

## Original article

# A comparative study of free-hand fine needle aspiration cytology and ultrasound guided fine needle aspiration cytology in the diagnosis of thyroid swellings at BP Koirala Institute of Health Sciences- a tertiary care centre in Nepal

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## Abstract

**Background:** Thyroid lesions are commonly encountered in clinical practice and it is mandatory to know and record the nature of pathology prior to definitive therapy. Fine needle aspiration cytology (FNAC) is a time tested, cheap, reliable and safe method to establish a cytological diagnosis of the nature of the disease. Ultrasound guided FNAC has the potential to reduce inadequacy rates and is regarded as the optimal cytological method for diagnosis. **Objective:** To compare the results of free-hand and ultrasound-guided FNAC of thyroid swellings and to find out the diagnostic reliability of free-hand FNAC and ultrasound-guided FNAC using histological diagnosis as the gold standard. **Methods:** Fifty-five patients with thyroid swelling who were subjected to free-hand and ultrasound-guided FNACs and who subsequently underwent surgery over one year were studied. **Results:** Ultrasound guided FNAC results revealed 72.75 % benign lesions and 25.45 % of malignant lesions, and free hand FNAC revealed 52.73 % benign and 16.36% malignant cases. A 14.55 % inadequacy rate was seen in the free hand group. Histological gold standard diagnosis comprised of 60 % benign and 40 % malignant cases. Sensitivity and specificity of free-hand and ultrasound guided FNAC in diagnosing malignancy of the thyroid were 56.25% and 100%; and 63.64% and 96.97% respectively. **Conclusion:** Free hand FNAC of thyroid swellings is more convenient and cost effective as compared to ultrasound guided FNAC. However, the diagnostic yield in ultrasound guided FNAC is significantly more in terms of accuracy especially in cystic and tiny lesions.

**Keywords:** biopsy, colloid goitre, fine needle aspiration cytology, medullary carcinoma, papillary carcinoma, thyroid lesions, thyroiditis

## Introduction

Thyroid lesions are commonly encountered in clinical practice and it is mandatory for the surgeons to know the nature of the pathology before definitive therapy. Fine needle aspiration cytology (FNAC) technique for thyroid originated in Scandinavia in the 1950s and 1960s.<sup>1</sup>

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Majority of thyroid nodules turn out to be benign, the small subset of cancerous nodules needs to be accurately identified for optimal and timely management. FNAC has been established as the first line diagnostic test for thyroid lesions and has proven to be the most valuable modality for preoperative distinction of benign from malignant nodules and to confirm the diagnosis.<sup>1</sup>

The accuracy of FNAC and the inadequacy rates are influenced by operator technique, experience and the reliability of inserting the needle into the area of interest particularly in cystic nodules.<sup>2</sup> Ultrasound guided FNAC has the potential to reduce inadequacy rates, to facilitate accurate targeting of the lesion, to sample the part most likely to yield diagnostic material and to sample the solid portion of cystic nodules which are too small for palpation<sup>2</sup>.

This study was done to compare the results of free-hand and ultrasound-guided FNAC in cases of thyroid swellings and to compare the reliability rates for ultrasound-guided and free-hand FNAC and to correlate cytological and histological findings.

### Methods

All the cases of thyroid swelling who presented to the departments of Otorhinolaryngology and General Surgery of B.P. Koirala Institute of Health Sciences, Dharan, Nepal from January to December 2008 were subjected to FNAC in the Department of Pathology and subsequently underwent surgery were included in the study. The cases that were subjected to FNAC but did not undergo surgery were excluded from the study. Fifty-five cases were enrolled in the study. Each of these cases underwent free hand FNAC followed by ultrasound-guided FNAC and subsequently underwent surgery. Cytological and histological correlation was observed.

After taking informed consent a free hand FNAC was performed from the thyroid gland and the patient was called for an ultrasound (USG) guided FNAC of the thyroid lesion at the next available date. Both free hand and USG guided FNAC were performed using a 10 ml Dispovan™ syringe with a tight fitting 21-23 gauge needle. Rapid smearing was done to avoid clotting. Two to three slides were immediately fixed in 95% ethyl alcohol for Papanicolaou stain and two to three slides were allowed to dry in the air for May-Grunwald's Giemsa (MGG) stain. Both free hand and USG guided FNAC smears findings were observed.

The study was carried out after obtaining ethical clearance from the Institute Ethical Review Board (IERB) of B. P. Koirala Institute of Health Sciences, Nepal.

### Histopathological Examination

Thyroid specimens were received in 10% formaldehyde in the histopathology department. Specimens were processed for the histopathological examination as per the routine protocol. The sections were stained with hematoxylin and eosin and were studied microscopically. Results of FNACs and histology were correlated.

### Statistical Analysis

Data were entered in Microsoft Office Excel 2000 and converted to SPSS PC+10.0 version for statistical analysis. To find out the descriptive statistics we calculated percentage, proportion and ratio and for presentation different types of diagrams were made. For inferential statistics we compared free-hand FNAC and ultrasound-guided FNAC with histopathology as gold standard.

### Results

The 55 patients who underwent surgery for their thyroid swellings following free-hand and ultrasound-guided FNAC were studied and the following observation was made.

The age of the patients ranged from 14 to 72 years. The mean age was 36.5 years with a SD of 13.17.

**Table 1: Age distribution in years**

Age distribution in years	Frequency	Percentage
11- 20	7	12.72
21- 30	13	23.62
31- 40	17	30.90
41- 50	9	16.3
51- 60	7	12.72
61- 70	1	1.81
≥70	1	1.81
Total	55	100

Forty-six (83.6%) of our patients were females and 9 (16.4%) males. The Female: Male ratio was 5.1:1. Thirty three (60%) patients were from the hills or the foothills, and 22(40 %)

patients were natives of the plains. The mean duration of symptoms was 59.98 months (range 1 month – 480 months). Three patients had hypothyroidism and were taking levothyroxine and another three had hyperthyroidism under control with medication. At the time of surgery all the patients were euthyroid. The largest swelling was 10cm in diameter where as the smallest that could be identified clinically was 1 cm in diameter. Swelling size of 2-3 cm was the most frequent. (Table 2).

**Table 2: Diameter of the thyroid swelling**

Size of the swelling ( maximum diameter)	Frequency	Percentage
<1 cm	2	3.63
1-2 cm	12	21.84
2-3 cm	13	23.65
3-4 cm	4	7.27
4-5 cm	10	18.18
5-6 cm	6	10.92
6-7 cm	1	1.81
7-8 cm	2	3.63
8-9 cm	1	1.81
9-10 cm	4	7.27
<b>Total</b>	<b>55</b>	<b>100</b>

On free hand FNAC of the thyroid swellings in 8 (14.55%) cases, the sample obtained was inadequate; and in 29 (52.73%) cases the lesions were benign, in 9 (16.36%) cases malignant, 8 (14.55%) cases were indeterminate and 1 (1.8%) case was a follicular neoplasm. The specific results of free hand FNAC are shown in table no 3.

**Table 3: Free Hand FNAC Results**

Free Hand FNAC Variants	Frequency	Percentage
No Material	8	14.5 %
Colloid, Macrophages, Lymphocytes, No Follicular cells	8	14.5 %
Thyroiditis	1	1.8 %
Colloid Goitre	21	38.3%
Colloid Goitre with papillary hyperplasia	3	5.5 %
Hyperplastic Nodule	1	1.8 %
Thyroglossal Cyst	3	5.5 %
Follicular Neoplasm	1	1.8 %
Medullary Carcinoma	1	1.8 %
Papillary Carcinoma	8	14.5 %
<b>Total</b>	<b>55</b>	<b>100 %</b>

On USG guided FNAC, 40 (72.75%) patients had benign lesions, 1 (1.8%) follicular neoplasm, and 14 (25.45%) malignant lesions. The cytological diagnosis on ultrasound guided FNAC are shown in table no. 4.

**Table 4: USG guided FNAC Results**

USG Guided FNAC Results	Frequency	Percentage
Thyroiditis	1	1.8 %
Colloid Goitre	32	58.2 %
Colloid Goitre with papillary hyperplasia	1	1.8 %
Hyperplastic Nodule	3	5.5 %
Thyroglossal Cyst	3	5.5 %
Follicular Neoplasm	1	1.8 %
Medullary Carcinoma	1	1.8 %
Papillary Carcinoma	12	21.8 %
Papillary Carcinoma with Metastasis	1	1.8 %
<b>Total</b>	<b>55</b>	<b>100 %</b>

#### **Histopathological Examination**

On histopathological examination it was observed that 33 (60%) cases were benign and 22 (40 %) cases were malignant and are shown in table no 5.

**Table 5: Histopathological Diagnosis**

Histological diagnosis	Frequency	Percentage
Thyroiditis	3	5.5
Adenoma	3	5.5
Colloid goiter	24	41.8
Thyroglossal Cyst	3	5.5
Follicular Carcinoma	1	1.8
Medullary Carcinoma	1	1.8
Papillary Carcinoma	20	36.3
<b>Total</b>	<b>55</b>	<b>100</b>

The histopathology report was taken as the gold standard and a comparison was made between the free -hand FNAC and the ultrasound- guided FNAC using standard statistical methods. It was seen that when free hand FNAC was compared with the histological findings, 31 (81.5%) cases were similar; whereas 7 (18.5%) cases were not. The 8 (14.5%) cases with no material or only blood aspirated and 8 cases with only macrophages or colloid with no follicular cells were not included in this comparison. The sensitivity and specificity of free-hand FNAC

were -56.25% and 100% respectively (Table no 6 or diagram 1).

**Table 6: Comparison of USG with histological examination (gold standard) for diagnosis of malignancy**

	Malignancy present	Malignancy absent
Test Positive	True Positive (a) n = 13	False Positive (c) n = 1
Test Negative	False Negative (b) n = 8	True Negative (d) n = 32
Sensitivity (a/a+b)	63.64%	95% CI: 40.67% to 82.76%
Specificity (d/c+d)	96.97%	95% CI: 84.18% to 99.49%
Positive Predictive Value (a/a+c)	93.33%	95% CI: 67.98% to 98.89%
Negative Predictive Value (d/b+d)	80.00%	95% CI: 64.35% to 90.92%

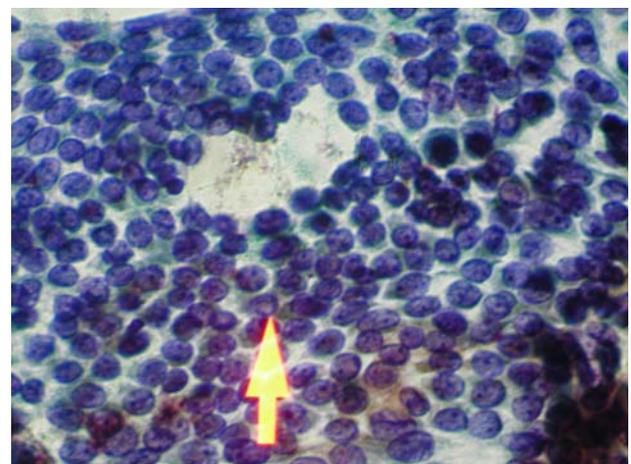
**Comparison of free hand biopsy with histological examination (gold standard) for diagnosis of malignancy**

	Malignancy present	Malignancy absent
Test Positive	True Positive (a) n = 9	False Positive (c) n = 0
Test Negative	False Negative (b) n = 3	True Negative (d) n = 26
Sensitivity (a/a+b)	56.25%	95% CI: 29.92% to 80.17%
Specificity (d/c+d)	100.00%	95% CI: 84.43% to 100.00%
Positive Predictive Value (a/a+c)	100.00%	95% CI: 66.21% to 100.00%
Negative Predictive Value (d/b+d)	75.86%	95% CI: 56.45% to 89.66%

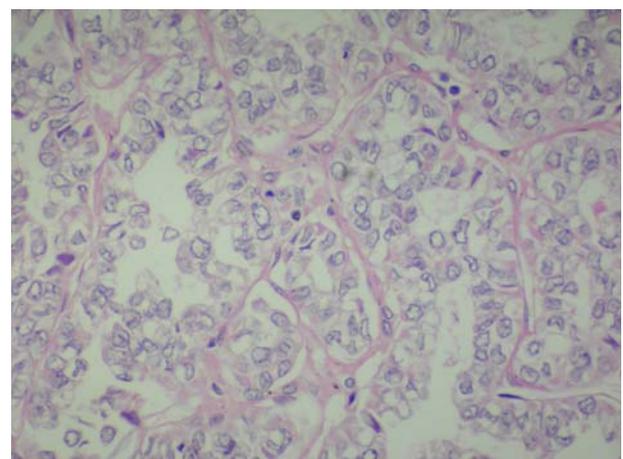
**Comparison of USG and freehand biopsy in diagnosis of malignancy**

	Biopsy Positive	Biopsy Negative
USG Positive	True Positive (a) n = 9	False Positive (c) n = 0
USG Negative	False Negative (b) n = 7	True Negative (d) n = 22
Sensitivity (a/a+b)	75.00%	95% CI: 42.84% to 94.22%
Specificity (d/c+d)	100.00%	95% CI: 86.65% to 100.00%
Positive Predictive Value (a/a+c)	100.00%	95% CI: 66.21% to 100.00%
Negative Predictive Value (d/b+d)	89.66%	95% CI: 72.62% to 97.69%

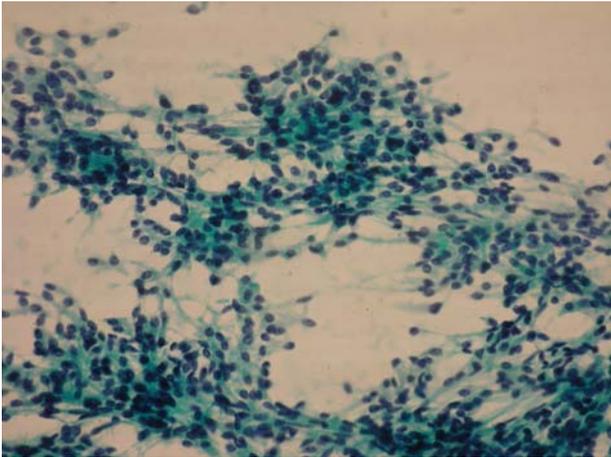
The USG guided FNAC when compared to the histological findings showed that 45(83.3%) cases matched or was in agreement with each other, while 9 (16.7%) cases did not match. It was observed that 83.3% of the ultrasound guided FNAC agreed with the histological findings but only 81.5% of the free hand FNAC matched with the histological findings. There was a difference of 1.8% between free hand and ultrasound guided FNAC. Ultrasound guided FNAC showed a 1.8 % greater agreement with histology. The sensitivity and specificity of Ultrasound guided FNAC were 63.64% and 96.97% respectively (Table no 6 or diagram 1).



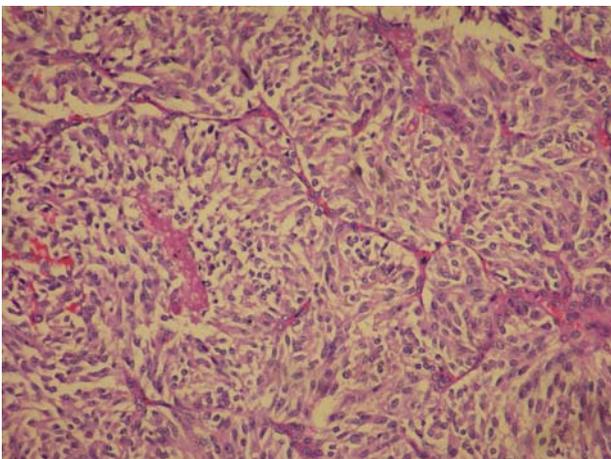
**Figure 1:** Papillary Carcinoma; intranuclear inclusion (arrow) and nuclear groove. (PAP stain X400)



**Figure 2:** Papillary carcinoma showing enlarged optically clear nuclei, nuclear crowding and nuclear grooving (H&EX400)



**Figure 3:** Medullary Carcinoma, dispersed and clustered spindle cells(PAP X 100)



**Figure 4:** Medullary Carcinoma thyroid (H&E X200)

### Discussion

Fine needle aspiration cytology (FNAC) is widely accepted as the most accurate, sensitive, specific and cost-effective diagnostic procedure in the assessment of thyroid nodules and helps to select patients preoperatively for surgery. The combined use of ultrasound guided FNAC has been proposed to optimize diagnostic yield and accuracy. However, this dual operator approach has manpower, time and cost implications.

It was observed that the maximum numbers of patients were in the age group of 31-40 years with a mean of 36.5 years. The youngest patient was 14 years old and the eldest was 72 years old. This compares with the findings of RD Bapat et al who observed the median age of 35 years<sup>3</sup>.

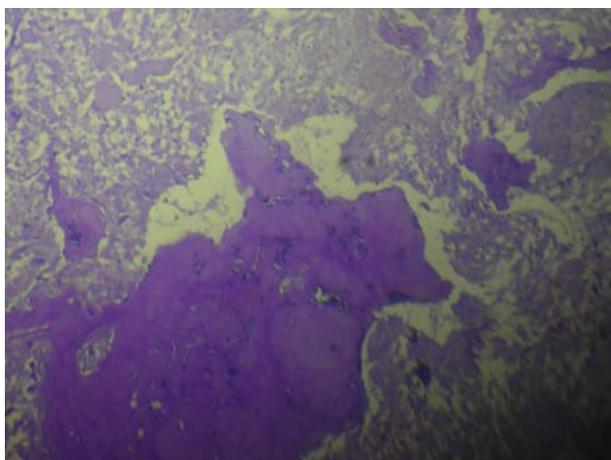
G H Sakorafas observed that the mean age of thyroid lesions was 38.37 years for males and 48 years for females in their study.<sup>4</sup> There were three cases of thyroglossal cysts and the age in 2 of these patients was 14 years and the third patient was 24 years old. Ranadive NU et al observed that the incidence of the thyroglossal cysts varied between 7 and 54 years because the lesion is usually asymptomatic.<sup>5</sup> The mean age of patients with papillary carcinoma in our study was 34.15 years which is similar to the study done by others who observed that papillary carcinoma occurred most frequently below the age of 40 years.<sup>6</sup>

Most studies report the majority of the patients with thyroid swellings to be females. In this study also we observed that the major bulk of patients were females. We found 46 (83.6%) females and 9(16.4%) males. Safirulla et al in their study also observed that 90% of the patients were females and males comprised of only 10%.<sup>7</sup> We observed that benign cases predominated with a percentage of 60 % in comparison to malignant with a percentage of 40 %. Among the 22 malignant cases 18 were seen in females and 4 in males with F: M ratio of 4.5:1. Papillary carcinoma was also observed more in females than males with F: M ratio of 4.25:1.

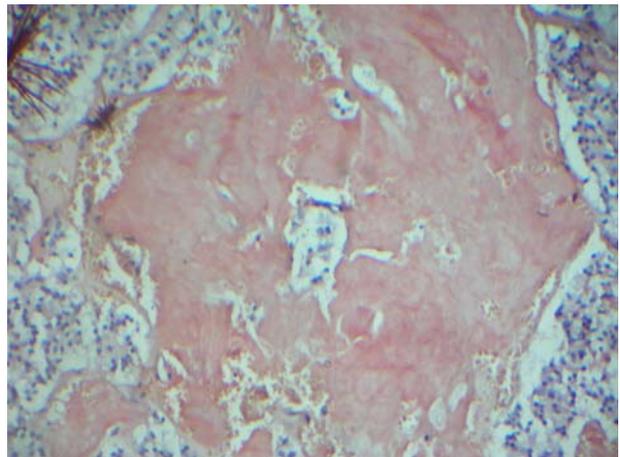
In our study majority (60%) of the patients belonged to hilly region whereas 40% were natives of the plains of Eastern Nepal. Duration of swelling in patients varied from months to years with a mean average of 59.98 months; the longest duration being 40 years. Most of our patients presented with only thyroid swelling and no other symptoms. Some patients presented with other symptoms like hoarseness of voice, dysphagia, pressure symptoms, sweating, palpitations, and increase in size of the swelling. One patient presented with a unilateral cervical lymph node enlargement which on free hand FNAC was seen to be a metastatic deposit of papillary carcinoma in a cervical lymph node. Three of our patients had

hyperthyroidism and 3 had hypothyroidism and rests of the patients were euthyroid. Pressure symptom was observed in 1(1.8%) case. Bapat RD et al in 1993 in their study of 334 cases also observed hyperthyroidism in only 14.67% of cases. Pressure symptom was seen in only 1.5 % cases in their study.<sup>3</sup>

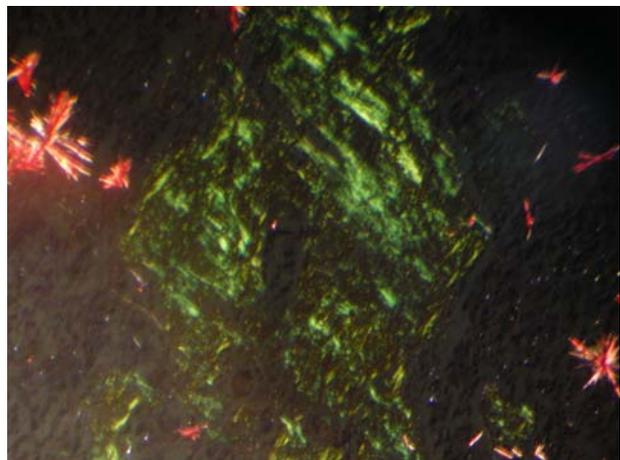
On free-hand FNAC 8 (14.5%) cases the sample was inadequate and in another 8 (14.5%) cases it was indeterminate. Benign lesions were commonest finding on free-hand FNAC which comprised of 29 (52.73%) cases among which 21 (38.2%) cases were colloid goitre, 3 (5.5%) thyroglossal cysts, 3 (5.5%) colloid goitre with papillary hyperplasia, one (1.8%) hyperplastic nodule and one thyroiditis. Malignant lesions comprised of 9 (16.36%) cases with 8 (14.5%) cases of papillary carcinoma and 1 (1.8%) case of medullary carcinoma. One case was of follicular neoplasm and could not be categorised as benign or malignant because a complete histological evaluation is required to make a diagnosis of follicular carcinoma. Mundasad B et al reported that FNAC analysis revealed 13.88% non-neoplastic, 65.27% neoplastic and 4.16% suspicious aspirate; 13.88% samples were inadequate and 2.77% samples were indeterminate<sup>8</sup>. The inadequate (non-diagnostic) sampling rate of 14.55% in free hand FNAC in this study was similar to 12 to 19 % rates reported by Cai et al<sup>2</sup> and 14% by Guhamallick.<sup>9</sup>



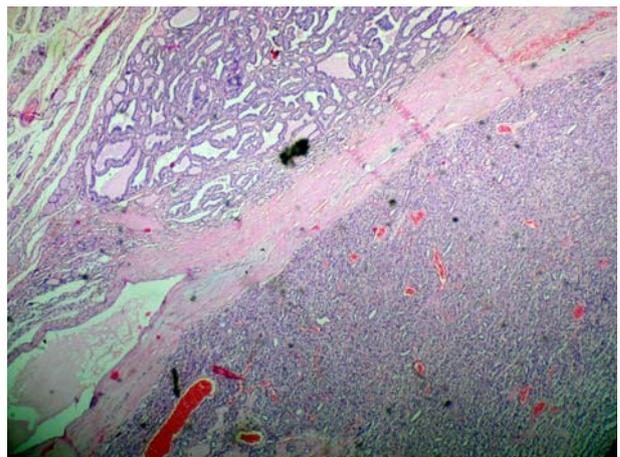
**Figure 5:** Crystal violet stain showing amyloid in Medullary Carcinoma



**Figure 6:** Congo Red stain showing amyloid



**Figure 8:** Follicular carcinoma showing capsular invasion. (H&E X 100)



**Figure 7:** Apple Green birefringence under polarized light in Medullary Carcinoma

On USG guided FNAC it was observed that in the eight cases which were inadequate on free hand FNAC, a diagnosis was made. Among these we observed that in 6 cases a diagnosis of colloid

goitre was made, one of these colloid goitres was found to have a hyperplastic focus and another one was a colloid goitre with secondary cystic changes. The case who presented with cervical lymphadenopathy on FNAC a diagnosis of metastatic papillary carcinoma was made. On free hand FNAC it was indeterminate. In 2006, Kelly NP et al reported that on ultrasound guided FNA of non palpable thyroid nodules adequate material may be obtained for a specific cytopathological diagnosis and in 17 (89%) cases specific cytological diagnosis was made.<sup>10</sup> In the indeterminate category 4 cases were found to colloid goitre with cystic changes, and three cases were reported as colloid goitre due to adequate material. One midline swelling clinically diagnosed as thyroglossal cyst turned out to be papillary carcinoma on biopsy.

The main limitation of thyroid FNAC is the inability to distinguish between follicular adenoma and carcinoma and a complete histopathological examination is required.<sup>11-14</sup> The same dilemma was faced during this study for categorization of follicular neoplasm as carcinoma without a complete histopathological examination similar to as observed by others.<sup>2, 5, 9</sup>

On histopathological examination also benign thyroid lesions were more common than malignant lesions. We observed 33 (60%) benign and 22 (40 %) malignant cases. Mundasad B reported 81.94% benign and 18.05% malignant cases in his study.<sup>8</sup> Haruna A et al studied histological findings of 69 patients and reported 73.9% benign and 26.1% malignant lesions- a predominance of benign lesions.<sup>15</sup> Similarly Bapat also reported 92.02% benign lesions.<sup>6</sup> RD Bapat et al in 1993 in their study observed that 92.02% were benign lesion and 8.98% were malignant. Among the benign lesions adenomatous goitre was the most common, comprising of 23 (41.8%) cases in our study. This agrees with the findings of Bapat et al who reported 57.78% of nodular goitres in their study.<sup>3</sup>

Papillary carcinoma (Fig 1, 2) is the most common type of thyroid malignancy.<sup>16</sup> Among the malignant cases in this study papillary carcinoma was the commonest i.e. 20 (36.4 %) cases. One (1.8%) case of medullary carcinoma (Fig 3, 4) and one (1.8%) case of follicular carcinoma was also seen. One case which was an occult papillary carcinoma, on sectioning the gross specimen a tumour of 0.5 cm was seen which on histological examination revealed multicentric papillary carcinoma. Eight cases which were reported as colloid goiter on FNAC were found to be papillary carcinoma on histological examination. Two cases reported as benign colloid goitres on FNAC were also seen as papillary carcinoma similarly. Sakorafa GH in 2007 reported that the incidence of microscopic papillary thyroid cancer is not an uncommon incidental finding in patients treated surgically for presumably benign thyroid disease.<sup>4</sup> Three cases which had hyperplastic foci on cytological examination were also diagnosed as papillary carcinoma in our study. One case which was falsely diagnosed as papillary carcinoma on cytology was seen to be a nodular goitre with papillary hyperplasia. One case of medullary carcinoma was observed in this study which correlates with the cytological diagnosis. It was observed that this patient with the medullary carcinoma was a male, as observed by Desai SS et al in 2005 who showed a male predominance in medullary carcinoma of the thyroid.<sup>17</sup> Presence of amyloid was confirmed by special stains using Congo-red and Crystal-violet (Fig 5,6,7) in the histopathological examination. One case of follicular neoplasm on FNAC was confirmed to be a follicular carcinoma with the presence of capsular and vascular invasion on histology (Fig 8). This observation agrees to the similar observations made by various other authors.<sup>3, 18</sup> In the present study a comparative study was done between free-hand FNAC and ultrasound guided FNAC taking histopathological results as the gold standard. It was seen that in 31 (81.5%)

cases the free hand FNAC results matched with the ultrasound guided FNAC results, while in 7 (18.5%) cases there was no agreement between the free-hand FNAC and the USG guided FNAC. The sensitivity of free hand FNAC in diagnosing malignant lesions of the thyroid was 56.25% which is similar to those reported by others. Mundasat et al in 2006 reported free hand FNAC to have a sensitivity of 52.6% for diagnosing thyroid malignancy, which is similar to our study. They also reported that their data suggests an overall accuracy rate of 75 % in the detection of thyroid malignancy.<sup>8</sup> Safirulla et al conducted a study to know the validity of FNAC in the diagnosis of thyroid swellings and reported that free-hand FNAC has high accuracy with 94.2% sensitivity and 94% specificity in diagnosis of malignant thyroid disease.<sup>7</sup>

We observed that the sensitivity and specificity of free-hand FNAC and USG guided FNAC in predicting thyroid malignancies were 56.25 % and 100 %; and 63.64% and 96.97% respectively. The positive predictive value and negative predictive for free-hand FNAC and ultrasound guided FNAC with histology as the gold standard were found to be 100 % and 75.86%; and 93.3% and 80 % respectively; which is similar to the findings of the study conducted by Moon H et al who reported that ultrasound guided FNAC has a high diagnostic accuracy with the sensitivity and specificity of 65% to 98% and 72% to 100% respectively.<sup>19</sup> Ogawa Y et al in their retrospective study of 1012 samples from 806 thyroid nodules by USG guided method reported that the accuracy of FNAC as 75 % and the rate of indeterminate diagnosis as 16 %. The false negative rate was 13 % and the positive malignancy rate was 99%.<sup>20</sup> Cai XJ et al in 2006 also reported their comparative study of free-hand FNAC and USG guided FNAC in 434 patients with thyroid nodules and compared the cytological results with the histological results of 69 cases. They found that the overall accuracy of FNAC for malignancy was 97% with sensitivity 83.3%,

specificity 98%, positive predictive value 71.4% and negative predictive value 98.4%.<sup>2</sup>

There was a 7.39 % greater sensitivity of ultrasound guided FNAC in detecting malignant lesions of the thyroid over free hand FNAC in our study.

#### ***Limitation of the study***

Since both free hand and ultrasound guided FNAC was done in this study majority of thyroid lesions could be diagnosed by cytology alone. However, it is well known that the main limitation of thyroid FNAC is the inability to distinguish between follicular adenoma and carcinoma and a complete histopathological examination is required for capsular or vascular invasion which applies for this study as well.

#### **Conclusion**

This was a small study conducted on a hospital-based sample at BPKIHS, Dharan, in Eastern part of Nepal. Free hand FNAC of thyroid swellings is convenient, safe, and cost effective as compared to ultrasound-guided FNAC. However, the diagnostic yield in ultrasound-guided FNAC is significantly more in terms of accuracy especially in cystic lesions and small swellings.

#### **References**

1. Söderstrom N. Puncture of goiters for aspiration biopsy. A preliminary report. *Acta Med Scand* 1952; 144:235- 244.
2. Cai XJ, Valiyaparambath N, Nixon P, Waghorn A, Giles T, Helliwell T. Ultrasound guided fine needle aspiration cytology in the diagnosis and management of thyroid nodules. *Cytopathology* 2006; 17(5):251-6.
3. Bapat RD, Pai P, Shah S, Bhandarkar SD. Surgery for thyroid goitre in western India. A prospective analysis of 334 cases. *J Postgrad Med* 1993; 39:202.
4. Sakorafas GH, Stafyla V, Kolettis T, Tolumis G, Kassaras G, Peros G. Microscopic papillary thyroid cancer as an incidental finding in patients treated surgically for presumably benign thyroid disease. *J*

- Postgrad Med 2007; 53:23-26.
5. Ranadive NU, Shroff CP. Thyroglossal cyst (a clinicopathological evaluation with special reference to its malignant potential). *J Postgrad Med* 1984; 30(3):175-8.
  6. Gupta C, Sharma VK, Agarwal AK, Bisht D. Fine needle aspiration cytology of solitary nodule of thyroid and its histopathological correlation. *Journal of Cytology* 200; 18(3):151-156.
  7. Safirullah, Mumtaz N, Khan A. Role of Fine Needle Aspiration Cytology (FNAC) in the diagnosis of thyroid swellings. *J postgrad Med Inst* 2004; 18(2):196-201.
  8. Mundasad B, Mcallister I, Carson J, Pyper PC. Accuracy of fine needle aspiration cytology in diagnosis of thyroid swellings. *The Internet Journal of Endocrinology* 2006; 2: 1540-2606
  9. Guhamallick M, Sengupta S, Bhattacharya NK, Basu N, Roy S, Ghosh AK, Chowdhury M. Cytodiagnosis of thyroid lesions – usefulness and pitfalls: A study of 288 cases. *J Cytol* 2008; 25:6-9.
  10. Kelly NP, Lim JC, DeJong S, Harmath C, Dudiak C, Wojcik EM. Specimen adequacy and diagnostic specificity of ultrasound guided fine needle aspirations of nonpalpable thyroid nodules. *Diagn Cytopathol.*2006 Mar; 34(3):188-90
  11. Sidaway MK ,Del Vecchio DM ,Knoll SM. Fine-needle aspiration of thyroid nodules .Correlation between cytology and histology and evaluation of discrepant cases. *Cancer (Cancer Cytopathol)*1997;81:253-259
  12. Giard RWM, Hermans J. Use and accuracy of fine-needle aspiration cytology on histologically proven thyroid carcinoma.An Audit using a national pathology data base. *Cancer (Cancer Cytopathol)* 2000;90:330-334
  13. Oertel YC, Burman K, Boyle L, Ringel M, Wartofsky L, Van Nostrand D, et al.. Integrating fine-needle aspiration into a daily practice involving thyroid disorders: the Washington hospital center approach. *Diagn Cytopathol* 2002;27:120-122
  14. Yang GCH, Liebeskind D, Messina AV. Should cytopathologists stop reporting follicular neoplasms on fine-needle aspiration of the thyroid? Diagnosis and histological follow-up of 147 cases. *Cancer (Cancer Cytopathol)* 2003; 99: 69-74
  15. Nggada HA, Musa AB, Gali BM, Khalil MIA. Fine needle aspiration cytology of thyroid nodule(s): a Nigerian tertiary hospital experience. *The Internet Journal of Cardiovascular Research.*2006; 5 (1).
  16. Schlumberger MJ. Papillary and follicular thyroid carcinoma. *N Engl J Med* 1998;338:297-306
  17. Desai SS, Sarkar S, Borges AM. A study of histopathologic features of medullary carcinoma of the thyroid. Cases from a single institute in India. *Indian J Cancer* 2005; 42:25-29
  18. Bajaj Y, De M, Thompson A. Fine needle aspiration cytology in diagnosis and management of thyroid disease. *J Larynol Otol.* 2006; 120(6):467-9
  19. Moon HG, Jung EJ, Park ST, Ha WS, Choi SK, Hong SC et al. Role of ultrasonography in predicting malignancy in patients with thyroid nodules. *World J Surg* 2007;31:1410-1416
  20. Ogawa Y, Kato Y, Ikeda K, Aya M, Ogisawa K, Kitani K et al. The value of ultrasound-guided fine needle aspiration cytology for thyroid nodules: an assessment of its diagnostic potential and pitfalls. *Surgery Today* 2001; 31 (2):97-101