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Research Article

Accuracy of Fine Needle Aspiration Cytology of Thyroid Compared to Final Histopathology in Total Thyroidectomy.

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Background

Thyroid nodules considered as common clinical presentation in head and neck clinic with a prevalence of thyroid nodule ranging from 2%–6% within palpation, 19%–35% using ultrasound imaging, and 8%–65% in autopsy data [1]. Majority of patient presented with thyroid nodule appear to begin with fewer cases of neoplastic disease [2]. Details history and full head and neck examination is important to reach the accurate diagnosis and it must address the risk factor for malignancy like age of the patient, progression of disease and exposure to radiation [3]. A lot of diagnostic modalities have been mentioned in literature like ultrasonography, fine needle aspiration, histopathology, CT scan and even MRI [3].

FNAC become the most important tools in diagnosis of thyroid nodule, its easy office procedure requires no general anesthesia and non-invasive, quick and reliable [3]. The main goal of thyroid Fine-Needle Aspiration (FNA) is to identify the nodules that require surgery and decrease the overall incidence of thyroidectomy among patients with benign disease [4]. However, many studies reported that FNAC has limitations related to specimen adequacy, sampling techniques, and skill of clinician performing the aspiration. In addition to that, it has low accuracy in suspicious cytology and follicular neoplasm. Thus, even if noninvasive techniques such as FNAC can provide an initial diagnosis, histopathological examination of the excised thyroid tissue is required for the final diagnosis [7]. Despite several studies showing a high accuracy with FNAC, emerging studies especially in tropical Africa and other developing countries with a high prevalence of nodular thyroid disease, have shown the accuracy of FNAC to be lower than previously reported and its diagnostic performance has been shown to vary across different studies [8]. So, in our study we wanted to know the accuracy compared to the final histopathology report in our region compared to the actual international percentage to avoid any unnecessary invasive procedure and to improve our accuracy if needed and overcome the false negative and false positive result. Furthermore, we studied the effect of larger thyroid nodule above 4cm to assist the accuracy of FNA as it was more risk for malignancy compared to smaller size [5,6].

Problem Statement: Thyroid nodules are a common clinical problem and they affect about 5% of the World's population. Currently, many diagnostic tests are used to diagnose thyroid swellings with Fine-Needle Aspiration Cytology (FNAC) being the gold standard test, in which it helps in planning extent of surgery. However, in some studies, FNAC has been found to have a low accuracy for malignancy.

Justification: For the past 2 decades, FNAC has become the diagnostic tool of choice for the initial evaluation of thyroid nodules. FNAC is a noninvasive, cost-effective, reliable, and quick to perform procedure in the Out Patient Department (OPD). However, some studies reported that FNAC has many limitations related to specimen adequacy, sampling techniques, and skill of clinician performing the aspiration. So, in our study we wanted to know the accuracy compared to the final histopathology report in our region compared to the actual international percentage to avoid any unnecessary invasive procedure and to improve our accuracy if needed and overcome the false negative and false positive result.

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Study Objective: The objective of this study was to evaluate diagnostic accuracy of FNAC in the diagnosis of thyroid nodules and its correlation with histopathological findings at Aseer Central Hospital in Abha, Saudi Arabia.

Hypothesis: It was anticipated that this study will reveal high specificity and low sensitivity of Fine Needle Aspiration Cytology (FNAC) at detecting malignancy in thyroid nodules.

Abbreviations: FNAC: Fine-Needle Aspiration Cytology; FNA: Fine-Needle Aspiration; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; OPD: Outpatient Department; PTC: Papillary Thyroid Cancer; SPSS: Statistical Package for Social Sciences; PPV: Positive Predictive Value; NPV: Negative Predictive Value.

Literature Review

Thyroid nodules are a common clinical presentation. Epidemiological studies show a prevalence of 2%–6% with palpation, 19%–35% using ultrasound imaging, and 8%–65% in autopsy data. The majority of clinically diagnosed thyroid nodules are nonneoplastic and fewer than 5% are malignant and require surgical intervention. There are many risk factors that increase the incident of thyroid nodules such as increasing age, female gender, iodine deficiency, and radiation exposure. [7]

FNAC of the thyroid gland is now a well-established, first-line diagnostic test for the evaluation of diffuse thyroid lesions as well as of thyroid nodules with the main purpose of confirming benign lesions and thereby, reducing unnecessary surgery [9].

Background Routine application of Fine Needle Aspiration Cytology (FNAC) has decreased unnecessary referral of thyroid nodules for surgical treatment and has also increased the cancer rates found in surgery materials. Success of thyroid FNAC depends on skilled aspiration, skilled cytological interpretation and rational analysis of cytological and clinical data. [10]

A study was conducted in Saudi Arabia by *Sameer Al-Bahkaly* in the year 2020 to correlate the FNAC findings with the histopathology of the excised specimens. It was a retrospective review of 98 patients undergoing thyroidectomy in the Department of ENT, Head and Neck Surgery at King Abdulaziz Medical City in Riyadh, Saudi Arabia. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of FNAC for the diagnosis of solitary thyroid nodules were 55.56%, 88.73%, 65.22%, 84%, and 79.59%, respectively [7].

Another study was done by *Robert Masereka* in Uganda in the year 2016 to estimate the sensitivity and specificity of FNAC in detecting malignancy for thyroid disease using histopathology as the gold standard. In total, 99 patients were recruited, the F:M ratio was 15.5:1 and median age was 42 years (IQR 34–50). The median duration of symptoms was 364 weeks (IQR 104–986). The proportion of patients with malignancy was 13.3% with papillary thyroid carcinoma being the most predominant type and colloid goiter was the most predominant benign thyroid disease. The sensitivity was 61.5% and specificity 89.5% [8].

Meanwhile in Turkey, *Taskin Erkinuresin* conducted a study in the year 2020 on the same topic. The sensitivity of thyroid FNAC for malignant cases was 57.89%, specificity was 88.10%, false-positive rate was 11.90%, false-negative rate was 42.11%, positive predictive value was 52.38%, negative predictive value was 90.24% and accuracy rate was 82.52%. "Focus number" variable was detected as the factor that affected the accurate prediction of FNAC and thyroidectomy results by the pathologist [10].

Again, in Saudi Arabia, *Hayfa Alolayan conducted a study in the year 2020 to* determine the accuracy of FNA in evaluating thyroid nodules to assess the ability of FNA in detecting malignancies of the thyroid gland and to evaluate the role of FNA in the reduction of unnecessary surgeries for the patients with a thyroid nodule. Part of the main results indicated that the accuracy of FNA was 88.6% in diagnosing the Follicular Carcinoma and 90.8% in diagnosing Follicular Adenoma. FNA's overall sensitivity was found to be 91.2%, while the specificity was found at 71.65%. Previous studies placed FNA sensitivity between 89% and 90% [11].

Lastly, a study was done in the UK in the year 2021 by *Ahmad K. Abou-Foul* on the same topic. The histological reports of 659 consecutive cases of thyroid surgery between 2006 and 2015 were retrieved from our hospital database. Among the 471 patients (71.5%) who underwent preoperative FNAC, the postoperative histology was reported as benign in 352 (74.7%) and malignant in 119 cases (25.3%). Papillary Thyroid Cancer (PTC) was the commonest histological diagnosis. Thy1 grade was reported in 165 (30%) cases, with 19.4% having a final histological diagnosis of malignancy. In the Thy2 group, 85.3% of patients had a benign final histological diagnosis, while 14.7% had malignancy (false-negative results). Malignancy was found in 89% of Thy4 and 100% of Thy5 group patients [12].

Materials and Methods

This retrospective review was carried out among patients undergoing thyroidectomy in the Department of ENT, Head and Neck Surgery at Aseer Central Hospital, Abha, Saudi Arabia. Period of study was from 1-1-2015 to 1-10-2019. All patients' records during the study period were included in this study (total coverage). Each patient's data was obtained from electronic records.

Local examination of the swelling and FNAC of thyroid goiters was performed on OPD basis as per standard protocol. Depending on the nature of the goiter as reported in FNAC and depending on the thyroid function status decision was taken regarding the need and extent for surgery. Thyroidectomy specimens preserved in 10% formalin were sent for histopathology examination to the pathology department in our hospital. All FNAC reports were correlated with histopathology diagnosis.

Inclusion Criteria

All patients above the age of 14 presenting with thyroid swellings or referred to the ENT OPD were included in the study.

All patient underwent FNA cytology for thyroid mass then underwent thyroid surgery

Exclusion Criteria

Patients with neck swellings caused by nonthyroidal gland related pathology like lymphadenopathy, branchial cysts, and others were excluded from the study.

Data Collection

Data was collected using data collection sheets including all aspects of the objectives.

Data Analysis

After data were collected, it was modified, coded and entered to statistical software IBM SPSS version 22(SPSS, Inc. Chicago, IL). All statistical analysis was done using two tailed

tests. P value less than 0.05 was considered to be statistically significant. Descriptive analysis based on frequency and percent distribution was done for all variables including demographic data, and FNA and histopathological findings. Thyroid profile was described using median value with range due to high variability of measures in relation to nodule nature. Mann-Whitney test was used to compare thyroid profile median value among benign and malignant masses. Cross tabulation was used to test for the distribution of FNA, histopathology and thyroidectomy procedure according to nodule size using exact probability test of significance. FNA diagnostic accuracy was tested using sensitivity (true positive rate), specificity (true negative rate), Positive Predictive Value (PPV), Negative Predictive Value (NPV), and diagnostic accuracy.

Results

A total of 357 patients were included in the study. Patients ages ranged from 18 to 88 years old with mean age of 39.7 11.6 years old. Exact of 299 (83.8%) patients were females. Total thyroidectomy was the surgical procedure among 240 (67.4%) and hemithyroidectomy was the procedure among 116 (32.6%) patients (Table 1).

Table 2 illustrates thyroid mass clinical data among patients undergone thyroidectomy. As for thyroid mass size, it was 5cm or more among 217 (60.8%) patients, 1-4cm among 122 (34.2%) patients and less than 1cm among 18 (5.0%) patients. Considering fine needle aspiration biopsy, it was benign among 311 (87.1%) patients. Considering histopathology findings, multinodular goiter was detected among 194 (54.3%) patients, followed by papillary thyroid cancer (18.8%), Hashimoto thyroiditis (13.7%), Follicular carcinoma (2.5%), Anaplastic thyroid cancer (0.8%), and Hurthle cell carcinoma (0.6%).

Table 3 shows thyroid profile among patients with thyroid mass who undergone thyroidectomy. TSH level ranged from 0.01-100 with median value of 1.52 among benign mass cases compared to 2.17 (0.01-77) among malignant mass (P=.091). T3 level ranged from 0.01-16 with median value of 4.47 among benign mass cases compared to 3.91 (0.0-77) for cases with malignant mass (P=.189). As for T4, it ranged from 0.5-41 with median value of 11.25 among cases with benign mass in comparison to 5.97 (2.2-52) among cases with malignant mass (P=.008).

Table 4 demonstrates distribution of thyroid mass clinical findings according to the mass size. Exact of 16.7% of masses less than 1cm were malignant by FNA compared to 12.3% of masses sized 1-4cm and 12.9% of masses sized more than 5cm with no statistical significance (P=.875). Exact of 38.9% of masses sized less than 1cm were found to be papillary thyroid cancer by histopathology compared to 21.3% of masses sized 1-4cm and 15.7% of masses sized more than 5cm. Also, 60.4% of masses sized more than 5cm were found to be multinodular goiter compared to 45.9% of masses of 1-4cm and 38.9% of those which sized less than 1cm (P=.098). Total thyroidectomy was done for 72.2% of masses sized less than 1 cm compared to 62.3% of those sized 1-4cm and 69.9% of masses of more than 5cm (P=.324).

Table 5 shows diagnostic indices of Fine-Needle Aspiration Cytology (FNAC) relative to histopathology according to the thyroid nodule size categories. In group A (nodule size <1cm), the sensitivity, specificity, PPV, NPV, and diagnostic accuracy were 42.9%, 100%, 100%, 73.3%, and 77.8%, respectively. In group B (nodule size 1-4cm), these values were 51.7%, 100%, 100%, 86.9%, and 88.5%, respectively. In group C (nodule size >5cm), these values were 55.6%, 98.3%, 89.3%, 89.4%, and 89.4%, respectively. Therefore, overall FNAC sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 53.1%, 98.9%, 93.5%, 87.8%, and 88.5%, respectively.

Table 1: Bio-demographic data of patients with thyroid mass undergone thyroidectomy.

Bio-demographic data	No	%
Age in years		
<40 years	176	49.3%
40-49 years	114	31.9%
>49 years	67	18.8%
Gender		
Male	58	16.2%
Female	299	83.8%
Procedure		
Total thyroidectomy	240	67.4%
Hemi thyroidectomy	116	32.6%

Table 2: Thyroid mass clinical data among patients undergone thyroidectomy.

Thyroid mass data	No	%
Mass size		
<1cm	18	5.0%
1-4cm	122	34.2%
>5cm	217	60.8%
FNA		
Benign	311	87.1%
Malignant	46	12.9%
Histopathology		
Multinodular goiter	194	54.3%
Papillary thyroid cancer	67	18.8%
Hashimoto thyroiditis	49	13.7%
Follicular adenoma	25	7.0%
Follicular carcinoma	9	2.5%
Hurthle cell adenoma	7	2.0%
Anaplastic thyroid cancer	3	0.8%
Hurthle cell carcinoma	2	0.6%
Hyperplastic nodule	1	0.3%

Table 3: Thyroid profile among patients with thyroid mass who undergone thyroidectomy.

Thyroid profile	Total		Histopathology findings				P-value
			Benign		Malignant		
	Median	Range	Median	Range	Median	Range	
TSH	1.69	0.01-100	1.52	0.01-100	2.17	0.01-77	.091
T3	4.34	0.0-77	4.47	0.01-16	3.91	0.0-77	.189
T4	10.35	0.5-52	11.25	0.5-41	5.97	2.2-52	.008*

P: Mann-Whitney test
*P<0.05 (significant)

Table 4: Distribution of thyroid mass clinical findings according to the mass size.

Mass data	Mass size						P-value
	<1cm		1-4cm		>5cm		
	No	%	No	%	No	%	
FNA							
Benign	15	83.3%	107	87.7%	189	87.1%	.875
Malignant	3	16.7%	15	12.3%	28	12.9%	
Histopathology							
Follicular adenoma	2	11.1%	15	12.3%	8	3.7%	.098
Follicular carcinoma	0	0.0%	2	1.6%	7	3.2%	
Hyperplastic nodule	0	0.0%	0	0.0%	1	.5%	
Multinodular goitre	7	38.9%	56	45.9%	131	60.4%	
Hashimoto thyroiditis	2	11.1%	20	16.4%	27	12.4%	
Hurthle cell carcinoma	0	0.0%	1	.8%	1	.5%	
Hurthle cell adenoma	0	0.0%	2	1.6%	5	2.3%	
Papillary thyroid cancer	7	38.9%	26	21.3%	34	15.7%	
Anaplastic thyroid cancer	0	0.0%	0	0.0%	3	1.4%	
Procedure							
Total thyroidectomy	13	72.2%	76	62.3%	151	69.9%	.324
Hemi thyroidectomy	5	27.8%	46	37.7%	65	30.1%	

P: Exact probability test

Table 5: Diagnostic indices of Fine-Needle Aspiration Cytology (FNAC) relative to histopathology according to the thyroid nodule size categories.

Mass size	FNA	Histopathology				Sensitivity	Specificity	PPV	NPV	Accuracy
		Benign		Malignant						
		No	%	No	%					
<1cm	Benign	11	61.1%	4	22.2%	42.9%	100%	100%	73.3%	77.8%
	Malignant	0	0.0%	3	16.7%					
1-4cm	Benign	93	76.2%	14	11.5%	51.7%	100%	100%	86.9%	88.5%
	Malignant	0	0.0%	15	12.3%					
>5cm	Benign	169	77.9%	20	9.2%	55.6%	98.3%	89.3%	89.4%	89.4%
	Malignant	3	1.4%	25	11.5%					
Overall	Benign	273	76.5%	38	10.6%	53.1%	98.9%	93.5%	87.8%	88.5%
	Malignant	3	0.80%	43	12.1%					

Discussion

The current study aimed to assess if the tumor size influences the diagnostic accuracy of Ultrasound-Guided Fine-Needle Aspiration Cytology (FNAC) for thyroid Nodules. Fine-needle aspiration cytology is a corner stone diagnostic test and cost-effective method for the differential diagnosis of thyroid nodules [13-15]. FNAC was firstly known in the 1950s, [17] and has now it become a frequently used method, especially after the appearance of ultrasound- (US-) guided FNAC. This new technique significantly improved the diagnostic accuracy of FNAC [18,19] US particularly improved accuracy of FNAC on nonpalpable small (≤1cm) thyroid nodules. This has greatly improved the diagnosis and surgical treatment of Papillary Thyroid Microcarcinoma (PTMC) [20-23].

The current study revealed that total thyroidectomy was done for two thirds of the study patients with nodule size more than 5cm among two thirds of them. Small nodules (<1cm) were detected among very few numbers of cases. Regarding nodule nature, FNA detected benign features were detected among most of the cases (nearly 1 out of each 10 cases). A lower portion of benign findings was detected by histopathology (77%) as more than half of the cases had multinodular goiter, while papillary thyroid carcinoma was diagnosed among nearly 1 out of each 5 cases followed by follicular carcinoma which was detected among few cases (2.5%). These findings were approximately similar to literature classification of thyroid nodules where nearly 23% of solitary nodules are actually dominant nodules within a multinodular goiter [10]. Thyroid carcinoma diagnosed among about 5 to 10 % of palpable nodules [23].

Regarding FNAC as a diagnostic tool, the current study revealed that it had higher specificity for detecting benign nodules but low sensitivity. The overall classification accuracy of FNAC relative to histopathology was about 88% with specificity higher than 98% but specificity of 53% which means, in general FNAC had very good ruling in criteria (detecting benign lesions) but moderately poor ruling out (poor capacity for excluding malignant lesions). The performance of FNAC was higher among larger nodules (better ability to detect benign features) than small nodules (<1cm). False negative rates (being malignant and defined as benign) was higher among small nodules (22.2%) compared to larger nodules (9.2%) with an overall rate of 10.6%. These findings were lower than to what reported by Koo DH et al, [24] who found that Overall FNAC sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 95.4%, 98.2%, 99.4%, 86.4%, and 96.0%, respectively. False-Negative Rates (FNRs) of different nodules according to size which ranged from <0.5cm to >4cm were 3.2%, 5.1%, 1.3%, 13.3%, and 50%, respectively. Accuracy rates of all sizes were 96.8%, 94.8%, 99%, 94.7%, and 87.5%, respectively. Authors also concluded that large thyroid nodules (>4cm) with benign cytology carry a higher risk of malignancy, which indicate that those should be deemed for rigorous follow-up or repeated biopsy. Other studies found similar findings where the diagnostic accuracy of FNAC for small thyroid nodules (<1cm) was found to be lower than for those with diameter exceeding 1cm [13-15]. On the other hand, many other studies revealed that FNAC is still a useful tool for small nodules (less than 1cm in diameter) [28-30].

Berker et al, [31] found that malignancy rate was 3-fold high in sub-centimeters nodules compared to larger nodules and recommended that FNAC should be performed for smaller hypoechoic nodules with microcalcification and round shape. Though, Mazzaferri et al, [32] reported increased rate of false negative classifications of FNAC results in sub-centimeters nodules. In contrast on the other hand the study of Koo et al, [24] showed that sensitivity and specificity of FNAC was 96.8% and 100% in sub-centimeters nodules, respectively.

These variations may depend upon the success of a biopsy which based on the adequacy of the specimen and skill of the cytopathologist. In skilled hands, the false negative rate is less than 5%, and the false positive rate less than 1%. The technique can be performed in ambulatory patients without local anesthesia. Discomfort is usually mild. Specimens can be taken from several parts of the nodule, and slides smeared immediately. Immediate staining of some slides allows evaluation of the adequacy of material while the patient is still present and further passes if material is inadequate. There is a small risk of bleeding, which settles quickly with ice packs. Ultrasound guidance is preferred by some practitioners and is needed for impalpable lesions that warrant fine-needle aspiration biopsy [33,34].

Conclusion

As overall, this study can conclude that FNAC has a high specificity and low sensitivity at detecting malignancy in thyroid nodules. It remains a simple, safe, and cost-effective diagnostic modality for thyroid carcinoma. It is recommended as the first-line investigation for the diagnosis of solitary thyroid nodule.

- Recommendations FNAC is recommended as the first-line investigation for the diagnosis of solitary thyroid nodule.
- Health providers must keep in mind that FNAC has a low sensitivity and more tests should be done in order to give the right diagnosis.
- Increasing the training among the team players in the endocrine surgery unit must be done in order to get the best outcome.

More studies on this topic should be conducted in Saudi Arabia to strengthen this evidence base for clinical decision making.

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