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Diagnostic Accuracy of Fine Needle Aspirate Cytology A Study of Moi Teaching and Referral Hospital, Eldoret Kenya

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Abstract

Thyroid masses/nodules are common clinical manifestations with a worldwide prevalence of 4–7% in the general adult population and 0.2% – 1.2% in children. The vast majority of thyroid nodules are benign; fewer than 5% are malignant. 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. Fine Needle Aspiration Cytology (FNAC) of thyroid is 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) Eldoret Kenya. Its objective was to assess the accuracy of FNAC in diagnosing thyroid masses. FNAC and corresponding histological findings of 118 patients 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. 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. The accuracy, sensitivity, specificity, positive predictive value and negative predictive values of FNAC were 90.80%, 54.54%, 96.05%, 66.66% and 94.58% respectively. 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.

Keywords

Fine Needle Aspiration Cytology, Thyroid Masses, Histological Examination

1. Introduction

Thyroid nodules are common clinical manifestations, their prevalence varies with the populations studied and the screening method used [1]. The reported prevalence is 4–7% in the general adult population and 0.2% - 1.2% in children [2]. On the screening methods used, numerous studies suggest a prevalence of 2-6% with palpation, 19-35% with ultrasound, and 8-65% in autopsy [3]. The majority of adult thyroid

nodules are benign neoplasm's, however fewer than 5% are malignant [4]. 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 [5]. The large number of benign thyroid masses relative to the small number of the malignant ones creates a clinical dilemma; how to manage patients with thyroid nodules that most probably are benign [6]. Neoplasms of thyroid have a wide phenotype spectrum ranging from benign follicular lesions to the violently anaplastic carcinoma [7] 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% [8]. 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 [9]. 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 [10]. 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 [11]. The distinction of benign lesions from malignant nodules cannot be based reliably on the clinical presentation alone [12]. 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 [13]. 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 [14]. 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 [15].

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 [16]. 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% [17]. Because of this, FNAC Has become the diagnostic tool of choice for the initial evaluation of solitary thyroid nodules, and therefore has reduced the number of patients undergoing thyroid surgery for benign diseases like thyroiditis, with resultant decrease in the cost of health care [18, 19]. Complications due to FNA are extremely rare but may include persistent pain, hematoma, infection, and recurrent laryngeal nerve palsy [20]. 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 [21]. 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 [22]. 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 [23].

The main aim of thyroid FNAC is to identify nodules that require surgery and those benign nodules that can be observed clinically and decrease the overall thyroidectomy rate in patients with benign diseases such as thyroiditis [24]. Though FNAC can reduce the number of thyroidectomies by identifying benign lesions that need not be removed, it does not eliminate all diagnostic operations [25].

This study was undertaken to correlate and compare FNAC findings of thyroid with corresponding histopathologic evaluation findings with a view of recommending whether FNAC of thyroid should be relied upon in the evaluation of thyroid nodules, thus reducing the rate of unnecessary thyroidectomies in benign pathologies, thereby reducing the cost of living and the risks associated with surgeries. Its aim was to demonstrate the effectiveness of FNAC (in the form of sensitivity, specificity and accuracy) in the diagnosis of different thyroid lesions and to highlight probable causes of errors in the cases showing discrepancy between cytological and histological diagnoses.

2. Materials and Methods

Patients were enrolled into the study if they had a pre-operative FNAC performed and subsequently a thyroid resection for a definitive histologicaldiagnosis. A proforma was used to collect the data; the proforma had provisions for participant's registration number, age, gender, cytology number, FNAC findings, histology number and histological evaluation findings. The cytology and histology reports of patients who underwent FNAC procedure and then underwent thyroid surgery respectively from January 2007 to December 2014 were accessed from the file copies in the archives of the anatomical pathology laboratory. 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 Papillary carcinoma, Follicular carcinoma, Medullary carcinoma and Anaplastic carcinoma. Histological evaluations were categorized as either benign or malignant. FNAC diagnoses were then compared with the gold standard histopathologic diagnoses. FNAC findings that were in agreement with those of corresponding histological evaluation were summarized as correlating. FNAC results that differed 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.

3. Results

118 patients met the study criteria within the study period were recruited into the study. There were 88 females and 30 males, accounting for 74.6% and 25.4% of the study populations respectively. This was a male: female ratio of 1:3. The ages of the patients were between 17-88 years with a mean of 40.61, standard deviation of +14.93, a median of 37.50, a mode of 28 years and a range of 71.

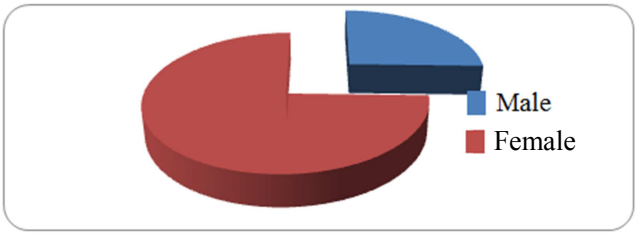

Figure 1. *Gender distribution.*

Table 1. *Age and gender distributions of patients n=118.*

Age (years)	Males	Females	Total	Percentages
10-19	0	5	5	4.2
20-29	3	20	23	19.5
30-39	6	32	38	32.2
40-49	5	20	25	21.2
50-59	6	3	9	7.6
60-69	9	3	12	10.2
70-79	1	4	5	4.2
80-89	0	1	1	0.8
	30	88	118	100

3.1. Cytological Diagnoses of Thyroid Masses

FNAC diagnoses were categorized into 4 categories; inadequate to make a diagnosis, suspicious for malignancy, non neoplastic and neoplastic. The 118 FNAC yielded 17 cases (14.4%) as inadequate to make a diagnosis, 14 (11.9%) cases suspicious for malignancy, 78 (70.27%) non neoplastic cases and9 (7.6%) neoplastic cases. The non neoplastic cases consisted predominantly of colloid goiter at 62 (52.5%), thyroiditis at 12 (10.2%) and 4thyroid cysts (3.4%). The neoplastic lesions consisted of 6 papillary carcinomas (5.1%) and 3 (2.5%) Medullary carcinomas

Table 2. *Summary of FNAC diagnoses (n=118).*

FNAC category	Frequency	%
Inadequate	17	14.4
Suspicious	14	11.9
Non neoplastic n=78		
Colloid goiter	62	52.5
Thyroiditis	12	10.2
Thyroid cysts	4	3.4
Neoplastic n=9		
Papillary carcinoma	6	5.1
Medullary carcinoma	3	2.5

3.2. Correlation of FNAC Diagnoses with Those of Corresponding Histological Diagnoses

FNAC diagnostic categories were compared with the corresponding gold standard histopathological diagnosis. 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 revealed 6 papillary carcinomas and 3 medullary carcinomas. When correlated with the final histology evaluation findings, 4 papillary carcinomas correlated and 2 were discrepant and turned out to be 1 colloid goiter and 1 thyroiditis. Of 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. Out of the 9neoplastic FNAC diagnoses, 6 correlated with corresponding histological diagnoses and 3 were discrepant. The 3 discrepant were non neoplastic on histology evaluation. 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.

3.3. Diagnostic Performance of FNAC

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.

Table 3. *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
Totals	11	76	87

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.

Table 4. *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

4. Discussion

As reported in the literature, age and gender are associated factors of thyroid lesions. In the present study there was a female predominance giving a male female ratio of 1:3. There were 88 females (74.6%) and 30 males (25.4%). Their ages ranged from17 to 88 years with a mean of 40.61 and SD of 14.93. The mean age of male patients was greater than that of female patients; 49.7 and 37.51 respectively. The male: female ratio (1:3) is comparable to other studies conducted nationally and internationally [26];Wahid *et al* reported 57 females and 25 males, with female: male ratio of 2.28: 1, age range of 16-65 years, with mean age of 42.56 S.D +11.60 years[27]. E.A. Sinna and N. Ezzat reported a female to male ratio of 5.2:1, and a median age of 44 years[28]. Muratli *et al* reported age range of 17-89 years and a mean of 51.24 [29]. In the current study, we also found that most of the patients were in their 3rd decade. This is in accordance with the study by Bamanikar [30]).

On the cytological patterns of thyroid masses, Esmaili and Taghipour reported 9.2% unsatisfactory, 64.3% benign, 7.8% malignant and 18.66% suspicious. [6]. In my study, the unsatisfactory rate is at 13.6%, benign 65.3%, malignant 8.6% and 12.7% suspicious. This is consistent with previous studies that have reported inadequacy rate of 0 to 25% [31, 32]. Bhatta *et al* (2012) reported colloid goiter as the commonest benign thyroid mass and papillary carcinoma as the commonest malignant thyroid lesion[33]. In my study, the commonest benign thyroid lesion was colloid goiter which is in keeping with the findings of a study by Bhatta *et al.,* and wahid *et al*.,

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. Unsatisfactory/ inadequate samples in this study were 13.6%, which is consistent with previous studies that have shown inadequacy rate of between 0 to 25% [31, 32]. 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 case of follicular neoplasm's where the differentiation between follicular carcinoma and follicular adenomas is based on the evaluation of the capsule. 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 2 follicular adenomas. 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, 10 correlated with histological diagnoses whereas2 were discrepant. The 2 discrepant cases were histologicaly diagnosed as 1 follicular carcinoma and 1 follicular adenoma. This 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, 1 was 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 rather than from the tumour 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.

76 FNAC diagnoses correlated with the corresponding histological evaluation diagnoses (70 true negatives and 6 true positives) and 11 FNAC diagnoses were discrepant with the corresponding histological evaluation diagnoses (3 false positives, 5 false negatives and 3 true 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% [34]**.** 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 9.8%[35]. Bhatta *et al* reported a false negative rate of 14.28% and false positive rate of 7.69% [33]. In my study, the concordance rate, false positive rate and false negative rate are 90.80%, 3.44% and 5.74% respectively. The concordance rate of my study is somewhat comparable to that of Pandey *et al* (80.28%). The false negative and false positive rates are within the ranges reported by Gharib.

The diagnostic sensitivities reported in the literature, range widely from 50% to 100% and specificity ranges from 64.6% and 100% (Bamanikar *et al* 2014, Gulia *et al* 2011*,* Muratli *et al* 2014). Factors contributing to such a broad range are how pathologists handle the category of "suspicious" and how they define the false-positive and false-negative results. Some pathologists include follicular neoplasms in the malignant/neoplastic category; others categorize them in the negative group, whereas others exclude them from the calculations. In the current 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. Gulia *et al* reported sensitivity, specificity, PPV, NPV and accuracy of 100%, 90.0%, 100%, 90.5% and92.3% respectively[36]. Bhatta *et al* reported a sensitivity, specificity, PPV, NPV and accuracy of 85.7 %,92.3 %,92.31%, 85.72% and 90 % respectively[33]. Pandey *et al* reported sensitivity, specificity, PPV, NPV and accuracy of 57.14%, 90%, 70.58%, 83.33% and 80.28% respectively [35]. Muratli *et al* reported sensitivity, specificity, PPV, NPV and accuracy of 87.1%, 64.6%, 76.1%, 79.5% and 77.3% respectively[29]. Mahar *et al* reported sensitivity, specificity, PPV, NPV and accuracy of 98%, 70%, 91%, 93% and 91% respectively [37]. Bamanikar *et al* reported a sensitivity of 50%, specificity of 100%, positive predictive value of 100%, negative predictive value of 93.8% and accuracy of 94.2% [30]. The diagnostic yield of FNAC in our study is comparable to those of other studies as demonstrated in table 5

Table 5. *A comparison of various parameters of FNAC between other studies and current Study.*

Series	Accuracy	Sensitivity	Specificity	PPV	NPV
Gulia *et al*	92.3%	100%	90.0%	100%	90.5%
Bhatta *et al*	90 %	85.7 %,	92.3 %,	92.31%	85.72%
Mahar *et al*	91%	98%	70%	91%	93%
Muratli *et al*	77.3%	87.1%	64.6%	76.1%	79.5%
Pandey *et al*	80.28%	57.14%	90%	70.58	83.33%
Bamanikar *et al*	94.2%	50%	100%	100%	93.8%
Current study	90.80%	54.54%	96.05%	66.66%	93.58%

5. Conclusion

FNAC of thyroid is a simple and easy to perform procedure; it's safe, cost-effective and minimally invasive with few complications. The results of our study and the results reported by other similar studies confirm that FNAC of thyroid is highly accurate and has a low rate of false-negative and false-positive diagnoses. In view of these, we conclude that FNAC should be adapted and relied upon as an initial investigation tool in evaluating thyroid nodules. FNAC helps reduce the cost of health care and avoids unnecessary surgeries in patients with benign thyroid lesions, thereby improving the overall quality of life for patients with thyroid nodules.

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