



RESEARCH ARTICLE

FINE NEEDLE ASPIRATE CYTOLOGY OF THYROID; A REVIEW OF DIAGNOSTIC PATTERNS AND COMPARISON OF FINDINGS WITH HISTOLOGY THE GOLD STANDARD, AT MOI TEACHING AND REFERRAL HOSPITAL

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ABSTRACT

Thyroid masses are common surgical presentations with a worldwide prevalence of 4–7% in the general adult population. The vast majority of adult thyroid nodules are benign neoplasms, however, less than 10% are malignant, which makes it important to screen the nodules in order to offer appropriate surgery and avoid unnecessary surgery for benign nodules. 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) is known to play a pivotal role in the screening and management of thyroid swellings. This study was carried out at the Moi Teaching and Referral Hospital its objective was to assess FNAC patterns of thyroid masses and compare its findings with corresponding histological findings to find out if FNAC can be relied upon in evaluating thyroid in order to establish a basis of whether or not to incorporate its findings in the management of these masses pre-operatively. This was a retrospective study where FNAC and corresponding histological evaluation findings of 118 patients aged 17-88 years 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 and compared for concordance and discordance. Of the 118 FNAC, 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. The benign cases consisted predominantly of colloid goiter (54.54%) whereas the malignant ones consisted predominantly of papillary carcinomas (5.08%). 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. 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 hence can be adopted and relied upon in evaluating thyroid nodules pre-operatively. Use of FNAC reduces the rate of unnecessary surgeries, the cost of health care and the risks associated with surgeries, resulting in better outcome of patient's care.

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INTRODUCTION

Thyroid nodules are common clinical manifestations with a prevalence of 4–7% in the general adult population and 0.2% - 1.2% in children (Ridgway, 1986). The vast majority of adult thyroid nodules are benign neoplasms, however, less than 10% are malignant, which makes it important to screen the nodules in order to offer appropriate surgery and avoid unnecessary surgeries for benign nodules (Nyonyintono et al., 2011). 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., 1968) 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

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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). In sub-Saharan Africa, where Kenya is situated, most thyroid nodules are a result of Iodine deficiency (Watters and Wall, 2007). Iodine deficiency is defined as a median urinary iodine concentration less than 50 µg/L in a population (Watters and Wall, 2007). These iodine deficiency nodules are treated by giving iodinated oil like Lipiodol or Brassiodol. Within 3 months of treatment, 98% of these nodule regress and do not require surgery but iodine (Watters and Wall, 2007) 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 preference for operation is 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 like thyroiditis (Fernandes *et al.*, 2009). Fine needle aspiration cytology is a technique for obtaining cellular material for cytological examination, which is minimally invasive, and provides rapid diagnosis. However, it does not preserve its histological architecture (Obaseki, 2009). Fine needle aspiration cytology is unable to differentiate follicular and Hurthle cell carcinomas from their benign counterparts because it cannot establish the presence of capsular and/or vascular invasion (Theoharis *et al.*, 2009). The accuracy of FNAC depends highly on the experience of the operator and the cytopathologist reading it and in very experienced hands the false negatives are as low as 1- 6% (Mehanna *et al.*, 2009). An Ethiopian study on FNAC showed a 96.9% accuracy for diagnosing simple goiter (Bekele, 2007). A study done at King Khalid University hospital in Saudi Arabia found that FNAC on thyroid nodules had a sensitivity of 71.4% and a specificity of 96.4% (Khairy and Murshid, 2004). Chandanwale *et al.*, (2012) showed a sensitivity and specificity of 90% and 100% respectively. While a Study in Oman done by Al-Yaarubi *et al.*,(2011) showed a poor result of 16% sensitivity. A study done at Cairo University, Egypt on 296 cases of thyroid nodules that had diagnostic thyroid FNAC reported 98 (33.1%) cases as benign, 40 cases (13.5%) as follicular lesion of undetermined significance, 49 cases (16.5%) as follicular neoplasm, 30 cases (10.1%) as suspicious for malignancy, 58 cases (19.5%) as malignant, and 21 cases (7.1%) as unsatisfactory. Nodular hyperplasia represented the majority of benign cases (89.8%), while papillary carcinoma was the most frequent malignant lesion (72.4%) (Sinna and Ezzat, 2012).

Esmaili and Taghipour (2012) conducted a study in Iran on 1639 aspirates of thyroid masses, 151 (9.2%) cases were unsatisfactory, the remaining 1488 cases were classified as 1054 (64.3%) benign, 128 (7.8%) malignant, and 306 (18.66%) suspicious. Benign lesions included 996 (94.4%) cases of multinodular goiter, 55 (5.2%) cases of Hashimoto's and chronic non-specific lymphocytic thyroiditis, 2 (0.2%) cases of sub-acute thyroiditis, and 1 (0.1%) case of Riedel's thyroiditis. The current study is based at the Moi Teaching and Referral Hospital in Kenya, its objective was to review FNAC findings of thyroid and compare with the corresponding histological evaluation findings.

## MATERIALS AND METHODS

Approval to carry out the study was sought from MTRH and Moi University Institutional Ethics and Review committee (IREC) via approval no 0001408. This was a retrospective comparative descriptive survey study in which FNAC reports and histological evaluation reports of patients who had FNAC diagnosis of thyroid and subsequently thyroidectomy for definitive histological diagnosis between January 2007 and December 2014 were reviewed. FNAC findings were then compared with the corresponding histological evaluation diagnosis for concordance and discrepancy. FNAC diagnoses reports were classified into 4 categories; unsatisfactory for diagnosis, indeterminate (suspicious), benign and malignant. "Unsatisfactory" for diagnosis encompassed reports of 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. Fine needle aspirate cytology diagnoses were then compared with the gold standard histopathologic diagnoses. The data generated were double checked and corded in SPSS version 20.0 for analysis. Contingency table analysis was done to determine the diagnostic accuracy of FNAC. Descriptive statistics was carried out for continuous variables (age) using mean and range. Frequency listings were done for categorical variables. Kappa statistics was done to measure whether there was significant agreement between FNAC of thyroid and the gold standard histological technique.

## RESULTS

118 participants who met the study criteria within the study period were recruited into the study. 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 and 9 (7.6%) neoplastic cases. The non-neoplastic cases consisted predominantly of colloid goiter at 62 (52.5%), thyroiditis at 12 (10.2%) and 4 thyroid cysts (3.4%). The neoplastic lesions consisted of 6 papillary carcinomas (5.1%) and 3 (2.5%) medullary carcinomas.

**Table 1. 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)

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. The youngest participant was 17 years diagnosed with colloid goiter and the oldest was 88 years diagnosed with papillary carcinoma. The mean age of Male participants was 49.7; the mean age of the females was 37.51.

histological evaluation diagnoses while 1 was histologically diagnosed as thyroiditis.

### DISCUSSION

As reported in the earlier literature, age and gender are associated factors of thyroid lesions (Vander *et al.*, 1968). In the current study there were 88 females (74.6%) and 30 males

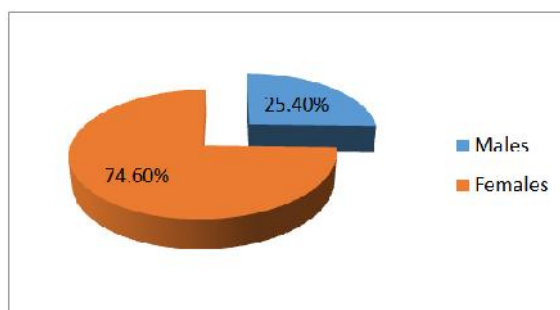


Figure 1. Gender distribution

Table 2. Comparison of FNAC findings with corresponding histological findings

FNAC Diagnosis	Gold standard histological evaluation diagnoses							
	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 carcinoma n= 3	-	-	1	-	-	-	2	-

The youngest and old participants were both females. Malignancy was diagnosed in 11 participants; 4 males and 7 females. The mean age of males with malignancy was 52.25 while that of females was 43.57. The youngest female diagnosed with malignancy was aged 20 years while the youngest male was aged 27 years. Out of the 7 females diagnosed with malignancy, 4 were aged below 40years. 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 (11 follicular 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 2 follicular 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

(25.4%), this was a female predominance giving a male female ratio of 1:3. This could be due to the fact that thyroid nodules are more common in women (Vander *et al.*, 1968). The male female ratio is comparable to those of other studies; Wahid *et al* (2011) reported 57 females and 25 males, with female: male ratio of 2.28: 1. Sinna and Ezzat reported a female to male ratio of 5.2:1 (Sinna and Ezzat, 2012). The ages of patients in the current study ranged from 17 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. Wahid *et al* reported an age range of 16-65 years, with mean age of 42.56 S.D +11.60 years (Wahid *et al.*, 2011). Muratli *et al* reported age range of 17-89 years and a mean of 51.24 (Muratli *et al.*, 2014). The age range is comparable to that of a study by Muratli *et al.* The mean ages of the patients are similar to that of Wahid *et al.* In the current study, we found that most of the patients were in their 3<sup>rd</sup> decade. This is comparable to that of a study by Bamanikar (Bamanikar *et al.*, 2014) who reported that most patients were aged between 30 and 40 years. On the cytological patterns of thyroid masses, Esmaili and Taghipour reported 9.2% unsatisfactory, 64.3% benign, 7.8% malignant and 18.66% suspicious. (Esmaili and Taghipour, 2012). In the current study, the unsatisfactory rate is at 13.6%, benign 65.3%, malignant 8.6% and 12.7% suspicious. This is comparable with previous studies that have reported inadequacy rate of 0 to 25% ( Gharib and Goellner, 1993; Shenovi *et al.*, 1995). Bhatta *et al* (2012) reported colloid goiter as the commonest benign thyroid mass and papillary carcinoma as the commonest malignant thyroid lesion (Bhatta *et al.*, 2012). In this current study, the commonest benign

thyroid lesion was colloid goiter which is in keeping with the findings of a study by Bhatta and Wahid. On cytohistologic correlations in this study, 17 (14.4%) FNAC were unsatisfactory to make a diagnosis. This is in agreement with previous studies that have shown inadequacy rate of between 0 to 25% (Gharib and Goellner, 1993; Shenovi et al., 1995). Alta Villa et al (1990) reported an inadequacy rate of 16.11%; this is slightly higher than for the current study (14.4). This can be explained on the basis that Alta Villa et al examined a larger population than the current study. Inadequate FNAC in this study could have resulted from sampling error, aspiration of sclerotic or calcified lesions and also nodules with large areas of cystic degeneration or necrosis. Sampling errors could have been mitigated with the use of ultrasound scan to help locate the nodule and guide aspiration. Thyroid ultrasonography gives details about the characteristics of the nodule and its potential risk of malignancy (Mehanna et al., 2009). The current study reported 14 (11.9%) suspicious FNAC cases.

This is comparable to that of a study by Sinna and Ezzat (2012) which reported 10.1 % suspicious FNAC. However, the suspicious FNAC in this study is higher than that reported by Kumar et al (2014) which reported 4 suspicious cases. This may be explained on the basis that Kumar et al used ultrasound imaging to guide FNAC procedure and this improved the specimen adequacy. The suspicious cases in the current 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. In FNAC, it's difficult to aspirate the capsule which is very crucial in thyroid diagnosis. 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 rejection of the null hypothesis (the two test procedures are independent) at 5% level of significance. Thus the current study concludes that the two tests (FNAC and histological evaluation) have a significant level of overall agreement.

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