

# Accuracy of Fine Needle Aspiration Cytology of Solitary Thyroid Nodules in Tertiary versus Community Hospital

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## ABSTRACT

**Background:** Fine needle aspiration cytology (FNAC) is considered as the gold standard diagnostic test for the diagnosis of solitary thyroid nodules (STN). **Aim:** To compare the accuracy of FNAC in diagnosis of thyroid nodules in Al Khor community hospital versus that of tertiary hospital (Hamad General Hospital) in Qatar. **Methods:** Retrospective, descriptive and comparative study of 320 patients of any age group and both sexes who have thyroid nodules and are subjected to surgical treatment [160 patients from Al Khor community hospital (group A) and 160 patients from Hamad General Hospital (group B)] during the period from May 2005 to Dec 2012. Each group was subdivided into free hand FNAC (done by physicians) and ultrasonography guided FNAC. All samples were prepared in the same histopathology laboratory and interpreted by the same histopathology team. **Results:** Free hand FNAC in group A and group B achieved a sensitivity of (10% vs. 50%), specificity of 93% in both groups, positive predictive value of (25% vs. 17%), negative predictive value of (82% vs. 98%), and a total accuracy of (82% vs. 94%) respectively, while US guided FNAC in group A and group B achieved a sensitivity of (10% vs. 86%), specificity of (98% vs. 94%), positive predictive value of (50% vs. 60%), negative predictive value of (86% vs. 98%), and a total accuracy of (85% vs. 97%) respectively. **Conclusion:** The overall accuracy of FNAC of STN in tertiary hospital was better than community hospital. More training is required for community hospital staff.

**Keywords:** Needle Aspiration; Solitary Thyroid Nodules; Accuracy

## 1. Introduction

Thyroid nodules are common clinical findings and have a reported prevalence of 4% - 7% of adult population. However, fewer than 5% of adult thyroid nodules are malignant, and the vast majority is non-neoplastic lesions [1]. Solitary thyroid nodule (STN) is defined clinically as the localized thyroid enlargement with apparently normal rest of the gland. The main goal of evaluating these nodules is to identify nodules with malignant potential [2]. FNAC is safe, simple and quick with a low complication rate so considered as the gold standard initial investigation in the diagnosis of thyroid swellings [3-5]. With the increase use of imaging over the last decades, the number of incidentally discovered thyroid nodules is rising [6]. Either palpation (free hand) or ultrasonography (US) may

be used for guidance of FNA, but US has several advantages over palpation [7,8]. Limitations of FNAC include false negative and false positive results and a proportion of FNA results that are not obviously benign or malignant and fall into the indeterminate or suspicious group [9]. Moreover, the pitfalls of FNAC are related to specimen adequacy, sampling techniques, the skill of the physician performing the aspiration, the experience of the pathologist interpreting the aspirate and the overlapping cytological features between some benign and malignant thyroid lesions [10]. No previous researchers studied if the level of hospital (community or tertiary) affects the accuracy of FNAC. This study aimed to compare the accuracy of FNAC in STN in a tertiary versus community hospitals and to determine the possible reasons of differences in accuracy if present. #

## 2. Methods

This is a retrospective comparative descriptive study of 320 Consecutive diagnosed cases of STN treated surgically from two hospitals; 160 patients from Al Khor community Hospital (group A) and 160 patients from Hamad General tertiary Hospital (group B) during the period from May 2005 to Dec 2012. Informed consents were taken from all patients. Institution research committee approved the study. Detailed history, physical examination, thyroid function tests, neck ultrasonography, FNAC, surgical intervention and post-operative histopathology were reviewed. All cytological and postoperative histopathology specimens were prepared in the same cyto/histopathology laboratory and interpreted by same cyto/histopathology team. Each group was subdivided into free hand FNAC (done by surgeons in the outpatient clinic) and ultrasonography guided FNAC. Free hand FNAC were performed using aspiration technique when a 23-gauge needle was connected to a 10-ml syringe mounted on a syringe holder. Multiple needle passes were made within the lesion 3 - 4 times at varying angles and depths and with constant negative pressure (never emerging outside the skin). Before final withdrawal, the negative pressure was released prior to the needle emerging from the skin. The cytological material was transferred on to glass slides. For US-guided FNAC Technique, after the lesion is localized using a high-resolution (7.5 - 15 MHz) linear-array transducer, the patient is instructed not to swallow or speak during the insertion of the needle. A freehand biopsy technique is used, and the syringe attached to the needle is placed just above the transducer. During the procedure, all needle movements should be continuously visualized in real time. It is recommended that aspiration be performed at least twice. Before aspiration, scanning is performed in the transverse plane for lesion localization, followed by color Doppler mapping to depict any large blood vessels in and around. The collected material is placed on four glass slides, smeared, and fixed in 95% ethyl alcohol for about 30 minutes. All the slides were stained with Papanicolaou stain. We categorized our results into insufficient for diagnosis, benign, atypical follicular lesion of undetermined significance, follicular neoplasm, suspicious for malignancy, and malignant sampling according to the recent Bethesda classification [11]. The smear was considered adequate if there were at least five groups of well-visualized follicular cells, each group containing ten or more cells [12]. All patients subsequently had a thyroid resection and a definitive diagnosis was reached FNAC results were then compared with the definitive histological diagnosis which was considered the gold standard. No blinding was done, in Al Khor community hospital group (A) we included all STN FNAC specimens during the study period while in tertiary hospital

group (B) we included only the first consecutive 160 FNAC specimen done during the same period. Follicular neoplasm Specimens were excluded from our results. We studied the details of inconclusive specimen.

We excluded patients with inconclusive and follicular adenoma/neoplasm results. Total number of Group A specimens became 120 vs. 134 in group B. Free hand FNAC was 55 in group A vs. 64 in group B. US guided FNAC was 65 in group A vs. 70 in group B. We compared the results of free hand FNAC and US guided FNAC in both hospitals separately. Data were analyzed statistically using SPSS software to assess the sensitivity, specificity and accuracy of the result. Diagnostic accuracy represents combination of sensitivity and specificity.

## 3. Results

The FNAC results in community hospital group A vs. tertiary hospital group B included; benign diagnosis in [114 patients (71.2%) vs. 123 (76.8%)], malignant in [6 patients (3.7%) vs. 11 (6.8%)], follicular neoplasm in 9 patients (5.6%) vs. 8 (5%)] and inconclusive specimens in 31 patients (19.4%) vs. 18 (11.2%)] (**Table 1**).

Inconclusive specimens in free hand FNAC were 29% and 15% in group A and B respectively, while in US FNAC were 10% and 6.25% in group A and B respectively. Free hand FNAC repeated twice in group A and group B was (15% vs. 10%) while US FNAC repeated twice in group A and group B was (6% vs. 5%). 90% of the repeated FNAC revealed satisfactory results. The remaining 10% (5 patients) underwent total thyroidectomy; 3 of them were papillary carcinoma. We excluded patients with inconclusive and follicular adenoma/neoplasm results. Total number of Group A specimens became 120 vs. 134 in group B. Free hand FNAC was 55 in group A vs. 64 in group B. US guided FNAC was 65 in group A vs. 70 in group B. FNAC results were compared to that of postoperative histopathology. Free hand FNAC in both groups (**Table 2**) and US guided FNAC in both groups (**Table 3**).

Free hand FNAC in group A and group B achieved a sensitivity of (10% vs. 50%), specificity of 93% in both groups, positive predictive value of (25% vs. 17%), negative predictive value of (82% vs. 98%), and a total accuracy of (82% vs. 94%) respectively (**Table 4**). While in US guided FNAC in group A and group B achieved a sensitivity of (10% vs. 86%), specificity of (98% vs. 94%), positive predictive value of (50% vs. 60%), negative predictive value of (86% vs. 98%), and a total accuracy of (85% vs. 97%) respectively (**Table 5**).

## 4. Discussion

In current study, we can notice a significant difference in accuracy of FNAC of STN in tertiary versus community hospital. While the sensitivity of free hand FNAC in the

**Table 1. Results of FNAC.**

FNAC Results	Group A	Group B
Inconclusive	31 (19.4%)	18 (11.2%)
<b>Benign</b>	114 (71.2%)	123 (76.8%)
Nodular colloid	112 (98.2%)	122 (99.1%)
Hashimoto's thyroiditis	2 (1.8%)	1 (0.9%)
Follicular adenoma/neoplasm	9 (5.6%)	8 (5%)
<b>Malignant</b>	6 (3.7%)	11 (6.8%)
Papillary carcinoma	5 (83.3%)	11 (100%)
Non Hodgkin lymphoma	1 (16.6%)	0 (0.0%)

**Table 2. Free hand FNAC.**

Group A free hand FNAC	
Cytological Diagnosis	Histopathological Diagnosis
Benign (n 51)	Benign Neoplastic
Suspicious and malignant (n 4)	42 (TN) 9 (FN) 1 (FP) 3 (TP)

  

Group B free hand FNAC	
Cytological Diagnosis	Histopathological Diagnosis
Benign (n 59)	Benign Neoplastic
Suspicious and malignant (n 5)	56 (TN) 3 (FN) 1 (FP) 4 (TP)

TN: true negative; FN: false negative; TP: true positive; FP: false positive.

**Table 3. US Guided FNAC.**

Group A US Guided FNAC	
Cytological Diagnosis	Histopathological Diagnosis
Benign (n 63)	Benign Neoplastic
Suspicious and malignant (n 2)	54 (TN) 9 (FN) 1 (FP) 1 (TP)

  

Group B US Guided FNAC	
Cytological Diagnosis	Histopathological Diagnosis
Benign (n 64)	Benign Neoplastic
Suspicious and malignant (n 6)	63 (TN) 1 (FN) 1 (FP) 5 (TP)

TN: true negative; FN: false negative; TP: true positive; FP: false positive.

tertiary hospital was higher than that of the community hospital (50% and 10% respectively), both groups had similar specificity (93%). Moreover the tertiary hospital had higher negative predictive and total accuracy values. Similarly, US guided FNAC in tertiary hospital achieved higher sensitivity, positive predictive, negative predictive and accuracy values.

Despite FNAC has about 95% accuracy in distinguishing between benign and malignant thyroid nodules, FNAC is unable to distinguish between benign and malignant follicular lesions in the absence of nuclear features of papillary carcinoma. The indeterminate diagnosis of follicular neoplasm encompasses a number of heterogeneous thyroid lesions including cellular adenomatoid nodule, follicular adenoma, and follicular carcinoma [13].

**Table 4. Free hand FNAC.**

	Group A Free hand	95% confidence intervals	Group B Free hand	95% confidence intervals
Total	55		64	
M/F	18/37		22/42	
Mean age	44		47	
False negative rate	0.17	0.08 - 0.31	0.01	0.001 - 0.09
False positive rate	0.75	0.22 - 0.98	0.83	0.36 - 0.99
Prevalence	0.18	0.09 - 0.31	0.03	0.005 - 0.1
Sensitivity	10%	0.005 - 0.46	50%	0.03 - 0.97
Specificity	93%	0.80 - 0.98	93%	0.83 - 0.97
Positive predictive value	25%	0.01 - 0.78	17%	0.009 - 0.63
Negative predictive value	82%	0.69 - 0.91	98%	0.90 - 0.99
Total accuracy	82%		94%	

**Table 5. US guided FNAC.**

	Group A US Guided	95% confidence intervals	Group B US Guided	95% confidence intervals
Total	65		70	
M/F	25/40		19/51	
Mean age	41		45	
False negative rate	0.14	0.07 - 0.26	0.01	
False positive rate	0.5	0.03 - 0.97	0.6	
Prevalence	0.15	0.08 - 0.27	0.093	0.04 - 0.19
Sensitivity	10%	0.005 - 0.46	86%	0.42 - 0.99
Specificity	98%	0.89 - 0.99	94%	0.85 - 0.98
Positive predictive value	50%	0.03 - 0.97	60%	0.27 - 0.86
Negative predictive value	86%	0.74 - 0.93	98%	0.90 - 0.99
Total accuracy	85%		97%	

In this study we excluded all cases of follicular neoplasm to avoid this limitation as much as possible.

False negative and positive results were found particularly with small tumors and when there is associated degenerative or inflammatory change in adjacent thyroid tissue. In addition, there is a group of lesions which overlap benign and malignant features. For instance, the distinction between a cellular colloid goiter and a follicular neoplasm may be impossible [14]. FNAC false negative rate (FNR) ranged from 1% to 16% in different series [15-19]. Factors implicated for this rate include technique, slide preparation and interpretation of results by a cytopathologist. It is also well recognized that certain thyroid pathologies have similar cytological features which make diagnosis extremely difficult [20,21].

In our series FNR for free hand FNAC were high in both community and tertiary hospitals (17% and 14% respectively) compared to 1% (FN) in US guided group

in both hospitals.

FNAC false positive rate (FPR) indicates that a patient with malignant FNAC result was found on histological examination to have benign lesion. In our series the FPR for free hand FNAC were significantly low in tertiary hospital group for both free hand and US guided FNAC (5% and 6% respectively) compared to higher values in community hospital group for both free hand and US guided FNAC (75% and 83% respectively) which agrees with other series that ranged from 0% to 8% [21].

FNAC has inherent limitations related to inadequate sampling, reportedly from 10% to 31% [22-24]. Specimen procurement may be affected by the level of operator experience, accuracy of localization of the lesion and the needle, method of guidance (palpation or US), number of aspirations, needle gauge, sampling technique, capability for immediate on-site cytologic analysis, and many other factors. Unsatisfactory specimen may be due to cystic fluid, bloody smears or poor technique in obtaining the sample and/or preparing the slides. The Papanicolaou Society of Cytopathology task force on Standards of Practice recommends that aspirators who persistently produce a high rate of unsatisfactory aspirates (>15%) should be identified and given remedial training. To develop and maintain the necessary level of staff expertise in an institution, the number of staff members who perform aspiration biopsies and the interpreting cytopathologists should be kept small. Each staff member who performs aspiration biopsies must complete at least 1 - 5 such procedures per month [25]. Criteria of specimen adequacy are: 1) a minimum of five or six groups of well-preserved cells, with each group containing approximately 10 - 15 cells; 2) six clusters of benign cells on at least two slides prepared from separate FNA biopsy samples; 3) 10 clusters of follicular cells, with each cluster containing at least 20 cells. Adherence to rigid criteria leads to higher nondiagnostic rates and lower false-negative rates; and high nondiagnostic rates exacerbate patient anxieties and lead to the performance of unnecessary repeat aspiration and unnecessary surgical excision, thereby reducing the overall efficiency and cost-effectiveness of the FNA biopsy procedure [26]. In our study, Inconclusive specimens were higher in community hospital for both free hand FNAC (29% vs. 15%) and US FNAC (10% vs. 6.25%).

A large nodule is easier to sample than a smaller one, and the diagnostic yield from FNA of large nodules may be higher. Degirmenci *et al.* reported that the highest specimen adequacy rate was observed among nodules smaller than 1 cm (76.4%) and the lowest rate was observed among nodules larger than 3 cm (56.9%). They inferred that the lower rate in larger nodules probably resulted from increased vascularity and the larger size of blood vessels, with resultant blood staining of the mate-

rial acquired at fine needle biopsy [18]. Another probable cause of the inadequacy of specimens from larger nodules in the study by Degirmenci *et al.* is that large nodules more often are cystic and contain necrotic areas. Selecting finer needles (24 - 25 G) for sonography-guided FNB of thyroid nodules and using the capillary-action technique decreased the rate of inadequate material in cytological examination [18]. One of the limitations of this study was that we did not include the STN size and site. Moreover we did not mention in cancer cases if the lesions originated from the same STN or originated from other foci.

FNAC has high sensitivity and specificity for predicting thyroid malignancies averaging 83% and 92% respectively [27,28]. Inpatients with thyroid nodules 4 cm or larger, the FNAC results are highly inaccurate, misclassifying half of all patients with reportedly benign lesions. Furthermore, those patients with a non diagnostic FNAC result display a high risk of differentiated thyroid carcinoma. Therefore, Scott N. Pinchot *et al.* recommended that diagnostic lobectomy be strongly considered in patients with thyroid nodules 4 cm or larger regardless of FNAB cytologic test results [29]. A possible way to reduce such error is to do aspirations from different parts which could reveal the typical nuclear features of papillary carcinoma [30]. The determinant factor for such a wide range of sensitivity, specificity and accuracy may be how the cytopathologists classify "suspicious" as well as false positive and negative samples. Some authors include follicular lesion in malignant/neoplastic group, whereas others exclude them from the calculations. In our study sensitivity rate was low compared to others as three out of four (75%) "indeterminate" FNAC results were later found to have malignancy on histological examination. This was despite adequate number of cells (by definition) and suggests that the FNAC interpretation is operator dependent. Our positive predictive values and negative predictive values for both techniques in both hospitals were comparable with published data [31,32].

The accuracy of US-guided FNA was significantly higher than that of palpation-guided FNA (68% vs. 48%), particularly for tumors smaller than 2 cm and those that were cystic or in deep locations. In our study the total accuracy of free hand FNAC was higher in tertiary hospital (94% vs. 82%) similarly, total accuracy of US guided FNAC was higher in tertiary hospital (97% vs. 85%).

US-guided FNA is the best available diagnostic procedure to evaluate thyroid nodules to submit to surgery [33]. Kim DW *et al.* showed a good adequacy and efficacy of US-FNAC for thyroid nodules despite one-sampling [34]. Specimen adequacy is not dependent on the vascularity and echogenicity of the sampled thyroid nodule but on components such as cystic change, calcifica-

tion, and fibrosis.

Similarity, in our study US guided FNAC had better accuracy and less inconclusive results than free hand FNAC.

One of the limitations of this study group is that it comprised FNAC samples taken by different operators, hence with varying skill levels and experience. Moreover, patients' selection process not similar in both hospitals as it is consecutive 160 patients in the community hospital (all patients done in this hospital) and we selected randomly 160 patients from the about 700 patients done in the tertiary hospital.

It is anticipated that improvement in diagnosis will develop from specific cytopathological training in thyroid FNAC, consideration of the cytopathologist performing the aspiration biopsy, and the development of immunohistochemical and molecular techniques applied to the cytologic smears.

## 5. Conclusion

The overall accuracy of both free hand and US guided FNAC in tertiary hospital was better than community hospital. We recommend better training of community hospital staff and encourage more liberal use of US guided FNAC.

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