

Cyto-Histopathological Diagnosis of the Thyroid Lesions: A Comparative Study.

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Abstract

Fine-needle aspiration cytology FNAC is the single most important diagnostic test for the evaluation of patients with thyroid lesions, it has been almost universally recognized as constituting the most significant advance of the past 20 years in the diagnostic evaluation of patients who present with palpable nodules of the thyroid gland. In this study, the effectiveness of fine needle aspiration cytology was evaluated through the identification of the correlation between the cytology diagnosis of thyroid fine needle aspiration cytology and the postoperative histopathological diagnosis. This is a retrospective study was performed on 80 cases underwent to both thyroid cytological and histopathological diagnosis, reports were retrieved from pathology archive of Aden Diagnostic Center/ Aden Governorate, during the period of 2012-2013. The inclusion criteria is that all patients, irrespective of sex and age; having thyroid lesion, diagnosed cytologically and confirmed histologically. Whereas the exclusion criteria: (1) Patients having history of recurrent thyroid carcinoma after lobectomy (2) patients who underwent fine needle aspiration cytology but did not undergo subsequent histopathological diagnosis (3) patients undergoing chemotherapy. Cytological study results in (85%) benign and (15%) malignant cases, while histological examination revealed (64%) benign cases and (16%) malignant cases. The most common benign lesion diagnosed by both cytologically and histologically was colloid goiter (63.7%) and (56.2%) respectively, followed by follicular adenoma, cytologically(15%) and histologically (21.25%), while Hashimotos` thyroiditis was the less common lesion which is, by cytological diagnosis (6.25%) and by histological diagnosis (2.5%). The main malignant lesion was papillary carcinoma, (15%) of the cases were diagnosed cytologically and (20%) were diagnosed histologically. Fine needle aspiration cytology sensitivity was (62.5%), specificity (97%), Positive predictive value (83.3%), negative predictive value (91.1%), and accuracy (90%). Benign lesions were the most common than malignant, as diagnosed by both cytologically and histologically. The most common benign lesion diagnosed by both methods was colloid goiter, followed by follicular adenoma. The main malignant lesion was papillary carcinoma by methods of diagnosis. False negative cases represent 7.5% and false positive represent 2.5%. Statistical analysis for cytological diagnosis revealed that it was moderately sensitive, highly specific, and accurate. So it is recommended to be applied as routine preoperative investigation.

Keywords: Thyroid lesions, benign thyroid lesions, malignant thyroid lesions, cytological and histological diagnosis.

Introduction

Around 5% of the population have a goiter or benign thyroid lump or enlargement. Up to 50% most thyroid lesions are benign, but some may produce excess thyroid hormone and other thyroid lumps may be cancerous [5].

Despite the improvement in the diagnosis of thyroid lesions using ultrasonography and radio-nucleotide scanning, fine needle aspiration cytology (FNAC) of thyroid is still the method of choice to conclusively prove the diagnosis of cancer[2]. It is the single most important diagnostic

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test for the evaluation of patients with thyroid lesions because it is a simple and safe procedure that has been almost universally recognized as constituting the most significant advance of the past 20 years in the diagnostic evaluation patients who present with palpable nodules of the thyroid gland[3].

Fine needle aspiration cytology (FNAC) is a well-established technique for pre-operative investigation of thyroid nodule(s) [22]. The technique is the most noninvasive, cost-effective and efficient method of differentiating benign and malignant thyroid nodules [14].

The fine needle aspiration cytology (FNAC) of the thyroid is the predominant method of preoperative tissue diagnosis of thyroid lesions. The routine use of FNAC has reduced the rate of unnecessary surgery for thyroid nodules [8]. Early diagnosis still maintains its importance for higher life expectancy due to the low malignant potential of thyroid nodules and slow progressing characteristics of thyroid gland cancers [17].

Objective: The purpose of the present study is to compare the cytological diagnosis with the final postoperative histological diagnosis in order to evaluate the effectiveness of FNAC in the diagnosis of thyroid lesions.

Material and methods: This is a retrospective study performed on 80 patients underwent thyroid cytological examination, compared with histopathological results for the same patients. FNAC and histopathologic reports were retrieved from pathology archive of Aden Diagnostic Center/ Aden Governorate, during the period of 2012-2013,

Inclusion criteria were FNAC and histopathological examination was performed for each patient with thyroid lesion, regardless the sex and age. Exclusion criteria were: (1) Patients having history of recurrent thyroid carcinoma after lobectomy (2) Patients who underwent FNAC but not performed subsequent histopathological diagnosis, and (3) Patient experienced chemotherapy.

Ethical consideration: Permission of Aden Diagnostic Center authorities. The obtained data were analyzed manually to determine the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of FNAC findings. The following values concerning the diagnostic accuracy were calculated in this study.

Measurement of validity [11]:

Sensitivity: The sensitivity of a diagnostic test refers to the ability of the test to correctly identify those patients with disease.

Specificity: The specificity of a diagnostic test refers to the ability of the test to correctly identify those patients without disease.

Measurement of feasibility:

Positive Predictive value: The probability of having malignancy when the results of FNAC are positive.

Negative Predictive value: the probability that a tumor is benign when the results of FNAC are negative.

Accuracy: the proportion of true results (namely true positive - true negative) among all results.

True positive: the patients has the disease and the test is positive

False positive: the patient does not have the disease but the test is positive.

True negative: the patient does not have the disease and the test is negative.

False negative: the patient has the disease but the test is negative.

Equations of the diagnostic test [18]:

$$1) \text{ Sensitivity} = \frac{\text{true positive}}{\text{true positive} + \text{false negative}}$$

$$2) \text{ Specificity} = \frac{\text{true negative}}{\text{true negative} + \text{false positive}}$$

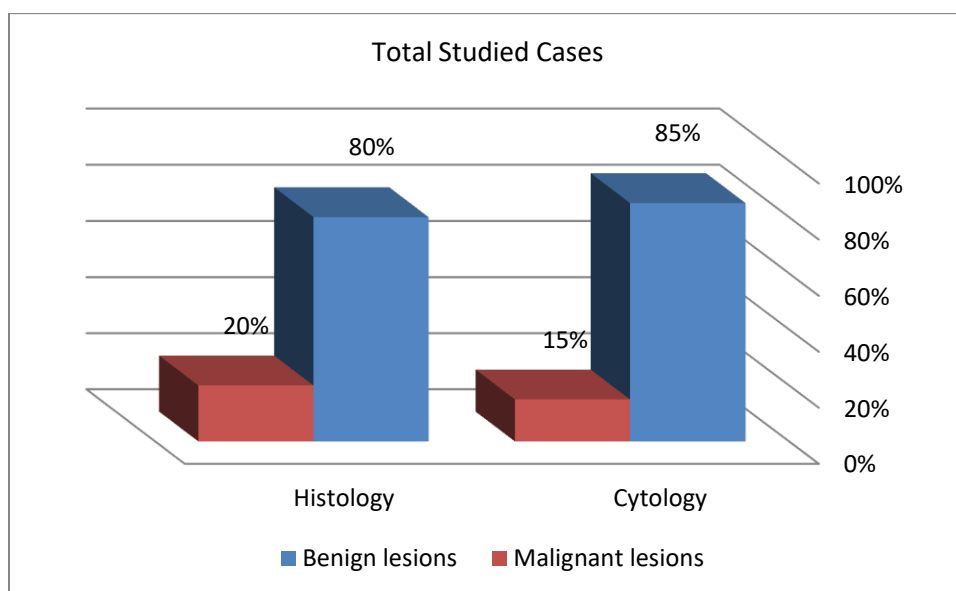
$$3) \text{ Positive Predictive Value} = \frac{\text{true positive}}{\text{true positive} + \text{false positive}}$$

$$4) \text{ Negative Predictive Value} = \frac{\text{true negative}}{\text{true negative} + \text{false negative}}$$

$$5) \text{ Overall Accuracy} = \frac{\text{true positive} + \text{true negative}}{\text{True positive} + \text{false positive} + \text{true negative} + \text{false negative}}$$

$$6) \text{ Unsatisfactory rate} = \frac{\text{false positive} + \text{false negative}}{\text{True positive} + \text{false positive} + \text{true negative} + \text{false negative}}$$

Results



Graph 1: Total studied cases

Graph 1 shows that the total benign lesions diagnosed by cytology were 68 cases, represented (85%). While the malignant lesions were 12 cases representing (15%). On the other hand, the histological diagnosis reveals that 64 cases (80%) were benign lesions and 16 (20%) were malignant lesions.

Table 1: Thyroid lesions diagnosed by cytology and histology

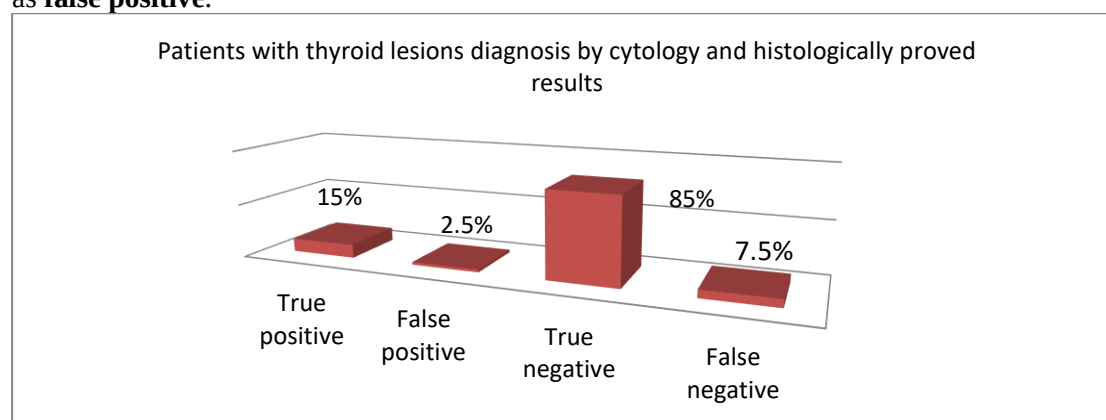
Type of lesion	Cytology diagnosed cases		Histology diagnosed cases	
	No.	%	No.	%
Benign lesions				
Colloid goiter	51	63.75	45	56.25
Hashimoto's thyroiditis	5	6.25	2	2.5
Follicular adenoma	12	15.0	17	21.25
Malignant lesions				
Papillary carcinoma	12	15.0	16	20.0
Total	80	100	80	100

Table 1reveals that the thyroid lesions diagnosed by both cytological and histological methods. Cytology, the colloid goiter were represent 51cases (63.75%), Hashimotoś thyroiditis 5 cases(6.25%),follicular adenoma 12 cases (15%), while papillary carcinoma represent 12 cases (15%).On the other hand, the histology reveals that the colloid goiter was 45cases(56.25%), Hashimotoś thyroiditis 2 cases (2.5%),follicular adenoma 17 cases(21.25%), while papillary carcinoma were 16 cases (20%)

Table 2: patients with thyroid lesions by cytology and histology results

Cytology	Histology									
	Colloid goiter		Hashimotos` thyroiditis		Follicular adenoma		Papillary carcinoma		Total●	
	No.	%	No.	%	No.	%	No.	%	No.	%
Colloid goiter	37	46.25	0	0.0	11	13.7	3*	3.75	51	63.7
Hashimotos`thyroiditis	3	3.75	1	1.25	0	0.0	1*	1.25	5	06.3
Follicular adenoma	5	6.25	1	1.25	4	5.0	2*	2.5	12	15.0
Papillary carcinoma	0	0.0	0	0.0	2**	2.5	10	12.5	12	15.0
Total●●	45	56.25	2	2.5	17	21.2	16	20.0	80	100
<i>*false negative cases (6), **false positive cases(2)</i> <i>Total ● of rows,</i> <i>Total ●● of columns</i>										

Table2:Shows the cytological and histological diagnosis for each thyroid lesion; by cytological diagnosis, colloid goiter which are 51 cases (63.7%), 37 cases (46.25%) of them confirm histologicallyas colloid goiter, while 11 cases (13.7%) of colloid goiter diagnosed by histology as follicular adenoma, and 3 cases(3.75%) of colloid goiter were approved as papillary carcinoma, they are considered as **false negative**. By cytology, Hashimotoś thyroiditis 5 cases (6.25%),while by histology only one case (1.25 %) confirmed as Hashimotos`thyroiditis, other 3 cases representing (3.75) diagnosed as colloid goiter, and one case (1.25%) diagnosed as papillary carcinoma; considered as **false negative**. 12 cases diagnosed cytologically as follicular adenoma representing (15%), by histological diagnosis 4 cases (5%) were diagnosed as follicular adenoma, Hashimotoś thyroiditis one case (1.25%), and papillary carcinoma two cases (2.5%) which are considered as **false negative**. Out of 12 patients diagnosed as positive malignancy by cytology, only 10 (12.5%)of them were proved as positive malignancy by histology and were considered as true positive (10 cases), other 2 cases were proved as benign by histology and therefore, considered as **false positive**.



Graph 2:Patients with thyroid lesions diagnosis by cytology and histologically proved results

Graph 2Shows that the true positive were15 %, while the true negative represented 80%. On the other hand 2.5 % and 7.5 % diagnosed as false positive and false negative respectively.

Equations of Diagnostic Test:

1-Sensitivity = True positive/True positive +false negative $\times 100$

=10/ (10 +6) $\times 100$ = **62.5%**

2-Specificity =True negative/True negative + False positive $\times 100$

= 62/62+ 2 $\times 100$ = **96.88%**

3-Positive predictive value =True positive/ True positive +false positive $\times 100$

=10/10 +2 $\times 100$ =**83.33%**

4-Negative predictive value= True negative/ Truenegative +false negative $\times 100$

=62/62+6 $\times 100$ = **91.17%**

5-Accuracy =True positive + true negative/Total number of cases $\times 100$

=10 + 62/ 80 $\times 100$ =**90%**

6-Unsatisfactory rate: is the portion of the incorrect results, false positive and false negative in relation to all cases studied =false positive + false negative/Total number of cases $\times 100$

= 2+6/80 $\times 100$ = **10%**

Table 3: Performance and predictive values of FNAC diagnosis

Values	%
Sensitivity	62.5
Specificity	96.88
Positive predictive value	83.3
Negative predictive value	91
Unsatisfactory rate	10
Overall accuracy of the test	90

Table 3 shows that the proportion of patients classified with the test, calculated the proportion of true results (Overall Accuracy) was 90% and conversely, the unsatisfactory rate was 10 %. The capacity to detect the malignancy given by the sensitivity was 62.5% and the capacity to detect benign given by the specificity was 96.8%.

The probability of being malignancy with positive test, Positive Predictive Value was 83% and the probability of being benign with negative test, Negative Predictive Value was 91%.

Discussion

The total number of studied cases were 80, the benign cases diagnosed cytologically were (85%), and malignant cases (15%), while by the histological diagnosis the benign were (80%) and malignant cases (20%).Our results were consistent with the results of a study performed by Gulia et al.,[6] who reported that the benign lesion represents(82.85%) and malignant cases (15.72%), also the study performed by Hirachand et al.,[10] showed that the benign lesions were(91.57%) and the malignant were (5.86%).In the Swamys` et al., study[21], the cytological results showed that (83.66%) were benign and (16.66%)were malignant, histological examination showed that (81.66%) were benign, and (18.33%) were malignant.

Colloid goiter was the common benign lesion representing (85%), and (80%) by histological examination, this result is in line with the results of Gulia et al.,[6]Hirachand et al.,[10]Sinna& Ezzat,[20]Esmaili&Taghipour, [4]considered that the colloid goiter is the most common benign lesion.

Hashimotos` thyroiditis representing the less common benign lesion was seen in (6.25%) by cytological examination and 2.5% by histological examination, this result is compatible with the

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result of a study done by Esmaili& Taghibour,[4]reported that Hashimotos` thyroiditis 5.2% by cytological examination, Gulia et al.,[6] who reported that Hashimotos` thyroiditis represents 3.51% of the total cases as diagnosed cytologically.

In our study, it is found that the second common benign lesion was follicular adenoma (by cytological diagnosis was (15%), and (21.25%) by histological diagnosis), which was in line with Sinna& Ezzat,[20] study, who reported that follicular adenoma represented 24.59% by FNAC diagnosis, while Hirachand,[10] reported that follicular adenoma which diagnosed by FNAC represent 1.10% only. Swamy et al.,[21] who reported that the common benign lesion in both cytological and histological was colloid goiter then follicular adenoma.

Papillary carcinoma was the only one type of malignant tumors in our study which represent (15%) of cases which were diagnosed cytologically, and in 20% of the cases that were diagnosed histologically, this result is in consistent with a result of a study performed by Hajmanoochehri& Rabiee, [9] who reported that papillary carcinoma represents the major type of malignancy forming 84.6% from the total cases of malignant lesions. Gumlu et al.,[7] reported that the papillary carcinoma is the more common in the cases of thyroid swelling diagnosed by FNAC.

Out of the total, diagnosed cytologically as colloid goiter(51), there were 3 cases (3.75%) diagnosed as papillary carcinoma, which considered as false negative cases, one case(1.25%) also diagnosed histologically as papillary carcinoma from the total 5 cases diagnosed cytologically as Hashimotos`thyroiditis, which were considered as additional false negative case, additional two cases(2.5%) of false negative cases were seen in histological diagnosis of the previously and cytologically diagnosed (12 cases) as follicular adenoma, so the total false negative cases were 6 (7.5%).This result was in line with Esmaili& Taghipour,[4]and Gulia et al.,[6] results, who reported 4 cases as false negative,, while Sikder et al.,[19] reported 8 cases of false negative. Gulia et al., [6] reported that the incidence of false negative usually attributable to overlooking of malignancy in favor of follicular adenoma, cystic lesions, and Hashimotos` thyroiditis.The false negative rate is defined as the percentage of patients with benign cytology in whom malignant lesions are later confirmed on thyroidectomy. The false negative FNAC results may occur because of sampling error, coexistence of benign and malignant lesions, or cytomorphologic overlap between benign and low grade malignant tumors [21].

Two cases out of the total 12 cases of follicular adenoma by FNAC, were diagnosed histologically as papillary carcinoma which was considered as false positive cases. Our result is consistent with Sharma [18] and Sikder et al.,[19] who reported 2 false positive cases.Swamy et al.,[21]also reported 4 cases false positive. Gulia et al.,[6]reported that the false positive diagnosis is the result of misinterpretation of the nature of benign cell than a sampling error, false positive diagnosis are usually encountered in Hashimotos` thyroiditis, follicular adenoma, and colloid goiter. The false positive rate indicates that a patient with malignant FNAC result was found on histological examination to have benign lesion [21].

Regarding the sensitivity, specificity, diagnostic accuracy, PPV and NPV of cytological method of diagnosis, our results showed that the sensitivity is 62.5% which was similar with the results of Afroze et al.,[1]61.9%, and higher than Mudasal et al.,[12] 52%,it was less than Sinna &Ezzat,[20] 92.8% Esmaili &Taghipour[4] 91.6% in Iran, and Gulia et al.,[6] 80%.The differences could be explained by the different study design, different instruments for data collection. The specificity of FNAC in our study was 96.88%, it was higher than Swamy, et al.,[21](83%) and Sinna & Ezzat,[20](94.2%) and Mudasal et al.,[12](86.6%), and similar with Sharma,[18](98%) and Rabia et al.,[16](97.7%), and less thanEsmaili& Taghipour, [4] Sikder, et al,[19]and Bagga &Mahaian [2]all of them report 100%. Positive predictive value PPV of our study was 83.3%, it was higher than Rabia, et al.,[16] 80% and Swamy, et al.,[21]81.8%, it is approximately near to Sharma [18]84.6%, and less than Sinna & Ezzat [20](95%),Gulia et al.,[6] 100%. Negative predictive value NPV of our study was 91%, it was equal to Sinna &Ezzat(91.8%) [20], near to Afroze, et al.,[1](92.8%); & Gulia, et al., [6](90.5%), and higher than Sikder et al.,[19](87.2%), and less than Sharma [18](98.6%) and Rabia, et al.,[16](97.7%). The diagnostic accuracy was 90%, it was similar to Sikder, et al., [19]90%,Gulia, et al.,[6]92.3%, and less than Sharma [18] (97%), and Swamy et al.,[21] (96.6%).We conclude that statistical analysis for cytological diagnosis reveals

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moderate sensitivity, highly specificity, and accurate, which allow for early diagnosis, treatment, and management of thyroid lesions, especially malignant tumors.

Conclusion: Benign lesions were the most common thyroid lesion, as diagnosed by both cytologically and histologically. The most common benign lesion diagnosed by both methods is colloid goiter, followed by follicular adenoma. The main malignant lesion is papillary carcinoma by both methods of diagnosis.

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التشخيص الخلوي - النسيجي لإصابات الغدة الدرقية (دراسة مقارنة)

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الملخص

فحص الخلايا بطريقة السحب بالإبرة الدقيقة يُعد لفحص الأهم لتشخيص حالات المرضى المصابين بالعقدة الدرقية، ويشكل تقدماً مهماً في السنوات العشرين الأخيرة في تشخيص وتقييم حالات مرضى الغدة الدرقية. هدف الدراسة هو المقارنة بين نتائج الفحص الخلوي والفحص النهائي النسيجي لنسيج الغدة الدرقية، وذلك لمعرفة وتحديد دقة الفحص الخلوي بالسحب بالإبرة. دراسة ارتجائية لـ 80 نتيجة فحوصات لأمراض الغدة الدرقية التي تم تشخيصها بكلتا الطريقتين بالفحص الخلوي بواسطة الفحص بالإبرة وفحص الأنسجة لكل حالة. جُمعت الحالات من أرشيف مركز عدن التشخيصي في مدينة المنصورة بمحافظة عدن، خلال المدة 2012-2013م. مواصفات حالات البحث: كل المرضى بغض النظر عن الجنس والعمر الذين يعانون مرض الغدة الدرقية وخضعوا لكلا الفحصين، المعايير المستبعدة: 1- المرضى الذين يعانون من تكرار حدوث الورم السرطاني للغدة الدرقية، 2- المرضى الذين خضعوا لفحص التشخيص الخلوي ولم يخضعوا للفحص النسيجي 3- المرضى الخاضعين للعلاج الكيماوي. العدد الكلي لنتائج الحالات المختارة للدراسة هي 80 حالة التي أخضعت للفحص بكلتا الطريقتين، نسبة الحالات الحميدة بالفحص الخلوي 85% وحالات الأورام الخبيثة 15%، بينما بالفحص النسيجي كانت نسبة الأمراض الحميدة 80% والخبيثة 20%. المرض الحميد الأكثر شيوعاً هو تضخم الغدة الغروي بنسبة 63.75% بالفحص الخلوي ونسبته بالفحص النسيجي 56.25%، ثم يليه الورم الغدي الحميد بنسبة 15% بالفحص الخلوي و21.25% بفحص الأنسجة، بينما كان الأقل شيوعاً الالتهاب المناعي للغدة الدرقية (الهاشيموتو) شكل نسبة 6.25% بالفحص الخلوي و2.5% فقط بالفحص النسيجي. بالنسبة للأورام السرطانية وجدنا بأن الورم الوحيد هو الدنف السرطاني الحليمي الذي شكل نسبة 15% بالفحص الخلوي و20% بالفحص النسيجي. التحليل الإحصائي أظهر بأن حساسية الفحص الخلوي 62.5% والخصوصية 96.9%، القيمة التوقعية الإيجابية 83.3%، القيمة التوقعية السلبية 91% ودقة الفحص الخلوي 90%.

من خلال دراستنا، وجدنا بأن استعمال الفحص الخلوي لإصابات الغدة الدرقية أظهر حساسيته المتوسطة وخصوصيته ودقته العالية في التشخيص وقد كانت نتائج فحص الخلايا قريبة جداً لنتائج فحص الأنسجة التأكيدية النهائية. نوصي أنه لا بد من تطبيق التشخيص الخلوي كفحص روتيني قبل إجراء العمليات الجراحية.

الكلمات المفتاحية: إصابات الغدة الدرقية الحميدة، إصابات الغدة الدرقية الخبيثة، التشخيص الخلوي، التشخيص النسيجي.