in Papillary carcinoma,1 case in medullary carcinoma ,while as Anaplastic carcinoma, Hurthle's cell carcinoma and Lymphoma were each one by both the techniques. Number of unsatisfactory smears were 4 and 1 in free and USG Guided FNAC respectively. We categorised the study sample as per Betheseda System. In USG-guided unsatisfactory were 4, benign were 87, Atypia of Undetermined Significance was none, Suscipicious for malignancy was none and malignant were 39.In Free-hand FNAC, unsatisfactory were 15,,*

benign were 81, stypia Of Undetermined Significance was none, suscipicious for malignancy was none and malignant were 36.In USG guided FNAC, Sensitivity was 96.96%, Specificity was 93.3%. Positive predictive value was 96.96%, Negative predictive value was 93.33% and Diagnostic accuracy was 95%.In Free Hand FNAC, Sensitivity was90.0%, Specificity was 80.0%. Positive predictive value was 90.0 %, Negative predictive value was 80% and Diagnostic accuracy was 86.66%.

Conclusion*: There was significant difference in the comparison of USG- guided FNAC and Conventional FNAC in Benign and Malignant lesions. The statistical significance of USG-guded FNAC as: Sensitivity 96.96%, Specificity 93.3%, Positive predictive value 96.96%,negative predictive vale 93.33%,diagnostic accuracy 95%.The statistical significance of USG-guded FNAC as: Sensitivity 90%, specificity 80%, positive predictive value 90%, negative predictive vale 80%, diagnostic accuracy 86.66%.*

Key Words: *Thyroid lesions, goiter, FNAC,ultrasonic –guided FNAC*

INTRODUCTION

Thyroid nodules are commonly encountered in clinical practice, with a prevalence of 2% to 5% for palpable thyroid nodules[1] and 19% to 46% for nodules detected by thyroid ultrasonography[2].Thyroid nodules are more common in women, and the incidence increases with age, history of radiation and diet containing giotrogenic material[1] .Various studies have shown that the risk of malignant involvement of thyroid palpable nodules[3] is 4% to 7%.

Thyroid nodules are the most common endocrine disorders particularly in countries where dietary iodine intake is low [4] .Clinically thyroid lesions present as goitre or thyroid enlargement which can be nodular

(solitary or multiple) or diffuse[5] .FNAC has surpassed most of other tests for the evaluation of thyroid nodules. [6]

Fine-needle aspiration cytology (FNAC) is a standard diagnostic test for evaluating palpable thyroid nodules. The procedure is regarded as a valuable method of distinguishing between malignant from those with benign nodules that can be followed clinically[7].

The sensitivity, specificity and accuracy of FNAC or malignancy detection have eclipsed the diagnostic utility of other diagnostic methods such as scintigraphic scanning. As a result, this relatively simple procedure have assumed dominant role in determining the management of patients with thyroid nodules. As a diagnostic test, FNAC can be used to diagnose most benign nodular goitres, cysts, thyroiditis and neoplasms (papillary, medullary, anaplastic, poorly differentiated and metastatic malignancy) with high degree of accuracy based on cyto-morphological features[8].The main objective of FNAC is to identify the thyroid nodules that can be safely left in situ, except carcinomas[9]. By differentiating benign from malignant lesions, FNAC has resulted in an overall decline in the number of thyroidectomise to 40% [10] and increased the yield of cancer [11]. FNAC is not a substitute for conventional surgical histopathology, but it should be regarded as extremely valuable component to it and is itself becoming indispensable[12].

The diseases of thyroid form a major share of head and neck surgery. Clinical examination, although very accurate in most cases, is

inadequate in some areas especially, in staging of thyroid malignancies and in detecting the multi-nodularity of the gland.Rapid evolution in sonographic technology has made ultrasound an important adjunct to the practice of head and neck surgery. Ultrasound of the neck is extremely sensitive in detecting thyroid pathology and is felt to be the most complete and cost-effective imaging method for the evaluation of the thyroid gland[13].

Rizatto et al [14] in 1973, introduced USG guided-FNAC, helps to accurately select the patients for surgery, avoids unnecessary diagnostic thyroidectomies.

Ultrasound guidance serves as a valuable aid in improving the diagnostic yield of fine-needle aspiration (FNA) cytology of thyroid nodules. The reported incidence of thyroid nodules in children and adolescents is estimated to be between 1% and 2%. However, this incidence may be increasing because diagnostic radiological procedures are detecting incidental thyroid nodules in children[15].

From a large study with 9683 subjects, Danese and coworkers[16] (1998) reported the sensitivity, specificity and accuracy of palpation-guided thyroid FNAs as 91.8%, 68.8% and 70.9% and of USG-guided FNAs as 97.1%, 70.9% and 75.6%, respectively.

FNAC and USG are thus used in association with clinical features. The present study is undertaken to evaluate usefulness of FNAC and USG in managing thyroid nodules. Thus, there is a need of comparative study between conventional FNAC and USG guided FNAC and to find the correlation between the two.

MATERIAL AND METHODOLOGY

The study was conducted in the Teaching hospital in Northern India. & was a prospective hospital based study in which FNAC of new cases of thyroid lesions was done. In each case, a brief clinical history and physical examination along with evaluation of relevant investigation was carried out. Fine Needle Aspiration Cytology of thyroid gland was done by (a) palpable method and (b) Ultrasound guided. The slide smears were stained by May-Grunwald Giemsa (MGG) and Papnincolaou (PAP) staining method.

PROCEDURE FOR PALPABLE FNAC

Patients were explained about whole of the procedure. The consent for the procedure was taken in all patients & the Palpable FNAC was carried out by positioning patient in supine position on an examination couch. During the procedure, the thyroid nodule was manually fixed in position & fine needle aspiration was performed .At least 2 passes in different quadrants of the thyroid nodule were performed to achieve a detailed cytologic picture keeping in mind that the majority of thyroid lesions are heterogeneous in morphology Smears were air-dried & then stained with May Grunwald Giemsa (MGG) stain. Some of the smears were fixed with 95 % ethanol. Those smears were then stained with Papanicolau's stain.

PROCEDURE FOR USG GUIDED FNAC:

USG guided FNAC was performed whereby the lesion were identified and the Fine Needle was introduced under continuous guidance of ultrasound. The procedure was done both in axial or sagittal plane. Correlation of the two methods was done by statistical evaluation using SPSS 11.5 software.

OBSERVATIONS

THE BETHSEDA GRADING FOR REPORTING CYTOPATHOLOGY

CATEGORY I **Non diagnostic /unsatisfactory smears:**

Smears containing few follicular cells or only blood without colloid were considered unsatisfactory or inadequate for diagnosis.

CATEGORY II **Smears negative for malignancy:**

The minimum criteria for calling a smear negative for malignancy was a total of six groups or clusters of well preserved benign appearing thyroid epithelial cells and a large quantity of colloid.

CATEGORY III **Atypia of undetermined significance:**

CATEGORY IV **Follicular Neoplasm:**

CATEGORY V **Smears suspicious for malignancy:**

The term suspicious /indeterminate was applied for follicular proliferation with minimal or no colloid and profuse presence of follicular cells and findings suggestive of, but not conclusive for malignancy. The distinction between follicular adenoma and follicular carcinoma was not possible on cytological grounds.

CATEGORY VI**: Smears positive for malignancy:**

The lesions designated as malignant included Papillary Carcinoma, Follicular Neoplasm, Medullary Carcinoma and Anaplastic Carcinoma. Detailed cytological examination of differently stained smears was carried out

OBSERVATION

TABLE 1: Distribution of Various Malignant Lesions on USG guided FNAC:

Age(yrs)	P.T.C.	M.C.	H.C.C.	A.C.	LYM.	Total
<10	0	0	0	0	0	0
11-20	3	0	0	0	0	3
21-30	7	0	0	0	0	7
31-40	10	1	1	0	0	12
41-50	9	0	1	0	0	10
51-60	2	1	0	0	0	3
61-70	1	1	0	1	0	3
>70	0	0	0	0	1	1
Total	32	3	2	1	1	39

P.T.C.= Papillary Cell Carcinoma, **M.C.**= Medullary Carcinoma, **H.C.C**.=Hurthle Cell Carcinoma, **A.C**.=Anaplastic Carcinoma, **LYM**.=Lymphoma

In the present study 39 out of 139 cases were cytologically diagnosed as neoplastic lesions in ultrasound guided FNAC. The most common neoplastic lesion by ultrasound guided FNAC was Papillary carcinoma accounting for 32, 3 cases of Medullary carcinoma, 1 Anaplastic carcinoma, 2 cases of Hurthle's carcinoma and 1 Lymphoma.

TABLE 2: Distribution of Various Malignant Lesions on Free Hand FNAC:

Age	P.T.C.	M.C.	H.C.C.	A.C.	LYM.	Total
<10	0	0	0	0	0	0
11-20	2	0	0	0	0	2
21-30	7	0	0	0	0	7
31-40	9	0	1	0	0	10
41-50	9	0	1	0	0	10
51-60	2	1	0	0	0	3
61-70	1	1	0	1	0	3
>70	0	0	0	0	1	1
Total	30	2	2	1	1	36

P.T.C.= Papillary Cell Carcinoma, **M.C**.= Medullary Carcinoma, **H.C.C**.=Hurthle Cell Carcinoma, **A.C**.=Anaplastic Carcinoma, **LYM**.=Lymphoma

In Free hand FNAC, 36 out of 139 patients were cytologically diagnosed as neoplastic cases were diagnosed. Two cases of papillary carcinoma and one case of medullary carcinoma were not picked up in Free hand FNAC and was diagnosed in USG Guided FNAC, which yielded representative material for cytological study.

TABLE 3: Comparison of Malignant Lesions between USG-guided FNAC and Free-Hand FNAC:

Thyroid lesion	USG guided FNAC	Percentage (%)	Free hand FNAC	Percentage (%)
Papillary carcinoma	32	80	30	75
Medullary carcinoma	3	7.5	2	5.0
Anaplastic carcinoma	1	2.5	1	2.5
Hurthle cell carcinoma	2	5.0	2	5.0
Lymphoma	1	2.5	1	2.5
Unsatisfactory	1	2.5	4	10.0
Total	40	100	40	100

Comparison of neoplastic lesions results both by USG guided FNAC and Free Hand FNAC in 38 patients shows difference of 2 cases in Papillary carcinoma,1 case in medullary carcinoma ,while as Anaplastic carcinoma, Hurthle's cell carcinoma and Lymphoma were each one by both the techniques. Number of unsatisfactory smears were 4 and 1 in free and USG Guided FNAC respectively.

TABLE 4: Results of FNAC as per Betheseda System:

CATEGORY	NAME	USG-FNAC	FREE-FNAC
I	Unsatisfactory	4	15
II	Benign	87	81
III	AUS	0	0
IV	Follicular Neoplasm	9	7
V	Suscipicious of Malignancy	0	0
VI	Malignant	39	36

AUS=Atypia of Undetermined Significance.

We categorised the study sample as per Betheseda System. In USG-guided unsatisfactory were 4, benign were 87, Atypia of Undetermined Significance was none, Suscipicious for malignancy was none and malignant were 39.In Free-hand FNAC, unsatisfactory were 15,, benign were 81, stypia Of Undetermined Significance was none, suscipicious for malignancy was none and malignant were 36.

TABLE 5: Comparison of USG Guided versus FREE HAND-FNAC:

Lesions	USG - guided FNAC		Free hand FNAC	
	Number	Percentage	Number	Percentage
benign	87	62.58	81	58.27
Follicular neoplasm	9	6.47	7	5.04
Papillary carcinoma	32	23.02	30	21.58
Medullary carcinoma	3	2.16	2	1.44
Anaplastic carcinoma	1	0.72	1	0.72
Hurthle cell carcinoma	2	1.44	2	1.44
Lymphoma	1	0.72	1	0.72
Unsatisfactory	4	2.88	15	9.35
Total	139	100	139	100

TABLE 6: STATISCAL COMPARISON BETWEEN USG AND FREE HAND FNAC:

VALUE	USG	FREE-HAND
Sensitivity	96.96%	90%
Specificity	93.3%	80%
Positive Predictive value	96.96%	90%
Negative Predictive value	93.33%	80%
Accuracy	95%	86.66%

In USG guided FNAC, Sensitivity was 96.96%, Specificity was 93.3%. Positive predictive value was 96.96%, Negative predictive value was 93.33% and Diagnostic accuracy was 95%.In Free Hand FNAC, Sensitivity was90.0%, Specificity was 80.0%. Positive predictive value was 90.0 %, Negative predictive value was 80% and Diagnostic accuracy was 86.66%.

DISCUSSION

The study was conducted in the teaching Hospital in Northern India & was a prospective hospital-based study. In the present study Ultrasound guided and Free handed Fine needle aspiration was performed in 139 patients with thyroid swelling. The present study aimed at studying the Cytological features of Thyroid lesions by Ultrasound guided Fine needle aspiration and compared with Free-hand Fine needle aspiration. Fine needle aspiration cytology (FNAC) is the fundamental method for evaluation of thyroid nodules. Examination of the material obtained by FNAC enables to differentiate between benign and malignant lesions. However, FNAC of thyroid has its own limitations. Ultrasound guidance allows continuous visualization of the needle during insertion and sampling which results in pinpoint accuracy with a high level of safety. Ultrasound guided Fine needle aspiration cytology improves the yield of cancer detected at surgery.[17] The incidence of solitary and diffuse nodules was 79.1% and 20.8%, respectively in the present study.

FINDINGS ON FNAC

In the present study, fine needle aspiration of thyroid lesion results are interpreted as per Bethesda system (Table 7). The results obtained by USG-guided FNAC of benign, malignant. Intermediate and Unsatisfactory subgroups, are incorporated in the following table and compared with results of studies by other authors.

Table 7: Comparison of results of present study with Other Authors:

Cytological results	A Martinek et al	A S Can et al	Present Study
Benign	4	147	87
Malignant	36	5	39
Indeterminate	8	9	9
Unsatisfactory	8	23	4

Aspiration was done from at least 2-6 sites. Laurie et al(1996) stresses the importance of doing multiple aspirations as the thyroid can be affected by more than one disease process[18].

Aspirates done by Ultrasound guided FNAC were satisfactory for cytological evaluation in 135 cases and unsatisfactory in 4 cases where as aspirates done by conventional FNAC were satisfactory in 124 cases and unsatisfactory in 15 cases with the percentage of inadequate samples being 2.87 % and 10.79 % respectively. This when compared to study by P Mehrotra et al [19], the percentage of inadequate samples is lower in both free hand and guided FNAC.

In present study, USG guided FNAC showed/diagnosed 87 smears as non-neoplastic 39 were neoplastic lesions and 4 were unsatisfactory. The non-neoplastic to neoplastic ratio was 2.23:1 by ultrasound guided FNAC. In conventional FNAC, 81 were non neoplastic lesions and 36 were neoplastic, 13 were unsatisfactory with non-neoplastic to neoplastic ratio being 2.25:1. Many authors have studied cytology of thyroid lesions with ratio of non neoplastic to neoplastic lesions ranging from 0.46:1 to 12.5:1. Ratio when compared to other studies it was comparable to Erik K Alexander [20] et al study but non-neoplastic were higher in number of patients when compared to study by A Martinek [21] and Antonello Accurso [22] et al. (Table 8).

Table No. 8: Showing non-neoplastic to neoplastic ratio in different studies and the present study.

Study	Non-neoplastic	Neoplastic	Ratio
A Martinek et al	189	56	3.37:1
Erik K Alexander et al	929	340	2.73:1
Antonello Accurso	239	14	17.07:1
Present study	87	39	2.23:1

In the present study, the most common malignant lesion in ultrasound guided FNAC was Papillary carcinoma 32, Follicular neoplasm 9, Medullary carcinoma 3, Hurthle Cell Carcinoma 2, Anaplastic carcinoma 1 and Lymphoma one case were seen. Free hand FNAC showed the commonest were Papillary carcinoma 30, follicular neoplasm 7, Medullary carcinoma 2, Hurthle cell carcinoma 2 and 1 lymphoma/ anaplastic carcinoma. There were 15 unsatisfactory samples. Papillary carcinoma was the common neoplastic lesion in the present study similar to the study by A Martinek et al[21].

n the present study, Goitre was the commonest thyroid lesion accounting for 51(57.3%) by USG-guided FNAC. Similar observation was made by A Martinek et al[21] who reported 156 (50.4%) out of 309 cases10.

In the present study the most common neoplastic lesion by ultrasound guided FNAC was papillary carcinoma accounting for 32(82.05 %), followed by Medullary carcinoma 3 (7.69 %), Hurthle's Cell Carcinoma 2(5.1 %), Anaplastic carcinoma 1(2.5 %) and Lymphoma 1(2.5 %) and follicular neoplasm cases 9(6.4%).Similar figures were seen in Free hand FNA with papillary carcinoma 30 (83.3 %), Medullary Carcinoma 2(5.55 %), Hurthle's Cell Carcinoma 2 (5.55 %) followed by Anaplastic carcinomas and lymphoma one (2.77 %) each and follicular neoplasm 7(5.03 %).

Distribution of different neoplastic lesions is comparable to A Martinek et al [21]study. The most common thyroid lesion was Papillary Carcinoma followed by Follicular Neoplasm, similar to that of our study. On the other hand, Jen Der Lin et al [22] shows follicular neoplasm as commonest

neoplastic lesion whereas in our study shows papillary carcinoma is the commonest neoplastic lesion.

In the present study, 9 cases of follicular neoplasm were diagnosed in both USG guided FNAC and Free hand FNAC, aspirate from all cases were scanty, semisolid. Similar observations were seen in the study by A Martinek et al[21]. But when compared to Jen Der Lin et al [23], the incidence was less.

In the present study cytological diagnosis of papillary carcinoma was made in 32 cases. Histopathological study was possible only in 17 cases and diagnosis remained same in all 17 cases.

In the present study cytological diagnosis of Medullary carcinoma was made in 03 cases. The incidence was comparable to study by A Martinek et al [21]and higher when compared to the study by Jen- Der Lin et al[23].In the present study one case of lymphoma was diagnosed by both ultrasound guided FNAC and free hand FNAC constituting 2.0 % of malignant lesions. Similar observations were made in study by A Martinek et al [21] in which also 1 case of lymphoma was diagnosed making 2.08% of total cases.

The efficiency of fine needle aspiration is responsible for a marked increase of the rate at which neoplasms are found at surgery. Out of 139 cases 48 were operated, of which 33 were neoplastic and 15 were benign as per cytological studies.

The ratio of non-neoplastic to neoplastic was 2.23:1 and 2.5:1 on free and USG guided cytology respectively

Study	Sensitivity	Specificity	PPV	NPV	Accuracy
Takashima et al	96%	91%	96%	91%	94%
Baloch et al	87.84%	78.5%	33.51%	98.13%	79.53%
Kim et al	96.9%	93.4%	86.1%	98.6%	94.4%
Cesur et al	93.5%	26%	43%	86%	54%
Kwak et al	96.4%	74.5%	92.7%	94.9%	80.9%
Rosen et al	60.9%	100%	100%	80%	85%
Present Study	96.96%	93.33%	96.96%	93.33%	95%

In this study we have achieved a sensitivity of 96.96% by ultrasound guided FNA which is comparable with that of Kim et al [24](96.9%), Takashama et al[25] (96%) , Kwak et al [26](96.4%) and Cesur et al[27] (93.5%) and higher compared to Cai et al [28](83.3%) study but lower than AS Can et al [29](100%).

Specificity of our study was 93.33% which was comparable with Kim et al[24](93.4%) and A S Can et al [29] (94.0%) but higher than Kwak et al

[26](74.5%), A Martinek et al[21] (85.0%), Takashima et al [25](91.0%) and lower than Cai et al [28](98%).The present study had Positive predictive value 96.96%. It is comparable with Takashima et al [25](96%), but higher than Cesur et al [27](43.0%), AS Can et al[29] (67%) and Cai et al[28] (71.0%). The negative predictive value of the study was 93.33%. It was comparable with Takashima et al [25] (91%) but higher than Cesur et al [27] (86%) but lower than AS Can et al [29](100%), Kim et al (98.6%) and Cai et al [28](98.4%). Negative predictive value of nearing 93.33 % is an indication of best screening test.Positive likelihood ratio and negative likelihood ratio was 14.54% and 0.03% respectively.Diagnostic accuracy of the present study is 95.83% which is comparable to Kim et al [24](94.4%) and Takashima et al [25](94%) but higher than Kwak et al [26] (80.9%) and A Martinek et al [21](86%).

The agreement between the USG guided FNAC and Free hand FNAC is highly significant shown by kappa k = 94 %.

CONCLUSION

The present work compromised of One year prospective analysis of thyroid lesions by USG-guided and conventional method fine needle aspiration cytology (FNAC).The study compromised of 139 patients of thyroid lesions who were subjected to USG-guided and conventional method fine needle aspiration cytology (FNAC). Following conclusions were inferred from the study:

- The diagnosis of thyroid lesions as per Betheseda System by USG and conventional FNAC was respectively ,as follows:

I	Unsatisfactory :	04,15
II	Benign :	87,81
III	Atypia of undetermined significance: none	
IV	Follicular Neoplasm :	09,07
V	Suspicious of malignancy : none	
VI	Malignant :	39,36.

- The distribution of malignant lesions on USG- guided FNAC was as: Papillary Carcinoma 32, Medullary Carcinoma 03, Anaplastic Carcinoma 01, Hurthle Cell Carcinoma 02 and Lymphoma 01. The distribution of malignant lesions on Conventional FNAC was as: Papillary Carcinoma 30, Medullary Carcinoma 02, Anaplastic Carcinoma 01, Hurthle Cell Carcinoma 02 and Lymphoma 01.
- The number of unsatisfactory samples were 4 and 15 by USG- guided FNAC and Conventional FNAC, respectively.
- The number of Follicular Neoplasm were 9 and 7 by USG- guided FNAC and Conventional FNAC, respectively.
- There was significant difference in the comparison of USG- guided FNAC and Conventional FNAC in Benign and Malignant lesions.
- The statistical significance of USG-guded FNAC as: Sensitivity 96.96%, Specificity 93.3%, Positive predictive value 96.96%,negative predictive vale 93.33%,diagnostic accuracy 95%.
- The statistical significance of USG-guded FNAC as: Sensitivity 90%, specificity

80%, positive predictive value 90%, negative predictive vale 80%, diagnostic accuracy 86.66%.

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