

*Research Article*

## A Study to Determine the Diagnostic Accuracy of Fine Needle Aspiration Cytology of Thyroid Nodules at El-Demerdash Hospital: A Cross-Sectional Study.

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### Abstract

**Introduction:** Thyroid nodules are one of the common surgical presentations in Africa and are of great concern because of their potential to be malignant. However, there are no pre-operative cellular or intra-operative tissue diagnoses of the thyroid nodules done before thyroidectomy making it difficult to plan for an optimal and definitive management. Fine needle aspiration cytology (FNAC) is known to play a pivotal role in the management and screening of thyroid swelling. This study serves to assess the diagnostic accuracy of FNAC on thyroid nodules at El-Demerdash Hospital in order to give us a basis of introducing its use in the management of thyroid nodules. **Objectives:** To evaluate the accuracy of FNAC in the diagnosis of thyroid nodules as compared to histopathology at El-Demerdash Hospital. **Methods:** This was a prospective cross-sectional study done from September 2014 to January 2016 at El-Demerdash Hospital surgery department. 73 patients who presented with palpable thyroid nodules and underwent thyroidectomy during the study period were enrolled in the study. A structured questionnaire was used to gather information from patient and record files. FNAC was then done pre-operatively by Assistant Professor Remon Zaher. The FNAC diagnosis of the patients was compared to the post operation histopathology results. **Results:** Females made up the majority of the patients (n=67, 91.8%). The ages of the patients ranged from 18 to 78 years. The mean age was 44.3 years and peak age of incidence was in fourth decade. All patients were clinically euthyroid at the time of enrolment because they were either naturally or pharmacologically stabilised for thyroidectomy. The FNAC cytopathology findings included 23 cases reported as unsatisfactory (31.5%), 29 cases of benign (39.7%), and 2 cases of atypical (2.7%), 6 cases of suspicious (8.2%), and 13 cases of malignant (17.8%). Histopathology was available on all 73 participants, of which 55 (75.3%) was benign and 18 (24.7%) was malignant. Among the 18 malignant cases identified by histology, the most common cancer was follicular cancer (n=9, 50%), followed by papillary carcinoma (n=6, 33.3%) and undifferentiated carcinoma (n=3, 16.7%). FNAC in this study had sensitivity, specificity, positive and negative predictive values of 100%, 83.78%, 71.42 and 100% respectively. **Conclusion:** The sensitivity, specificity, and predictive value of FNAC of thyroid nodules at El-Demerdash Hospital is high and therefore can be adopted as a pre-operative tool for diagnosis of thyroid nodules. It also demonstrates that benign thyroid pathology is the most common thyroid disease and follicular carcinoma is the commonest malignancy followed by papillary carcinoma.

**Keywords:** Thyroid nodules, malignant, Fine Needle Aspiration

### Introduction

The thyroid gland is named after the thyroid cartilage and the name thyroid comes from a Greek word meaning shield shaped. It is a butterfly-shaped and highly vascular endocrine organ, whose primary function is the production of the hormones tri-iodothyronine (T3), thyroxine (T4) and calcitonin. It is situated at the front and sides of the neck. It consists of

right and left lobes connected across the midline via the isthmus (Barker, L.W. 1907).

A thyroid nodule is a discrete lesion within the thyroid gland that is palpable and/or ultrasonographically distinct from the surrounding thyroid parenchyma (Cooper et al., 2006). Incidentalomas are thyroid nodules that are incidentally found during imaging studies like

ultrasound and are not palpable (Cooper et al., 2006). By and large, only nodules larger than 1 cm should be evaluated, because they have the potential to be clinically malignant (Cooper et al., 2006).

Thyroid nodules are one of the common surgical presentations and are of great concern because of their potential to be malignant. Depending on the method of screening, the prevalence of thyroid nodules varies. Using ultrasound the prevalence is 30% to 50% while at clinical examination it is 5% to 7% (McDougall I.R 2007).

Fine needle aspiration cytology (FNAC) is known to play a pivotal role in the management and screening of thyroid swelling. According to Frable WJ and Frable MA. (2014) FNAC is a safe, sensitive and specific technique in the initial evaluation of thyroid nodules, and a correct cytological diagnosis can be achieved in a majority of cases, thus obviating the need for a second surgical intervention.

Therefore, FNAC of the thyroid nodules prior to thyroidectomy will readily give cytological diagnosis of the nodules as benign, suspicious or malignant. This is critical because it will allow surgeons prioritize patients and avoid unnecessary operations which are not only costly but may be a source of morbidity and mortality. This will also enable optimal pre-operative planning of treatment and avoid repeated thyroidectomies which are equally expensive and a source of morbidity to the patient.

This study serves to assess the diagnostic accuracy of FNAC on thyroid nodules at El-Demerdash Hospital in order to give us a basis of introducing its use in the management of thyroid nodules.

## Patients and methods

### General objective

$$TP+FN = \frac{Z^2 \times SN(1-SN)}{(W)^2}$$

$$N = \frac{TP+FN}{P}$$

TP= True Positive

FN= False Negative

To evaluate the accuracy of FNAC in the diagnosis of thyroid nodules as compared to histopathology El-Demerdash Hospital.

### Specific Objective

- To determine the frequency of various pathologies of thyroid nodules
- To determine the sensitivity and specificity of FNAC in the diagnosis of thyroid nodules
- To determine the positive and Negative predictive value of FNAC in the diagnosis of thyroid nodules

### Research Methods

**Study site:** This study was conducted in the Departments of surgery at El-Demerdash Hospital.

**Study design:** This was a prospective cross-sectional study

### Inclusion criteria:

- Patients with palpable thyroid nodules and admitted in surgical wards at El-Demerdash Hospital sites scheduled for elective thyroidectomy
- Patients of age 18 years and above
- Patients who gave informed consent

### Exclusion criteria:

- Patients who had diffuse thyroid enlargement.
- Patients with toxic goitres
- Patients with a bleeding disorder, hepatic or renal failure

### Sampling

Convenience sampling was used, with consecutive patients being recruited in order to eliminate bias. The aim was to capture all the patients who were scheduled for thyroidectomy for thyroid enlargement.

**Sample size:** based on the sensitivity sample size formula is

SN= Sensitivity (96%)  
 N = Sample required  
 Z = Z statistic (usually 1.96)  
 P = the expected prevalence = 50%  
 W = acceptable accuracy range (+/- 5%)  
 $TP+FN = \frac{(1.96)^2 \times 0.96(1-0.96)}{(0.05)^2} = 59$

$N = \frac{59}{0.5} = 118$

: based on the specificity sample size formula is

$TN+FP = \frac{Z^2 \times SP(1-SP)}{(W)^2}$

$N = \frac{TN+FP}{(1-P)}$

TN= True Negative

FP= False Positive

SP= Specificity (97%)

N = Sample required

Z = Z statistic (usually 1.96)

P = the expected prevalence = 50%

W = acceptable accuracy range (+/- 5%)

$TN+FP = \frac{(1.96)^2 \times 0.97(1-0.97)}{(0.05)^2} = 44.7$

$N = \frac{44.7}{0.5} = 89$

### Study Procedures

Patients who presented with thyroid nodules were recruited. Data was collected from the patients with the aid of a data collection sheet. Enrolment was then determined by exclusion criteria.

After proper patient counselling, all patients were requested to fill in a written informed consent.

### Technique

Ultrasound imaging is central to the evaluation of most thyroid nodules. Ultrasound uses a high-frequency probe in the 7.5- to 12-MHz range.

Advantages of ultrasound over other imaging modalities include portability, availability, cost-effectiveness, and lack of ionizing radiation.

Fine-Needle Aspiration Biopsy (FNAC) is a cost-effective and valuable tool in the evaluation of thyroid nodules.

**FNA is performed with a small-gauge needle** (needle of sterile 3ML syringe 25 gauge) and

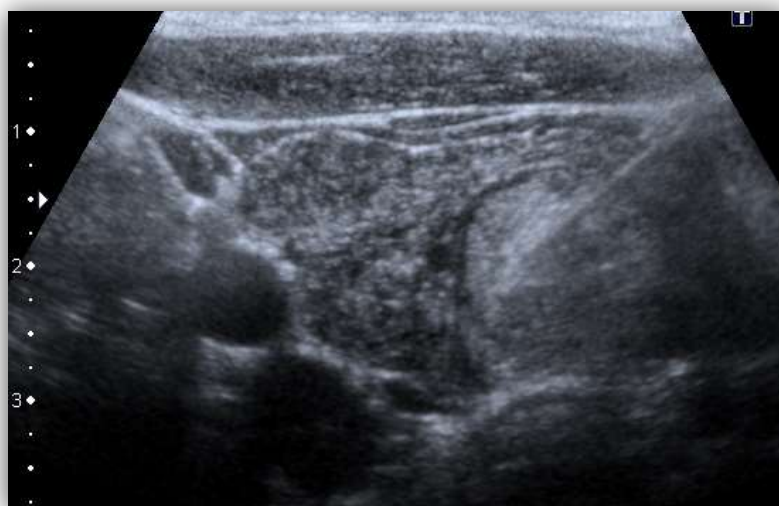
may be performed with capillary or suction technique. Use of small-gauge needles has resulted in a marked decrease in the complication rate while maintaining diagnostic accuracy.

**FNAC** is done under US-guidance for palpable, nonpalpable nodules, posteriorly located, or cystic nodules and results in a lower rate of nondiagnostic cytology and sampling error.

Under US guidance, small-gauge needle is inserted into the thyroid nodule and a **brisk back-and-forth oscillating-type movement** of the needle through the nodule.

Ultrasound guidance clearly increases the diagnostic yield of thyroid FNA

**Ultrasound findings** within a nodule that are considered suspicious for malignancy include micro calcifications, hypoechogenicity, hypervascularity, infiltrative irregular margins, being taller than wider appearance on transverse view. These findings can guide the decision to biopsy or direct the biopsy to the most worrisome nodules in the setting of multinodularity.



**US-guided FNAC from solid hyperechoic right thyroid lobe nodule showing needle within the center of the thyroid nodule**



**US-guided FNAC from solid hypochoic right thyroid lobe nodule showing needle within the center of the thyroid nodule**



**Specimen preparation**

The aspirate was spread onto 6 slides and spread thinly, and then 3 slides were air dried for 5 to 10 minutes and other 3 slides were alcohol fixed. The slides were then stained with Giemsa, papneaccou, H&E. The slides were then taken for reporting to a consultant pathologist.

**Data entry/ analysis:** Data collected was stored on data capture sheet in SPSS Version 21, IBM Armonk US

**Descriptive statistics:**

Continuous variables were presented as means and/or medians, and percentages. Categorical variables were presented as percentages or proportions.

**Statistical Analysis**

The diagnostic value of FNAC was determined by calculating its sensitivity, specificity, positive and negative predictive values. Sensitivity, Specificity and predictive value analysis were done with the aid of a 2x2 table. The histopathology results will be taken as gold standard and the FNAC result matching with histopathology as true positive.

**Table 1:** The 2X2 table

Cytopathology	histopathology	
	Malignancy	No Malignancy
Positive	TP	FP
Negative	FN	TN

**Sensitivity** = TP/TP+FN

**Negative Predictive Value** = TN/TN+FN

**Specificity** = TN/TN+FP

**Positive Predictive Value** = TP/TP+FP

**Ethical Considerations**

Participation in this study was voluntary. This study did not affect patients’ management during period of study. Patients were not remunerated. All information obtained was being kept confidential.

All the investigations were done by qualified personnel. FNAC was the minimally invasive procedure and the anticipated risks to patients included pain and bleeding. This was mitigated with local anesthesia and application of

pressure at puncture site respectively. A written consent was obtained from every patient.

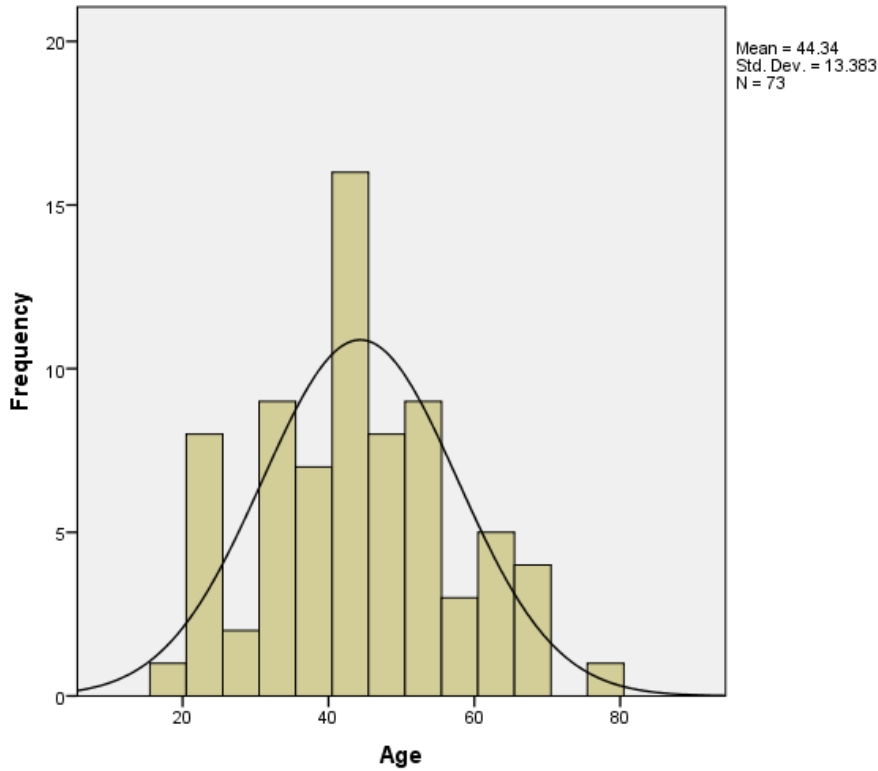
**Results**

**Characteristics of the Participants**

The study enrolled 84 participants however only 73 where eligible for analysis. All the participants had enlarged thyroid glands and had an FNAC and a thyroidectomy done on them.

**Age**

The age range was between 18years and 78years with a mean age of 44.34 years (fig. 1).



**Figure 1:** Age distribution of the study.

**Sex distribution**

In this study the participants sex distribution was 67 females and 6 males representing 91.8% and 8.2% respectively.

**Table 2:** Sex distribution

n=73	N	%
<b>Male</b>	6	8.2
<b>Female</b>	67	91.8

**Clinical characteristics**

The duration of the goitre ranged from 1 year to 35 year with the median age of 8 years at presentation to the hospital. Most of goitres

(89.9%) were described as slow growing and 94.5% were clinically nodular of which 59.9% were multinodular and 41.1% solitary. All the 73 participants were clinically euthyroid.

**Table 3:** Clinical characteristics of the Goitre

n=73	n	%
<b>Type of Thyroid Enlargement</b>		
Diffuse	4	5.5
Nodular	69	94.5
<b>Type of Nodularity</b>		
Solitary	30	41.1
Multinodular	43	59.9
<b>Functional State</b>		
Euthyroid	73	100.0
<b>Rate of Growth</b>		
Slow	62	89.9
Fast	11	15.1

**Thyroid profile**

The thyroid hormone profile in this study had no role to determine the predictability of a positive or negative cytology for malignancy as the p value is more than 0.5.

**Table 4:** TSH, T3 and T4 Levels by Cytopathology (n=50)

	Positive Cytopathology	Negative Cytopathology	Statistics	
	n(%)	n(%)	$\chi^2$	p
<b>TSH Levels</b>			0.31	0.577
Normal	18(97.4)	28(90.3)		
Low	1(5.3)	3(9.7)		
<b>T3 Levels</b>			0.26	0.878
Normal	13(64.4)	19(61.3)		
Low	4(21.1)	8(25.8)		
High	2(10.5)	4(12.9)		
<b>T4 Levels</b>			1.14	0.567
Normal	11(57.9)	20(64.5)		
Low	3(15.8)	2(6.5)		
High	5(26.3)	9(29.0)		

**Cytopathology**

The cytopathology findings on the 73 thyroid FNACs performed during 12months period included 23 cases of unsatisfactory (31.5%), 29 cases of benign (39.7%), and 2 cases of atypical (2.7%), 6 cases of suspicious (8.2%), and 13 cases of Malignant (17.8%).

**Table 5:** Cytopathology findings

	n	%
<b>Non Diagnostic</b>	23	31.5
<b>Benign</b>	29	39.7
<b>Atypia Undetermined Significance</b>	2	2.7
<b>Suspicious for Malignancy</b>	6	8.2
<b>Malignant</b>	13	17.8



**Histopathology**

All the 73 participants had a thyroidectomy with a subsequent histopathology done. Fifty five (75.3%) was benign and eighteen (24.7%) was malignant. Among 18 malignant tumours

identified, the most common cancer was follicular cancer (50%), followed by papillary carcinoma (33.3%) and undifferentiated carcinoma (16.7%).

**Table 6:** histopathology findings

n=73	n	%
Malignant	18	24.7
Benign	55	75.3
<b>Benign</b>		
Follicular Adenoma	6	10.9
Others	49	89.1
<b>Malignant</b>		
Follicular Carcinoma	9	50.0
Papillary Carcinoma	6	33.3
Undifferentiated Carcinoma	3	16.7

**Comparison of FNAC and histopathology**

Figure 6 shows the FNAC diagnosis and their corresponding histopathology diagnosis for all the patients.

**Table 7:** Fnac-Histopathology

FNAC	n (%)	HISTOPATHOLOGY	n (%)
Non Diagnostic	23 (31)	Other Benign	18 (24)
		Follicular adenoma	2 (3)
		Follicular carcinoma	2 (3)
		Papillary carcinoma	1 (1)
Benign	29 (40)	Other Benign	29 (40)
Atypia Undetermined Significance	2 (3)	Other Benign	2 (3)
Suspicious for Malignancy	6 (8)	Follicular carcinoma	4 (6)
		Papillary carcinoma	1 (1)
		Anaplastic carcinoma	1 (1)
Malignant	13 (18)	Follicular adenoma	4 (6)
		Follicular carcinoma	3 (3)
		Papillary carcinoma	4 (6)
		Anaplastic carcinoma	2 (3)

**False Positive Cases**

The table shows the 6 FNAC false positive for malignancy results and their corresponding histopathology results.

**Table 8:** False Positive Cases

Age/sex	FNAC Diagnosis	Histopathology diagnosis
25/Female	malignant	Follicular Adenoma
18/Female	malignant	Follicular Adenoma
42/Female	Atypia of undetermined significance	Other benign
45/Female	Atypia of undetermined significanc	Other benign
41/Female	Malignant	Other benign
32/Female	Malignan	Follicular Adenom



**The 2x2 Table**

The table shows a 2x2 table used to calculate FNAC’s sensitivity, specificity, positive and negative predictive values.

**Table 9:** The 2X2 table

Cytopathology	histopathology	
	Malignancy	No Malignancy
Positive	TP	FP
Negative	FN	TN

Cytopathology	histopathology	
	Malignancy	No Malignancy
Positive	15	6
Negative	0	31

**Sensitivity** = TP/TP+FN = 15/15+0 = 15/15 = **100%**

**Specificity** = TN/TN+FP = 31/31+6 = 31/37 = **83.78%**

**Negative Predictive Value** = TN/TN+FN = 31/31+0 = 31/31 = **100%**

**Positive Predictive Value** = TP/TP+FP = 15/15+6 = 15/21 = **71.42%**

FNAC showed 21 cases positive for malignancy of which 15 were true positive and 6 were false positive. There was no false-negative diagnoses .All the 29 negative for malignancy FNAC were true negatives.

**Surgical procedures**

Subtotal thyroidectomy was the commonest surgical procedures accounting for 41.1%, followed by total thyroidectomy 31.5% and lobectomy 24.7%.

**Table 10:** Surgical procedures

	n	%	malignant	benign
Lobectomy/hemi- thyroidectomy	20	24.7	2	18
Subtotal Thyroidectomy	31	41.1	2	29
Total Thyroidectomy	22	31.5	14	8

**Discussion**

The total number of patients enrolled was 84 although only 73 were eligible for analysis this was because the other 11 cases (13.1%) had either lost slides, cytopathology or histopathology results.

This study had most of the patients females at 91.8% (67) and males at 8.2% (6) and the ratio was 11.2:1. This is because of the fact that thyroid nodules are more common in women.

The ages of the patients ranged from 18 to 78 years. The mean age was 44.34 years and peak age of incidence was in fourth decade. This is slightly different to a study done by Khageswar Rout et al., (2011 ) whose peak incidence was third decade.

The clinical presentation of the all patients was euthyroid this is because all patients were

enrolled at the time when they were prepared for thyroidectomy thus where stabilised in terms of thyroid function. It is for the same reason why the thyroid hormone profile in this study could not be used to help predict the cytology outcomes for malignance as shown in table 6 in which all the P values are more than 0.5. Thyroid function tests helps to exclude nodules which are associated with either hyperthyroidism or hypothyroidism. When TSH level is normal, assay of serum free T4 adds no further information because TSH is the most sensitive thyroid function test. Although calcitonin levels were not measured in this study, in a suspected case of medullary carcinoma, calcitonin levels should be measured for it is both sensitive and specific to it.

The duration of the thyroid gland tumour was from 1year to 35 years. This wide range can be attributed to the general poor health seeking

behaviour of the general populous and because of the difficulties most patients encounter to seek specialised treatment.

This study emphasises the importance of FNAC as a pre-operative assessment tool in thyroid nodules as recommended by the American Thyroid Association and the National Comprehensive Cancer Network Yang, J. et al., (2007). The cytopathology findings included 23 cases of unsatisfactory (31.5%), 29 cases of benign (39.7%), and 2 cases of atypical (2.7%), 6 cases of suspicious (8.2%), and 13 cases of malignant (17.8%). Benign was the commonest finding in this study which is similar to other studies done by Wu et al., (2006) and Yang, J. et al., (2007). The unsatisfactory cases were mainly due to the initial inexperience of the radiologist' residents in the collection and preparation of the FNAC as it was their first experience. However, this improved when the assistant professor did it by himself. The other sources of error that were identified in the study included.

The unsatisfactory cases were ideally supposed to have been repeated however, in this study they were not repeated because of the way the research was setup. At the time the FNAC results were out thyroidectomy would have already been done on the patient. On all the participants a thyroidectomy with a subsequent histopathology diagnosis was done, of which 75.3% (55) was benign and 24.7% (18) was malignant. This is similar to the findings in the study done within Egypt that benign goitres are the commonest thyroid pathology by Mohamed et al., (2018). Among the 18 malignant tumours identified by histology, the most common cancer was follicular cancer at 50%, followed by papillary carcinoma at 33.3% and undifferentiated carcinoma at 16.7%.

The diagnostic value of FNAC was determined by calculating its sensitivity, specificity, positive and negative predictive values. Sensitivity was defined as the test diagnosed positive for malignancy by FNAC divided by the total positive diagnosis for malignancy as demonstrated by histopathology after thyroidectomy. Specificity was defined as the test diagnosed negative for malignancy divided by the total negative diagnosis for malignancy as demonstrated by histopathology after thyroidectomy. The predictive value was the ratio of the number of times FNAC was correct

divided by the total number of either positive or negative FNAC result and was expressed in percentage.

The diagnostic value of FNAC of thyroids varies because of many reasons among them is the differences in data analysis of the indeterminate categories (atypical, Follicular Neoplasm, and suspicious for malignancy). In this study these categories were considered positive for malignancy as recommended by most authors (Yang, J. et al., 2007). This increases the sensitivity of the study while reduces its specificity. Out of the 73 cases of FNAC only 21 cases were positive for malignancy of which 15 were true positive and 6 were false positive. Thus, FNAC in this study had a sensitivity, specificity, Positive and negative predictive values of 100%, 83.78%, 71.42 and 100% respectively. This is comparable to other studies by Chandanwale et al., (2012) and Khairy and Murshid (2004) whose Sensitivity and specificity were 90% and 100%, and 71.4% and 96.4% respectively.

Khairy and Murshid (2004) indicated that centres that utilised FNAC as a pre-operative diagnostic tool reduced the number of unnecessary thyroid operation by 40%. Therefore, FNAC of thyroid nodules can be used as a pre-operative tool to diagnose thyroid malignancy as it is a simple, safe and cost effective. It also allows appropriate and immediate surgery for patients with thyroid malignancy thus enormously eliminate the unnecessary and inappropriate thyroid operations.

### Conclusion

This study demonstrates that the sensitivity, specificity, and predictive value of FNAC of thyroid nodules at El-Demerdash hospital is high and therefore can be adopted as a pre-operative tool for diagnosis of thyroid nodules. It also demonstrates that benign thyroid pathology is the most common thyroid disease and follicular carcinoma is the commonest malignancy followed by papillary carcinoma.

### Study Limitations

Some limitations have been identified as the study was taking place as follows:

1) The participants' numbers were not large enough to enable us make some of the conclusions confidently.

- 2) The study was dependant on surgical thyroid operation thus successful enrolment of patient was limited to those patients with thyroid goitre and has undergone a thyroid operation.
- 3) Delays in producing the Cytology results and losing of some samples from the laboratory reduced the sample size.

### Recommendations

- 1) FNAC should be made as part of the initial evaluation of all patients with thyroid nodules.
- 2) Since FNAC is simple and safe all registrars and consultants in surgery department should be trained in the method of performing it.
- 3) No thyroid operation should be done before having a pre-operative diagnosis in order to avoid inappropriate and unnecessary thyroid operations.
- 4) The efficiency of the laboratory at El-Demerdash should be improved and dedicated cytopathology stream set up in order to improve cytology output.

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