The diagnostic value of fine needle aspiration cytology in thyroid swellings in a University Hospital, Yemen

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ABSTRACT

Objective: To evaluate the correlation between the fine needle aspiration (FNA) cytology and the histopathological findings in cases of the thyroid swellings and to assess the accuracy of cytological examination of thyroid nodules.

Methods: This study was carried out at Kuwait University Hospital, Sana'a, Yemen. There were 243 thyroid FNAs of which 199 had subsequent excisional histopathological examination in the period 1997 to 2001. All the records of cytology and histology were reviewed. Cases were classified into 6 subsets: benign follicular lesion, thyroiditis, follicular neoplasm, suspicious for papillary carcinoma, malignant, and non-diagnostic aspirate. For statistical analysis, we excluded cases, which had not had subsequent histopathological examination (n=44), and cases with non-diagnostic aspirate (n=3), so only the histology and medical records of 196 cases were reviewed and correlated with the cytology results.

Results: There were 156 (78.4%) cases of benign aspirate, 31 (15.6%) cases of follicular neoplasm, 4 (2%) cases that were suspicious for papillary carcinoma, 4 (2%) cases of papillary carcinoma, and 3 (1.5%) cases of non-diagnostic aspirates. The 196 cases, which underwent cytological and histopathological examinations, were classified as non-neoplastic and neoplastic (including follicular neoplasm and malignancy) according to postoperative histopathology and correlation which, was carried out with preoperative cytology. There were 115 true negatives, 26 true positives, 42 false negatives, and 13 false positives. This gives a sensitivity of 38%, specificity of 89.9%, positive predictive value of 66.7%, negative predictive value of 73.2%, and accuracy of 72%.

Conclusion: The sensitivity of FNA cytology in this study is very low compared to published studies, which had adversely affected the surgical decision making as well as the outcome. We should realise that negative FNA cytology does not exclude malignancy and we have to seriously evaluate the situation and to rethink on how to raise the scale of sensitivity in FNA cytology in the diagnosis of thyroid nodules, and to improve the level of expertise in cytology.

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The management of thyroid swellings remains a clinical problem, especially in the light of the difficulties in the differentiation between benign and malignant lesions. It has been reported that thyroid nodules occur in 4-7% of the population,[1] but the situation is completely different in this region, since it is an endemic area with goitre, and the total goitre rate has been estimated recently to be 16.8%.[2] Excision of all thyroid nodules is impractical, as most thyroid nodules are benign and thyroid surgery has got its own risks. Therefore, an effective screening test is needed to identify those who need surgery, and this has been

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achieved by fine needle aspiration (FNA) cytology, which has been advocated as the first investigation of choice when assessing thyroid nodules.[3]

Fine needle aspiration cytology is simple, and a non-expensive procedure whereby we try to detect those nodules containing malignant growth. On the basis of the current literature, it's a well-established diagnostic procedure, which is used, in the initial screening for patients with thyroid nodules, and has become the diagnostic tool of choice in the initial evaluation of thyroid nodules. It has been shown that this procedure has reduced the number of patients requiring surgery for non-neoplastic lesions from 40-3% of the screened population.[4,5] In the management of thyroid patients in Yemen, this procedure is of paramount importance as the endemicity of goitre and due to the high percentage of malignancy among Yemeni goitre patients, which were found in one series to be as high as 30%.[6]

In this study we are trying to evaluate the effectiveness of FNA cytology to detect neoplastic lesions of the thyroid gland by presenting an analysis of the results of FNA cytology and those results obtained by histopathological examination and make a comparison between the 2 procedures in a 5-year period at the Kuwait University Hospital (KUH), Sana'a, Yemen. This is regarded as the first study on FNA cytology of the thyroid in Yemen.

Methods. The clinical data was collected from the clinical records of patients in KUH who had FNA cytology due to thyroid swelling (n=243) in the last 5 years (1997 to 2001). The procedures were carried out by pathologists, using aspiration technique. No ultrasonic imaging guidance was used.

Diagnostic categories. Cytological diagnoses have been classified in 6 subsets: benign follicular lesion (including colloid and nodular goitre, and hyperplasia), thyroiditis, follicular neoplasm, suspicious for papillary carcinoma, malignant, and non-diagnostic aspirate. Non-Diagnostic aspirates are those with non-adequate smear (adequate smear is defined as the presence of 6 clusters of follicular cells, with 10 cells per cluster) all patients who underwent both procedures, that is FNA cytology and histopathological evaluation have been included in this study; we excluded cases with non-diagnostic aspirates (n=3). The reports of histopathology of these cases (n=196) were reviewed and correlated with the cytology results.

Data were entered into a spreadsheet of statistical package for social sciences software for statistical analysis (Version 10.0). For the purpose of statistical analysis all of the subsets were classified into 2 categories: non-neoplastic (benign and thyroiditis subsets), and neoplastic (follicular neoplasm, suspicious for papillary carcinoma and malignant). True negative (TN) cases were reported as being non-neoplastic by FNA cytology; they were also shown to be benign following histological examination. False negative (FN) cases were reported as being benign by FNA cytology but were shown to be neoplastic (including follicular adenoma) following histological examination. True positive (TP) cases were reported as having neoplastic lesion (follicular neoplasm, suspicious for papillary carcinoma or malignant) by FNA cytology and were neoplastic (including follicular adenoma) following histological examination. False positive (FP) cases were reported as neoplastic by FNA cytology but were shown to be non-neoplastic following histological examination. The sensitivity, specificity, positive & negative predictive values, and diagnostic accuracy, were calculated.

Results. There were 243 FNA cytology samples from 219 females (90.1%) and 24 males (9.9%). The mean age was 36.36 ± 11.95 years (range 14-80 years). The diagnostic categories of all FNAs carried out are shown in **Table 1**. During the same study period, follow-up histological information was available for 199 (82%) of all FNA cytology cases, 3 cases had non-diagnostic aspirate. **Table 2** depicts the cytology-histology correlation of 196 cases, which underwent both procedures, after exclusion of the 3 cases with non-diagnostic aspirates. Of the 3 non-diagnostic aspirates, 2 cases were diagnosed as colloid goitre and one case as papillary carcinoma. Follow up biopsy specimens showed that there were 13 cases of false positive cases, 10 cases of which showed nodular and colloid goitre, and 3 cases showed thyroiditis. There were 42 cases of false negative, which were diagnosed by FNA cytology as being benign, but histopathological examination showed 22 cases of papillary carcinoma and 18 cases of follicular adenoma. There were 26 cases with true positive results and 115 cases with true negative results. **Table 3** shows the summary of the statistical analysis and the calculated values of sensitivity, specificity, positive and negative predictive values, and accuracy of FNA cytology in the diagnosis of neoplastic lesions. The false negative rate is 61.8%, and the false positive rate is 10%. Sensitivity in the diagnosis of papillary carcinoma is 15.4%, cases with false negative cytological diagnoses showed the following histopathological results: 22 cases diagnosed to have colloid or nodular goitre, and 9 cases as follicular neoplasm. The diagnostic sensitivity of follicular neoplasm was 35.5%.

Discussion. Fine needle aspiration cytology of the thyroid gland is considered as the most effective screening test for investigating thyroid nodules and extremely sensitive with a high specific diagnostic field in experienced hands. Unfortunately, sensitivity and specificity of this procedure are lower in thyroid gland if compared to other organs as of the inability to diagnose some malignancies as follicular carcinoma, that their cells are morphologically and cytologically similar to those of follicular adenoma. Nevertheless, there is a

Table 1 - Diagnostic categories of fine needle aspiration of the thyroid (N=234).

Diagnosis	n of samples (%)
Benign follicular lesion	184 (75.7)
Thyroiditis	7 (2.9)
Follicular neoplasm	36 (14.8)
Suspicious for papillary carcinoma	4 (1.6)
Papillary carcinoma	7 (2.9)
Non-diagnostic*	5 (2.1)
Total	**243 (100)**

* Aspirates which are inadequate, for example < 6 clusters of cells, each of 10 cells

Table 2 - Cytohistological correlation of fine needle aspirations of the thyroid (N=199).

	Histopathology					
FNA Cytology	**Multinodular & colloid goitre**	**Follicular adenoma**	**Papillary carcinoma**	**Thyroiditis**	**Diffuse hyperplasia**	**Total**
Benign follicular lesion	98	18	22	8	5	**151**
Thyroiditis	2	2	-	2	-	**6**
Follicular neoplasm	9	11	9	2	-	**31**
Suspicious for PA	1	-	2	1	-	**4**
Papillary carcinoma	-	-	4	-	-	**4**
Non-diagnostic	2	-	1	-	-	**3**
Total	**112**	**31**	**38**	**13**	**5**	**199**

PA - papillary carcinoma, FNA - fine needle aspiration

Table 3 - Summary of statistical analysis (N=196).

	Histology	
Cytology	**Neoplastic**	**Non-neoplastic**
Neoplastic	26 (TP)	13 (FP)
Non-neoplastic	42 (FN)	115 (TN)

Sensitivity = (TPx100) / (TP+FN) = 38%

Specificity = (TNx100) / (TN+FP) = 89.8%

Positive predictive value = (TPx100) / (TP+FP) = 66.7%

Negative predictive value = (TNx100) / (TN+TN) = 73.2%

Accuracy = [(TP+TN)x100] / (TP+TN+FP+FN) = 72%

3 cases with non-diagnostic aspirates were excluded
TP - true positive, FP - false positive
TN - true negative, FN - false negative

Table 4 - Results from previous studies of fine needle aspiration cytology of the thyroid.

Study	n of FNA cytology	n of histological samples	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
Piromalli et al 1992[12]	795	216	95	97.5	94.5	97	-
Holleman et al 1995[13]	112	53	84	52	53	83	65
Sanders et al 1996[14]	899	345	92	97	-	-	-
Leonard and Melcher 1997[15]	335	184	88	78	46	97	80
Lopez et al 1997[16]	827	827	90	99.8	98	99	99
Bakhos et al 2000[17]	625	625	93	96	-	-	-
Present study	243	196	38	89.9	66.7	73.2	72

FNA - fine needle aspiration

range of FNA cytology sensitivities and specificities that any centre should check if its corresponding results fall within the reported range. Yemen, as any developing country, is lacking an accepted level of expertise in this field, something that makes it mandatory to continuously monitor and evaluate how valid this procedure is. The sensitivity and specificity of FNA cytology are more than 90%.[7] Nevertheless, numerous studies have cited FNA cytology sensitivity and specificity of different rates. **Table 4** shows comparisons between some studies and the current study in terms of sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. Obviously, the sensitivity of FNA cytology in this study (38%) does not lie within the range of sensitivities in previous studies, which is less than half of any listed sensitivity. Extensive reported experience of FNA cytology in the literature shows a false positive rate for malignancy of less than 2% and a false negative rate of around 5%.[8] This is so far from the results we reached which were 61.8% for false negative rate and 10% for false positive rate. In addition to that, the sensitivity to diagnose papillary carcinoma is much less than reported, which is 85%,[9] whereas in our series it was 15.4%. Many factors interact and might cause this discrepancy between FNA cytology and histopathology. In our setting we believe that the most important factor is the unavailability of experienced cytologists who can correctly and efficiently diagnose the neoplastic lesions by FNA cytology. Other factors which might play a role such as the sampling error, sub optimal material and the coexistence of papillary carcinoma in a diffuse goitre. The false negative rate for neoplasm is high and disappointing, and we should seriously evaluate the reasons of this marked cytohistopathological discordance. It's a difficult decision to take regarding aspirates that are diagnosed as being benign for many reasons: 1. The low sensitivity of the procedure in our setting 2. The high malignancy rate in Yemen among patients with goitre (30%)[6] 3. The unavailability of a careful follow up of patients with benign nodules. So, the patients who are due to have FNA cytology for the thyroid gland should be carefully selected. Clinically, solitary nodules are more common than multinodular goitre according to the published literature,[10] but this is not true in Yemen where most of the cases are with multinodular goitre rather than solitary nodules, so this might decrease the sensitivity of the procedure. Perhaps the FNA cytology will be more yielding if confined to the solitary nodules, since they are more prone to harbor malignancy, and this is a questioned statement since it has been shown that solitary nodules have the same cancer risk as multinodular goitre.[11]

The FNA cytology should be used in conjunction with clinical, laboratory, and radiological evaluation since it is regarded as an adjunct to the work up rather than a diagnostic test, at the same time cases have to be classified according to the risk models, and high-risk groups have to be dealt with aggressively.

It is important to stress that negative FNA cytology does not exclude neoplasm, especially if there are other clinical data suggesting the contrary, so surgical intervention is important in many cases as of the uncertainty and as of the indolence of the disease if not completely resected. The sensitivity of FNA cytology for thyroid nodules in KUH is low if compared with the published studies. Results might be improved if we improve the level of expertise and if clinical picture is taken into consideration, and to select cases to undergo FNA cytology. The clinical picture and imaging studies also should be considered in conjunction with the procedure to increase its sensitivity.

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