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Original Research Article

Correlation between thyroid fine needle aspiration cytology and postoperative final histopathology: a 5-year single-centre retrospective study

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ABSTRACT

Background: Thyroid nodules are common problems encountered in our routine practice. Fine needle aspiration cytology (FNAC) is the most accurate and cost-effective method for evaluating thyroid nodules. It is the procedure of choice for identifying patients who require surgical excision.
Methods: This is a retrospective single-center observational study in Salmaniya Medical Complex, a tertiary care center, in Kingdom of Bahrain that aims to to correlate preoperative FNAC results with the post-surgical histopathology report, and to compare our diagnostic performance results to previously published literature.
Results: The post-operative histology was reported as benign in 62% of patients and malignant in 38% of patients. Bethesda II was the most common category in our sample, with 14.3% having a final histopathological diagnosis of malignancy (false negative results). Malignancy was found in 84% and 96.8% of Bethesda V and VI, respectively. Our FNAC data achieved an 80.95% sensitivity, specificity of 93.51% specificity, and a total accuracy of 87.86%. The positive predictive value was 91.07%, and an 85.71% negative predictive value, which were comparable to data from published series.
Conclusions: FNAC remains the most accurate and cost-effective method for evaluating thyroid nodules. However, its diagnostic value varies among different institutions. Our results demonstrated higher rates of malignancy compared to other published series in both category I and II. Due to the chance of false negative rates in these categories and the slow-growing nature of thyroid malignancy, it is important that patients with benign FNAC should have periodic clinical and radiological follow up.

Keywords: Fine-needle aspiration, Thyroid cancer, Histopathology, Bethesda

INTRODUCTION

Thyroid nodules are common problems encountered in our routine practice. Studies suggest a prevalence of 2-6% with palpation, 19-35% with ultrasound, and 8-65% in autopsy data. Their incidence increases with age as well as in women and in people with iodine deficiency and those with a history of radiation exposure.[1-3] Although thyroid nodules are mostly benign, the incidence of malignancy was found to be around 5% making it one of the most common endocrine malignancies; it is listed as the seventh most common cancer affecting women and as the fifteenth most common cancer affecting men worldwide.[4-6] In Bahrain, thyroid cancer was the fourth most common female cancer between 1998 and 2011 accounting for 4.9% of all cancer cases in Bahraini females, with an average annual ASR of 6.0/100,000 people.[7]

The challenge facing clinicians dealing with thyroid nodules is to achieve an accurate preoperative diagnosis of malignancy.[8] Methods for evaluating thyroid nodules

include the thyroid palpation exam, thyroid-stimulating hormone (TSH) test, ultrasonography, and fine needle aspiration (FNA). FNA is the most accurate and cost-effective method for evaluating thyroid nodules. It is the procedure of choice for identifying patients who require surgical excision.[9] In Bahrain practice, FNAC specimens are reported according to Bethesda system for reporting thyroid cytopathology (TBSRTC). As per Chirag et al, FNAC was assessed to have a diagnostic accuracy of 94.5%, with a sensitivity of 84.2% and a specificity of 97.2%, respectively. The positive predictive value was 88.3%, whereas the negative predictive value was 96% [10].

The aim of this retrospective study is to correlate preoperative FNAC results with the post-surgical histopathology report, and to compare our diagnostic performance results to previously published literature.

METHODS

Study subjects, sampling and data acquisition

We conducted a retrospective single-center observational study in Salmaniya Medical Complex, a tertiary care center, in Kingdom of Bahrain. Patients with thyroid lesions who underwent pre-operative FNACs followed by surgical option, lobectomy or total thyroidectomy, which yielded a final histopathologic examination over a five-year period, between January 2018 and December 2022, were included. Details of the all patients who applied to the inclusion criteria were pulled from the internal data system at the hospital and arranged as a database. Investigated clinical parameters include age, gender, details of FNAC and final histopathological diagnosis. In cases with multiple abnormal aspirates taken from more than one nodule, the most abnormal result was used for analysis. Our exclusion criteria were patients outside of our center, patients outside of our designated timeframe, and those who did not undergo a surgical option following FNAC.

Fine needle aspiration sample processing

In our institutions, FNAC samples are routinely aspirated under ultrasound guidance using 23-gauge needle with 10 ml disposable syringes. Each specimen contains at least an air-dried slide for Giemsa stain and an alcohol-fixed slide for Papanicolaou stain (Pap stain).

Data management

All FNAC date was sorted into six groups according to Bethesda system for reporting thyroid cytopathology (TBSRTC).[11] It categorizes findings into 6 main categories. Bethesda I being non-diagnostic or unsatisfactory, containing cystic fluid, acellular specimen, or other non-diagnostic findings (e.g., obscuring blood, and clotting artificial). Bethesda II are benign, consistent with a benign follicular nodule (includes adenomatoid nodules, and colloid nodules), or lymphocytic (Hashimoto) thyroiditis in the proper clinical context, or consistent with benign follicular nodules (includes adenomatoid nodules, and colloid nodules). Bethesda III is atypia of undetermined significance or follicular lesion of undetermined significance. Bethesda IV is a follicular neoplasm or suspicious for follicular neoplasm. Bethesda V is suspicious for malignancy (e.g., papillary, medullary, metastatic or lymphoma). Bethesda VI is malignant, which includes findings in line with papillary thyroid carcinoma, poorly differentiated carcinoma, medullary thyroid carcinoma, anaplastic carcinoma, squamous-cell carcinoma, carcinoma with mixed features, metastatic carcinoma, non-Hodgkin lymphoma, and others.

Statistical analysis

The data collected is used to calculate the sensitivity, specificity, diagnostic accuracy, positive predictive value (PPV), and negative predictive value (NPV) for our thyroid cytology. Statistical analysis was performed using IBM statistical package for the social sciences (SPSS) statistics (version 20.0).

Ethical approval

This study was approved by the ethical committee in the research department in Salmaniya Medical Complex. It is in compliance with all its rules and regulations.

RESULTS

During our study's timeframe, a total of 200 patients from our center underwent FNAC for a thyroid nodule followed by a definitive surgical option which yielded a histopathological diagnosis. The age of the patients ranged from 17 to 79 years, with a mean age of 44.25 years, with 11% male and 89% female patients' distribution. Out of the 200 patients in the study population, 5 patients (2.5%) were reported as non-diagnostic or unsatisfactory, 84 patients (42%) as benign, 32 patients (16%) as atypia of undetermined significance or follicular lesion of undetermined significance, 23 patients (11.5%) as follicular neoplasm or suspicious for a follicular neoplasm, 25 patients (12.5%) suspicious for malignancy, and 31 patients (15.5%) as malignant (Table 1).

The distribution of Bethesda scores varied between the two genders as shown in Table 1, with the majority of patients in both genders having Bethesda scores in the range of II to VI. Specifically, 90.5% of female patients and 9.5% of male patients had Bethesda II, which was the most common score in the sample. For Bethesda III, 78.1% of female patients and 21.9% of male patients had this score. Similarly, for Bethesda IV, 87% of female patients and 13% of male patients had this score. For Bethesda V, 96% of female patients and 4% of male patients had this score. Finally, for Bethesda VI, 87.1% of female patients and 12.9% of male patients had this score.

Table 1: Cross-tabulation distribution – Bethesda and gender.

Bethesda category	Gender		Total	% of each category
	F	M		
Bethesda I				
Number of cases	5	0	5	2.5
% within category	100	0	100	
Bethesda II				
Number of cases	76	8	84	42
% within category	90.5	9.5	100.0	
Bethesda III				
Number of cases	25	7	32	16
% within category	78.1	21.9	100.0	
Bethesda IV				
Number of cases	20	3	23	11.5
% within category	87.0	13.0	100.0	
Bethesda V				
Number of cases	24	1	25	12.5
% within category	96.0	4.0	100.0	
Bethesda 6				
Number of cases	27	4	31	15.5
% within category	87.1	12.9	100.0	
Total				
Number of cases	24	1	25	100
% of all categories	96.0	4.0	100.0	

Table 2: Bethesda classifications, its risk of malignancy and histopathology diagnosis types.

Bethesda	Histopathology diagnosis		Total	Risk of malignancy (%)
	Malignant	Benign		
1				
Count	1	4	5	20.0
% within Bethesda	20.0	80.0	100.0	
2				
Count	12	72	84	14.3
% within Bethesda	14.3	85.7	100.0	
3				
Count	6	26	32	18.8
% within Bethesda	18.8	81.3	100.0	
4				
Count	6	17	23	26.1
% within Bethesda	26.1	73.9	100.0	
5				
Count	21	4	25	84.0
% within Bethesda	84.0	16.0	100.0	
6				
Count	30	1	31	96.8
% within Bethesda	96.8	3.2	100.0	
Total				
Count	76	124	200	38.0
% within Bethesda	38.0	62.0	100.0	

Table 2 shows that out of the 200 patients in the study population, 124 (62%) had a benign histopathology report, and 76 (38%) were malignant. The distribution of Bethesda scores varied significantly between the two diagnosis types. Specifically, for Bethesda I, 20% of patients had a malignant diagnosis, while 80% had a benign diagnosis. For Bethesda II, out of 84 samples, 72 were actually benign, while 12 turned out to be malignant,

making the risk of malignancy 14.2% in that sample with a 12 false positives as shown in Table 3. For FNAC samples with atypia of undetermined significance or follicular lesion of undetermined significance, 6 out of 32 were malignant, with a 18.75% risk of malignancy in that group. As for FNAC samples with follicular neoplasm or suspicious for a follicular neoplasm, 6 out of 23 were malignant, making the risk of malignancy 26.1%. For FNAC samples with a suspicion for malignancy, 21 out of 25 were malignant, making the risk of cancer 84.0% and 4 false negatives, while for malignant FNACs, 30 out of 31 were correctly labeled as malignant with a 96.8% risk of cancer in this category and 1 false negative.

As demonstrated in Table 3, to properly assess the sensitivity and specificity of the FNAC in comparison to the histopathology, we needed to exclude undetermined results. Therefore, Bethesda II were categorized as benign, and Bethesda V and VI were categorized as malignant. Our FNAC data achieved an 80.95% sensitivity, specificity of 93.51% specificity, and a total accuracy of 87.86%. The positive predictive value was 91.07%, and an 85.71% negative predictive value.

Table 3: Final FNAC versus histopathology results.

FNAC	Histopathology result		Total
	Benign	Malignant	
Benign	72	12	84
Malignant	5	51	56
Total	77	63	140

Table 4: Accuracy measures of FNAC compared to histopathology reports.

Parameters	Percentage
Sensitivity	80.95
Specificity	93.51
Positive predictive value (PPV)	91.07
Negative predictive value (NPV)	85.71
Total accuracy	87.86

DISCUSSION

FNAC is an essential part in the work-up of thyroid nodules. It can differentiate between benign and malignant nodules with varied, but for the most part, accurate results. Its effectiveness in the guidance of therapy of thyroid nodules led to more operated malignant lesions.[10] However, evaluating its reliability is essential in each center as well as comparing results with ones from all around the world. In this study, we correlate FNAC results of thyroid nodules to the final histopathology in a 5-years-period in Salmaniya Medical Complex, Bahrain.

The study results showed that out of all benign FNACs, 72 (85.7%) were actually benign, yielding 12 (14.3%) false positives. While out of all the malignant FNACs, 51 (91.1%) were, in fact, malignant, with 5 (8.9%) false negatives. If we delve deeper into each FNAC category's risk of malignancy and compare it to the available literature, Table 6, our results showed higher rates of malignancy in category I compared to the data from published series. This can be partially attributed to poor sampling techniques as well as unsatisfactory sample preparation and preservation, especially from cystic lesions.[12]

The category II also had a higher rates of malignancy in our study, 14.3% compared to 3.7 % in a large meta-analysis conducted by Bongiovanni et al literature as shown in Table 5.[13] Abou-Foul et al highlighted that the majority of the false-negative cases in this category were in lesions <1 cm, which can further explain the sampling challenges of smaller lesions. Moreover, the risk of malignancy figures can be skewed dramatically due to selection bias in patients with category I and II results, as they only undergo surgery if they show suspicious clinical or radiological features; as some studies found that only 10% of patients with benign cytologic findings underwent surgery, making it challenging to determine the valid rate of false-negative results.[8,13,14]

The limitation of FNAC to precisely identify follicular pattern lesions and cystic papillary thyroid carcinoma (PTC) was also reported.[15] It is thought to be due having similarities between papillary cancer and conditions such as adenomatous goiter, thyroiditis, nodular goiter, and follicular neoplasm.[16] Therefore, we agree with the published guidelines that advocate repeating FNAC for all patients in category I and II with suspicious clinical or radiological features. Table 6 summarizes the recommended clinical action for each Bethesda category.[17]

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Table 5: FNAC cytology categories and the implied risk of malignancy in our study and the published literature.

FNAC category	Risk of malignancy (%)		
	Bethesda system guidelines	Bongiovanni et al.; pooled %	Current study
I: Non-diagnostic or unsatisfactory	5 – 10	16.8	20
II: Benign	0 – 3	3.7	14.3
III: Atypia of undetermined significance /follicular lesion of undetermined significance	6 – 18	15.9	18.8
IV: Follicular neoplasm / suspicious for follicular neoplasm	10 – 40	26.1	26.1
V: Suspicious for malignant	45 – 60	75.2	84
VI: Malignant	94 – 96	98.6	96.8

Table 6: Recommended clinical actins for each Bethesda category.

Bethesda category	Recommend clinical action
I: Non-diagnostic or unsatisfactory	Repeat FNA with ultrasound-guidance
II: Benign	Clinical and sonographic follow up
III: Atypia of undetermined significance / follicular lesion of undetermined significance	Repeat FNA, molecular testing or lobectomy
IV: Follicular neoplasm / suspicious for follicular neoplasm	Molecular testing, lobectomy
V: Suspicious for malignant	Near-total thyroidectomy or lobectomy
VI: Malignant	Near-total thyroidectomy or lobectomy

Although our results demonstrate similar rates of malignancy higher rates of malignancy patients with category III, IV and VI, they show higher rates of malignancy in patients with category V results.

Our FNAC data achieved an 80.95% sensitivity, specificity of 93.51%, and a total accuracy of 87.86% with a positive predictive value of 91.07%, and a negative predictive value 85.71%. These results were comparable with the results from other published series. Sharma et al. estimated sensitivity, specificity, and accurate of FNAC of 84%, 100%, and 90%, respectively.[11] While Hawkins et al values were 86.3%, 95.3%, and 93.7%.[18] Alhassan et al estimated values were 80.2%, 98.9%, and 89.9%, respectively.[5] The diagnostic accuracy was found to be 87.86% which is lower than Frable and Singh et al who reported a diagnostic accuracy of 94% and 95.71%, respectively.[10]

The main limitation of the study is being a retrospective single-center study with a small sample size size due to the strict selection criteria of cytology-histopathology correlation, excluding numerous FNAC results without final Histopathology diagnosis. Another limitation of the study is the lack of thyroid nodules size, which might affect the accuracy of the FNAC results.

CONCLUSION

In conclusion, FNAC remains the most accurate and cost-effective method for evaluating thyroid nodules. However, its diagnostic value varies among different institutions. Our results demonstrated higher rates of malignancy compared to other published series in both categories I and II. Due to the chance of false negative rates in these 2 categories and the slow-growing nature of thyroid malignancy, it is important that patients with benign FNAC should have periodic clinical and radiological follow up.

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