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# Demographic distribution of papillary carcinoma on USG-guided biopsy and compare the same with free guided biopsy in a study population and its subsequent confirmation by histopathology

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### ABSTRACT

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 and to find their correlation with histopathology. To Study the Demographic distribution of Papillary carcinoma of thyroid on USG-guided biopsy with free guided biopsy` and confirm the same with cytohistopathological diagnosis. The study was conducted in a teaching hospital for a period of 1 year. It was a prospective hospital based Study. Patients 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 followed by histopathological examination wherever possible. Out of 139 patients, maximum numbers of patients were in 31-40 age group i.e., 43 and minimum patients were in < 10 years and > 70 year age group. 24 patients were males and rest 115 were females. The diagnosis of thyroid lesions as per Betheseda System by USG and conventional FNAC. Cytological diagnosis of papillary carcinoma was made in 32 cases in ultrasound guided FNAC. Out of 32 patients, 30 were clinically euthyroid and 2 had clinical toxic features. Two cases was reported as unsatisfactory smears in free hand FNAC while as guided aspirates proved to be papillary carcinoma. Age ranged from 8 to 68 yrs., with mean age of 39.5 yrs. Majority were female numbering 27 and 5 were male. 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. Number of unsatisfactory smears were 4 and 1 in free and USG Guided FNAC respectively. The Histo-pathological results were same as that seen cytological study. Out of 30 cases of papillary carcinoma diagnosed on Free-Hand FNAC histopathology was available in only in 15 cases. 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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### Introduction

In clinical practice palpable thyroid nodules occur with a prevalence of 2% to 5%<sup>1</sup> and 19% to 46% for nodules detected by thyroid ultrasonography<sup>2</sup>. The incidence of thyroid nodules increases with age, radiation exposure and giotrogenic diet<sup>1</sup> Women are affected more than males. The risk of malignant involvement of thyroid palpable nodules<sup>3</sup> is 4% to 7%.

Thyroid nodules are the most common endocrine disorders particularly in developing countries<sup>4</sup>. Clinically thyroid lesions present as goitre or thyroid enlargement which can be nodular (solitary or multiple) or diffuse<sup>5</sup>.

Clinicians have used clinical examination, biochemical lab. tests (T3, T4, TSH), transcutaneous ultrasonography, scintigraphy with (I-123 or Tc-99 mm) and fine needle aspiration cytology (FNAC) for the evaluation of thyroid nodules. FNAC has surpassed most of other tests<sup>6</sup>.

Fine-needle aspiration cytology (FNAC) is a standard diagnostic test for evaluating palpable thyroid nodules<sup>7</sup>. The

procedure is regarded as a valuable method of distinguishing between malignant from those with benign nodules that can be followed clinically<sup>8</sup>. A successful thyroid FNAC requires an adequate specimen, high-quality smear preparation, and experience on the part of the both aspirator and cyto-pathologist<sup>9</sup>.

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<sup>10</sup>. Though conventional FNAC plays a key role in diagnosing thyroid lesions, it has its own limitations. By differentiating benign from malignant lesions, FNAC has resulted in an overall decline in the number of thyroidectomise to 40%<sup>11</sup> and increased the yield of cancer<sup>12</sup>

Detailed cytologic assessment helps to highlight the differentiating features between various types of goitres. The parameters for cytologic assessment include cellularity, colloid

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content, acinar formation, intranuclear cytoplasmic inclusions, marginal vacuoles, nuclear grooves, hurthle cells and various inflammatory cells<sup>12</sup>.

The diseases of thyroid form a major share of head and neck surgery. In some Cases where Clinical examination is inadequate , in staging of thyroid malignancies and in detecting the multi-nodularity of the gland the advancements in management of thyroid pathology has been possible, because of developments in the field of imaging radiology. 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<sup>13</sup>.

Rizzato et al<sup>14</sup> in 1973, introduced USG guided-FNAC. Thereafter, several studies have reported that USG guided-FNAC reduces the inadequacy rate , helps to accurately select the patients for surgery, avoids unnecessary diagnostic thyroidectomies. Ultrasound guided-FNAC had a significantly higher rate of diagnostic accuracy compared to palpable FNAC<sup>15</sup>. Various authors recommend FNAC to be undertaken with ultrasound guidance with a pathologist in attendance to assess sample adequacy<sup>16</sup>.

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<sup>17</sup>.

The majority of thyroid fine needle aspiration Cytology (FNAC) are performed by palpation. Not infrequently, patients are sent to radiology for an ultrasound-guided FNAC. Real-time ultrasound FNAC allows for continuous visualization of the needle during insertion and sampling<sup>18</sup>.

It is reported that 9 to 47% of palpation-guided and 4 to 21% of ultrasound-guided FNA smears are inadequate<sup>19</sup>. Hatada and co-workers<sup>20</sup> (1998) reported that for nodules less than 2 cm in diameter, the sensitivity and accuracy of USG-guided FNA biopsies are significantly better than manual FNA . From a large study with 9683 subjects, Danese and coworkers<sup>21</sup> (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. Thus, there is a need of comparative study between conventional FNAC and USG guided FNAC and to find correlation with histopathology.

#### Methodology

The study was conducted in the Postgraduate Department of Pathology in a tertiary care hospital. It 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 radiologist and cyto-Pathologist carried out Ultrasound-guided FNAC. The slide smears were stained by May-Grunwald Giemsa (MGG) and Papnicolaou (PAP) staining method. The results of FNAC were correlated with histopathology, wherever available.Statistical evaluation was done using SPSS 11.5 software

#### Results

Cytological diagnosis of papillary carcinoma was made in 32 cases in ultrasound guided FNAC. Out of 32 patients, 30 were clinically euthyroid and 2 had clinical toxic features and 3 patient had pain and difficulty in swallowing, duration of symptoms varied from 4 months to 8 years.4 patients complained of rapid increase in size of the swelling and one

patient had undergone lobectomy previously for similar complaints.

**Table 1. Age and Sex Distribution of Papillary Thyroid Carcinoma on USG guided FNAC**

Age(yrs)	Male	Percentage(%)	Female	Percentage(%)
<10	0	0	0	0
11 to20	1	20	2	7.4
21 to 30	0	0	7	22.9
31 to 40	1	20	9	33.3
41 to 50	1	20	8	29.6
51 to 60	2	40	0	0
61 to 70	0	0	1	3.7
> 70	0	0	0	0
Total	5	100	27	100

**Table 2: Age and Sex Distribution of Papillary Thyroid Carcinoma on Free Hand FNAC**

Age(yrs)	Male	Percentage(%)	Female	Percentage(%)
<10	0	0	0	0
11 to20	1	20	1	4
21 to 30	0	0	7	28
31 to 40	1	20	8	32
41 to 50	1	20	8	32
51 to 60	2	40	0	0
61 to 70	0	0	1	4
> 70	0	0	0	0
Total	5	100	25	100

Cytological diagnosis of papillary carcinoma was made in 30 cases in free hand FNAC. Two cases was reported as unsatisfactory smears in free hand FNAC while as guided aspirates proved to be papillary carcinoma. Age ranged from 8 to 68 yrs., with mean age of 39.5 yrs. Majority were female numbering 27 and 5 were male.All of the 32 patients presented with solitary hard nodule measuring 2 to 6 cms .

**Table 3. Comparison of Malignant Lesion Papillary Carcinoma between USG-guided FNAC and Free-Hand FNAC**

Thyroid lesion	USG guided FNAC	Percentage(%)	Free hand FNAC	Percentage(%)
Papillary carcinoma	32	80	30	75

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.Number of unsatisfactory smears were 4 and 1 in free and USG Guided FNAC respectively.

**Table 4: Distribution of malignant lesions on Histopathological diagnosis**

Age Group	Papillary thyroid carcinoma	Others
<10	0	0
11-20	2	1
21-30	4	2
31-40	7	4
41-50	3	1
51-60	1	4
61-70	0	3
>70	0	1
Total	17	16

Out of 32 cases of papillary carcinoma diagnosed on usg-guided FNAC histopathology was available in only 17 cases. The Histo-pathological results were same as that seen cytological study.Out of 30 cases of papillary carcinoma diagnosed on Free-Hand FNAC histopathology was available in only in 15 cases.

**Table 5: Cyto-histopathological correlation of Papillary Carcinoma**

CYTOLOGIC DIAGNOSIS		Histopathological Diagnosis
Papillary Carcinoma		Papillary Carcinoma
USG-Guided FNAC	Free-hand FNAC	17
17	15	

## Discussion

The study was conducted in the Postgraduate Department of Pathology. It 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 (viz-a-viz papillary carcinoma of thyroid) by Ultrasound guided Fine needle aspiration and compared with Free-hand Fine needle aspiration. Furthermore, the cytological findings were confirmed with Histopathology examination (HPE), wherever it was available.

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. 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.<sup>22</sup> In the present study, fine needle aspiration of thyroid lesion results are interpreted as per Bethesda system

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<sup>23</sup>. 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<sup>24</sup>, the percentage of inadequate samples is lower in both free hand and guided FNAC.

For considering the aspirate adequate for interpretation, it requires five to six groups of well preserved cells with each group consisting of 10 or more cells. Many studies have applied the same criteria for satisfactory aspirates. 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<sup>25</sup> et al study but non-neoplastic were higher in number of patients when compared to study by A Martinek<sup>26</sup> and Antonello Accurso<sup>27</sup> et al

Papillary carcinoma was the common neoplastic lesion in the present study similar to the study by A Martinek et al<sup>26</sup>. Histopathological study was possible in 4 cases of goitre which confirmed cyto-diagnosis in all the 04 cases. In the present study the most common neoplastic lesion by ultrasound guided FNAC was papillary carcinoma accounting for 32(82.05 %).

Similar figures were seen in Free hand FNA with papillary carcinoma 30 (83.3 %). Distribution of different neoplastic lesions is comparable to A Martinek et al<sup>26</sup> 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<sup>28</sup> shows follicular neoplasm as commonest neoplastic lesion whereas in our study shows papillary carcinoma is the commonest neoplastic lesion.

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. On comparing USG-guided FNAC with Histopathology findings, one case of Papillary carcinoma was proved to be Hyalinizing Trabecular Adenoma. One case of colloid goitre with cystic degeneration diagnosed on cytology was proved to be Papillary Carcinoma on Histopathology.

On comparing Free-hand FNAC with Histopathology findings, three cases found to be malignant on conventional FNAC were proved to be benign on Histopathology. They are described as: Two cases of follicular neoplasm was proved to be follicular adenoma and one case of Papillary carcinoma was proved to be Colloid goitre. However three cases found to be colloid goitre were proved to be Papillary carcinoma. 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.

In this study we have achieved a sensitivity of 96.96% by ultrasound guided FNA which is comparable with that of Kim et al<sup>29</sup> (96.9%) and higher compared to Cai et al<sup>30</sup> (83.3%) study but lower than AS Can et al<sup>15</sup> (100%). Specificity of our study was 93.33% which was comparable with Kim et al<sup>29</sup> (93.4%) and A S Can et al<sup>15</sup> (94.0%) but higher than Kwak et al<sup>31</sup> (74.5%), A Martinek et al<sup>26</sup> (85.0%), Takashima et al<sup>32</sup> (91.0%) and lower than Cai et al<sup>30</sup> (98%).

The present study had Positive predictive value 96.96%. It is comparable with Takashima et al<sup>32</sup> (96%), but higher than AS Can et al<sup>15</sup> (67%). The negative predictive value of the study was 93.33%. It was comparable with Takashima et al<sup>32</sup> (91%) but higher than Cesur et al<sup>33</sup> (86%) but lower than AS Can et al<sup>15</sup> (100%). 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.

The agreement between the USG guided FNAC and Free hand FNAC is highly significant shown by kappa k = 94 %. The agreement between the USG guided FNAC and histopathology is shown by kappa k = 96 %. The agreement between the Free hand FNAC and histopathology is shown by kappa k = 74 %.

## Summary

The present study was conducted in the Post-graduate Department of Pathology, in a tertiary care hospital. The present work comprised of:

- One year prospective analysis of thyroid lesions (viz-a-viz papillary carcinoma of thyroid) by USG-guided and conventional method fine needle aspiration cytology (FNAC).
- Correlation of findings of FNAC with Histopathological findings, wherever, available.

The study comprised 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:

1) Out of 139 patients, maximum number of patients were in 31-40 age group 24 patients were males and rest 115 were females.

2)The major complaint was swelling in neck i.e., in 134, rest presented with local pain (3) and discomfort (2). Furthermore, majority of patients were euthyroid i.e., 123. Only 13 patients proved hypothyroid and 1 patient was thyrotoxic.

3) The diagnosis of thyroid lesions as per Bethesda 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.

4)The distribution of malignant lesions on USG- guided FNAC was as: Papillary Carcinoma 32, Others 7. The distribution of malignant lesions on Conventional FNAC was as: Papillary Carcinoma 30, others 6.

5)The number of unsatisfactory samples were 4 and 15 by USG-guided FNAC and Conventional FNAC, respectively.

6)There was significant difference in the comparison of USG-guided FNAC and Conventional FNAC in Benign and Malignant lesions.

7)Histopathological study was possible in 48 cases of USG-guided FNAC, out of which 32 were malignant and 14 were benign cases. 1 case diagnosed as Papillary Carcinoma by USG-FNAC was found to be Colloid Goitre by

8)Histopathology. One case diagnosed by USG-FNAC was Colloid Goitre with Cystic degeneration while as Histopathology proved to be Cystic Papillary Carcinoma.

9)Histopathological study was possible in 45 cases of Conventional FNAC, out of which 30 were malignant and 15 were benign cases. 3 cases diagnosed as Papillary Carcinoma by USG-FNAC were found to be Colloid Goitre with cystic change by Histopathology. Furthermore, three case by USG-FNAC was Colloid Goitre with Cystic degeneration that on Histopathology proved to be Cystic Papillary Carcinoma.

10)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%.

11)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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