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Research Article

CYTOHISTOLOGICAL CORRELATIONS OF THYROID MASSES FINDINGS AT THE MOI TEACHING AND REFERRAL HOSPITAL, KENYA

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ABSTRACT

Thyroid masses are common clinical manifestations with a worldwide prevalence of 4–7% in the general adult population and 0.2% – 1.2% in children. Thyroid nodules are 4 times more common in females than in males and increase in frequency with age. The vast majority of thyroid nodules are benign; fewer than 5% are malignant. The distinction of benign from malignant nodules is fundamental, as it is preferred to operate only on those patients with suspicion of malignancy, while strict patient follow-up is necessary in dealing with benign cases. Fine Needle Aspiration Cytology (FNAC) of thyroidis simple, minimally invasive, cost effective, readily available, time saving and an easy to perform outpatient procedure. The study was carried out at Moi Teaching and Referral Hospital (MTRH); its objective was to assess the FNAC findings of thyroid masses with those of corresponding histological evaluation findings. FNAC and corresponding histological findings for 118 participants who had a pre-operative FNAC and subsequently a thyroid resection for definitive histological diagnosis between January 2007 and December 2014 were accessed from the archives of MTRH pathology laboratory. Therewere88 (74.60%) females and 30 (24.40%) Males; with a male, female ratio of 1:3.Their ages ranged between 17-88 years with a mean of 40.61 and SD of 14.93. Majority of the participants were in their third decade. Of the 118 FNACs, 17(14.40%) were inadequate to make a diagnosis, 14(11.86%) were suspicious for malignancy, and 78 (66.1%) were benign while 9 (7.62%) were malignant. FNAC diagnoses were compared with the corresponding histological evaluation diagnoses for correlations and discrepancies. However the suspicious and inadequate FNAC diagnoses were excluded from statistical calculations analysis owing to their non-diagnostic importance. The concordance, false positive and false negative rates were 90.80%, 3.44% and 5.74% respectively. There was a significant agreement between the two tests (p= 0.34). FNAC of thyroid is accurate and has a low rate of false-negatives and false-positives diagnoses and can be adopted and relied upon in evaluating thyroid nodules, thus reducing the rate of unnecessary surgeries, the cost of health care and the risks associated with surgeries, resulting in better outcome of patients care.

INTRODUCTION

Thyroid nodules are common clinical manifestations, their prevalence varies with the populations studied and the screening method used (Mackenzie and Mortimer, 2004). The reported prevalence is 4–7% in the general adult population and 0.2% - 1.2% in children (Ridgway, 1996). On the screening methods used, numerous studies suggest a prevalence of 2-6% with palpation, 19-35% with ultrasound, and 8-65% in autopsy (Wang and Crapo, 1997). With the widespread use of sensitive imaging in clinical practice, incidental thyroid nodules are being discovered with increasing frequency (Gharib and Goellner, 1993).

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The vast majority of adult thyroid nodules are benign neoplasms; however fewer than 5% are malignant (Bakhos *et al.,* 2000). Increased suspicion of malignancy is associated with male gender, females of ages less than 15 years and greater than 45 years, history of radiation exposure, and personal or family history of conditions known to be associated with thyroid cancer (Network, 2008). Thyroid nodules are 4 times more common in women than in men (Vander *et al.,* 1998) and increase in frequency with age and with decreasing iodine intake (Reiners *et al.,* 2004). The gender disparity is perhaps explained by the hormonal influences of both estrogen and progesterone, as increasing nodule size and new nodule development have been demonstrated to be related to pregnancy and multiparity (Jonklaas *et al.,* 2006). Neoplasms of thyroid have a wide phenotype spectrum ranging from

benign follicular lesions to the violently anaplastic carcinoma (Abdul-Jabar and Lynn, 2004). The most common diagnoses and their approximate distributions are colloid goiters, cysts, and thyroiditis in 80%; benign follicular neoplasms in 10-15%; and thyroid carcinoma in 5% (Mistry *et al.,* 2011). Different diagnostic modalities have been used to evaluate and diagnose thyroid nodules efficiently; they include Clinical examinations, thyroid function test (TFT), ultrasonography (USG), fine needle aspiration cytology (FNAC) and histopathological examination. However, clinical assessment, TFT, and USG have been poor parameters in assessing thyroid nodules (Shirish Chandanwale, 2012). The main goal of evaluating thyroid nodules is to identify and surgically treat patients with malignancies, while identifying and avoiding surgery in those with benign, asymptomatic thyroid nodules (Orell *et al.,* 2005). The distinction of benign from malignant nodules is important as it is preferred to operate only on those patients with suspicion of malignancy, while strict patient follow-up is recommended in dealing with benign cases, thus avoiding unnecessary surgeries in patients with benign lesions (Fernandes *et al.,* 2009). The distinction of benign lesions from malignant nodules cannot be based reliably on the clinical presentation alone (Roman, 2003). The main stem of diagnosis of nodular thyroid swelling is by clinical means, fine needle aspiration cytology (FNAC) and histopathological (histopathology) examination of the biopsy. However they differ in many occasions and therefore this study is carried out with a view of making correlations between FNAC findings and its corresponding histological diagnoses findings.

Histological examination of the thyroid is the most accurate way of determining the pathology. However, it is expensive since it requires prior preparations and long procedures like surgery anesthesia, hospitalization and sometimes even over treatment (McCaffrey, 2000). Surgery involvement exposes patients to the risks of anesthesia, postoperative infection, and the possibility of tumor seeding. A percentage of patients may require overnight admission to the hospital and extra time away from work (Bailey *et al.,* 2006). Thyroid surgeries are further complicated by post-operative thyroid hormone imbalance, hyperparathyroidism, recurrent laryngeal nerve injury, bleeding, or infection; thus, there has to be efforts to limit unnecessary surgeries in asymptomatic patients with benign lesions (Saeed *et al.,* 2013). Fine-needle aspiration cytology of thyroid is simple, minimally invasive, cost effective, readily available and reliable, time saving and an easy to perform outpatient procedure (Caruso, 1991). FNAC has greatly improved the clinical management of thyroid nodules. Previous studies have shown that the sensitivity of thyroid FNAC ranges from 80 to 98 percent and its specificity from 58 to 100% (Shepherd *et al.,* 2006). Complications due to FNA are rare but may include persistent pain, hematoma, infection, and recurrent laryngeal nerve palsy (Rosen and Stone, 2006). Due to the simplicity, low cost and absence of major complications of FNAC, it is being performed on an increasing number of patients, which has led to detection of thyroid cancer at earlier stages, resulting in better outcome of patients (Tyler *et al.,* 1999). Like any other test, FNAC has limitations and diagnostic pitfalls. The pitfalls are overlapping cytological features between some benign and malignant thyroid lesions, specimen adequacy, sampling techniques, the skills of the physician performing the aspiration, and the experience of the pathologist interpreting the aspirate (Baloch *et al.,* 1998). The reported limitations are the proportion of FNA results that are not obviously benign or malignant and fall into the indeterminate or suspicious group, the false negative and false positive results (Galera, 1997). Though FNAC can reduce the number of diagnostic thyroidectomies by identifying benign lesions that need not be removed, it does not eliminate all diagnostic operations (Cytopathology, 1997).

MATERIALS AND METHODS

Patients were enrolled into the study if they had a preoperative FNAC performed and subsequently a thyroid resection for definitive histological diagnosis. A proforma was used to collect data. The proforma had provisions for the patient's age, gender, FNAC diagnosis and histological diagnosis. The cytology and histology reports of patients who met the study criteria between January 2007 and December 2014 were accessed from the archives of the anatomical pathology laboratory MTRH. The cytology and histology numbers in the respective registers were used to access and retrieve the FNAC and histological reports respectively. The participant's age, gender, FNAC findings and its corresponding histological diagnosis were entered in the data collection forms. FNAC diagnoses were classified into 4 categories; unsatisfactory for diagnosis, indeterminate (suspicious), benign and malignant. "Unsatisfactory" for diagnosis encompassed Smears with insufficient cellularity or poor quality due to delayed or improper fixation and aspirates consisting only of cyst fluids. The indeterminate (suspicious) category encompassed aspirates with atypical features suggestive of, but not diagnostic for malignancy and included follicular neoplasm's, cellular adenomatoid nodules, hurthle cell proliferations and lesions suspicious for papillary carcinomas. Smears classified as "benign" were smears without atypical or malignant features and included colloid goiter, colloid or adenomatous nodules, thyroglossal duct cyst, Hashimoto's, sub-acute thyroiditis and other types of thyroiditis. The malignant category encompassed smears with cytological findings of primary or secondary malignancy and included Papillarycarcinoma, Follicularcarcinoma, Medullary carcinoma and Anaplastic carcinoma. Histological evaluations were categorized as either benign or malignant. FNAC diagnoses findings were then compared with those of the corresponding 'gold standard' histopathologic diagnoses. FNAC findings that were in agreement with those of corresponding histological evaluation were summarized as correlating. FNAC results that disagreed with the corresponding histological evaluation findings were summarized as discrepant. The discrepant findings were defined as either false negatives or false positives. False negatives were those cases in which FNAC failed to confirm malignancy while histopathology showed malignancy and false positives were those cases in which FNAC showed malignancy but histopathology showed no evidence of malignancy.

RESULTS

118 participants met the criteria and were included in the study (31 Males and 87 Females). Of the 118 FNAC, 87 were determinate, 17 were inadequate to make a diagnosis and 14were indeterminate (suspicious for malignancy). FNAC findings were compared with the corresponding gold standard histopathological diagnosis as illustrated in Table1.

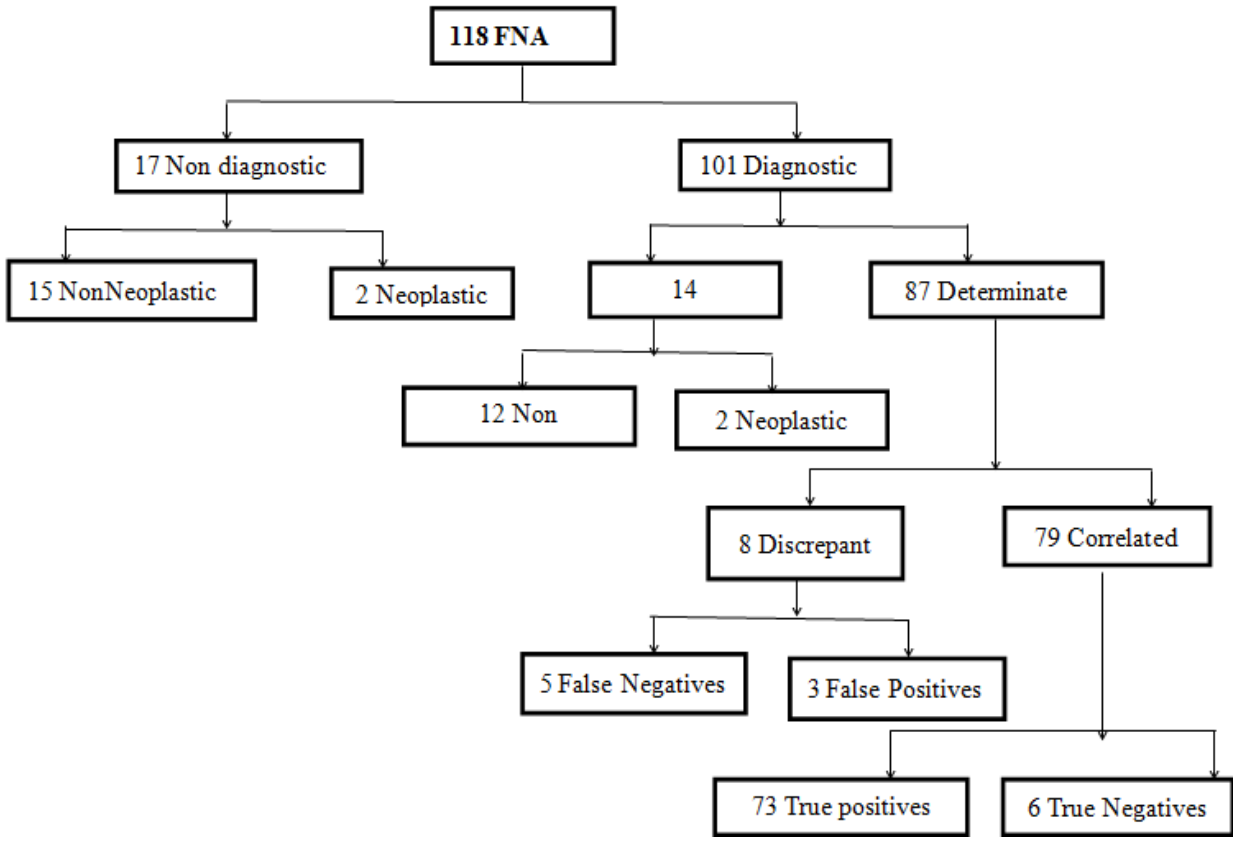

Figure 1. Cytohistological correlations of thyroid masses

Table 1. Summary of FNAC findings with corresponding histological findings Gold standard histological evaluation diagnoses

FNAC Diagnosis	Colloid goiter	Follicular Adenomas	Thyroiditis	Thyroid cysts	Papillary carcinoma	Follicular carcinoma	Medullary carcinoma	Anaplastic carcinoma
Inadequate n=17	6	1	1	7	-	1	-	1
Suspicious n = 14	1	11	0	-	0	2	-	-
Colloid goiter n=62	57	2	-	-	2	-	1	-
Thyroid cyst n=4	-	-	-	3	-	-	-	1
Thyroiditis n=12	-	1	10	-	-	1	-	-
Papillary carcinoma n =6	1	-	1	-	4	-	-	-
Medullary carcinoman= 3	-	-	1	-	-	-	2	-

The 17 inadequate FNAC diagnoses were histologically diagnosed as; 7 thyroid cysts, 6 colloid goiters, 1 follicular adenoma, 1 thyroiditis 1 follicular carcinoma and 1 anaplastic carcinoma. The 14 suspicious FNAC cases on histological evaluation revealed 1 colloid goiter and 13 follicular neoplasms (11follicular adenomas and 2 follicular carcinomas). On the non neoplastic category; the 62 colloid goiter diagnoses on FNAC, 57 correlated with histological diagnoses and 5 cases were discrepant; the discrepant cases histologically turned out to be 2 papillary carcinomas, 1 medullary carcinoma and 2follicullar adenomas. Of the 4 thyroid cysts on FNAC 3 correlated with final histological diagnoses, 1 was discrepant and was diagnosed histologically as medullary carcinoma. Of the 12 cases of thyroiditis, 10 correlated with the histological diagnosis whereas 2 were discrepant and histologically turned out to be follicular neoplasm's (1 follicular carcinoma and 1 follicular adenoma). The neoplastic FNAC category diagnoses were 6 papillary carcinomas and 3 medullary carcinomas. When correlated with the final histology evaluation findings, 4 papillary carcinomas correlated and 2 were discrepant.The discrepant ones turned out to be 1 colloid goiter and 1 thyroiditis. On the 3 medullary carcinomas,2 correlated with histological evaluation diagnoses while 1 was histologically diagnosed as thyroiditis. Out of the 78 non neoplastic FNAC diagnoses, 70 cases correlated with corresponding histological evaluation diagnoses whereas 8 (5 neoplastic and 3 non neoplastic) were discrepant. Of the 9neoplastic FNAC diagnoses, 6 correlated with corresponding histological diagnoses and 3 were discrepant. The 3 discrepant were non neoplastic on histology (2 thyroiditis and 1 colloid goiter). Generally 79 cases correlated (6 true positives and 73 true negatives) and 8were discrepant (3 false positives and 5 false negatives), translating to a concordance and discordance rate of 87.40% and 12.60% respectively. Upon comparing FNAC diagnoses with the corresponding histological evaluation diagnoses for correlations and discrepancies, the study yielded 79 FNAC diagnoses that correlated with the corresponding histological evaluation diagnoses(73 true negatives and 6 true positives) and 8 FNAC diagnoses that were discrepant with the corresponding histological evaluation diagnoses(3 false positives and 5 false negatives). In general, there were 73 true negatives, 6 true positives, 5 false negatives and 3 false positives. The suspicious and inadequate FNAC diagnoses were excluded from the statistical analysis owing to its non diagnostic importance.

The diagnostic performance of FNAC were calculated as follows;

Sensitivity= TP/ TP+FN * 100
=6/I1*100 = 54.54%

Specificity= TN/TN+FP * 100
=73/76 * 100 = 96.05%

Positive predictive value = TP/TP+FP *100
= 6/9 *100 = 66.66%

Negative predictive value = TN/TN+FN*100
= 73/78 * 100 = 93.58%

Accuracy = TP+TN/Total No *100
=79/87*100 = 90.80%

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of FNAC compared with the gold standard histological evaluation was 54.54%, 96.05%, 66.66%, 93.58% and 90.80% respectively. The kappa statistic of agreement had a chi- square distribution with 1 df under the null hypothesis (Ho: the test procedures, FNAC and histological evaluation of thyroid are independent (do not agree). The associated p-value was 0.34.

Table 2. Results of 87 patients of FNAC with histopathologic correlation Histological diagnosis

Test (FNAC)	Disease +ve	Disease –ve	
Disease +ve	6 (TP)	3 (FP)	9
Disease -ve	5 (FN)	73 (TN)	78

Table 3. Statistical analysis findings of FNAC in detecting malignant lesions

Parameter	Percentages
Sensitivity	54.54
Specificity	96.05
Accuracy	90.80
Positive predictive value	66.66
Negative predictive value	93.58

DISCUSSION

On cytohistologic correlations in this study, 17 unsatisfactory/inadequate FNAC were histologically diagnosed as; 7 thyroid cysts, 6 colloid goiters, 1 thyroid adenoma, 1 thyroiditis 1 follicular carcinoma and 1 anaplastic carcinoma. The inadequacyrate in this study was 13.6%, which is in keeping with previous studies that have shown inadequacy rate of between 0 to 25%; [4] (Shenovi *et al.,* 1995). Inadequate FNAC in this study may be attributed to sampling error, faulty techniques and sampling from highly vascular or focal lesions. Fourteen suspicious FNAC cases on histological evaluation were diagnosed as 1colloid goiter and 13 follicular neoplasms. The follicular neoplasms were 11 follicular adenomas and 2 follicular carcinomas. The suspicious cases in this study may be attributed to overlapping cytological features between some benign and malignant thyroid lesions especially in the cases of follicular neoplasm's where the differentiation between follicular carcinoma and follicular adenoma is based on the evaluation of the capsule (Nepali and Banita, 2012). In FNAC of thyroid, it's difficult to aspirate the capsule which is very crucial in thyroid diagnosis. In the 62 colloid goiter diagnoses, 57 correlated with histological diagnoses and 5 cases were discrepant; the discrepant cases histologically turned out to be 2 papillary carcinomas, 1 medullary carcinoma and 2follicularadenomas. The discrepancies in this case may be explained on the basis of the relatively low cellularity in these lesions that may have led to misdiagnosis in FNAC. There were 12 thyroiditis on FNAC, of which 10 correlated with final histological diagnoses and 2 were discrepant. The 2 discrepant cases were histologicaly diagnosed as 1 follicular carcinoma and 1 follicular adenoma. These discrepancies may be attributed to the low cellularity of the follicular neoplasms that may have led to misdiagnosis in FNAC. Of the 4 thyroid cysts on FNAC, 3 correlated with final histological diagnoses, 1was discrepant and was histologically diagnosed as medullary carcinoma. The discrepancy may be due to sampling error; the sample may have been aspirated from the cystic part of the tumor rather than from the tumor itself. On the neoplastic FNAC category, there were 6 papillary carcinomas and 3 medullary carcinomas.

On histological diagnosis, 4 correlated with FNAC findings and 2 were discrepant; 1 thyroiditis and 1colloid goiter. In the medullary carcinomas, 2 correlated and 1 was discrepant. The discrepant one was histologically diagnosed as thyroiditis. The discrepancies in the neoplastic category may be attributed to poor sampling and over diagnosis on cytological reporting by the cytopathologists. 79 FNAC diagnoses correlated with the corresponding histological evaluation diagnoses (70 true negatives and 6 true positives) whereas 8 FNAC diagnoses were discrepant with the corresponding histological evaluation diagnoses (3 false positives and 5 false negatives). In general, there were 73 true negatives, 6 true positives, 5 false negatives and 3 false positives translating to a concordance rate of 90.80%, false negative rate of 5.74% and a false positive rate of 3.44%. Gharib reported a false negative rate of 1% to 11%, a false positive rate of 1% to 8% (Gharib and Goellner, 1993). Pandey *et al* reported cytohistological concordance of 80.28% and discordance of 19.72%. Of the discordant cases, false positives accounted for 11.60% and false negatives for 8.12% (Pinki Pandey *et al.,* 2012). Bhatta *et al* reported a false negative rate of 14.28% and false positive rate of 7.69% (Bhatta *et al.,* 2012). In my study, the concordance rate, false positive rate and false negative rate are 90.80%, 3.44% and 5.74% respectively. The Kappa statistical analysis for agreement showed a significant agreement between FNAC of thyroid and histological evaluation technique with associated p-value of 0.34. This observation gives credence to the rejection of our null hypothesis (the two test procedures are independent) at 5% level of significance. Thus we conclude that the two tests (FNAC and histological evaluation) have a significant level of overall agreement.

The concordance rate of my study is somewhat comparable to that of Pandey *et al* (80.28%) (Pinki Pandey *et al.,* 2012). The false negative and false positive rates are within the ranges reported by Gharib (Gharib and Goellner, 1993). In our study, the diagnostic yield of FNAC of thyroid masses including sensitivity, specificity, PPV, NPP and accuracy is 54.54%, 96.05%, 66.66%, 93.58% and 90.80% respectively. The findings compares well with those of other previous studies; Gulia *et al* reported sensitivity, specificity, PPV, NPV and

accuracy of 100%, 90.0%, 100%, 90.5% and 92.3% respectively (Gulia *et al.,* 2011). Bhatta *et al* reported a sensitivity, specificity, PPV, NPV and accuracy of 85.7 %,92.3 %,92.31%, 85.72% and 90 % respectively (Bhatta *et al.,* 2012). Pandey *et al* reported sensitivity, specificity, PPV, NPV and accuracy of 57.14%, 90%, 70.58%, 83.33% and 80.28% respectively (Pinki Pandey *et al.,* 2012). Muratli *et al* reported sensitivity, specificity, PPV, NPV and accuracy of 87.1%, 64.6%, 76.1%, 79.5% and 77.3% respectively (Muratli *et al.,* 2014). Mahar *et al* reported sensitivity, specificity, PPV, NPV and accuracy of 98%, 70%, 91%, 93% and 91% respectively (Saeed Mahar and Najmul Islam, 2005). Bamanikar *et al* reported a sensitivity of 50%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 93.8% and accuracy of 94.2% (Bamanikar *et al.,* 2014).

Conclusion

FNAC of thyroid is a simple and easy to perform procedure, it's safe, minimally invasive with few complications and moreover it's cost effective. Our study reveals that FNAC of thyroid has low false negatives and false positives rates and as such it's accurate and therefore can be recommended and relied upon as the initial investigation tool in evaluating thyroid nodules, therefore avoiding unnecessary surgeries in patients with benign thyroid nodules, thus reducing the cost of health care of patients with thyroid nodules.

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