COMPARISON OF FINE NEEDLE ASPIRATION CYTOLOGY WITH HISTOPATHOLOGY FINDINGS OF THYROID LESIONS AT MUHIMBILI NATIONAL HOSPITAL

Husein M. Hassanali, MD

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By

Husein M. Hassanali, MD

A Dissertation Submitted in (Partial) Fulfilment of the Requirements for the Degree of Masters of Medicine (General Surgery) of Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by the Muhimbili University of Health and Allied Sciences the dissertation titled "**Comparison of Fine needle Aspiration Cytology with Histopathology findings of Thyroid Lesions at Muhimbili National Hospital"** in partial fulfilment of the requirements for the degree of Masters of medicine in General Surgery.

_____

Prof Charles Mkony

Supervisor

_____

Date

_____

Dr Amos Mwakigonja

Co Supervisor

_____

Date

DECLARATION AND COPYRIGHT

I **Husein Mufaddal Hassanali** declare that this **dissertation** is my own original work and has not been submitted for a similar award in any other university.

Signature…….. Date……

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DEDICATION

This dissertation is dedicated to my parents Mr Mufaddal Hassanali and Zainab Mufaddal who always taught me to be humble and strive for excellence and my wife and daughter Mariyah and Insiyah.

ABSTRACT

Background: Thyroid lesions due to iodine deficiency and other causes is an endemic disease in our set up. Over 70% of patients are found to be referred due to nodular lesions, in which some nodular lesions are malignant in nature. The risk of malignancy in solitary and multinodular goiter occurring in endemic goitre areas is reported to be higher than in control areas.[1]

Several investigations have been recommended to assess thyroid lesions and these include thyroid function test, ultrasonography, radionuclide scans and fine needle aspiration cytology. Cytology is considered to be a precise diagnostic screening test for malignancy. However for a satisfactory result, a representative specimen and an experienced cytologist are mandatory. In a developing country where sophisticated technology and an experienced cytologists may not be readily available, the challenges of identifying patients with malignancy in thyroid lesion is even greater.

Objective: The aim of the study was to determine sensitivity, specificity, positive predictive value, negative predictive value and accuracy of FNAC in comparison with gold standard histopathology findings.

Methodology: This hospital based descriptive crossectional study was intended to compare FNAC to histopathological tissue findings of thyroid lesions at Muhimbili National Hospital of hundred and twenty four patients. It included inpatients in general surgery wards and surgical outpatient clinics.

Results: A total of 124 patients with thyroid lesions were enrolled in the study. The mean age (± standard deviation) of the study participants was 40.5years (±11.66) years. Large percentages (33.1%) of the thyroid patients were in the 31-40 years age group. Fifteen (12.1%) of the 124 patients were male and 109 (87.9%) were female (M: F, 1:7.3). In FNAC a total of 124 patients with thyroid lesion, 80.6% showed benign lesion, 11.3% malignant lesion and 8.1% suspicious lesion.

In Tissue histopathology a total of 124 patients with thyroid lesion, 82.3% showed benign lesion, 17.7% malignant lesion. Most common benign thyroid lesions were colloid goiter 48 out of 102(47.1%).

Out of 124 patients, 114 patients were analysed, as 10 patients were indeterminate on FNAC. Of the 100 samples which were negative for malignancy on FNAC, 9 aspirates showed non neoplastic lesion while confirmed by histopathology as papillary carcinoma in 4(44.4%) and follicular carcinoma in 5(55.6%). Out of 14 malignancies on FNAC, 13(92.9%) were malignant. one patient showed papillary carcinoma on FNAC while histological diagnosis confirmed the diagnosis as follicular adenoma. Sensitivity of FNAC was 59.1%, specificity 98.9%, positive predictive value 92.9, negative predictive value 91% and accuracy was 91.2%. In FNAC out of 124 patients 70(56.5%) received their FNAC results by one week. The mean duration (± standard deviation) of reporting FNAC results was 8.2 days (±5.59) days. In Histology out of 124 patients 40(32.3%) received their histological results by third week. The mean duration (± standard deviation) of reporting histopathology results was 23.53 days (±17.17) days

Conclusion: The results of this study are comparable with the current published data and demonstrate that FNA cytology is a specific, and accurate initial diagnostic test for evaluation of patients with thyroid swellings. However, FNAC has low sensitivity. Cytodiagnostic errors of some cases with overlapping cytological features can be avoided by paying attention to the possible pitfalls. The suspicious results can be resolved by diagnostic surgical resection. A benign FNAC diagnosis should be viewed with caution as false negative results do occur and these patients should be followed up clinico-radiologically for any progression that will require repeated FNAC and/or surgery.

Recommendation: FNAC is a reliable preoperative tool for investigation. The sensitivity of the test could be improved by decreasing false negative rate through improving sample collection, appropriate sample preparation and accurate interpretation by cytopathologists.

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LIST OF ABBREVIATIONS

ACTH	Adrenocorticotrophic Hormone
CEA	Carcinoembryonic Antigen
FNAC	Fine Needle Aspiration Cytology
MEN	Multiple Endocrine Neoplasia
MNG	Multinodular Goitre
MNH	Muhimbili National Hospital
MTC	Medullary Thyroid Carcinoma
MUHAS	Muhimbili University of Health and Allied Sciences
PTH	Parathyroid Hormone
RAI	Radioactive Iodine
SPSS	Statistical Package for Social Sciences
STN	Solitary Thyroid Nodule
TL	Thyroid Lesion
US	Ultrasound

DEFINITIONS

True Positive

A true positive test result is one that detects the condition when the condition is present.

True Negative

A true negative test result is one that does not detect the condition when the condition is absent.

False Positive

A false positive test result is one that detects the condition when the condition is absent.

False Negative

A false negative test result is one that does not detect the condition when the condition is present.

Sensitivity

The ability of a test to give a positive finding when the tested person truly has the disease under the study. In other words it is the probability that the test will be reactive in a diseased individual. A test with a high sensitivity will detect a high percentage of diseased individuals.

Specificity

The ability of a test to give a negative finding when the tested person is truly free of the disease under study. In other words it is the probability that a test result will be non-reactive in an individual who is not diseased.

Positive Predictive Value

Denotes the proportion of diseased amongst all positive tests. In other words, it signifies the probability that a given patient with a positive test, indeed does have the disease. PVP is also known as the posterior probability or post-test probability of disease.

Negative Predictive Value

Denotes the proportion of healthy individuals amongst all negative tests. In other words, it signifies the probability that a given individual with a negative test, indeed does not have the disease.

Reliability

The proportion of the correct results true positive and true negative in relation to all cases studied.

Or process yielding values that are equal on average to the true underlying value for the diagnostic variable measured.

CHAPTER ONE

1.0 INTRODUCTION AND LITERATURE REVIEW

Iodine deficiency disorders are endemic in Tanzania and large numbers of patients requiring surgery for goiter are referred to the Muhimbili National Hospital (MNH), Dar es salaam (the major referral and teaching hospital for the country). Over 70% of patients with goitre referred to the Department of Surgery have nodular lesions and these include both solitary nodules and multinodular goitres. A higher incidence of malignancy in cold thyroid lesions by radionuclide scan has also been noted.[1]

A Study conducted in Tanzania on the frequency of carcinoma in solitary thyroid nodule and multinodular goitre, revealed females were mainly affected , papillary carcinoma was found to be more common in STN while follicular carcinoma to be more in MNG.[1]

In the West, the risk of carcinoma in a solitary nontoxic thyroid nodule is reported to vary from as low as 10% to as high as 50%[2,3,4,5].The risk has also been found to vary according to age, sex and family history of thyroid carcinoma in patients[4,6,7,8].

A study in North Western Ethiopia on pattern of goitre in a teaching hospital, cosmetic disfigurement and respiratory symptoms were the leading reasons for hospital visit. Simple goitres, thyroid carcinoma and toxic goitres occurred in 80%, 11.3% and 6.25% of the patient's respectively.[9]

Fine needle aspiration cytology (FNAC) of the thyroid gland is now a well-established, first-line diagnostic test for the evaluation of diffuse thyroid lesions as well as of thyroid nodules with the main purpose of confirming benign lesions and thereby, reducing unnecessary surgery. Although there is a large body of world literature claiming the accuracy and usefulness of thyroid cytology, there is also evidence showing possible limitations and pitfalls of this procedure. The possible pitfalls encountered were inadequate sampling in 14%, cytohistological discrepancy in 5.2% and others were dual pathology and errors in interpretation.[10]

Histological examination of the removed thyroid swelling is the most accurate way to determine the pathology. It requires preparation and long procedure like anaesthesia, hospitalization and sometime even over treatment.

The assessment of the patient with a thyroid nodule(s) includes the triple modalities of clinical examination, cytology and imaging investigations. The result of thyroid aspiration cytology is therefore only one factor governing the management decision. Indeterminate FNAC results and cytodiagnostic errors are unavoidable due to overlapping cytological features particularly among hyperplastic adenomatoid nodules, follicular neoplasms and follicular variants of papillary carcinomas. Ongoing correlation of cytology and histology is an important quality assurance measure and it allows laboratories to calculate their false positive and false negative rates.[11]

A study conducted in Pakistan to find out the role of FNAC in thyroid disease revealed FNAC is a reliable, safe and accurate method as a first line of evaluation in thyroid gland nodules before surgery. FNAC is more specific (100%) than sensitive (77%) in detecting thyroid gland malignancy and therefore its use as a reliable diagnostic test cannot be overemphasized.[12]

In our setup FNAC is done without Ultrasound (US) guidance comparing to other hospitals using US-FNAC. According to the literature, the routine use of US-FNAC allows a decrease in the rate of unsatisfactory specimens from 15% to 20% down to 5%.[13,14]
US-FNAC makes the diagnosis possible in 50% to 63% of initially unsatisfactory FNAC results.[15]
A study for assessment of cost of FNAC demonstrated that the cost of a given procedure for a true diagnosis exceeds its unit cost of production. The cost study of a diagnostic procedure should take into account its predictive value, that is, its errors and its failures (unsatisfactory specimens). Thyroid FNAC failures generate a much higher cost than errors. Routine use of US-FNAC and on-site assessment of the adequacy of cytopathologic specimens should dramatically reduce the rate of failures and, thus, the cost of a true diagnosis.[16]

Thyroid Malignancies

A study of Diagnosis of Thyroid enlargement with the use of FNAC conducted in Nigeria revealed out of 84 satisfactory smears for FNAC, 73.6% cases were nonneoplastic while neoplastic lesions accounted for 21.8%, cases.

3.4% smears were unsatisfactory. Colloid goitre, 57 (65.5%) cases, dominated the diagnosis and was followed by follicular carcinoma with 9 (10.3%) cases. The cytological diagnosis could be verified by histology in 68 cases. The study had one false-positive and two false-negative reports giving a diagnostic accuracy of 95.6%. One case was complicated by mild hemorrhage.[17]

Papillary Carcinoma

Papillary carcinoma accounts for 80% of all thyroid malignancies in iodine-sufficient areas and is the predominant thyroid cancer in children and individuals exposed to external radiation. Papillary carcinoma occurs more often in women, with a 2:1 female: male ratio; the mean age at presentation is 30 to 40 years. Most patients are euthyroid and present with a slow-growing painless mass in the neck. Dysphagia, dyspnea, and dysphonia are usually associated with locally advanced invasive disease. Lymph node metastases are common, especially in children and young adults, and may be the presenting complaint. The so-called "lateral aberrant thyroid" almost always denotes a cervical lymph node that has been invaded by metastatic cancer. Suspicion of thyroid cancer often originates through physical examination of the patient and a review of the patient's history. Diagnosis is established by FNA biopsy of the thyroid mass or lymph node. Distant metastases are uncommon at initial presentation, but may ultimately develop in up to 20% of patients. The most common sites are the lungs, followed by bone, liver, and brain.

Follicular Carcinoma

Follicular carcinomas account for 10% of thyroid cancers and occur more commonly in iodine-deficient areas. The overall incidence of this tumor is declining in the United States, probably as a result of iodine supplementation and improved histologic classification. Women

have a higher incidence of follicular cancer, with a female: male ratio of 3:1, and a mean age at presentation of 50 years. Follicular cancers usually present as solitary thyroid nodules, occasionally with a history of rapid size increase, and long-standing goitre. Pain is uncommon, unless hemorrhage into the nodule has occurred. Unlike papillary cancers, cervical lymphadenopathy is uncommon at initial presentation (approximately 5%), although distant metastases may be present. In less than 1% of cases, follicular cancers may be hyper functioning, leading patients to present with signs and symptoms of thyrotoxicosis. FNA biopsy is unable to distinguish benign follicular lesions from follicular carcinomas. Therefore, preoperative diagnosis of cancer is difficult unless distant metastases are present. Large follicular tumors (>4 cm) in older men are more likely to be malignant.

Hürthle Cell Carcinoma

Hürthle cell carcinomas account for approximately 3% of all thyroid malignancies. Under the World Health Organization classification, Hürthle cell carcinomas are considered to be a subtype of follicular thyroid cancer. Like follicular cancers, Hürthle cell cancers are characterized by vascular or capsular invasion, and therefore cannot be diagnosed by FNA biopsy. Tumors contain sheets of eosinophilic cells packed with mitochondria, which are derived from the oxyphilic cells of the thyroid gland. Hürthle cell tumors also differ from follicular carcinomas in that they are more often multifocal and bilateral (approximately 30%), usually do not take up RAI (approximately 5%), are more likely to metastasize to local nodes (25%) and distant sites, and are associated with a higher mortality rate (approximately 20% at 10 years). Hence, they are considered to be a separate class of tumors by some surgeons.

Management is similar to that of follicular neoplasms, with lobectomy and isthmusectomy being sufficient surgical treatment for unilateral Hürthle cell adenomas. When Hürthle cell neoplasms are found to be invasive on intraoperative, frozen-section, or definitive paraffin-section histology, then total thyroidectomy should be performed. These patients should also undergo routine central neck node removal, similar to patients with MTC, and modified radical neck dissection when lateral neck nodes are palpable. Although RAI scanning and

ablation usually are ineffective, they probably should be considered for ablation of any residual normal thyroid tissue and, occasionally, for ablation of tumors.

Medullary Carcinoma

MTCs account for about 5% of thyroid malignancies and arise from the parafollicular or C cells of the thyroid, which, in turn, are derived from the ultimobranchial bodies. These cells are concentrated superolaterally in the thyroid lobes, which is where MTC usually develops. C cells secrete calcitonin, a 32-amino-acid polypeptide that functions to lower serum calcium levels. In some animals, especially those that lay eggs with shells, calcitonin is a significant regulator of calcium metabolism, but in humans, it has only minimal physiologic effects.

Most MTCs occur sporadically. However, approximately 25% occur within the spectrum of several inherited syndromes such as familial medullary thyroid cancer, MEN2A, and MEN2B.

Patients with MTC often present with a neck mass that may be associated with palpable cervical lymphadenopathy (15 to 20%). Local pain or aching is more common in patients with these tumors, and local invasion may produce symptoms of dysphagia, dyspnea, or dysphonia. Distant blood-borne metastases to the liver, bone (frequently osteoblastic), and lung occur later in the disease.

The female: male ratio is 1.5:1. Most patients present between 50 and 60 years of age, although patients with familial disease present at a younger age. Medullary thyroid tumors secrete not only calcitonin and carcinoembryonic antigen (CEA), but also other peptides such as calcitonin gene-related peptide (CGRP), histaminadases, prostaglandins E_2 and F_2, and serotonin. Patients with extensive metastatic disease frequently develop diarrhea, which may result from increased intestinal motility and impaired intestinal water and electrolyte flux. Approximately 2 to 4% of patients develop Cushing's syndrome as a result of ectopic production of adrenocorticotropic hormone (ACTH).

Anaplastic Carcinoma

Anaplastic carcinoma accounts for approximately 1% of all thyroid malignancies in the United States and is declining in incidence. Women are more commonly affected, and the majority of tumors present in the seventh and eighth decades of life. The typical patient has a long-standing neck mass, which rapidly enlarges and may be painful. Associated symptoms, such as dysphonia, dysphagia, and dyspnea, are common. The tumor is large and may be fixed to surrounding structures or may be ulcerated. Lymph nodes usually are palpable at presentation. Evidence of metastatic spread also may be present. Diagnosis is confirmed by FNA biopsy revealing characteristic giant and multinucleated cells. Incisional biopsy is occasionally needed to confirm the diagnosis and isthmusectomy is performed to alleviate tracheal compression.

Lymphoma

Lymphomas account for less than 1% of thyroid malignancies and most are of the non-Hodgkin's B-cell type. Although the disease can arise as part of a generalized lymphomatous condition, most thyroid lymphomas develop in patients with chronic lymphocytic thyroiditis. Chronic antigenic lymphocyte stimulation has been suggested to result in lymphocyte transformation. Patients usually present with symptoms similar to those of patients with anaplastic carcinoma, although the rapidly enlarging neck mass often is painless. Patients may present with acute respiratory distress. The diagnosis usually is suggested by FNA biopsy, although needle-core or open biopsy may be necessary for definitive diagnosis. Staging studies should be obtained to assess the extent of extra thyroidal spread.[18]

FINE-NEEDLE ASPIRATION

FNA of the thyroid with a small-gauge needle has become increasingly popular and is now one of the initial diagnostic modalities in patients with thyroid nodules. Use of a smaller-gauge needle has allowed a marked drop in the complication rate associated with the use of large-bore or core needle biopsies while maintaining diagnostic accuracy. In a series of 561 patients, FNA was found to have a sensitivity of 86% and a specificity of 91%. Accurate diagnosis of

benign lesions has significantly decreased rates of surgery in patients with thyroid nodules. Additionally, preoperative FNA is replacing the use of intraoperative frozen section pathologic analysis. Despite the widespread use of ultrasound-guided FNA, this modality is also associated with a significant rate of initial nondiagnostic cytology approaching 20% to 25%. The finding of a malignant diagnosis on FNA is associated with a high rate of accuracy approaching 100%. Certain discrete cytologic characteristics of papillary carcinoma allow the use of FNA to be extremely accurate in diagnosis.[19]

The diagnosis of follicular carcinoma cannot be made with FNA. FNA diagnosis of medullary or anaplastic carcinoma is somewhat more difficult but can be accomplished by experienced cytopathologists. When FNA reveals follicular cells, an important decision must be made. Although most of these cases are benign (follicular adenoma), this diagnosis cannot be secure and ultimately depends on complete histologic examination of the resected specimen. Large series show malignancy in 6% to 20% of thyroid lesions when follicular cells are demonstrated on FNA.

The presence of colloid and macrophages within the aspirate strongly suggests a benign lesion. In this circumstance, a safe diagnosis of a colloid nodule or benign process can be made. The patient must understand, however, that this diagnosis depends only on the aspirated material. Tissue immediately adjacent to or contained within another part of the nodule may harbor malignant cells. The false-negative rate of FNA has been reported to be between 1% and 6%. Therefore, benign nodules diagnosed by FNA are monitored sequentially with ultrasound to ensure that their characteristics do not change. If FNA leads to a diagnosis that is “suspicious but not confirmatory,” an aggressive workup continues for the possibility of malignancy. Certain series state that more than half of such FNA results are associated with malignant cells. If the FNA findings are indeterminate, either repeat aspiration or close conservative follow-up of the nodule is undertaken.[19]

FNA can also be used for lesions that are determined to be cystic by ultrasound. A larger-bore needle can be used to aspirate the cystic fluid. Examination of most cystic fluid results in

benign cytologic findings; however, an occasional papillary carcinoma can be manifested as a cyst and diagnosed by cytologic examination of cystic fluid.[19]

The indications for FNAC are as follows:

1. The diagnosis of diffuse non-toxic goitre
2. The diagnosis of the solitary or dominant thyroid nodule.
3. Confirmation of a clinically obvious thyroid malignancy
4. To obtain material for ultra-structural study and clinical research
5. Emptying of simple thyroid cysts.
6. Diagnosis of thyroiditis

The main focus of FNAC in the thyroid is STN. The FNAC has been compared with the histological findings. Most of the studies so far performed have shown its predictive values as sensitivity, specificity and efficacy in the diagnosis of neoplastic lesion of more than 90%. The rate of false negative results is 1 to 30% and it may be due to:

1. Geographic misses
2. Dual pathology
3. Errors in interpretation
4. Inadequate sampling

As the false negative rate may delay the treatment and may worsen the prognosis, the clinical findings and thyroid scanning are very important and should be considered seriously. The cystic neoplastic lesions are more vulnerable for the false negative results. The overall rates of false positive results are usually less than 5% of the total number of malignancies. So it is stressed that the surgeon can think positively for the various treatment options when the FNAC indicates a malignant lesion. The FNAC has been compared with the frozen section biopsy preoperatively and some authors have preferred the former. The frozen section biopsy has little to offer over FNAC in the assessment of follicular neoplasms. These require

extensive sampling to exclude or prove capsular or vascular invasion. There is no absolute contraindication for the FNAC in STN. But it should be performed cautiously in children or uncooperative adults. These patients may move their head suddenly during the procedure. If FNAC is performed carefully complications are few.

The recognized complications are;

1. Hemorrhage in to tissue and hematoma formation. This may obscure the histological pattern of thyroid. Larger needles are more likely to cause this complication. The hematoma may be larger enough to compress the trachea. The transient laryngeal nerve palsy has been reported.
2. Puncture of trachea may cause cough and hemoptysis. The recovery is expected within a few minutes. Elevated level of thyroglobulin after FNAC has been reported.
3. So far the dissemination and implantation of tumor has not been reported following FNAC.[20]

A similar study of FNAC on thyroid lesion conducted in Honk Kong revealed fine-needle aspiration cytology had a high positive predictive value for thyroid cancer (100%), enabling to 'rule-in' malignant lesions with confidence. Among those with indeterminate fine-needle aspiration cytology, atypical cell lesions and age greater than 40 years conferred increased risk of malignancy.[20]

Fine Needle Aspiration Cytology (FNAC) is accepted at present as the most precise diagnostic screening procedure for differentiating benign from malignant thyroid nodules.[22] It is safe, inexpensive and accurate in experienced hands; it has a sensitivity of 90- 92% and specificity 74-83%, with few false positives 3.3%. However this high sensitivity and specificity may not represent the same picture between developed and developing country populations. Considering the differences in socioeconomic and people's awareness with regards to health, it is clear that majority of patients from developing countries present late to hospital with disease being more advanced and hence the pattern of thyroid disease might be different.

1.2 PROBLEM STATEMENT

Currently at Muhimbili, the diagnosis of thyroid lesions is mainly dependent on FNAC as a preoperative diagnostic investigation to plan the surgical treatment.

No study of comparison between FNAC and histopathology finding in thyroid lesion has been conducted in our setup.

Due to lack of reliability and accuracy of the test in our setting, it is difficult to scientifically rely on the results unless accuracy of FNAC is proven by knowing its sensitivity and specificity in our setup.

Discordance in results of FNAC and histopathology findings after thyroidectomy has also been observed in several cases, which leads to revision of surgery, increase in cost, occupancy of operating theatre and patient suffering.

1.3 RATIONALE

The aim of this study is to improve our knowledge on reliability and accuracy of FNAC in comparison with gold standard histological tissue findings in areas of sample collection, sample preparation, issues of appropriate timing and deficits of reagents and plan prompt treatment of thyroid cancer patients if FNAC turns out to be a reliable and dependable indicator in our set up. Other areas of improvement include human resource as the volume of work is a lot and also expertise with accurate interpretation.

It can significantly reduce morbidity as well as mortality of patients by making early and accurate differentiation of benign and malignant thyroid nodules with special focus on prevalence of malignancy in thyroid nodules, therefore bridging the gap between clinical evaluation and final surgical pathologic diagnosis in majority of cases.

1.4 RESEARCH QUESTION

Is FNAC reliable in comparison with a gold standard histopathological findings of thyroid lesion at Muhimbili National Hospital

1.5 OBJECTIVES

1.5.1 Main Objective

To determine the reliability of FNAC compared with histopathology tissue results as a standard diagnostic technique among patients with thyroid lesions attending General Surgery at MNH

1.5.2 Specific Objectives

1. To determine the proportions of patients with thyroid nodules diagnosed by Fine Needle Aspiration Cytology and by tissue histopathology over a twenty month period at MNH.

2. To analyze the sensitivity, specificity, positive predictive value and negative predictive value of FNAC in diagnosis of thyroid lesions in surgical patients at MNH using histopathology findings as the standard test.

3. To assess the reliability/efficiency of FNAC of thyroid lesions in surgical patients at MNH.

4. To record the duration (in days) from requesting of FNAC to the reporting of results compared to histopathology report in patients with thyroid lesions attending MNH.

CHAPTER TWO

2.0 METHODOLOGY

2.1 Study design

Hospital based descriptive prospective and retrospective cross sectional study

2.2 Study area

The study was conducted at MNH, which is the National referral hospital receiving patients from districts and regional hospitals within the country but in addition it serves as city hospital by receiving more patients from the three municipalities in the city and nearby district hospitals of Coast Region due to its geographical location. The hospital is a teaching hospital for MUHAS students both Undergraduates and Postgraduates located within Dar es Salaam city.

The hospital has a bed capacity of 1,500 of which 120 beds are set apart for adult general surgery services. The below listed departments were involved:

I. The Department of General surgery inpatients and outpatient clinics of all general surgical units.
II. Histopathology Laboratory, where FNAC and tissue specimens are collected processed, stained and interpreted by a pathologist at MNH
III. Medical Records Department of MNH

2.3 Study population

All Patients with diagnosed thyroid lesion who underwent FNAC, surgery and histopathological tissue findings at MNH for the period of twenty months

2.4 Sample size

Sampling unit – MNH

Sampling frame – General surgery

Sample size estimation – $n = (Z)^2P(1-P)/e^2$

Where n – sample size

Z – 1.96

P – Sensitivity of FNAC

By (Bhatta S, et al) [22]= 85%

e – margin of error = 3%

Therefore, $(1.96)^2 0.85(1 – 0.85)/(0.03)^2 = 544$

Applying finite population correction,

Adjusted sample size, n` = n/(1 + n/N)

Where n – 544

N – Anticipated number of patients undergoing FNAC with thyroid lesion; 160

Therefore, 544/(1 + 544/160) = **124**

2.5 Sampling procedure

Convenience sampling, all patients with FNAC results who underwent thyroidectomies and histopathological results of thyroid lesions between May 2012 and February 2014 at MNH.

2.6 Data collection

1. For retrospective part, 62 patients who had attended in the department of surgery at MNH who had FNAC, underwent surgery and histopathological results for the period of May 2012-February 2013 were recruited in the study, case notes of patients with thyroid lesion were retrieved from medical records department.

Names of patients who had their histopathology findings for thyroid specimen within the stated period and corresponding file numbers were traced from the pathology laboratory records. Then the file numbers were used to retrieve the corresponding files from the records department of Muhimbili National Hospital.

2. For prospective part, 62 patients who had been admitted to general surgery ward and as an outpatient clinic for both firms who had or underwent FNAC, surgery or Histopathological examination for thyroid lesion, the processing and interpretation of cytology samples as well as specimen samples provided by surgery for histopathology were conducted by the Histopathology Department, Muhimbili National Hospital for the period of March 2013-February 2014. A total of 124 patients were recruited in the study. All the above information was filled in a data collection tool.

FNAC

Fine Needle Aspiration Cytology was performed and reported by a pathologist. A palpable mass was aspirated using a 22 or 23G needle attached to a 10cc syringe held in a syringe holder (gun). The smears were made on three glass slides which were immediately fixed in 95% ether in alcohol for at least half an hour.

The smears were then stained by a standard papanicolau stain, mounted and cover-slipped ready for reporting. No anesthesia was required.

Histopathology

Post-surgery either thyroidectomy or lobectomy the specimen was immediately put in a container with 10% formalin for at least 24hrs for proper fixation and a form filled requesting histopathology examination. In the laboratory the tissues were cut into appropriate sizes, run in a machine with graded alcohol containers 70%, 80%, 95%, 95% for proper dehydration. Then the tissues were passed through three jars containing xylene to cleanse off the alcohol. The tissues were then run in a jar containing molten wax to infiltrate the tissue. Before they were removed from the machine the tissues were then blocked, sectioned by microtome into five

micron sections stretched in warm water and put on glass slides. Then the glass slides were put on hot plate to stretch further the tissue and put in oven for 15-30 minutes according to type of wax used. Then the sections on glass slides were stained by haematoxylin and eosin, mounted ready for reporting.

2.7 Data analysis

Sensitivity: Is the ability of the test to pick all those individual who truly have the characteristic of interest. Sensitivity of FNAC will be taken as the ability of FNAC to correctly make diagnoses similar to those made by histological tissue findings.

$$\text{Sensitivity} = \frac{\text{Total number of true positives(TP)}}{\text{Total number of individuals found positive on Histopathology(TP + FN)}} \times 100$$

$$\text{Sensitivity} = \frac{TP \times 100}{D+}$$

True positives (TP): All individuals who will test positive for a thyroid disease in both FNAC and histopathology

True Negatives (TN): All individuals who will test negative for a thyroid disease in both FNAC and Histopathology

False Positives (FP): Those individuals who will test positive in FNAC but negative on Histopathology

False Negatives (FN): Those individuals who will test negative in FNAC but positive on Histopathology

Specificity: is the ability of the test to give negative finding when the tested person is truly free of the disease under study. In other words- Specificity of FNAC will be taken as the ability of

FNAC to correctly detect benign lesion in an individual who has a non-reactive/benign lesion by histopathology.

Specificity = Total number of true negatives(TN)_ _____ x 100

Total number of individuals found negative on Histopathology(TN+FP)

Specificity = TN x 100

D-

Positive Predictive Value (PVP): Proportion of true diseased individuals amongst all positive tests by FNAC. In other words, signifies the probability that a given patient with positive test, indeed does have the disease.

PPV = True positives (TP) x 100

Total positive test on FNAC(T+)

Negative Predictive Value (NPV): The proportion of healthy individuals amongst all negative tests by FNAC or the probability that a given individual with a negative test indeed does not have the diseases.

NPV = TN x 100

T-

Accuracy of FNAC – The proportion of the correct results true positive and true negative in relation to all cases studied.

Or process yielding values that are equal on average to the true underlying value for the diagnostic variable measured.

Accuracy = (TP + TN) x 100

(Reliability/efficiency) N

Of FNAC

Diagnostic value of the Fine Needle Aspiration Cytology was checked by calculating the sensitivity, specificity, positive predictive value, negative predictive value and by calculating the percentage of false positive and false negative results.

The Histopathology tissue findings was taken as the gold standard and the results of fine needle aspiration which was matching with the histopathology, taken as positive cases. Analysis was done by Statistical package for social Sciences version 20.0, P-values less than or equal to 0.05 was considered significant.

2.8 Ethical consideration

MUHAS ethical committee was sought for ethical clearance of this study and permission to conduct the study was sought from the Director of Clinical Services – MNH.

In the Retrospective part permission to use data from MNH was sought and for Prospective part again data from general surgery wards and histopathological department was used with permission from MNH, For all the cases no patient handling or contact was done only information from files and histology records was used, at all levels the patients confidentiality was maintained, as no risk of harm to subjects and their rights and welfare will not be affected.

2.9 Inclusion criteria

I. All patients with diagnosed thyroid lesions who underwent FNAC, thyroid surgery and histopathological tissue findings at MNH between May 2012 and February 2014.

2.10 Exclusion criteria

I. Hot and toxic nodules and diffuse goitre with hyperthyroidism.
II. Patients who underwent FNAC but did not have thyroid surgery.
III. Patients with missing FNAC or Histopathological results.

2.11 Study limitation

Adequate cytologic interpretation depends on correct detection of the location of the suspected lesion, also the level of expertise of pathologist and on the aspiration technique. Wrong detection, interpretation and poor aspiration techniques cause most of the false-negative reports.

Delays in staining during periods where lack of staining staff, lack of reagents may interfere with the results.

Lack of experts for cytologic aspiration, processing and interpretation by some pathologists

Improper documentation of presenting illness in records.

The most important limitation of thyroid cytology lies in the differential diagnostics of cellular follicular lesions. It is especially difficult to distinguish benign from malignant follicular neoplasms by cytologic evaluation, because the diagnosis of cancer depends on demonstration of vascular or capsular invasion. In the case of follicular lesion the cytologic examination concludes relatively often as follicular lesion of uncertain biological character.[23]

CHAPTER THREE

3.0 RESULTS

3.1 Description of the study population

A total of 124 patients with thyroid lesions were enrolled in the study. The mean age (± standard deviation) of the study participants was 40.5years (±11.66) years. Large percentage (33.1%) of the thyroid patients were in the 31-40 years age group. Fifteen (12.1%) were male and 109 (87.9%) were female (M: F, 1:7.3). (Table 1) Commonest presenting symptom was painless neck swelling 98 (79%) of 124 patients.

Table 1: Socio-demographic characteristics of study participants

Characteristics	**Categories**	**Thyroid lesions**	**Percent (%) (N=124)**
Age Group	11- 20	4	3.2
	21- 30	21	16.9
	31- 40	41	33.1
	41- 50	35	28.2
	51- 60	17	13.7
	61+	6	4.8
Sex	Male	15	12.1
	Female	109	87.9
***Age (Mean ± SD)**			**40.5±11.66**

SD= Standard deviation

The commonest age group was found to be 31-40 years with both benign (33.3%) and malignant (31.8%) lesion as histology diagnosis. Of the age group 11-20 years none of the patients were found to have malignant lesion, only 4(3.9%) had benign lesion. (Table 2)

Out of 124 thyroid lesion patients, 109 (87.9%) were female, 21(19.3%) had malignancy and 88 (80.7%) had benign lesion on histology diagnosis. (Table 2)

Neither age nor sex of the patients show significant difference on histopathology results. (Table 2)

Table 2: Socio-demographic characteristics in relation to histology diagnosis

Characteristics	**Categories**	**Histopathology(N=124)**		**P value**
		Benign (%)	**Malignant(%)**	
Age Group	11- 20	4(3.9)	0 (0%)	0.512
	21- 30	15(14.7)	6(27.3)	
	31- 40	34(33.3)	7(31.8)	
	41- 50	30(29.5)	5(22.7)	
	51- 60	15(14.7)	2(9.1)	
	61+	4(3.9)	2(9.1)	
Sex	Male	14(93.3)	1(6.7)	
	Female	88(80.7)	21(19.3)	0.468

Both P values non significant

3.2 Patients with thyroid nodules diagnosed by fine needle aspiration cytology (FNAC) and by tissue histopathology

In FNAC, total of 124 patients with thyroid lesions, 80.6% showed benign lesions, 11.3% malignant lesions and 8.1% suspicious lesions. Most common benign thyroid lesion was colloid goitre, 51 out of 100(51%), malignant were follicular carcinoma, 7 out of 14(50%) while papillary carcinoma were 3(21.4%) and follicular neoplasm suspicious were found to be 10 out of 124(8.1%).(Table 3)

In tissue histopathology, total of 124 patients with thyroid lesions, 82.3% showed benign lesions and 17.7% malignant lesion. Most common benign thyroid lesion was colloid goitre, 48 out of 102(47.1%), followed by follicular adenoma 24 (23.5%). Common malignant lesions were papillary carcinoma 9 out of 22(41%) while follicular carcinoma were also 9(41%) and none were undetermined or not confirmed by histopathology. (Table 3)

There were 10 aspirates which were suspicious for neoplasm and all were confirmed by histopathology. (Table 3)

Table 3: Patients with thyroid nodules diagnosed by fine needle aspiration cytology (FNAC) and by tissue histopathology

Diagnosis	FNAC Conditions	Frequency(%)	Frequency(%)
Benign	Colloid Goitre	51(51)	48(47.1)
	Follicular Hyperplasia	31(31)	9(8.8)
	Multinodular goiter	9(9)	15(14.7)
	Follicular adenoma	3(3)	24(23.5)
	Thyroid Cyst	3(3)	1(0.98)
	Epidermal Cyst	1(1)	1(1)
	Haemorrhagic Cyst	1(1)	-
	Tuberculous thyroiditis	1(1)	-
	Apocrine Hidrocystoma + Squamous Metaplasia	-	1(0.98)
	Hashimoto Thyroiditis	-	2(2)
	Sub acute Granulomatous Thyroiditis (Dequervaitis)	-	1(0.98)
	Total	100(100)	102(100)
Malignant	Follicular Carcinoma Suspicious	7(50)	-
	Epithelial Carcinoma	1(7.2)	-
	Papillary Carcinoma	3(21.4)	9(41)
	Thyroid Malignancy	3(21.4)	-
	Follicular Carcinoma	-	9(41)
	Hürthle Cell Adenocarcinoma	-	1(4.5)
	Squamous Cell Carcinoma G2	-	2(9)
	Diffuse Large Cell Lymphoma	-	1(4.5)
	Total	14(100)	22(100)
Suspicious	Follicular Neoplasm Suspicious	10(100)	-
	Total	124	124

Table 4: Summary of cases Examined by FNAC and Histopathology

Feature	FNAC Diagnosis	Histopathology Diagnosis
	N0 (%)	**N0 (%)**
Benign	100(80.6)	102(82.3)
Malignant	14(11.3)	22(17.7)
Suspicious for Neoplasm	10(8.1)	-
TOTAL	124(100)	124(100)

3.3 Analysis of the sensitivity, specificity, positive predictive value, negative predictive value and to assess the reliability of FNAC in diagnosis of thyroid malignancy

114 patients were analysed, as 10 patients were suspicious on FNAC.

Out of 100 non-malignant lesions on FNAC, 9 aspirates showed non neoplastic lesion while confirmed by histopathology as papillary carcinoma 4(44.4%) and follicular carcinoma 5(55.6%).(Table 5)

Out of 14 malignant lesions on FNAC, 13(92.9%) were continued on histology to be malignant and 1 patient showed papillary carcinoma on FNAC while Histological diagnosis confirmed the diagnosis as follicular adenoma.(Table 5)

Sensitivity of FNAC 59.1%, specificity 98.9%, positive predictive value 92.9, negative predictive value 91% and Accuracy 91.2%.(Table 5)

Table 5: Accuracy of FNAC diagnosis of thyroid malignancy when comparing with gold standard histolopathology diagnosis among 114 cases

FNAC Diagnosis	**Definitive Histopathology Diagnosis**		**Total**	
	Malignant	**(Non-malignant)Benign**		
Malignant	**13** **59.1% TP**	**01** 1.1% **FP**	14	T+
Non malignant(Benign)	**9** 40.9% **FN**	**91** **98.9% TN**	100	T-
Total	22 D+	92 D-	114	N

NB 10 Suspicious for Neoplasm on FNAC

(P-value <0.001 statistically significant)

Sensitivity = $\frac{TP}{D+} \times 100$ $\frac{13 \times 100}{22} = 59.1\%$

Specificity = $\frac{TN}{D-} \times 100$ $\frac{91 \times 100}{92} = 98.9\%$

Positive Predictive Value = $\frac{\text{True Positive} \times 100}{\text{Total positives on FNAC}}$ $= \frac{13 \times 100}{14} = 92.9\%$

Negative Predictive Value = $\frac{\text{True Negatives} \times 100}{\text{Total Negatives on FNAC}}$ $= \frac{91 \times 100}{100} = 91\%$

Accuracy/Reliability/

Efficiency of FNAC = $\frac{TP + TN}{N}$ $= \frac{13 + 91}{114} = 91.2\%$

Table 6: Histological Diagnosis of the false Negative FNAC

FNAC	Histological Diagnosis	Frequency	Percent %
9 Aspirates showed Non-Neoplastic results	Papillary Carcinoma	4	44.4
	Follicular Carcinoma	5	55.6
	Total	9	100

3.4 Record of the duration from requesting FNAC to the reporting of results compared to Histopathology tissue

In FNAC, out of 124 patients, 70(56.5%) received their results by one week. The mean duration (± standard deviation) of reporting the results was 8.2 days (±5.59 days). Four (3.2%) patients received their results by 3 weeks and above. The minimum time for receiving result was less than a day. (Table 7)

In Histopathology, out of 124 patients, 40(32.3%) received their results by third week. The mean duration (± standard deviation) of reporting the results was 23.53 days (±17.17 days). Eighteen (18) patients (14.5%) received their results at 6 weeks. The minimum time for receiving result was 1 week 8(6.5%). (Table 7)

Table 7: Record of the duration from requesting FNAC to the reporting of results compared to histopathological tissue

Characteristics	Categories	FNAC (%) N=124	Histopathology (%) N=124
Duration	Less than a day	1(0.8%)	00
	1 Week	70(56.5)	8(6.5)
	2 Weeks	49(39.5)	31(25.0)
	3 Weeks	3(2.4)	40(32.3)
	4 Weeks	00	12(9.7)
	5 Weeks	00	15(12.1)
	6 Weeks	1(0.8)	18(14.5)
		124(100)	124(100)
***Duration FNAC (Mean ± SD)**			**8.2±5.59**
***Duration Histopathology (Mean ± SD)**			**23.53±17.17**

S.D= Standard Deviation

CHAPTER FOUR

4.0 DISCUSSION

Fine needle aspiration cytology continues to play an important role in the management of thyroid lesions in patients. However its reliability depends on the quality of the specimens. The assessment of the patient presenting with thyroid nodule includes three modalities of clinical examination, cytology and imaging investigations and the result of FNAC still remains as the only guiding factor in the decision of surgical management.[24]

Prehand information of nature of disease alters the treatment options greatly. In thyroid, benign nodules require partial thyroidectomy or lobectomy, whereas malignant disease demands extensive surgery, which is total thyroidectomy, neck dissection followed by radio iodine ablation and lifetime dependency on thyroxine supplement. In thyroid disease, this benefit of prehand knowledge of pathology is granted by FNAC which is a well-established technique for pre-operative assessment of thyroid nodules.[24] The FNAC is cost-effective, less traumatic, less invasive, and easily performed procedure.[25] FNAC is a useful tool in the diagnosis in thyroid nodules if a suspicion of cancer exists. It has reduced the need of imaging and surgery and increased the yield of cancer in patients who come for surgery.[26]

The important steps in FNAC of thyroid are careful sample procurement, appropriate sample preparation and accurate interpretation by cytopathologists. An appropriate diagnosis can only be offered when all these steps are performed properly. Improper sampling and over interpretation can lead to discrepant cytologic diagnoses. Prudence is recommended to meticulously and carefully scrutinize for various cytologic features so as to reduce the number of discrepant cases.[27]

4.1 Description of the study population

This study consisted of 124 patients with thyroid lesions. The age of patients studied ranged from 12 to 77 years, the mean age (± standard deviation) of the study participants was 40.5years (±11.66) years. There was similar pattern in a study done in Tanzania on goitre showing the mean and median ages were 42.7 and 42.5 years indicating consistent distribution. The minimum age was 13 years and the maximum was 72 years with a standard deviation of 12.27 years.[28] Similar mean age in this study was due to the fact that the study also included both patients with benign and patients with malignant thyroid lesions. In this study most of the patients presented in 3rd and 4th decade which is in accordance to the study of Bukhari and colleagues and also in a study in Iran.[29,30]

There is abundant literature showing that FNAC, when practiced in a multidisciplinary setting with the involvement of pathologist, radiologist and surgeons, is an extremely accurate test with high sensitivity, specificity, rapid and cost effective in the diagnosis of thyroid lesions.[27,31,35]

The largest percentages (33.1%) of the thyroid patients were in the 31-40 years age group. Fifteen (12.1%) of the 124 patients were male and 109 (87.9%) were female (M: F, 1:7.3). The commonest presenting symptom was painless neck swelling which constituted 98 (79%) out of 124 patients. A similar pattern was found in a study conducted in Tanzania, in which there were 106 females and 18 male patients with goitre constituting a male to female ratio of 1:6. Most patients were in the age group of 31- 40 and 41-50 years.[28] The commonest age group was found to be 31-40 years with both benign (33.3%) and malignant (31.8%) lesion as histology diagnosis. In this study the age group of 11-20 years none of the patients was found to have malignant lesion, only 4(3.9%) had benign lesion. Out of all female patients, 21(19.3%) had malignancy and 88(80.7%) had benign lesion on histology diagnosis which was similarly shown in studies conducted in Tanzania.[28]

4.2 Proportions of patients with thyroid nodules diagnosed by fine needle aspiration cytology (FNAC) and by tissue histopathology

In this study of FNAC, out of 124 patients with thyroid lesions, 80.6% showed benign lesion, 11.3% malignant lesion and 8.1% suspicious lesion. Most common benign thyroid lesion was colloid goitre, found in 51 out of 100(51%). Malignant lesions were follicular carcinoma in 7 out of 14(50%) while papillary carcinomas were 3(21.4%) and follicular neoplasm suspicious were found to be 10 out of 124(8.1%). In series of studies done in U.S.A and other parts of world benign cytologic diagnosis is reported for 50% to 90% of the specimens (average, 70%) [31,32,33,34,35]. From 10% to 30% of FNA cytologic specimens may be suspicious for malignancy or indeterminate (average, 20%).[34,35]The accuracy of FNAC in cases of follicular carcinoma is lower and estimated to be between 10% and 40%, because identification of structural features of cell groups and the capsule of the nodule are essential for diagnosis.[47,55,56]

In present study of tissue histopathology, a total of 124 patients with thyroid lesions, 17.7% were found having malignant lesion. Malignancies were papillary carcinoma, 9 out of 22(41%) while follicular carcinomas were also 9(41%), 2(9.1%) Squamous cell carcinoma, 1(4.5%) hürthle cell adenocarcinoma, 1(4.5%) diffuse large cell lymphoma and none were undetermined or not confirmed by histopathology. A study conducted in Tanzania on thyroid disease, incidence of malignancy was found to be 18%, similar trend as in present study.[28]Another study conducted in Tanzania on frequency of carcinoma revealed 15(6.3%) cases as malignant.[1] Possible rise in the frequency over the span of 18 years could be due to increase in use of different diagnostic techniques and possible rise in iodine deficiency in some regions of the country, despite rally of iodinization of table salt. The clinical picture and pattern of thyroid disease seen and reported in developed countries may be different from disease pattern in third world countries especially in goiter endemic areas. This is mainly affected by socioeconomic status and literacy.

Majority of patients in developed countries report to hospital early, and management is done accordingly, while patients with goitre in developing countries present late, as shown in a study by E. Nyawawa et al, in which the cases of patients who presented at an average of 4 years, the minimum time to report was 1year and the maximum was 20 years after onset of disease, with symptoms of pressure, cervical adenopathy and hoarseness of voice. Seventy four (60%) of their patients had multinodular disease and the incidence of malignancy was found to be high (15%). This suggested that there is a higher risk of malignant degeneration in patients with long standing history of goiter.[36]

Benign lesions were found to be 82.3%, with most common benign thyroid lesion being colloid goitre, 48 out of 102(47.1%), followed by follicular adenoma 24(23.5%), 1% as subacute thyroiditis and 2% as hashimoto's thyroiditis. A similar trend was seen in a study conducted in Tanzania showing benign lesion as 81.6%.[28] This was also in accordance with a study in Karachi, among the sixty cases included in the study FNAC diagnosed 50(83.33%) cases as benign and 10(16.66%) cases as malignant. Thirty cases (50%) were reported as nodular goitre, 9(15%) as follicular adenoma, 8(13.33%) as subacute thyroiditis and 3(5%) as hashimoto's thyroiditis.[37]

In this study, there were 10 aspirates which were Suspicious for neoplasm and all were confirmed by histopathology as benign lesions with 4 follicular hyperplasia, 3 follicular adenoma, 2 colloid goiter and one hashimoto's thyroiditis. Overall benign thyroid disease is more common than malignancy, while follicular and papillary carcinoma has almost a parallel trend throughout, with a slight recent increased rate. Reports from developed countries suggest that papillary carcinoma is the commonest malignant type (80%), follicular carcinoma (20%), medullary carcinoma (<5%) and anaplastic carcinoma (<1%).[38] In this study papillary and follicular carcinoma had similar prevalence, possibly due to presence of iodine deficient endemic areas still exists, while developed world its decreasing in iodine deficiency. None of the patients had either medullary or anaplastic carcinoma.

4.3 The sensitivity, specificity, positive predictive value, negative predictive value and to assess the reliability of FNAC in diagnosis of thyroid malignancy

Hundred and fourteen patients were analysed, as 10 patients were suspicious on FNAC. True positive were found in 13(92.9%) patients. Out of 100 non-malignant lesions on FNAC, 9(9.0%) aspirates showed non neoplastic lesion but they were confirmed by histopathology as papillary carcinoma 4(44.4%) and follicular carcinoma 5(55.6%) (false negative). The false negative FNAC results may occur because of sampling error or misinterpretation of cytology and are of great concern because they indicate the potential to miss malignant lesion.[39] Since only a small percentage of patients with benign cytological findings undergo surgery, it is difficult to state the true frequency of false negative results.[35] False negative rates(9.0%) in this study accords with the reports that suggest a range in literature from 1 to 11%.[35,40] This high rate of failure to diagnose cancer could be attributed to the failure of aspiration from precise locations. Also false negative cytology results in a delay in treatment and hence adversely affects the outcome in patients with thyroid cancer.[41]This is also consistent with recent reports in the literature that suggest a false negative rate of 1% to 16% in different series.[36,33,42]

Out of 14 malignancies on FNAC, 13(92.9%) were malignant(true positive) which showed 5(35.7%) papillary carcinoma, 4(28.6%) follicular carcinoma, 2(14.3%) squamous cell carcinoma, 1(7.1%) diffuse large cell lymphoma, 1(7.1%) Hürthle cell adenocarcinoma and 1(7.1%) patient showed papillary carcinoma on FNAC while histological diagnosis confirmed the diagnosis as follicular adenoma (false positive). Papillary type of smear was misinterpreted as carcinoma either possibly due to too much stress on cellularity and architectural pattern or cytomorphological features of papillary carcinoma were lacking during interpretation and thus papillary hyperplasia in adenomatous follicle was diagnosed on cytology as carcinoma. As papillary hyperplasia and hyperplastic nodules are well known to occur in adenomatous follicle.[43] In the present study sensitivity of FNAC was 59.1%, specificity 98.9%, positive predictive value 92.9, negative predictive value 91% and Accuracy 91.2%.

In the published data, the sensitivity, specificity and accuracy of thyroid FNAC in detecting malignancy ranges from 52-86%, 52-87% and 65-80% respectively.[44,45,46]Others reported sensitivity of FNAC is between 79% and 98% according to most authors in reviewing the literature[11,47,48,49,50,51], specificity ranges from 70% to 100% [11,47,48,49,50,51], and false-positive and negative results in 5–25% of cases 5. In our study overall sensitivity was calculated at 59.1% and specificity was analysed as 98.9% which matches the above mentioned figures from different studies. Accuracy of FNAC is estimated to be between 87% and 95%[11,47, 48, 49]and varies according to the histological evaluation. In this study overall accuracy was 91.2%, and positive and negative predictive values were 92.9% and 91% respectively which again matches the searched literature.[11, 50]

Another study done in Pakistan showed a similar trend of sensitivity which was 61.53% and specificity was 98.9%. Similarly concluded by Humberger as sensitivity around 65.53% and specificity 72–100%.[52]

The determinant factor for such a wide range of sensitivity, specificity and accuracy may be how the cytopathologists classify ‘suspicious' as well as false positive and negative samples. Some authors include follicular lesion in malignant / neoplastic group, whereas others exclude them from the calculations. In our study sensitivity rate was low compared to others as 9 aspirates which were nonneoplastic were later found to have malignancy on histological examination. This suggests that the FNAC interpretation is operator dependent. Our positive and negative predictive values are comparable with published data.[11,50]

FNAC is generally reported to have high sensitivity (74-83%) and specificity (92%) with low false positives (<5%)[53,54]. In our set up however this is not the case. The accuracy FNAC for thyroid disease like that reported for breast cancer (unpublished) in Tanzania has been shown to be low. In this study the sensitivity (59.1%) was low however; specificity (98.9%) was similar to other reported series.

FNAC can also be used for monitoring therapy. Also application of various techniques like advanced imaging techniques, immune-cytochemistry, immunologic analysis, analysis of hormone receptors and electron microscopic study can result in further reduction in misdiagnosis and can considerably expand the diagnostic range and increase the diagnostic accuracy.

4.4 Record of the duration from requesting FNAC to the reporting of results compared to Histopathology tissue

In this study, out of 124 patients 70(56.5%) received their FNAC results by one week. The mean duration (± standard deviation) of reporting FNAC results was 8.2 days (±5.59) days. Four (3.2%) patients received their results 3 weeks and above. The minimum time for receiving result was less than a day. Few studies conducted in Tanzania on FNAC with other organs, showed a delay, as 67.5% results were reported at 2 weeks and median duration was 10 days. [57,]

In this study, out of 124 patients 40(32.3%) received their histological results by third week. The mean duration (± standard deviation) of reporting histopathology results was 23.53 days (±17.17) days. Eighteen (18) patients (14.5%) received their results at 6 weeks. Studies conducted in Tanzania on other organs showed histopathology results reported at a duration of 21 days.[57] In both cases the delay is explained by the heavy patient load, poor follow up of results from up country, or poor communication from the surgeons/physicians who ordered the procedure and as well as unreliable supply of xylene, absolute alcohol, ether, glass slide, cover slips etc. It seems that possibility of processing these procedures more rapid (from less than a day in FNAC to 1 week in Histology) is high.

CHAPTER FIVE

5.0 CONCLUSION AND RECOMMENDATION

5.1 CONCLUSION

The assessment of the patient with a thyroid nodule(s) includes the triple modalities of clinical examination, cytology and imaging investigations (radionuclide thyroid scan). The result of thyroid aspiration cytology is therefore only one factor governing the management decision.
Thyroid disease in our setting and compared to others, occurs more commonly in female and in early 40's of age. The pattern of disease in thyroid lesions is mainly affected by socioeconomic status and literacy, when comparing with developed world.

On the basis of this study, high specificity and commonest thyroid lesions, benign lesion once diagnosed on FNAC, there is a high probability to be considered benign on histology.
Indeterminate FNAC results and cytodiagnostic errors are unavoidable due to overlapping cytological features particularly among hyperplastic adenomatoid nodules, follicular neoplasms and follicular variants of papillary carcinomas. Ongoing correlation of cytology and histology is an important quality assurance measure and it allows laboratories to calculate their false positive and false negative rates.

On the basis of this study the accuracy of FNAC at MNH is comparable to other studies done elsewhere, however the sensitivity which is relatively low 59.1%, which was influenced by high false negative results 9.0%. These findings were relatively lower compared to literature. The study showed several factors that contributed to these low findings, inadequate experience of some of the pathologist and technicians in aspirating, processing and interpreting the aspirates especially in the retrospective part of the study. In addition inadequate facilities, heavy patient load, financial constraints and unreliable supply of basic reagents like xylene,

absolute alcohol ether, glass slides, cover slips etc. All contributed to the delay on definitive diagnosis and management.

The duration for FNAC was almost 1 week and a number of them took 2- 3 weeks. This can be explained by the fact that at Muhimbili National Hospital, the demand for this service is overwhelming as indicated by long waiting list of cases. However the reason does not refute the fact that, duration for FNAC results if short, it provides opportunity for early discussion of treatment options with the patient. In this way patients are spared psychological traumatic experience of being uncertain of the diagnosis in the interval between the initial evaluation and surgical treatment.

The FNAC is very useful and readily available tool for evaluating thyroid nodules with high accuracy and specificity in picking up benign lesion and excluding the malignant disease. This is very helpful in patient counselling and defining the extent of surgery.

In summary the results of this study are comparable with the current published data and demonstrate that FNA cytology is a specific, and accurate initial diagnostic test for evaluation of patients with thyroid swellings. However, FNAC has low sensitivity. Cytodiagnostic errors of some cases with overlapping cytological features can be avoided by paying attention to the possible pitfalls. The suspicious results can be resolved by diagnostic surgical resection. A benign FNAC diagnosis should be viewed with caution as false negative results do occur and these patients should be followed up clinico-radiologically for any progression that will require repeated FNAC and/or surgery.

5.2 RECOMMENDATION

Cytological diagnosis should always be interpreted within the clinical context and if possible with the radionuclide thyroid scan findings.

Experience is not inborn rather an acquired attribute. By introducing a pure “Thyroid lesion Clinic” where not only the pathologists would perform the aspiration but surgeons, clinician and residents would fully participate and be trained would increase the number of aspirations, reduce load per practitioner, increases the volume of cases, chance of immediate assessment of specimen. Proper training should be given at all levels depending on the level of interests and financial availability. There should be standard guidelines for sampling procedures. Aspiration procedure should be annually reviewed for audit and a system providing feedback, by counselling and further training.

Unless adequate cellular thyroid elements are identified, it is best to classify the smear as inadequate rather than negative. This practice will reduce the false negative rate and contribute to effectiveness of this diagnostic technique.

Additional steps in false negative rate reduction is to perform:-

- Multiple aspirations from different parts of the lesion could give a clear picture of cytologic features, reduce overinterpretation and help in proper diagnosis

- Ultrasound-guided FNAC in cystic thyroid nodule results in better sample acquisition leading to low rate of false negative/ non diagnostic smears and high overall accuracy.

Proposed guidelines for FNAC:

FNAC should be performed by individuals who have had training in both thyroid examination and thyroid aspiration. Thyroid FNA in the hands of experienced operators achieves high diagnostic accuracy. Aspirates should be obtained from different portions of the nodule, preferably peripheral areas, in an organized and sequential manner. It is essential to ensure that

an adequate number of follicular cells is present. A cytopathologist, preferably one with experience in thyroid cytology, should review and interpret the slides. If reaspiration yields insufficient material, US-FNA biopsy is the next test. In the event that the final result is still insufficient, surgical excision is warranted for most nodules.

REFERENCES

1. Lema LEK, Aziz MR, Mbembati NA, Mwakyoma HA. Frequency of carcinoma in solitary thyroid nodules and in multinodular goiters. East and Central African journal of surgery. 1996; 2(1):11-14

2. Vander JB, Gaston EA and Dawber TR. Significance of solitary non toxic thyroid nodules. New Engl J Med. 1984;254:970-973

3. Figg DM, Bralt HJ, Vanvliet PD and Dean RE. Thyroid cancer, diagnosis and management Am J Surg. 1978;178;135:671-674

4. Belfore A, Ginfrida D, La Rosa GL, Ippolito O, Russo G, Fiumara A et al. High frequency of cancer in cold thyroid nodules occurring at young age Acta Endocrinologica. 1989;121:197-202

5. McCall A, Jarosz H, Lawrence AM and Paloyan E. The incidence of thyroid carcinoma in solitary cold nodules and in multinodular goiters Surgery. 1986;100:1128-1132

6. Wheelar MH, Malignant goiter Surgery 1994;26:161-168

7. McHenery C, Smith M, Lawrence AM, Jarosz H, Paloyan E. Nodular thyroid disease in children and adolescents: a high incidence of carcinoma Am Surg. 1988;54:444-447

8. Re Mine WH, Mc Conahey M. Management of thyroid nodules Surg Clin N AM. 1977;57:523-531

9. Abebe B, Mensur O. Goitre in a Teaching Hospital in North Western Ethiopia. East and Central African Journal of Surgery. 2006; 11(2): 21-27

10. Guhamallick M, Sengupta S, Bhattacharya NK, Basu N, Roy S, Ghosh AK, et al. Cytodiagnosis of thyroid lesions-usefulness and pitfalls. Journal of cytology. 2008; 25(1):6-9

11. Mahar SA, Husain A, Islam N. Fine needle aspiration cytology of thyroid nodule: diagnostic accuracy and pitfalls. Journal of Ayub Medical College, Abbottabad : JAMC. 2004; 18(4): 26–9

12. Kumar S, Aqil S, Dahar A. Role of fine needle aspiration cytology in thyroid diseases. Journal of Surgery Pakistan(international). 2008; 13(1): 22–25.

13. Carmeci C, Jeffrey RB, McDougall IR, et al. Ultrasound-guided fine-needle aspiration biopsy of thyroid masses. Thyroid. 1998;8:283-289.

14. Danese D, Sciacchitano S, Farsetti A, et al. Diagnostic accuracy of conventional versus sonography-guided fine-needle aspiration biopsy of thyroid nodules. Thyroid. 1998;8:15-21.

15. Alexander EK, Heering JP, Benson CB, et al. Assessment of nondiagnostic ultrasound-guided fine needle aspirations of thyroid nodules. J Clin Endocrinol Metab. 2002;87:4924-4927.

16. Borget I, Vielh P, Leboulleux S, Allyn M, Iacobelli S, Schlumberger M, et al. Assessment of the cost of fine-needle aspiration cytology as a diagnostic tool in patients with thyroid nodules. American journal of clinical pathology [Internet]. 2008 May [cited 2013 May 12];129(5):763–71. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18426737

17. Afolayan EA, Mohammed A. Diagnosis of thyroid enlargement: use of FNAC, Nigerian Journal postgraduate med. 2008;1(1):22-27

18. Beauchamp RD, Mark BE, Kenneth LM, John BH, Leslie JS. Sabiston text book of surgery.18th ed. Philladelphia: Saunders Elsevier;2008.Chapter 36, Thyroid.

19. Overview on Fine needle aspiration cytology of Thyroid nodule [internet]. 2007 [cited 2013 jan 23]. Available from: http://www.healthnet.org.np/resourse/thesis/othnsurgery/.../introduction.PDF

20. Cheung YS, Poon CM, Mak SM, Michael WM, Leong HT. Fine needle aspiration cytology of thyroid nodule-how well are we doing?. Honk Kong Medical Journal. 2007; 13(1):12-5

21. Gharib H. FNAC of thyroid nodules, advantages limitations and effect. Mayo Clin. Proc 1994; 69

22. BhattaS , Makaju R , Mohammad A. Role of fine needle aspiration cytology in the diagnosis of thyroid lesions. Journal of Pathology of Nepal. 2012; 2:186 – 188

23. Caplan RH, Kisken WA, Strutt PJ, Wester SM. Fine-needle aspiration biopsy of thyroid nodules, Thyroid nodule July, Postgrad Med. 1991; 90(1):183–190.

24. Tabaqchali MA, Hanson JM, Johnson SJ, Wadehra V, Lennard TWJ, Proud G. Thyroid aspiration cytology in Newcastle: a six year cytology/ histology correlation study. Ann R Coll Surg Engl 2000; 82: 149-55.

25. Safirullah, Mumtaz N, Khan A. Role of Fine Needle Aspiration Cytology (FNAC) in the diagnosis of thyroid. J Postgrad Med Inst 2004;18(2):196–201.

26. Ramsden J, Watkinson JC. Thyroid cancers.Scott-Brown's Otorhinolaryngology, Head and Neck Sugery. 7th edition, vol 2, Hodder Arnold, 2008:2663–701.

27. Pandey P, Dixit A, Mahajan NC. Fine-needle aspiration of the thyroid: A cytohistologic correlation with critical evaluation of discordant cases. Thyroid Res Pract 2012;9:32-9.

28. Nyawawa ET, Yongolo S, Tupa J. Radionuclide scan and other diagnostic studies in goiter patients in Tanzania. East And Central African Journal of Surgery.2006;11(2):15-20

29. Bukhari MH, Niazi S, Hanif G, Qureshi SS, Munir M, Hasan M, et al. An updated audit of fine needle aspiration cytology procedure of solitary thyroid nodule. Diagnos Cytopathol 2008; 36: 104-12.

30. Wahid FI, Khan SF, Rehman HU, Khan IA. Role of Fine Needle Aspiration Cytology in Diagnosis of Solitary Thyroid Nodules. 2011;23(4):111–8.

31. Goellner JR, Gharib H, Grant CS, Johnson DA. Fine needle aspiration cytology of the thyroid, 1980 to 1986.ActaCytol. 1987;31:587-90.

32. Singer PA. Evaluation and management of the solitary thyroid nodule. Otolaryngol Clin North Am. 1996;29:577-91.

33. Baloch ZW, Sack MJ, Yu GH, Livolsi VA, Gupta PK. Fine-needle aspiration of thyroid: an institutional experience. Thyroid. 1998;8:565-9.

34. Caruso D, Mazzaferri EL. Fine needle aspiration biopsy in the management of thyroid nodules. Endocrinologist. 1991;1:194-202.

35. Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. Ann Intern Med. 1993;118:282-9.

36. Tan GH, Gharib H, Reading CC. Solitary thyroid nodule. Arch Intern Med 1995**;155:**2418-2423.

37. Saddique M, Iqbal P, Baloch Q. FNAC : a reliable diagnostic tool in solitary thyroid nodule and multinodular goiter. 2008;24(3).

38. Lange G, MeyerBJ, VanNiekerk ACM. Cancer of thyroid. The MedicineJournal.2001**;3:** 1-7

39. Hall TL, Layfield LJ, Philippe A, Rosenthal DL. Sourse of diagnostic error in the fine needle aspiration of the thyroid. Cancer 1989;63:718-25.

40. Bakhos R, Selvaggi SM, Dejong S, Gordon DL, Pitale SU, Hermann M et al. Fine-needle aspiration of the thyroid: Rate and causes of cytohistopathologic discordance. Diagn cytopathol 2000;23:233-7.

41. Yeh MW, Demircan O, Ituarte P, Clark OH. False negative fine needle aspiration cytology results delay treatment and adversely affect outcome in patients with thyroid carcinoma. Thyroid 2004;14:207- 15.

42. Caraway NP Sniege N, Samaan. Diagnostic pitfalls in thyroid fine needle aspiration: a review of 394 cases. Diagn cytopathol.1993; 9: 345-50.

43. Kini SR. Thyroid. In: Kline TS, editor. Guides to clinical aspiration biopsy series, 2nd ed. New york: Igaku-Shoin;1996.

44. Holleman f, Hoekstra JB, Ruitenberg HM. Eualuation of fine needle aspiration cytology in the diagnosis of thyroid nodules. Cytopathology.1995, 6:175-186.

45. Cap J, Ryska A, Rehorkova P, Hovorkova E, Kerekes Z, Pohnetalova D. Sensitivity and specificity of the fine needle aspiration biopsy of the thyroid: clinical point of view. Clinical endocrinology 1999, 51:509-515.

46. Mundasad B, Mcallister I, Carson J, Pyper P. Accuracy Of Fine Needle Aspiration Cytology In Diagnosis Of Thyroid Swellings. The Internet Journal of Endocrinology.2005, 2(2).

47. Kessler A, Gavriel H, Zahav S. Accuracy and consistency of Fine- Needle Aspiration Biopsy in the Diagnosis and management of Solitary Thyroid Nodules. IMAJ June 2005; (7):371-73.

48. Martinek A, Dvorackova J, Honka M, Horacek J, Klvana P. Importance of guided fine needle aspiration cytology (FNAC) for the diagnostics of thyroid nodules- own experience. Biomed. Papers 2004; 148(1): 45-50.

49. Mandell DL, Genden EM, Mechanick JI, Bergman DA, Biller HF, Urken ML. Diagnostic accuracy of fine needle aspiration and frozen section in nodular thyroid disease. Otolaryngol Head Neck Surg2001; 124: 531–6.

50. Silverman JF, West RL, Larkin EW, et al. The role of fine needle aspiration biopsy in the rapid diagnosis and management of thyroid neoplasm. Cancer 1986;57: 1164–70.

51. Kaur K, Sonkhya N, Bapna AS, Mital P. A comparative study of fine needle aspiration cytology, ultrasonography. And radionuclide scans in the management of solitary thyroid nodule: a prospective analysis of fifty cases. Ind J Otolaryngology and head and neck surgery. April-June 2002; 54(2): 96-101.

52. Humburger JI. Diagnosis of thyroid nodules by fine needle aspiration biopsy: use and abuse. J Clin Endocrinol Metab 1994;79:335–9.

53. Gharib H, Goellner JR, Johnson DA. Fine-needle aspiration cytology of the thyroid: a 12 year experience with 11,000 biopsies. Clin.Lab Mzed.1993**;13:**699

54. Aschraft MW, Van Herle AJT. Management of thyroid nodule: history and physical examination, blood tests, x-ray tests and ultrasonography. Scanning technique, thyroid suppressive therapy and FNAC. Head and neck. Surg. 1981; **3:**216

55. Oertel YC, Oertel JE. Thyroid cytology and histology. Baillieres Best Pract Res Clin Endocrinol Metab 2000; 14:541–57.

56. Baloch ZW, Fleisher S, LiVolsi VA, Gupta PK. Diagnosis of "follicular neoplasm": a gray zone in thyroid fine-needle aspiration cytology. Diagn Cytopathol 2002; 26:41–4.

57. Mpongi JP. The diagnostic value of fine needle aspiration cytology for prostate lesions (Mmed dissertation). Muhimbili National Hospital: Muhimbili University of Health and Allied Sciences; 2007.

APPENDICES

Appendix 1: Questionnaire

A. Introduction

I. Serial N0:_____

Hospital Care file N0:_____

II. Patient's Age (in years): _____

III. Patients sex : a) M b) F

IV. Presenting symptoms _____

B. Main theme:

1. Date of requesting for FNAC _____
2. Date of reporting FNAC results _____
3. Duration (in days) from the time FNAC was requested to when report was made available _____
4. Diagnosis according to FNAC results, as reported: _____

_____

5. Was any other tissue diagnostic technique employed? Yes/No
6. What other tissue diagnostic technique was employed?
   a) Incisional biopsy
   b) Surgery:
      I. Lobectomy
      II. Excision
      III. Subtotal Thyroidectomy
      IV. Total Thyroidectomy
      V. Others (specify)_____
   c) Others (specify) _____

7. When was the histopathological tissue ordered? (state date)_____
8. When was the report for Histopathological tissue signed? (state date)

   _____

9. Duration (in days) from the time histology was ordered to when its results were made available _____

10. Diagnosis from Pathologist's report of the histopathological tissue results

    _____

    _____

11. The diagnosis made following FNAC, was it similar to the one made from histopathological tissue?
    Yes/No

12. FNAC suspicion
    a) Confirmed by histopathological tissue? YES/NO
    b) Refuted by histopathological tissue results? YES/NO
    c) Histopathological tissue results also remain inconclusive YES/NO