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# A Comparative Study on Fine Needle Aspiration Cytology versus Fine Needle Capillary Cytology in Thyroid Nodules

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## *Abstract*

**Objectives:** Fine needle aspiration cytology (FNAC/FNA) is the primary investigation for thyroid nodules. Fine needle capillary cytology (FNCC/FNC) is an alternative technique not commonly used, though it is easy to perform. Both the techniques have their own advantages and disadvantages. This study aims to compare these two cytological techniques for better specimen and cytological diagnosis.

**Methods:** This prospective study was conducted on 50 patients attending the FR Muller Medical College Hospital from May 2006 to April 2008. The patients with thyroid nodules (diagnosed by palpation) were subjected to both the cytological techniques; FNA and FNC. The specimen and results were compared and then correlated with the final histopathological findings wherever surgical specimens were available (38 cases).

**Results:** The mean age of the patients was 39.16 with a female predominance. The majority of cases were diagnosed to have nodular goiters. The FNC technique yielded 88% diagnostic superiority and adequate specimens compared to 94% by FNA. Sensitivity was 50% for FNC and 100% for FNA while specificity was 100% for both techniques; accuracy score was 97.4% for FNC and 100% for FNA in predicting malignancy. While sensitivity was 75% for FNC and 100% for FNA; specificity was 100% for both techniques, and accuracy score was 97.4% for FNC and 100% for FNA in the prediction of neoplasia.

**Conclusion:** The results indicated that there was no significant difference between the two techniques; if done in tandem can give better and accurate cytological diagnosis. In highly cellular lesions, in which abundant material was obtained, FNC was more likely to be diagnostically superior, but FNA can diagnose most of the lesions. In less cellular lesions, FNA is more likely to be diagnostically superior to FNC.

**Keywords:** Cytology; Fine needle biopsy; Needle biopsy; Thyroid gland; Non- aspiration.

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## Introduction

Fine needle aspiration cytology (FNAC/FNA) has played a pivotal role in diagnosing thyroid gland nodules and thus pulling investigations out of the laboratory into the outpatient department. But in this procedure, the pitfalls encountered were either due to less pressure, inadequate specimen or due to excess pressure; the cells are flushed away with blood. A growing technique for thyroid nodules, fine needle capillary cytology (FNCC/FNC) bears hope of being a more efficient clinical investigation. It is the technique of using the same fine needle without the negative pressure as done in FNAC. The studies have shown that the two techniques have unique results in different areas, the sensitivity depends on whether the tumor is vascular, necrotic or other factors.[1,2] In cases of thyroid lesions, promising results are encountered in favor of fine needle capillary cytology.[1,3]

Fine Needle Non Aspiration Cytology (FNCC), is a technique similar to FNAC which eliminates the need for aspiration by a syringe.[4] It is less painful, less traumatic and allows for much better control of the needle while in the lesion. FNA when performed in vascular organs like the thyroid and vascular tumors results in hemorrhagic distortion of cell morphology in the aspirate. This hampers the study and diagnosis of the lesion thereby changing the course of management.[5] This problem is overcome by the FNCC technique, which picks up a small amount of tissue in which the cell morphology and architecture is preserved. The advantages of FNCC are as follows: (a) it yields more material, (b) no hospitalization required for the procedure and (c) results are obtained rapidly within hours. However, the disadvantages are: (a) it compromises on cell concentration, (b) detrimental to cell morphology and active aspiration of blood, and (c) it relies heavily on the skill of the performer.[4]

FNC was developed in France by Brifford, Gentile and Hebert in 1982.[6] It avoids aspiration and relies on the physical property of capillary pressure to suck cells inside the needle bore. The French authors termed the technique "Cytopuncture." For thyroid lesions, this technique was first evaluated and compared with the conventional technique of FNA by Santos and Leiman.[3] Many studies have proved that FNCC seemed to be better for diagnosing malignant lesions while FNA appeared better for diagnosing benign lesions.[7,8,9,10,11] They opined that FNCC was more patient friendly, gave more cellular yield and that it will improve the quantity and quality of the material. Both the techniques should be used together yielding better diagnostic results.

With this idea in mind, the FNC technique can be used as a simple outpatient procedure in thyroid nodules. This study aims to compare the two cytopuncture techniques in our clinical set up to promote accurate diagnosis and better management.

## Methods

This was a prospective study comparing FNC and FNA on 50 patients with a thyroid swelling/nodule who were admitted to Fr. Muller Medical College Hospital, Karnataka, India, over a period of 2 years from May 2006 to April 2008. The ethical committee clearance was obtained and all biopsies were performed by the same investigator. The Pathologist was blinded for the technique used and all cytological and histopathological reporting was done by a single pathologist. Histopathological specimen was available in 38 cases. The inclusion criteria comprised of all the patients admitted to the hospital with thyroid nodules or swellings (diagnosed by palpation) and patients aged >15 years. The exclusion criteria consisted of patients who had undergone previous surgery and patients who had undergone previous irradiation.

After detailed clinical examination along with ensuring to note any doubtful sites on the thyroid gland, the patient was investigated with a thyroid function test and a needle biopsy. The patient was subjected to needle biopsies (not ultrasound guided) after obtaining informed consent. The order of FNC and FNA sampling was pre-planned; in 25 patients, FNC was performed first followed by FNA and the next 25 patients underwent FNA first followed by FNC. This was done to eliminate any bias (if present). Both techniques were performed at the same site by the same investigator. A 23G needle was used in both procedures, and an average of 4 slides was obtained by both the FNA and the FNC techniques.

Some of the smears were fixed in methanol and stained by Papanicolaou stain, the others were air dried and stained using the May-Grunwald-Geimsa stain. The smears of FNC and FNA were assessed by a single observer using a scoring system (modified scoring system of Mair and colleagues, (Table 1).[11] FNC and FNA results were correlated with histopathological findings whenever surgical specimens (38 cases) were available. The tissue was processed routinely and paraffin embedded blocks was prepared. Sections cut at 4-6 µm were stained with Hematoxylin and Eosin. The data collected was statistically analyzed and compared using the Receiver Operating Curve (ROC). The sensitivity, specificity and accuracy of both FNC and FNA were calculated. Sensitivity was defined as the ratio of true positives to the total number of patients with the disease; while specificity was defined as the ratio of true negatives to the total number of patients without the disease. Accuracy was defined as the ratio of true positives plus true negatives to the total number of patients.

The smears of FNC and FNA were assessed by a single observer using a scoring system which was a modified scoring system of Mair and colleagues.[12] It was based on the following: 1) Background blood or clot, 2) Amount of cellular material, 3) Degree of cellular degeneration, 4) Degree of cellular trauma, and 5) Retention of appropriate architecture. A score ranging from 0-2 was assigned to each of these criteria. A cumulative score between 0-10 points was allocated to each FNC and FNA specimen which was then assigned to one of the three categories based on total points scored.

| | |
|---|---|
| Unsuitable for cytodiagnosis | 0 - 2 |
| Diagnostically adequate | 3 - 6 |
| Diagnostically superior | 7 - 10 |

Unsuitable specimen mainly contained blood clots or low cellularity leading to inadequacy in diagnosis. Diagnostically adequate specimen was good enough to give a diagnosis and exhibited moderate cellularity which was sometimes trapped in blood clots. Diagnostically superior were those specimens in whom the cellularity was good, the architecture was not destroyed with the least amount of blood clots.

The data collected was statistically analyzed and compared using the Receiver Operating Curve (ROC). Each parameter was analyzed and plotted as a line diagram where FNC was compared to FNA. Hence, the straight line in the graph represents FNA while the curved line represents FNC. The area below the FNC curve is calculated and depending on the area, it is comparable to FNA as follows:

| **Area below the curve** | **Comparison** |
|---|---|
| 0.9 - 1.0 | Excellent |
| 0.8 - 0.9 | Very Good |
| 0.7 - 0.8 | Good |
| 0.6 - 0.7 | Average |
| 0.5 - 0.6 | Poor |

With the overall scores and the diagnostic description, FNC was correlated to FNA using the Kappa score.

| | | |
|---|---|---|
| <0.20 | - | Poor agreement |
| 0.21 - 0.4 | - | Fair agreement |
| 0.41 - 0.6 | - | Moderate agreement |
| 0.61 - 0.8 | - | Good agreement |
| 0.81 - 1.0 | - | Very good agreement |

**Table 1:** Scoring system developed by Mair et al.[7,12]

| Criterion | Qualitative description | Score | Patient's score | |
|---|---|---|---|---|
| | | | FNA | FNC |
| Background Blood & Clot | Large amount- diagnosis not possible | 0 | | |
| | Moderate amount- diagnosis possible | 1 | | |
| | Minimal amount- diagnosis easy | 2 | | |
| Cellularity Amount of Material | Minimal- diagnosis not possible | 0 | | |
| | Sufficient- diagnosis possible | 1 | | |
| | Adequate- diagnosis easy | 2 | | |
| Degree of cellular degeneration | Marked- diagnosis not possible | 0 | | |
| | Moderate- diagnosis possible | 1 | | |
| | Minimal- diagnosis easy | 2 | | |
| Degree of cellular trauma | Marked- diagnosis not possible | 0 | | |

## Results

In this study, the majority of the patients were aged between 40 and 49 years (36%), with a mean age of 39.16 (SD 11.47; Table 2). In this study, females comprised 94% of the study group, while males comprised only 6%. Thyroid function tests of all the patients were within normal limits, except for one patient who had elevated T-3 and T-4 values.

**Table 2:** Age Distribution.

| Age in years | Frequency | Percentage |
|---|---|---|
| 20-29 | 8 | 16-0 |
| 30-39 | 16 | 32.0 |
| 40-49 | 18 | 36.0 |
| 50-59 | 6 | 12.0 |
| > 60 | 2 | 4.0 |
| **Total** | **50** | **100.0** |

*(SD-11.472; range: 20-72)*

Clinically, 42 of the 50 cases were multi-nodular goiters, 5 were solitary nodules, 1 was a toxic nodular goiter and 2 were suspicious of malignancy. The cytological evaluation diagnosed 25 (50%) cases of nodular goiters, 10 (20%) cases of colloid goiters, 6 (12%) cases of Hashimoto's thyroiditis and 1 case (2%) each of anaplastic carcinoma and papillary thyroid carcinoma. (Table 3)

**Table 3:** Correlation between clinical diagnosis with FNAC and FNCC.

| Diagnosis | No. of cases -Clinical (Percentage) | No. of cases Cytological-FNA and FNC (Percentage) |
|---|---|---|
| Multinodular goiter | 42(84%) | 25(50%) |
| Solitary nodule | 5(10%) | 0(0%) |
| Colloid goiter | 0(0%) | 10(20%) |
| Toxic nodular goiter | 1(2%) | 1(2%) |
| Hashimoto's thyroiditis | 0(0%) | 6(12%) |
| Papillary Carcinoma | 2(4%) | 1(2%) |
| Follicular neoplasm(FN) | 0(0%) | 2(4%) |
| Adenomatous nodule(AN) | 0(0%) | 2(4%) |
| Adenomatous nodular hyperplasia(ANH) | 0(0%) | 1(2%) |
| Lymphocytic thyroiditis(LT) | 0(0%) | 1(2%) |
| Anaplastic carcinoma | 0(0%) | 1(2%) |
| **Total** | **50(100%)** | **50(100%)** |

A comparison between FNCC and FNAC is shown in Table 4. Of the 50 patients in the current study, six were diagnosed to have thyroid malignancy on final histopathology report. Four patients were not diagnosed by FNC nor FNA needle sampling but only on histopathology. All the four had microscopic foci of papillary carcinoma. The specimen of anaplastic carcinoma had typical characteristics in FNC and the FNA smears both were equally scored. The papillary carcinoma was diagnosed only with FNA since the FNC specimen was inadequate in material. But the one specimen which was diagnosed as anaplastic carcinoma, the FNC specimen was good and better than FNA with respect to the amount of cellularity and retention of architecture.

**Table 4:** Comparison between FNCC and FNAC diagnosis.

| Diagnosis | FNCC (Percentage) | FNAC (Percentage) |
|---|---|---|
| **Non-neoplastic:** | | |
| Nodular goiter(NG) | 25 (50%) | 25 (50%) |
| Nodular colloid goiter (NCG) | 10 (20%) | 10 (20%) |
| Hashimoto's thyroiditis (HT) | 6 (12%) | 6 (12%) |
| Adenomatous nodule (AN) | 2 (4%) | 2 (4%) |
| Adenomatous nodular hyperplasia(ANH) | 2 (4%) | 1 (2%) |
| Lymphocytic thyroiditis (LT) | 1 (2%) | 1 (2%) |
| Toxic nodular goiter(TNG) | 1 (2%) | 1 (2%) |
| **Neoplastic:** | | |
| Follicular neoplasm(FN) | 2 (4%) | 2 (4%) |
| Anaplastic carcinoma(ANC) | 1 (2%) | 1 (2%) |
| Papillary carcinoma(PTC) | 0 (0%) | 1 (2%) |
| **Total** | **50(100%)** | **50(100%)** |

**Table 5:** Comparison of FNCC and FNAC with Histopathology report of 38 cases.

| Diagnosis | FNCC | FNAC | Histopathology |
|---|---|---|---|
| **Non-neoplastic:** | | | |
| NG/MNG | 26 | 26 | 24 |
| HT | 4 | 4 | 3 |
| LT | 0 | 0 | 1 |
| AN | 2 | 2 | 2 |
| ANH | 2 | 1 | 0 |
| TNG | 1 | 1 | 0 |
| **Neoplastic:** | | | |
| FN | 2 | 2 | 0 |
| FA | 0 | 0 | 2 |
| HT+Micro PTC | 0 | 0 | 1 |
| MNG+ Micro PTC | 0 | 0 | 1 |
| FA+Micro PTC | 0 | 0 | 2 |
| ANC | 1 | 1 | 1 |
| PTC | 0 | 1 | 1 |
| **Total** | **38** | **38** | **38** |

Histopathological specimen were obtained in 38 cases which were correlated with both the needle biopsies (Table 5). Four patients exhibited microscopic focus of malignancy incidentally diagnosed on final histopathology. These cases could not be diagnosed on FNCC or FNAC. (Table 6)

**Table 6:** Correlation of FNCC and FNAC with histopathology report in six cases of malignancy.

| FNCC | FNAC | Histopathology |
|---|---|---|
| Hashimoto's thyroiditis | Hashimoto's thyroiditis | Hashimoto's thyroiditis+ micro papillary carcinoma |
| Anaplastic carcinoma | Anaplastic carcinoma | Anaplastic carcinoma |
| Nodular colloid goiter | Nodular colloid goiter | Multinodular goiter+ micro papillary carcinoma |
| Adenomatous nodular hyperplasia | Papillary carcinoma | Papillary carcinoma |
| Nodular colloid goiter | Nodular colloid goiter | Follicular adenoma+ micro papillary carcinoma |
| Nodular goiter | Nodular goiter | Follicular adenoma+ micro papillary carcinoma |

The diagnostic performance of FNC and FNA techniques indicated that FNA yielded more diagnostically superior cases (30%) compared to FNC (18%). But FNC produced more cases that were adequate for diagnosis (70%) than FNA (64%). Moreover, FNA exhibited half the number of diagnostically unsuitable cases (6%) compared to FNC (12% [Table 7]). The kappa value was 0.29, which was a fair agreement between the two techniques.

**Table 7:** Diagnostic performance.

| Performance | Technique | | | |
|---|---|---|---|---|
| | FNC | | FNA | |
| | No. of cases | Percentage | No. of cases | Percentage |
| Diagnostically Superior | 9 | 18% | 15 | 30% |
| Diagnostically Adequate | 35 | 70% | 32 | 64% |
| Diagnostically Unsuitable | 6 | 12% | 3 | 6% |

FNC showed 50% sensitivity and FNA showed 100%, while specificity was 100% for both the techniques; but the accuracy score was 97.4% for FNC and 100% for FNA for predicting malignancy. While for predicting neoplasia; sensitivity was 75% for FNC and 100% for FNA, specificity was 100% for both the techniques, while the accuracy score was 97.4% for FNC and 100% for FNA. (Table 8)

**Table 8:** Prediction of malignancy and neoplasia.

| | Prediction of malignancy | | Prediction of neoplasia | |
|---|---|---|---|---|
| | FNC (%) | FNA (%) | FNC (%) | FNA (%) |
| Sensitivity | 50 | 100 | 75 | 100 |
| Specificity | 100 | 100 | 100 | 100 |
| Negative predictive value | 97.3 | - | 97.1 | - |
| Positive predictive value | - | 100 | - | 100 |
| Accuracy | 97.4 | 100 | 97.4 | 100 |

## Discussion

Thyroid disorders vary in terms of their presentation and characteristics. An established first line of investigation for any evident thyroid swelling is a Fine Needle Aspiration Cytology (FNAC) after a thyroid function test.[4] It has gained popularity based on the given facts.[4] It is easy and quick to perform, and has a high degree of sensitivity and specificity. In the current study, the FNC and FNA techniques were compared on thyroid gland lesions using a modified scoring system by Mair et al.[12] The age incidence of thyroid gland disorders was between 40-49 years, which mainly comprises middle aged patients. This has previously been stated in literature and has also been observed by other authors.[1,3,13,14] Our study group was comprised of 94% female patients and 6% males; none of the male showed malignant disease.

In comparing both techniques on the parameter of blood clots; FNC was most likely to produce the least likelihood of hemorrhage, thereby giving a clear picture to the cytopathologist. This has also observed by Ali Rizvi,[1] and other authors.[3,14] The presence of blood cannot be totally prevented in thyroid gland cytology samples but its effect can be minimized by the capillary action of the FNC technique compared to the active high suction pressure of the FNA technique. In our study, for material with highly cellular lesions in which abundant material was obtained; FNC was more likely to be diagnostically superior; but FNA can diagnose most of the lesions. In less cellular lesions, FNA is more likely to be diagnostically superior to FNC. Some authors have reported similar findings,[10,12] but the majority found no significant difference.[3,11,12,13]

The cellular trauma and degeneration were generally the same in both techniques as these parameters depended on the method of smear making. FNA scored better since it had more cellular material, hence the destruction of some sheets of cells did not obscure the field for diagnosis. This is in contrast to Raghuveer et al. who opined FNC smears were better.[11] The architecture was retained to a greater extent in the FNA smears than the FNC smears due to the additional material yield in FNA. But the architecture was a text book picture in whichever FNC smears that had good material. Gosh and Misra observed this in their study of FNC on thyroid lesions.[15] This was the only parameter in which FNC scored much better than FNA, as reported by other authors.[3,11,14]

Three patients were diagnosed to have thyroid cysts; in two of these patients, FNC was performed first and a colloid overflow was encountered, it was drained using the FNA technique. There was no cellular material on any of these smears; hence they was not included into the study. This problem has also been previously encountered by Mair and team,[12] and also by Kate et al.[16] They documented that FNA is the procedure of choice for cystic lesions, as the fluid can be collected for cytological evaluation. The cysts usually disappear after the colloid is drained out completely; hence FNA becomes a therapeutic procedure. The specimen of anaplastic carcinoma had typical characteristics in FNC and the FNA smears, both were equally scored.

**Table 9:** Comparison of the current study with other studies.

| Parameter | Current Study | de Carvalho et al.[18] | McElvanna K et al.[21] |
|---|---|---|---|
| Number of patients | 50 | 260 | 70 |
| Mean age of the patients | 39.16 yrs | 43.2 yrs | 49 yrs |
| Diagnostically superior and adequate samples | FNAC – 94%<br>FNCC – 88% | FNAC – 91.6%<br>FNCC – 91.6% | FNAC –63%<br>FNCC – 74% |
| Sensitivity | FNAC – 100%<br>FNCC – 50% | FNAC – 85.7%<br>FNCC – 100% | FNAC – 81%<br>FNCC – 81% |
| Specificity | FNAC – 100%<br>FNCC –100% | FNAC – 100%<br>FNCC – 100% | FNAC – 90%<br>FNCC – 77% |

The papillary carcinoma was diagnosed only with FNA as the FNC specimen was inadequate in material. Hence in contradiction to the analyses by Santos and Leiman who stated that FNC specimen were better in neoplasms; we encountered some technical difficulty in assessing the quality of the FNC specimen in malignancies.[3] But in the one specimen which was diagnosed as anaplastic carcinoma, the FNC specimen was relatively good and generally better than FNA with respect to the amount of cellularity and retention of architecture.

On the diagnostic performance; FNA was notably better, producing more of the diagnostically superior specimen (n=15; 30%), compared to FNC (n=9; 18%); however, FNC exhibited more diagnostically adequate specimen (n=35; 70%). Santos and Leiman reported similar results which were 44% diagnostically superior, 50% diagnostically adequate and 3% diagnostically unsuitable with the FNC technique.[3] Rizvi and Hussain also reported that FNC yielded 44.7% diagnostically superior specimen, 53.3% diagnostically adequate and 2% diagnostically unsuitable specimen.[1]

In this study, FNC appears to be a good technique but only in certain aspects compared to FNA. Each of these techniques has its own advantages and disadvantages.[4] Sanjeev et al. conducted a similar study on lymph node lesions and the results proved the technical superiority of FNCC technique in cellular lymph node lesions.[17] While Carvalho et al. suggested that FNA and FNC provide similar sample adequacy and diagnostic accuracy.[18] Overall, the decision to chose which technique to adopt rests with the operator to select the method that will produce a high yield of good quality material, with minimal diagnostic failures. Though there was no significant difference between the two techniques, if done in tandem at two different sites on the same lesion; they can add up to ease the diagnosis.[19,20] The results of this study were compared to those reported by Carvalho et al.[18] and McElvanna et al.[21] who have also documented similar observations. (Table 9)

## Conclusion

In summary, both techniques FNC and FNA are advised to be used in tandem; however, they should be done on different sites of the same thyroid lesion. Preferably, FNC should be performed initially, and then followed by FNA in order to attain clear and accurate cytological diagnosis. In highly cellular lesions where abundant material was obtained, FNC was most likely to be diagnostically superior, although FNA can also diagnose most of the lesions. In less cellular lesions, however; FNA was most likely to be diagnostically superior to FNC.

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