# CHARACTERIZATION OF THYROID NODULES USING ACR 2017 TIRADS CLASSIFICATION SYSTEM AND CORRELATION WITH THE BETHSEDA FNAC SYSTEM AT KENYATTA NATIONAL HOSPITAL.

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**A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT FOR THE REQUIREMENTS OF MASTER OF MEDICINCE IN DIAGNOSTIC IMAGING AND RADIATION MEDICINE**

**UNIVERSITY OF NAIROBI**

**DECLARATION**

I hereby declare that the work contained herein is my original work that has not been presented at any other place to the best of my knowledge.

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**DEDICATION**

I dedicate this to my mother Dr Angeline Aywak and my sisters Valary and Dorothy Aywak whose tireless support and prayers kept me going.

**ACKNOWLEDGEMENTS**

Thanks to Almighty God for His grace and mercy that made it possible for me to finish this work.

I would like to convey my sincere, heartfelt thanks to both my supervisors, Dr Caroline Kebuka and Dr Alfred Odhiambo for their guidance, continuous support, and trust in my abilities during my study period.

Special mention goes to the following persons who played pivotal roles during the study.

- Mr. Maina Cytotechnologist at KNH Cytology Lab for his tireless support during data collection
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- Dr Nanabhai for assisting me with a portable ultrasound machine.
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I am indebted to my parents Mr. Walter Aywak and Dr Angeline Aywak and my siblings Dorothy, Allan, Aggrey, Valary and Valentine Aywak for their continued support and guidance in my career.

## LIST OF ABBREVIATIONS AND ACRONYMS

**ACR – American College of Radiology**

**TIRADS- Thyroid Imaging and Reporting Data System**

**FNAC- Fine Needle Aspiration Cytology**

**KNH- Kenyatta National Hospital**

**UON- University of Nairobi**

**DDIRM- Department of Diagnostic Imaging and Radiation Medicine**

**BIRADS – Breast Imaging and Reporting Data System**

**CT - Computed Tomography**

**MRI – Magnetic Resonance Imaging**

**DWI – Diffusion Weighted Imaging**

**FDG – PET - Fluorodeoxyglucose Positron Emission Tomography**

**USG- FNAC – Ultrasound guided FNAC**

**C- FNAC – Conventional FNAC**

**TBSRTC – The Bethseda System for Reporting Thyroid Cytopathology**

**NPV – Negative Predictive Value**

**PPV – Positive Predictive Value**

**% - Percentage**

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## ABSTRACT

**Introduction:** Thyroid gland pathology can be diffuse enlargement or focal nodules. Besides clinical examination, imaging and cytology play a key role in further evaluation of the varied thyroid pathology. All of these have resulted in improved evaluation of thyroid nodules, with the modality of first choice being high resolution ultrasound. Owing to this increased detection, an upsurge has been seen in the number of patients undergoing invasive procedures to discern benign from malignant nodules. Majority of these are found to be benign, leading to development of sonographic risk stratification models to help guide the clinician on which nodules require follow up or cytologic diagnosis. In Kenya, there is limited data comparing TIRADS and fine needle aspiration cytology (FNAC) in assessment of thyroid nodules and in most cases the TIRADS classification is not employed.

**Study Objective:** To subject all patients diagnosed with thyroid nodules and referred for FNAC to sonographic stratification using the ACR 2017 TIRADS and correlate with the FNAC Bethesda Classification.

**Materials and Methods:**

Following authorization by the by the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee a prospective cross-sectional study was conducted on 79 consenting patients who satisfied the inclusion criteria at Kenyatta National Hospital (KNH)**.** The study ran from November 2019 to May 2020.

Conventional B- mode and Color Doppler ultrasound of thyroid nodules was done by the principal investigator using a standard procedure and images saved and findings stratified. These were later verified by 2 consultant radiologists well versed with thyroid sonography and a score assigned according to the ACR TIRADS.

Ultrasound guided FNAC of the identified nodules was done aseptically using standard ultrasound guided free hand FNA procedure. Diagnostic quality of the aspirate was confirmed, and slides fixed by a qualified cytotechnologist. The slides were sent to a qualified cytopathologist for evaluation and classification according to the Bethesda Classification.

Data was captured using a standardized Microsoft Excel data collection tool. Demographic and clinical characteristics were summarized using proportions for categorical variables and means or medians for continuous variables. Prevalence of malignancy was summarized as a proportion and concordance rate defined as the number of classification agreement outcomes over the total number assessed. Analysis was done using Stata version 16. A comparison with other worldwide studies was made.

**Results**

A total of 79 patients were evaluated and of these, 72 (91.9%) were female and 7 (8.2%) were male. Majority of the patients were in the 4th decade of life accounting for 39.2% of the sample population, with a median age of 45yrs. Out of 108 nodules in our study, 106 were benign and 2

were malignant. Of these nodules, 5 were categorized as TIRADS 1, 40 as TIRADS 2, 37 as TIRADS 3, 24 as TIRADS 4 and 2 as TIRADS 5.

The percentage risk of malignancy based on TIRADS classification was found to increase with increase in TIRADS classification. TIRADS 1-3 had 0%, TIRADS 4 had 4.2% risk and TIRADS 5 had 50% risk of malignancy with a p value of <0.05. The overall risk of malignancy was 1.9%. The concordance of ACR TIRADS with Bethseda FNAC was 100% for TIRADS 1 to 3 with Bethseda II and 50% for TIRADS 5 with Bethseda V. Upon application of Cohen's Kappa, slight agreement was shown which was not statistically significant (p value of 0.2514). The ACR TIRADS diagnostic performance was calculated using FNAC as the gold standard test and was found to have an overall sensitivity of 100%, specificity of 77.36%, positive likelihood ratio of 4.42, negative likelihood ratio of 0.0, positive predictive value of 7.69%, negative predictive value of 100% and overall diagnostic accuracy of 77.78%. (p value < 0.05)

**Conclusion**

ACR 2017 TIRADS as a stratification system can identify almost all benign lesions as per this study owing to its high specificity and high concordance between TIRADS 1-3 and Bethseda II. It is simple to use in day to day practice owing to its point based format, allowing all nodules to be classified and provides a tool that can be used in management of thyroid nodular disease to avoid unnecessary biopsies.

# CHAPTER 1

## 1.1 INTRODUCTION

Thyroid pathology can be diffuse enlargement or focal nodules. Of the focal nodules several studies worldwide based on invasive procedures have shown that most are benign with approximately 4.0 to 6.5 % being malignant.[1]. Female preponderance has been noted, which has been attributed to increasing age and deficiency of iodine. Nodular disease of the thyroid is common worldwide with 4-8% of the population diagnosed by neck palpation while 67% have been diagnosed using ultrasonography and 50% at autopsy. [1]

Among the imaging modalities, ultrasonography has become the main modality in the assessment of thyroid nodular disease. [2] As it not only localizes the mass to the thyroid and its effect to surrounding structures but is also key in guiding intervention.

A meta-analysis of publications assessing the validity of Bethesda reporting system of thyroid cytology from January 2008 to September 2011, found that out of 6362 nodules 39 - 73.8% were found to be benign.[3] Locally in Kenya several studies have shown a trend of increased rates of benign thyroid nodules like other worldwide regions. A local retrospective study done at the Moi teaching and referral hospital, Kenya found that out of 118 patients comprising of 87 women and 31 men who underwent FNAC, 66% (78) were benign.[4]

FNAC is the foremost diagnostic investigation for all thyroid nodules that helps determine whether they are benign or malignant. [5] Ultrasound has further been used to aid in FNAC to visualize and characterize nodules and guide needle placement, thereby increasing diagnostic accuracy rates as compared to conventional FNAC. [5]

In 2007, upon recognizing the need for standardizing reporting of thyroid nodule aspirates, histopathologists developed the Bethesda classification, enabling them to communicate their findings uniformly to surgeons, radiologists and physicians.[6].Since 2009, numerous radiological studies have proposed thyroid imaging and reporting data systems comparable to the widely used and reliable BIRADS based on sonographic features of whether a nodule is benign or malignant.[7] Of these systems the 2017 ACR TIRADS has been found to be easiest to reproduce with the lowest false negative rate when correlated with FNA cytology.[8]

In KNH, there is no standardized sonographic reporting system in use and there is limited local data recorded comparing the use of a sonographic risk stratification system such as 2017 ACR TIRADS with FNAC findings. This study aims to form a standard baseline and add to the scientific knowledge.

## 1.2 LITERATURE REVIEW

### 1.2.1 Thyroid gland anatomy

The thyroid gland is found within the infrahyoid neck, surrounded by strap muscles anteriorly trachea and oesophagus posteriorly, carotid arteries and jugular veins laterally on either side of the gland. It is composed of 2 lobes on lying to the right and left of the trachea connected by the isthmus in the midline. In adults, each lobe measures 40-60mm in length, 13-18mm in height and 4-6mm in thickness. Blood supply is via the superior and inferior thyroid arteries and with the respective draining veins.[9]

### 1.2.2 Thyroid gland nodular disease

There are many disease processes affecting the thyroid. These are caused in part by changes in levels of hormone secretion, goiter or both. The main diseases are namely goiter that can be nodular or diffuse, in the setting of hypothyroidism as with conditions like Hashimoto's and Ord's thyroiditis. In hyperthyroidism the spectrum of diseases includes thyroid toxic adenoma, de Quervain's thyroiditis, Plummer's and Graves' disease, to name a few. [10]

In neoplastic diseases, adenomas are the most widespread benign tumors of the thyroid.[10] According to Global Cancer Observatory survey for 2018, the prevalence of thyroid carcinoma is currently at 2.46% with an incidence of 1.1% and a mortality of 0.37%.[11] Papillary carcinoma has been found to be more prevalent as compared to follicular carcinoma owing to the country's iodine status and that of the continent as a whole, with rates of 6.7% vs 4.9% respectively.[12]

A nodule refers to a lesion within the thyroid parenchyma with well-defined margins that is distinct from the contiguous normal parenchyma.[1] Clinically significant nodules are those that upon measurement in 3 dimensions are found to be >0.5cm in size. [13] They occur in all age groups, more so with advancing age and a female preponderance is noted. Most nodules are asymptomatic and benign, with a small but significant number found to be malignant.[1, 14]

### 1.2.3 Imaging Modalities

Thyroid nodular disease can be evaluated using the following imaging namely Conventional Radiography, Ultrasonography, CT, MRI and Radionuclide Imaging. Currently ultrasound is the imaging of first choice

#### 1.2.3.1 Conventional Radiography

Thyroid nodules may be an incidental finding in the setting of conventional radiography examinations of the cervical spine or chest area, and hence has an albeit limited role in the assessment of thyroid nodules as it mainly demonstrates tracheal deviation which alludes to retrosternal extension.[15]

### 1.2.3.2 Ultrasonography

Due to its superficial location, high resolution B mode and Color Doppler ultrasonography demonstrates normal thyroid anatomy and spectrum of pathology with clarity. [9] On ultrasonography the thyroid parenchyma is homogenously medium to high level echogenicity in relation to the surrounding strap muscles with the capsule visible as a thin hyperechoic line.[9] It is cost effective, non-ionizing, safe, reproducible and convenient tool in the assessment of clinically suspected thyroid lesions. [15]. It does have limitations as an imaging modality as it has difficulty in assessing ectopic thyroid tissue, it cannot predict the functional status of a nodule and is operator dependent.[15]Popli et al found that ultrasound could differentiate nodules as either malignant or benign with a sensitivity of 81.8 % and specificity of 87.2%.[16]

Ultrasound elastography is based on the ability to measure the elasticity of tissues using two main methods: shear wave and strain elastography. It can be used as an adjunct in determination of the benignity viz a vie the malignancy of a nodule. Benign ones tend to be softer and easier to compress as compared to malignant ones that are hard and less likely to deform on compression by the ultrasound probe. Its main disadvantage is inability to assess nodules not adequately enveloped by normal parenchyma.[13]

Several studies have proven ultrasonography's role in detection and characterization of thyroid nodular disease and thus raising its prevalence of nodular disease to 68% as it is able to detect nodules that as small as 2-3mm. [13] Studies have also been done to elucidate the sonographic characteristics of nodules based on the composition, size, margins, echopattern, presence or absence of microcalcifications and flow patterns on Color Doppler studies.[1]. Of these characteristics some have been found to be of predictive value in diagnosing malignancy.[1]

### 1.2.3.4 Computed Tomography

CT demonstrates the gland and its adjacent structural relations. On unenhanced CT it is uniformly hyperdense relative to soft tissue owing to its high iodine content. It enhances avidly and homogeneously post contrast due to its blood supply.[13] It has the limitation of having poor contrast resolution which necessitates the need for ultrasonography to further evaluate identified nodules.[13] It also delays use of radionuclide imaging be it for purely diagnostic or therapeutic in the event contrast has been used.[13]

### 1.2.3.5 Magnetic Resonance Imaging

On non-contrast MRI it is hyperintense on T1, T2 hyper to isointense and enhances homogenously post gadolinium administration. Advantage of this modality and CT is in staging of malignancy as they evaluate regional lymphadenopathy, loco-regional extension, spread into mediastinum and detection of distant and occult metastases.[13] DWI-MRI has been shown to be have an added benefit in the differentiation of nodules as malignant nodules tend to demonstrate low apparent coefficient values as compared to benign ones that show higher values. MR spectroscopy is an adjunct tool used as malignant nodules demonstrate high choline peaks which is however non-specific as this is seen in all carcinomas. [13] They are however not the primary imaging modality owing to inadequate spatial resolution and failure to identify features such as microcalcifications and nodule margins. [17]

#### 1.2.3.6 Nuclear Medicine

Nuclear imaging is used in the setting of reduced thyroid stimulating hormone levels. Technetium - 99m pertechnetate and Iodine 123 radionuclide imaging demonstrates the thyroid gland as uniform radiotracer uptake and delineation of the right and left lobe is possible. It can depict nodules based on amount tracer uptake referred to as either cold or hot nodule. Hot nodules being regarded to be benign while cold nodules are considered malignant.[18]. Iodine 131 is used mainly for whole body imaging and therapeutic purposes in ablation of thyroid tissue.[13] However, this is not adequate to determine benignity or malignancy of a nodule, as it has a specificity of 40%[1] thus further imaging is required for in depth evaluation. FDG-PET shows diffuse uniform low-level uptake with focal uptake depicting nodules being seen in 1-2% with a malignancy rate of 11-14%. Its main disadvantage is there is currently no standardized uptake threshold value that enables conclusive differentiation of benign and malignant nodules[17]

### 1.2.4 Role of Fine Needle Aspiration

FNAC remains the most applied and efficient test in ascertaining whether a nodule is malignant or benign and if surgical intervention is required.[5] USG-FNAC has improved the accuracy of the procedure as compared to that of C-FNAC [5] as it provides direct visualization and guidance of the needle during the procedure.[5]. A study by Jalan et al found that the specificity and sensitivity of C-FNAC was 90.91% and 71.43% respectively as compared to 92.31% and 100% with USG-FNAC.[5] Several studies have also shown that presence of a cytotechnologist at time of procedure helps determine the accuracy of the samples collected thus improving the accuracy rate of USG-FNA.[19]

### 1.2.5 Development of Management Guidelines for Thyroid Nodular Disease

Owing to improved detection rates of thyroid nodules an 'apparent epidemic' has risen leading to an increased number of FNACs. This has been associated with increased cost benefit, anxiety and procedural pain. A joint effort between the American, Italian and European endocrinology associations carried out in 2010, came up with guidelines as regards to both diagnostic and therapeutic management of thyroid nodular disease. [20]

#### 1.2.5.1 Bethesda Classification System

In 2007, histopathologists developed a standardized reporting system of the FNAC samples to help in communicating findings to surgeons, radiologists and physicians known as "The Bethesda System for Reporting Thyroid Cytopathology" (TBSRTC). [1] It basically assigns FNAC findings to six main categories giving each a malignancy risk percentage and recommendation for management as illustrated in the Table 1.

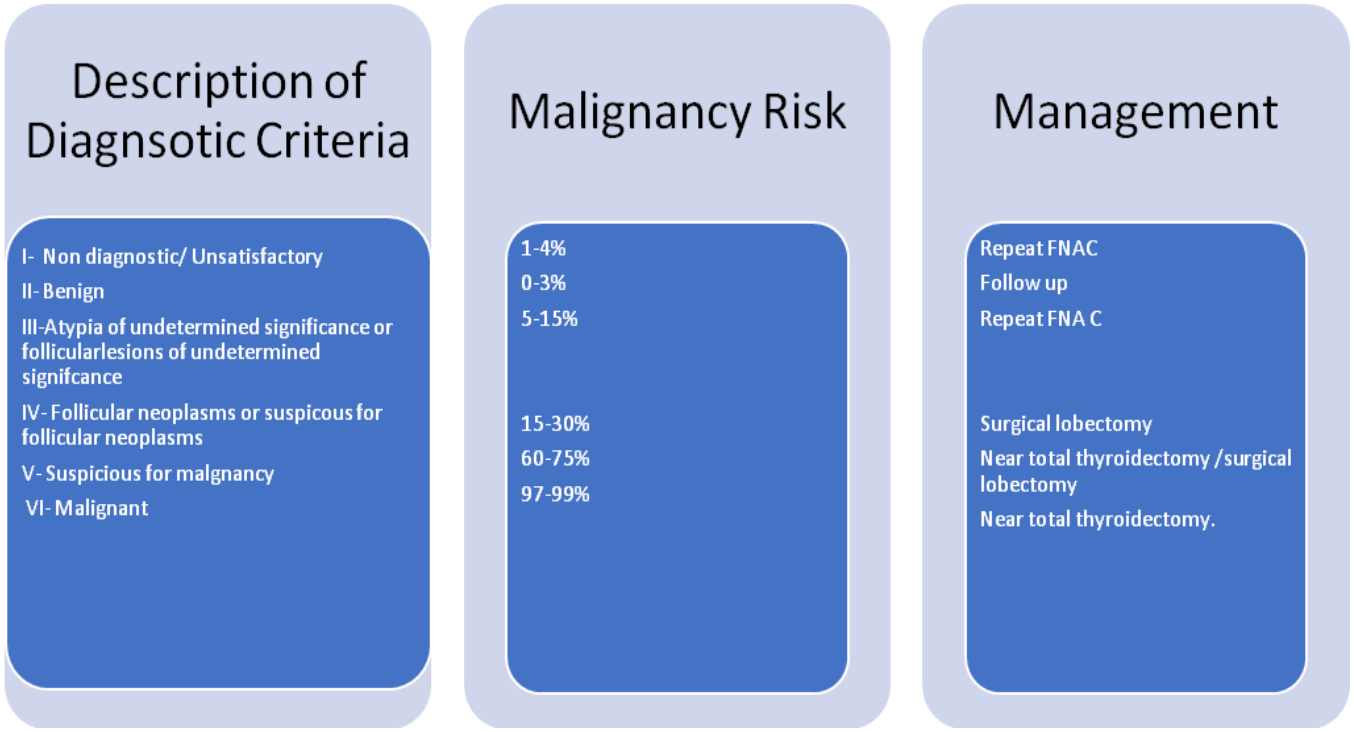



**Table 1: Bethseda Classification**

### 1.2.5.2 Development of Ultrasound Reporting System

In light with this, several radiological associations have since devised sonographic risk stratification systems, to characterize thyroid nodules, create a standardized approach to reporting the nodules, communicate to the clinicians on possible interventions and hence help to reduce unnecessary biopsies. Several systems have been developed based on the already well outlined and established sonographic features and out of the currently used systems the 2017 ACR TIRADS has been found to be the best in achieving these goals. [8]

ACR TIRADS is modelled on the widely accepted ACR BIRADS. It incorporates main ultrasound features and assigns points as to the risk of malignancy of nodules seen. The features considered, include the echogenicity, composition, margins, size, echogenic foci and shape. Each of which is assigned a score from 0-3 which are collated and the nodule given a score.[21] This is illustrated in Table 2 and the respective sonographic images presented.

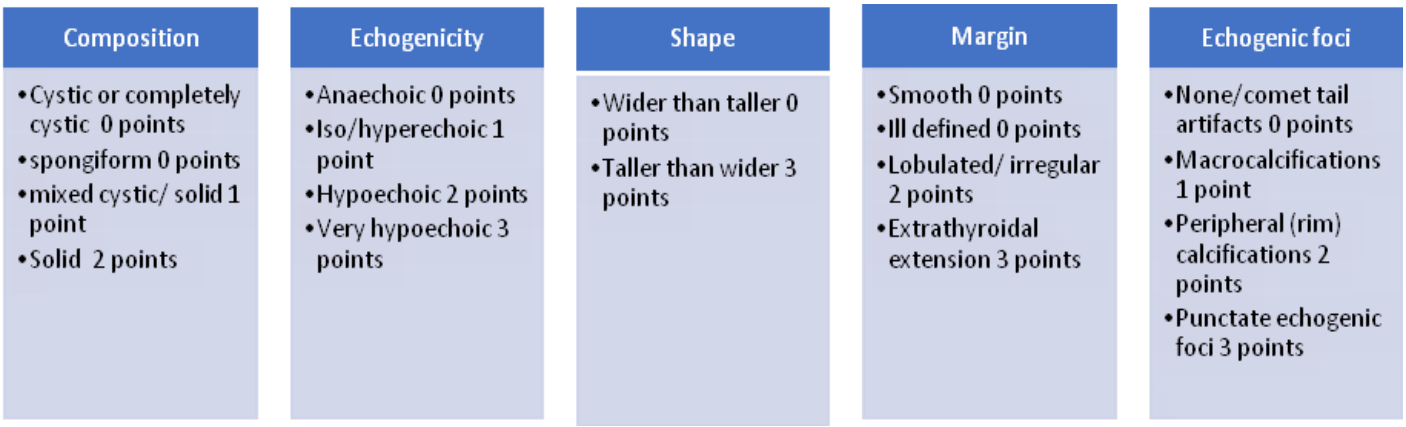



**Table 2 2017 ACR TIRADS Classification**

Once tallied it is given a TIRADS categorization as shown:

**0 points TIRADS 1 Benign No need for FNAC**
**2 points TIRADS 2 Not Suspicious No need for FNAC if ≥ 2.5cm.**
**3 points TIRADS 3 Mildly suspicious FNAC if≥ 2.5cm and follow up if≥ 1.5cm**
**4-6 points TIRADS 4 Moderately suspicious FNAC is ≥1.5cm and follow up if ≥1cm**
**7 points TIRADS 5 Highly suspicious FNAC if ≥1.5cm and follow up if ≥0.5cm**

**Composition**

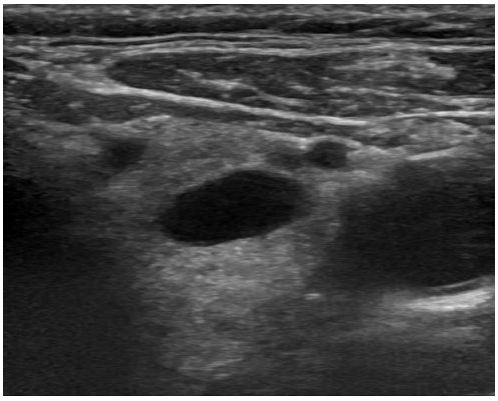


**Figure 1.1**

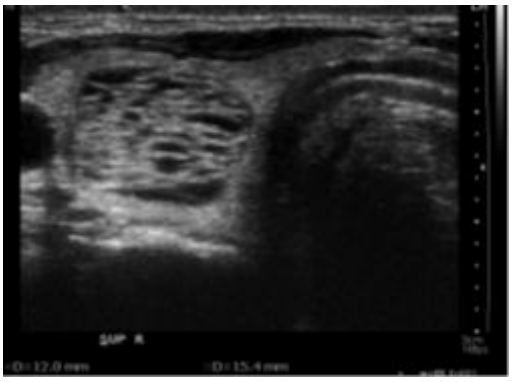
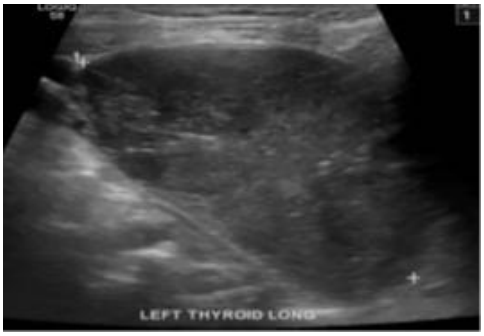


**Figure 1.2**

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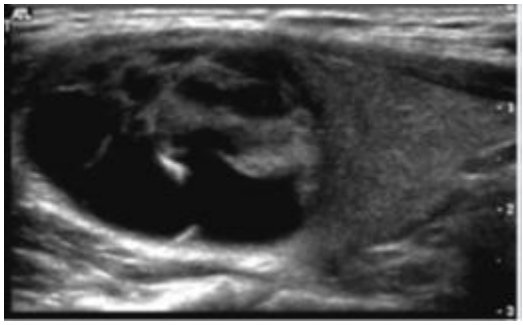


**Figure 1.4**

**Figure 1.1: Completely cystic. Figure 1.2: Spongiform. Figure 1.3: Solid. Figure 1.4: Mixed cystic/solid**

**Echogenicity:**

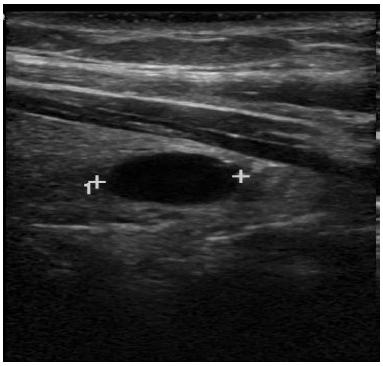
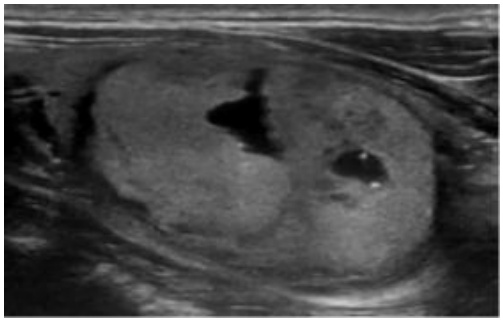


**Figure 1.5**



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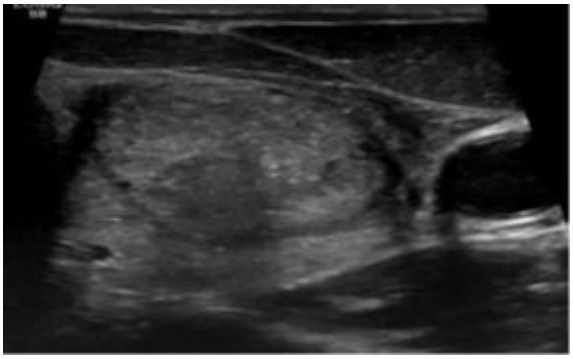

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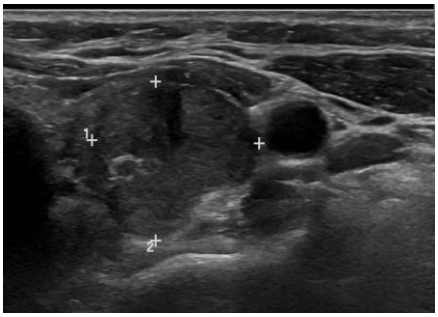


**Figure 1.8.**

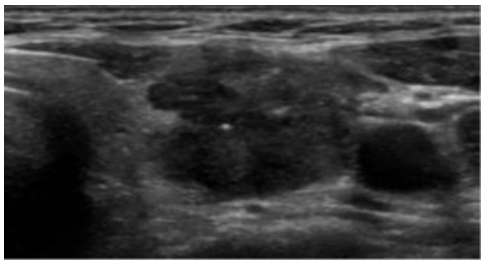
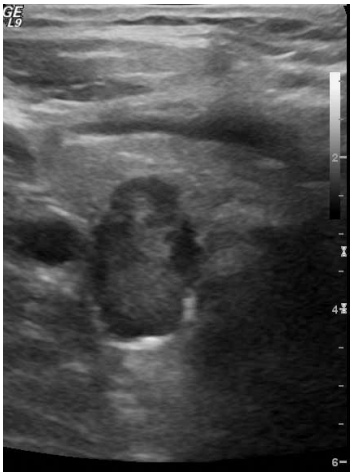


**Figure 1.9.**

**Figure 1.5: Anaechoic. Figure 1.6: Isoechoic. Figure 1.7: Hyperechoic. Figure 1.8: Hypoechoic. Figure 1.9: Very hypoechoic**

**Shape**



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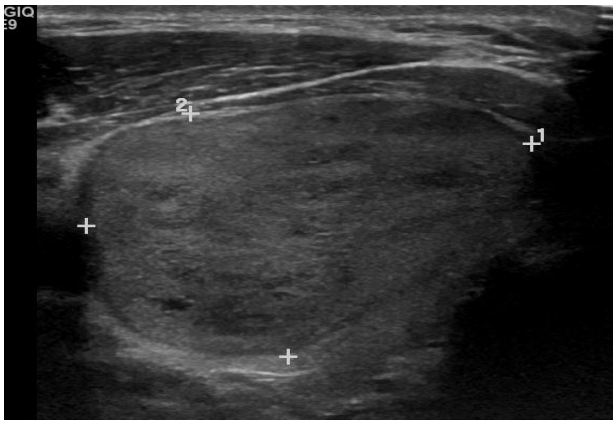


**Figure 1.11**

**Figure 1.10: Taller than wider. Figure 1.11: Wider than taller.**

**Margins**

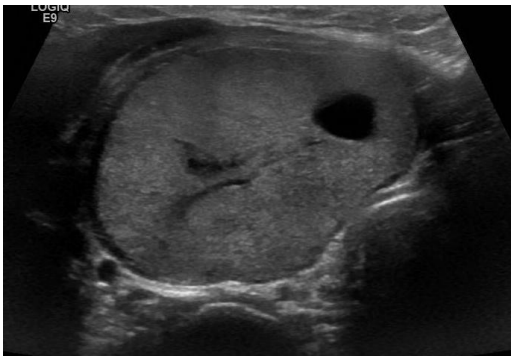


**Figure 1.12**

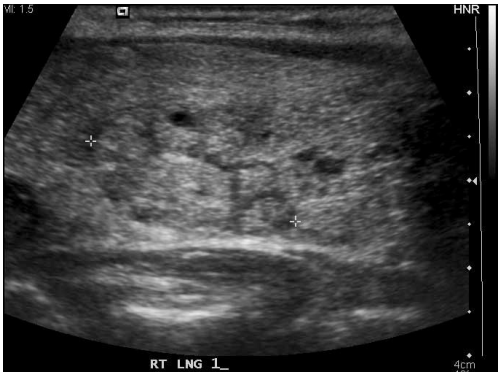



**Figure 1.13**

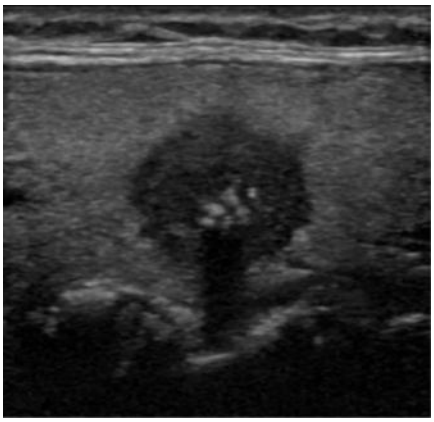
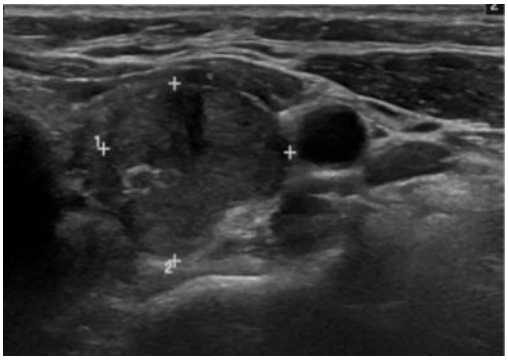


**Figure 1.14**



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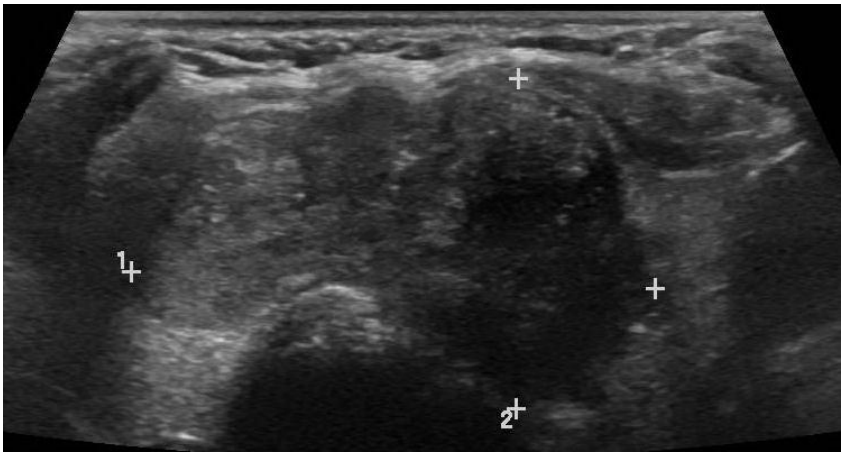


**Figure 1.16**

**Figure 1.12: Well defined. Figure 1.13: Ill defined. Figure 1.14: Irregular. Figure 1.15: Lobulated. Figure 1.16: Extrathyroidal extension**

**Echogenic Foci**

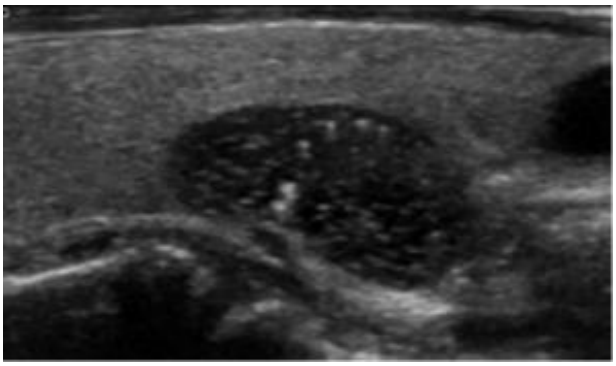


**Figure 1.17**

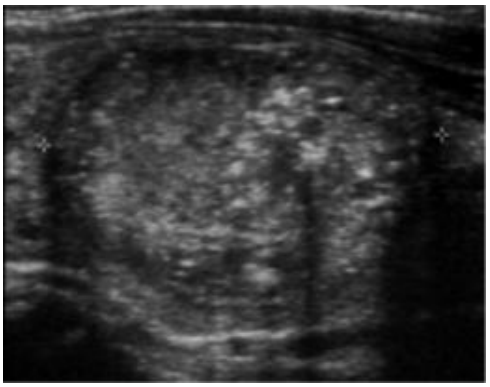


**Figure 1.18**

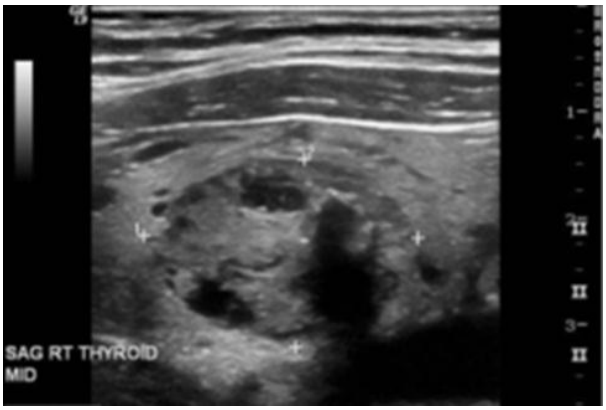



**Figure 1.19**

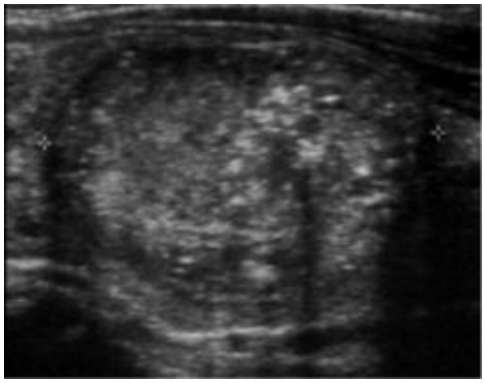


**Figure 1.20**

**Figure 1.17: Comet-tail calcifications. Figure 1.18: Macrocalcifications. Figure 1.19: Peripheral calcifications. Figure 1.20: Punctate echogenic foci**

# CHAPTER 2

## 2.1: STUDY RATIONALE AND JUSTIFICATION

Currently at KNH's imaging department, there is no standardized reporting protocol for patients undergoing thyroid ultrasound. This contrasts with the fact that the Bethesda Classification system has been adopted by the Cytology department. Many benign nodules are undergoing unnecessary FNAC which are costly, invasive and can be avoided.

There is limited local/regional data comparing the 2017 ACR TIRADS and FNAC in assessment of thyroid nodules. There is need to incorporate the ACR TIRADS into ultrasound reporting of thyroid nodules, which has been found to result in a reduction in unnecessary FNACs.[8]

Findings from this study will set pace for stratification of all thyroid nodules at KNH as well as contribute to scientific knowledge. The study findings will also aid in ascertaining the reliability of a sonographic risk stratification system in guiding management of thyroid nodular disease.

## 2.2 RESEARCH QUESTION

Does the use of a sonographic risk stratification system such as the 2017 ACR TIRADS help to determine benignity vs malignancy of thyroid nodules?

## 2.3: STUDY OBJECTIVES

### 2.3.1 Main objective

To subject patients diagnosed with thyroid nodules and sent for FNAC to sonographic risk stratification using the 2017 ACR TIRADS classification and correlate with the Bethesda classification of FNAC findings.

### 2.3.2 Specific objectives

1. To determine the prevalence of malignancy from thyroid nodules using the 2017 ACR TIRADS
2. To determine the concordance rate of 2017 ACR TIRADS classification with FNAC
3. To determine the accuracy of 2017 ACR TIRADS classification using FNAC as the gold standard

## 2.4 ETHICAL CLEARANCE AND CONSIDERATION

### 2.4.1 Ethical Clearance

Ethical clearance was sought from the KNH/UON Ethics Committee and permission sought from the KNH Research and Radiology departments prior to commencement of the study. The research study was done in agreement with the Helsinki Declaration (1975) that was revised in 2008.[22]

### 2.4.2 Ethical Consideration

Participation in the study was voluntary with the participants being free to pull out of the study at any juncture. Informed consent was taken prior to any data collection. The participants were not subjected to any harm and were treated with respect to maintain their dignity during the study.

All the data collected was coded and stored in an encrypted storage device to maintain patient's privacy and anonymity. Works of other authors used during the study was acknowledged using a referencing syst

## CHAPTER 3

### 3.1 STUDY DESIGN AND METHODOLOGY

A hospital based prospective cross-sectional study was carried at KNH Radiology Department, and the KNH FNA Clinic.

### 3.2 Study Population

Patients with thyroid nodules confirmed on ultrasound at KNH radiology department and referred for FNAC at KNH Radiology Department and FNA Clinic.

### 3.3 Sample Size Determination

Sample size was determined with interest in the positive likelihood ratio (LR) that combines the specificity and sensitivity of a test as uni-dimensional index.[23] A test with higher $LR^+$ has a greater value of rule in the disease (identifying those with malignancy in this study). The required sample size was determined as follows;

$$n = \frac{\left(Z_{\frac{\alpha}{2}}\sqrt{\frac{1-\widehat{P}_1}{\widehat{P}_1}+\frac{1-\widehat{P}_2}{\widehat{P}_2}}\right)^2}{\left(\log(\mathrm{LR}+)-\log\frac{\widehat{P}_1}{\widehat{P}_2}\right)^2}$$

Where;

$\widehat{P}_1$ = sensitivity (85%)

$\widehat{P}_2$ = 1-specificty (70%)

$LR^+ = \frac{\widehat{P}_1}{\widehat{P}_2}$

$Z_{\frac{\alpha}{2}}$ =1.96

$\alpha$ = 0.05

With assumed sensitivity of 85%, specificity of 70% and equal sample sizes for malignant and non-malignant $LR^+ = \frac{\widehat{P}_1}{\widehat{P}_2}$ cases, the = 2.83 and the required minimum sample size is 7

### 3.4 Sampling Method

This was via a consecutive sampling (total enumerative) method, where every patient who met the criteria of inclusion was selected until the required sample size was achieved.

### 3.4.1 Inclusion Criteria

1. All patients with thyroid nodules sent for FNAC
2. Informed consent
3. Patients who are 18years and above

### 3.4.2 Exclusion Criteria

1. Patients who have undergone previous FNAC or core biopsy.
2. Those who decline consent.
3. Patients who are under 18 years of age.

## 3.5: MATERIALS AND METHODS

The study was done using a Phllips Attimis 70G ultrasound machine at KNH radiology department and a GE LOGIQ V ultrasound at the FNA Clinic. All the patients who met the inclusion criteria and gave informed consent underwent a thorough ultrasound examination, followed by an ultrasound guided FNA.

### 3.5.1: Ultrasound technique

Ultrasound examination was done by the principal investigator, using a linear 7.5-12Mhz Phillips Attimis 70G and GE LOGIQ V. The patients were placed supine with the neck hyperextended, and the thyroid gland assessed. Neck hyperextension was achieved by placing a pillow beneath the patient's shoulder. The neck was scanned in both long and short axis using B-mode and Color Doppler settings. Patients were asked to swallow to ensure adequate assessment of the lower poles of both lobes.

All nodules once identified were categorized based on their characteristics of shape, echogenic foci, margins, echogenicity, and composition, in accordance with the 2017 ACR TIRADS lexicon[9]. Points were allocated to each nodule based on the individual categories, and the sum of which led to the final TIRADS classification based on the ACR TIRADS guidelines. TR 1 =0 points, TR2= 2 points, TR3= 3 points, TR4 = 4-6points, TR5 = 7 or more points[9]. All findings were confirmed by 2 consultant radiologists.

### 3.5.2: Ultrasound guided FNAC technique.

Ultrasound guided FNAC of the identified nodules was done aseptically, in the event more than 1 nodule was present, a maximum of 2 nodules underwent FNA. This decision was based on the recommendation in the 2017 ACR TIRADS.[9]

Samples from the identified nodules were collected using the capillary method with a 23- gauge needle and 10mL syringe. These were then aspirated onto 2-4 slides by the cytotechnologist and upon confirmation of adequacy fixed with 95% ethyl alcohol solution. The area was then cleaned, hemostasis achieved, and post procedural pain was alleviated by placing gauze soaked in cold saline.

### 3.5.3: Procedure for FNA specimen analysis.

A maximum of 2 slides per nodule were fixed and allotted a laboratory number upon collection. Upon arrival at the cytology laboratory, the slides were logged in using the allotted number and one slide was prepared using Hematoxylin and Eosin stain while the other using Papanicolaou stain. These were then mounted, dried, and examined under a microscope by a qualified cytopathologist and classified under the Bethesda System of Cytological Reporting used at KNH.

## 3.6: STUDY VARIABLES

**Demographics:**

- Age
- Sex

**Dependent Variables**

- Number of thyroid nodules per patient
- Ultrasound features of the thyroid nodules
- TIRADS classification of the thyroid nodules

**Independent Variable**

- Final cytological diagnosis of the thyroid nodules

## 3.7: QUALITY ASSURANCE PROTOCOL

Only patients who satisified the inclusion criteria were recruited into the study. A standardized sonographic worksheet was used during the ultrasound examination. Both the thyroid ultrasound and FNAC was done by the principal investigator and results verified by the two supervisors. The principal investigator used the ACR TIRADS Atlas to help in adequately identifying the different sonographic characteristics of the nodules when assigning scores. Use of ultrasound guidance during the FNAC ensured that the nodules identified were adequately sampled.

Adequacy of FNA samples was confirmed by the cytotechnologist at the time of collection. Fixation and labelling of samples will be done in the presence of the principal investigator and cytologist according to the standard operating procedures of the KNH Cytology laboratories. The FNA samples were assessed according to approved standard operating protocols at the KNH Cytology laboratories.

Use of the currently widely used standardized Bethseda classification system during interpretation of the FNAC samples. 10% of the FNA samples were sent to an independent laboratory for assessment by an independent histopathologist and thus helped in calibrating the cytologist. Daily review of the data collected during the study was done by the principal investigator.

## 3.8: DATA MANAGEMENT

### 3.8.1: Data Collection

Upon arrival to the KNH radiology department/FNA clinic, the study participants were explained to the details regarding the study and once they understood the nature of study, its basis of voluntary participation and agreed to participate, they then proceeded to sign a consent form.

All the patient's bio data, sonographic and cytological findings were then documented in a data collection form upon completion of the study procedure. This was then transferred to an Excel Spreadsheet and backed up to a flash drive and external hard drive.

### 3.8.2: Data Analysis

During analysis, demographic and clinical attributes were summarized using proportions for categorical variables and medians or means for continuous variables. Prevalence of malignancy was summarized as a proportion and presented in a pie chart. The concordance rate was defined as the number of classification outcomes that agree (same between TIRADS and cytological examination) over the total number assessed. The difference between the rate of agreement (concordance) that was observed and the rate of agreement that was expected purely by chance was measured using Cohen's kappa. Specificity sensitivity, negative and positive predictive values, and positive likelihood ratios were computed for features of thyroid nodules and specific TIRAD classifications and presented in tabular form. Statistical significance was interpreted at 5% level ($p$ value $< 0.05$). Analysis will be done using Stata version 16.[24]

# CHAPTER 4

# RESULTS

## 4.1 Sociodemographic Characteristics

A total of 108 nodules were classified under TIRADS and correlated with FNA results out of a sample size of 79 patients. 72 (91.9%) of whom were female and 7 (8.2%) were male. This is demonstrated in the pie chart below:

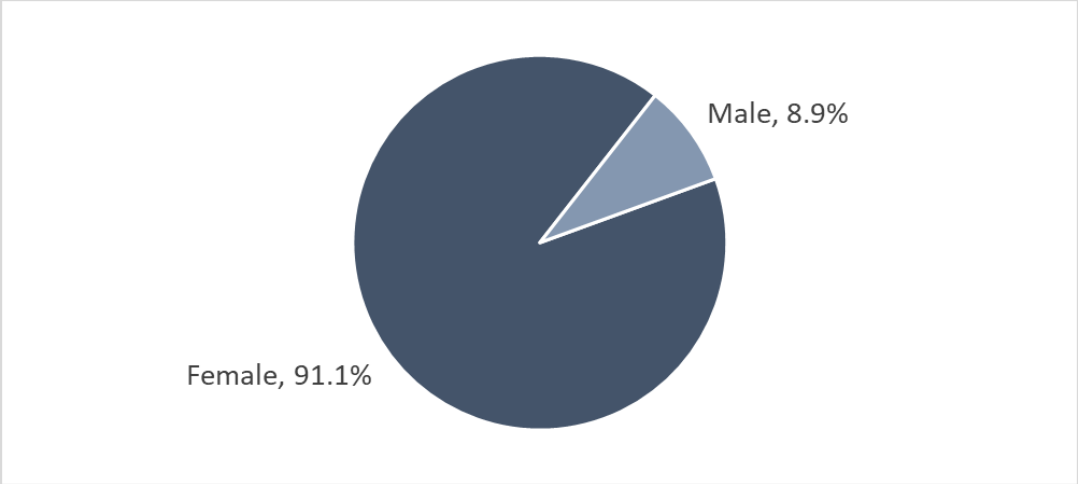
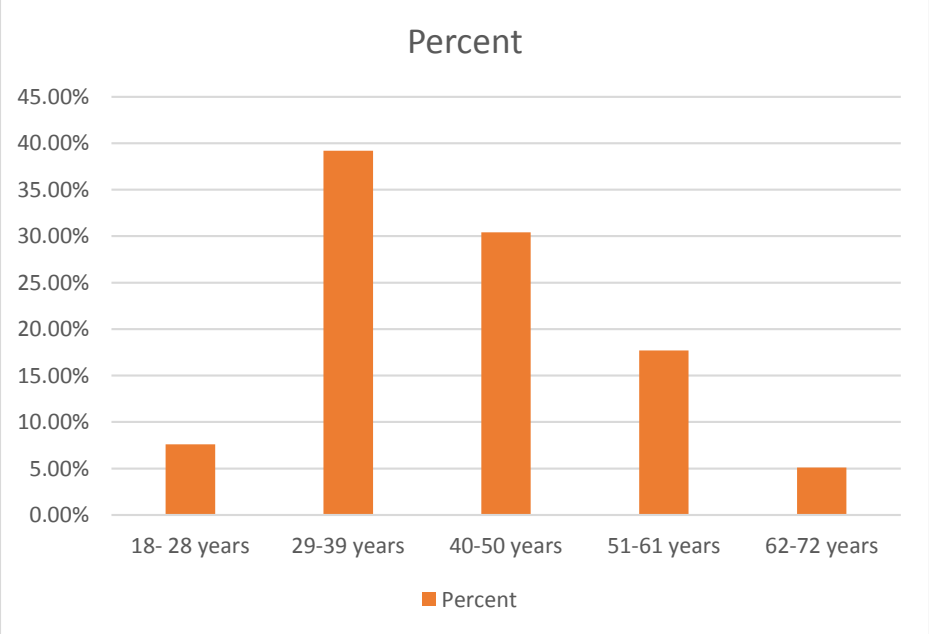



Figure 4.1.1. Pie chart displaying gender distribution

Majority of the patients were in the 29-39 age group, accounting for 39.2% of the sample population with a median age of 45yrs.

Figure 4.1.2: Bar chart demonstrating age range distribution



**4.2: ACR TIRADS classification and FNA diagnosis**

Out of a total of 108 nodules, 5 were categorized as TIRADS 1, 40 as TIRADS 2, 37 as TIRADS 3, 24 as TIRADS 4 and 2 as TIRADS 5. All the nodules classified as TIRADS 1 to 3 were found to be benign upon cytological correlation, with one TIRADS 4 and one TIRADS 5 lesion being found to be malignant. One nodule categorized as TIRADS 5 was found to be benign upon cytological assessment classified as chronic granulomatous thyroiditis. This is illustrated in the bar chart below:

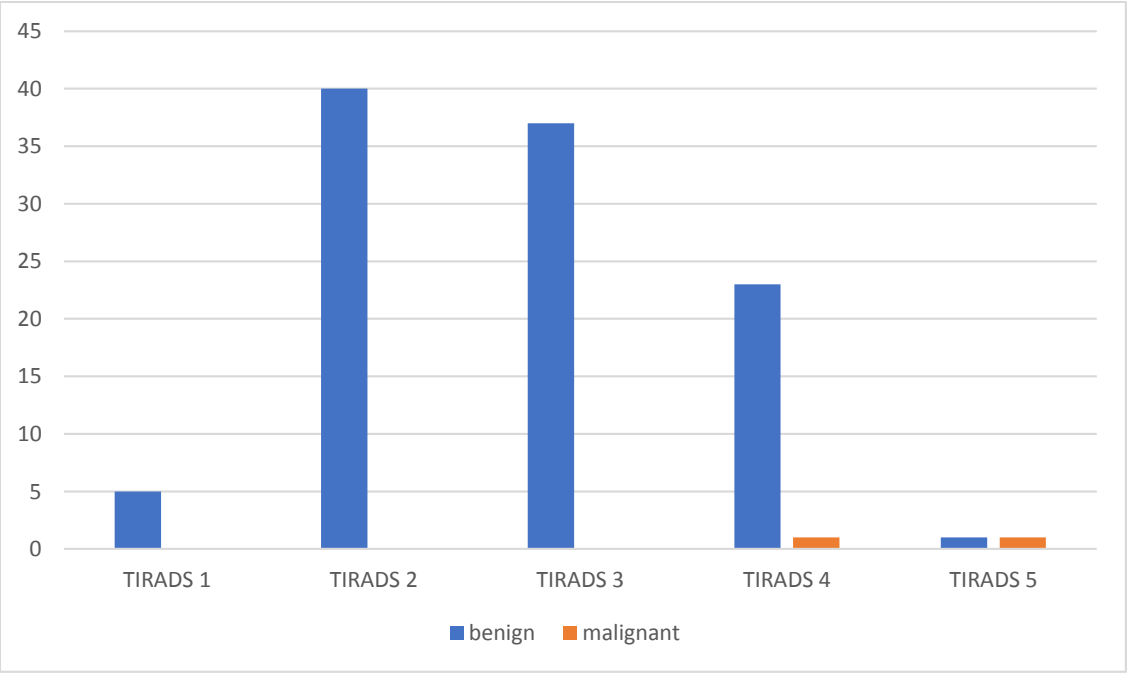



Figure 4.2.1: Distribution of malignant and benign nodules based on TIRADS category.

Cytological diagnosis of these 108 nodules found that 106 were benign while 2 were positive for malignancy. The commonest benign nodule was colloid goiter accounting for 103/108, while 3/108 were found to be granulomatous thyroiditis, and 2/108 had a diagnosis of papillary carcinoma.

Our study showed that sonographic features spongiform and mixed solid- cystic composition, hyper and iso-echogenicity, ill-defined margins and macrocalcifications had a 100% positive predictive value (PPV) and 100% sensitivity for benignity. Out of the 5 suspicious sonographic features, marked hypoechogencity had the highest PPV of 50%, specificity of 98.1%, sensitivity of 100% and negative predictive value (NPV) of 100% for malignancy.

The malignancy percentage risk based on TIRADS classification was found to increase with increase in TIRADS classification. TIRADS 1-3 were found to have 0% risk of malignancy while TIRADS 4 had a 4.2% risk and TIRADS 5 had a 50% risk. This resulted in an overall risk of malignancy of 1.9% which was inferred to be the prevalence of malignancy within our study sample.

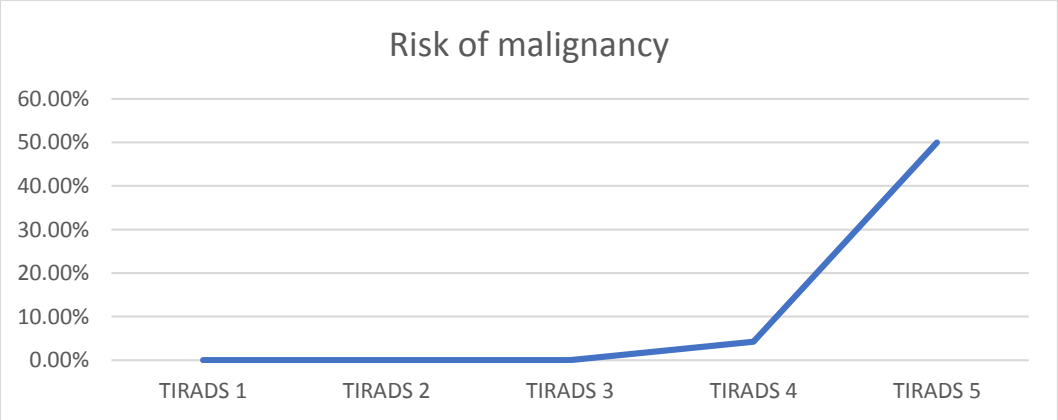



Figure 4.2.2: Increase in % risk of malignancy with increasing TIRADS category.

### 4.3: Concordance between ACR TIRADS and Bethseda FNAC

The concordance of ACR TIRADS with Bethseda FNAC as the gold standard was found to be 100% for TIRADS 1 to 3 with Bethseda 2, 4.2% of nodules categorized as TIRADS 4 and 50% classified as TIRADS 5 were found to be Bethseda V lesions. One of the nodules categorized as TIRADS 5 was found to be Bethseda 2 on FNAC.

| | FNA classification | | | | |
|---|---|---|---|---|---|
| TIRADS classification | Thy2 | Thy3 | Thy4 | Thy5 | Total |
| TIRADS 1 | 5 | 0 | 0 | 0 | 5 |
| TIRADS 2 | 40 | 0 | 0 | 0 | 40 |
| TIRADS 3 | 37 | 0 | 0 | 0 | 37 |
| TIRADS 4 | 23 | 0 | 0 | 1 | 24 |
| TIRADS 5 | 1 | 0 | 0 | 1 | 2 |
| Total | 104 | 2 | 1 | 1 | 108 |

Table 3: Concordance of TIRADS with Bethesda cytological classification

Upon application of Cohen's kappa test there was slight agreement with a kappa value of 0.0125, which was not statistically significant (p-value 0.2514) demonstrated between ACR TIRADS and FNAC Bethseda classification.

### 4.4: DIAGNOSTIC PERFORMANCE OF ACR TIRADS

The ACR TIRADS diagnostic performance was calculated using FNAC as the gold standard test and found to have an overall specificity of 77.36%, sensitivity of 100%, positive likelihood ratio of 4.42, negative likelihood ratio of 0.0, positive predictive value of 7.69%, negative predictive value of 100% and overall diagnostic accuracy of 77.78%. As illustrated in the table below:

| **Statistic** | **Value** | **95% Confidence interval** |
|---|---|---|
| Sensitivity | 100.00 % | 15.81% to 100.00% |
| Specificity | 77.36% | 68.21% to 84.92% |
| Positive likelihood ratio | 4.42 | 3.11 to 6.28 |
| Negative likelihood ratio | 0.00 | |
| Disease prevalence | 1.85 % | 0.23% to 6.53% |
| Positive predictive value | 7.69% | 5.54% to 10.59% |
| Negative predictive value | 100.00% | |
| Overall accuracy | 77.78% | 68.76% to 85.21% |

Table 4: Overall diagnostic performance of ACR TIRADS

Receiver operating curves (ROC) were generated for TIRADS 4 category, which was the cut off point for malignant nodules. The area under the curve was found to be highest for TIRADS 4 at 0.64 with a sensitivity of 50%, specificity of 78.3%, PPV - 4.2%, NPV - 98.8%.

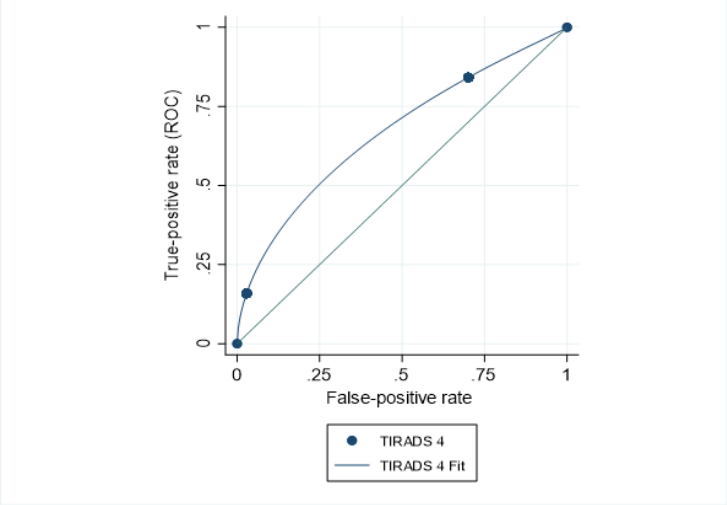



Figure 4.4.1: ROC curve illustrating diagnostic performance of TIRADS 4 in detecting malignancy.

A total of 82 nodules categorized as TIRADS 1-3 were found to be benign on cytology resulting in a specificity of 100% for classifying a nodule as benign. Assuming these cases did not undergo FNAC, the anticipated reduction in unwarranted biopsies in our study would be 75.9%

**4.5: CASES**

Case 1: A 43year old female patient with left anterior neck swelling for 3 months.

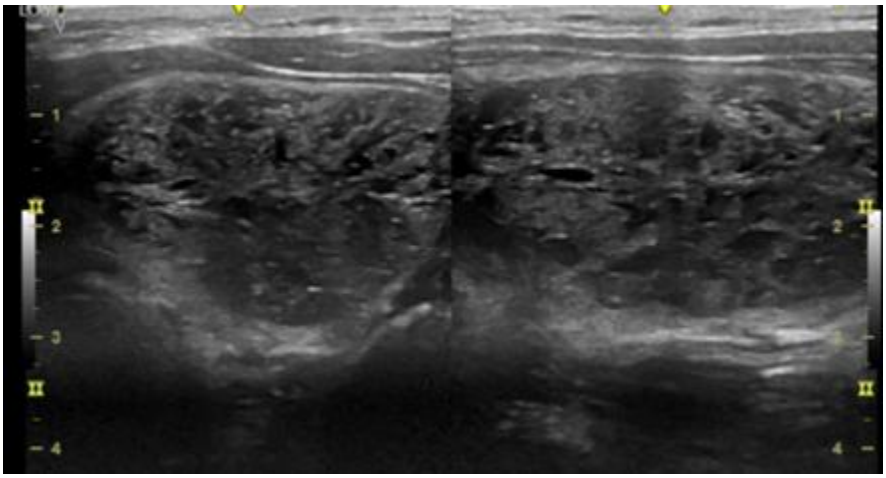


Figure 4.5.1: Gray scale images demonstrate a left spongiform, hypoechoic nodule with smooth margins classified as TIRADS 2 and was benign on cytology.

Case 2: A 39-year female with 8month history of an anterior neck swelling, initially associated with pain.

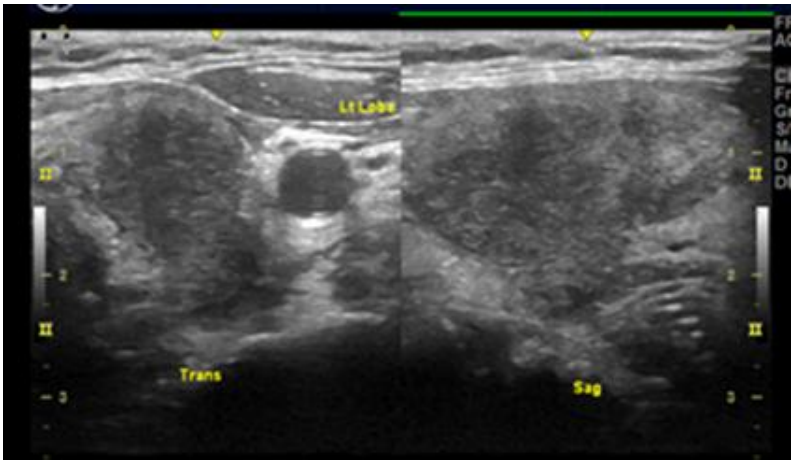



Figure 4.5.2: Gray scale image of left solid, hypoechoic nodule that was taller than wider with extrathyroidal extension, classified as TIRADS 5 but was found to be granulomatous thyroiditis on cytology

Case 3: A 70 year female with a 3 year history of anterior neck swelling that started to increase in size over a period of 3months

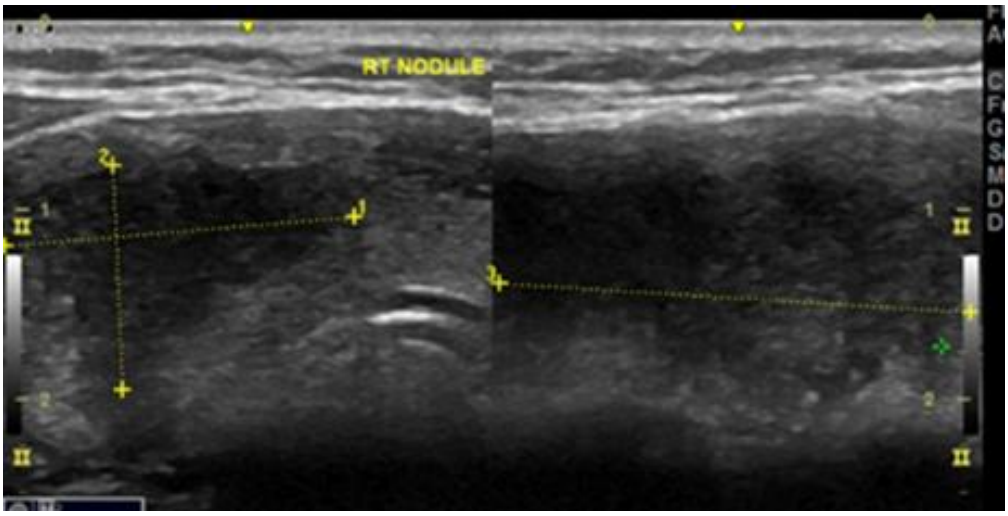



Figure 4.5.3: Gray scale image of a right markedly hypoechoic, solid, nodule with irregular margins given TIRADS 5 classification and upon cytology was papillary carcinoma.

Case 4: A 45year old male patient with history of right anterior neck swelling for the past 1year

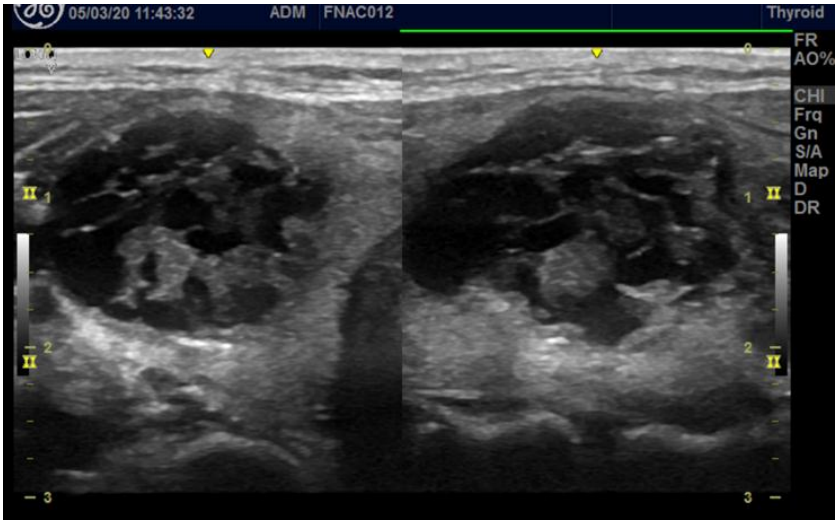



Figure 4.5.4: Gray scale image of a right thyroid nodule, isoechoic and mixed solid cystic nodule with well-defined margins, that is wider than taller which was classified as TIRADS 2 and was benign on cytology.

## CHAPTER 5

## DISCUSSION

A female preponderance was demonstrated in our study which similarly seen in South Africa by Mark Nicolaou et al who had 84 females vs 16 males.[25] In India, Dhanadia Shah et al found that the highest incidence was found in patients between 30-39yrs (30%), this was also seen in our study with patients between 29-39yrs accounting for 39.2%.[26] Our study found that the overall prevalence of malignancy to be 1.9% which is lower in comparison to the country's 5 year prevalence of 2.46%[11], this may be due to the number of cases and short study duration.

Mohanty et al in India observed that spongiform, cystic and mixed solid cystic composition, anaechoic echogenicity, ill-defined margins and long comet tail artefacts had 100% PPV, with 0% malignancy risk.[27] This corresponds to some extent, with our findings of spongiform and mixed solid- cystic composition, hyper and iso-echogenicity, ill-defined margins and macrocalcifications having a 100% PPV and 100% sensitivity for benignity. Srinivas et al stated that marked hypoechogenicity had a 54.5% PPV while in our study it was observed at 50% PPV.[28]

Our study revealed that the risk of malignancy increased with increase in TIRADS category upon correlation with FNAC results. TR1 to TR3 had a 0%, 4.2% in TR4 and 50% in TR5. In Egypt, Azab et al, established an elevated malignancy risk as the tally of points and subsequently the overall TIRADS level increased.[29] Allen San Shell Jabar et al, stated the risk of malignancy to be TR1- 0%, TR2-0%, TR3- 6.9%, TR4-29.2% and TR5- 80%.[30] Tessler et al, in the ACR TIRADS Committee White paper categorized the risk as <2% TR1&TR2, 2-5% TR3, 5-20% TR4 and >20% for TR5.[21]

Our study also looked at the concordance between the Bethesda and ACR TIRADS reporting systems. The most common consistency was found for Bethesda II with all nodules classified as TIRADS 1-3 having 100% concordance and 50% concordance for TIRADS 5 nodules with Bethesda V. Vargas et al reported the highest concordance between TIRADS 2 and Bethesda II and TIRADS 4 and Bethesda IV.[31]

However, when our study results were analyzed using Cohen's Kappa, they showed slight agreement which was not statistically significant in comparison to Vargas et al who reported good/substantial agreement and had a p value of <0.001. This could be postulated to be due to the higher number of malignant nodules and use of surgical histopathology in addition to FNAC in the study by Vargas et al.[31]

The diagnostic performance of ACR TIRADS with FNAC as the gold standard test was found to have an overall sensitivity of 100%, specificity of 77.36%, positive likelihood ratio of 4.42, negative likelihood ratio of 0.0, PPV of 7.69%, NPV of 100% and overall diagnostic accuracy of 77.78%. In 2019, a Turkish study by Bülent Çolakoğlu et al, similarly showed a sensitivity of 87%, specificity 71.7%, 97.4% NPV, 31.1% PPV, and 73.6% diagnostic accuracy.[32]

Our study observed the best cut off point to detect malignancy to be TIRADS 4 which had a 50%sensitivity, 78.3%specificity, 4.2% PPV, 98.8% NPV. Azab et al, had a similar cut off point with a 88.89% sensitivity, 96.77% specificity, 88.9 % PPV and 69.8% NPV.[29] The difference in our studies is in part to the higher number of malignant lesions found be Azab et al, in addition to their use of histopathology and thyroid scintigraphy.[29]

Our study showed an estimated reduction in unnecessary biopsies of 75.9%, as all nodules categorized as TIRADS 1-3 were found to be benign. Bülent Çolakoğlu et al, observed a slightly lower reduction of 64.1%[32] with Middleton et al observing a 52.9% reduction.[33]

## CONCLUSION

Our study compares well with other international studies and shows 2017 ACR TIRADS to be a good scoring system to use to diagnose benign lesions. Being point based it is easy to adopt in daily practice, allowing all nodules to be classified. It provides a tool that both the radiologist and clinician can use objectively in management of thyroid nodular disease and avoid unnecessary biopsies.

## RECOMMENDATIONS

There is a need to develop a multi-centric study whilst involving a multi-disciplinary team to gain a better representation of the country's population and enhance the validity of the study.

There is need to incorporate ACR TIRADS classification system in the radiology department in the daily reporting of thyroid nodular disease through education of staff performing the imaging studies and to the referring clinicians.

## STUDY LIMITATIONS

This study was based at a tertiary hospital and thus was not a true representation of the country's population. There was a lack of histological correlation which hindered ability to provide a confirmatory diagnosis of the suspicious nodules in TIRADS 4 and 5. The advent of COVID 19 resulted in a drop in patient numbers and follow up for those who required histopathological correlation

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**TIMETABLE**

| Activity | Action by | Period | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Mar 19 | Apr 19 | May 19 | Jun 19 | July 19 | Aug 19 | Sep19 | Oct 19 | Nov 19 | Dec 19 | Jan '20 | Feb '20 | Mar '20 | Apr '20 | May 2020 | Jun 2020 | July 2020 |
| Writing Research Proposal | Student | | | | | | | | | | | | | | | | | |
| Revising and Finalizing proposal | Student and Supervisor | | | | | | | | | | | | | | | | | |
| Ethical Approval | KNH-ERC | | | | | | | | | | | | | | | | | |
| Data Collection | Student | | | | | | | | | | | | | | | | | |
| Data Checks and Cleaning | Student | | | | | | | | | | | | | | | | | |
| Data Analysis and Interpretation | Student and Biostastician | | | | | | | | | | | | | | | | | |
| Writing up | Student and Supervisor | | | | | | | | | | | | | | | | | |
| Dissertation submission | Student | | | | | | | | | | | | | | | | | |

**BUDGET**

| ITEM | QUANTITY | UNIT PRICE | TOTAL |
|---|---|---|---|
| PRINTING PAPER | 5 RIMS | 500 | 2500 |
| NOTEBOOKS | 4 PIECES | 100 | 400 |
| FILES | 6PIECES | 90 | 360 |
| PRINTER CATRIDGE | 2 PIECES | 2400 | 4800 |
| INTERNET | 50GB DATA BUNDLE | 4000 | 4000 |
| FLASH DISK | 32GB – 1 PIECE | 900 | 900 |
| PRINTING DRAFTS AND FINAL PROPOSAL | 10 COPIES | 1000 | 10000 |
| PHOTOCOPIES OF QUESTIONAIRES | 100 COPIES | 10 | 1000 |
| PHOTOCOPIES OF FINAL PROPOSAL | 6 COPIES | 100 | 600 |
| BINDING OF FINAL PROPOSAL | 6 COPIES | 60 | 360 |
| AIRTIME | 1 | 3000 | 3000 |
| ETHICAL REVIEW FEE | 1 | 2000 | 2000 |
| SUBTOTAL | | | 28920 |
| PERSONNEL | | | |
| BIOSTATICIAN | 1 | | 25000 |
| RESEARCH ASSISTANT | 1 | | 25000 |
| SUB TOTAL | | | 50000 |
| DATA COLLECTION, DATA ANALYSIS AND THESIS DEVELOPMENT | | | |
| PRINTING OF THESIS DRAFTS | 10 COPIES | 1000 | 10000 |
| PRINTING OF FINAL THESIS | 6 COPIES | 1000 | 6000 |
| BINDING OF THESIS | 6 COPIES | 400 | 2400 |
| DISSEMINATION COST | | | 15000 |
| SUBTOTAL | | | 33400 |
| CONTINGENCY (10% OF TOTAL BUDGET) | | | 11232 |
| GRAND TOTAL | | | 112320 |

## APPENDICES

## APPENDIX I: PATIENT INFORMATION DOCUMENT

## TITLE OF STUDY: CHARACTERIZATION OF THYROID NODULES USING THE 2017 ACR TIRADS WITH FNAC CORRELATION.

Principal Investigator\and institutional affiliation: Dr Josephine Achieng Aywak University of Nairobi

Co-Investigators and institutional affiliation:

1. Dr Caroline Kebuka Kenyatta National Hospital
2. Dr Alfred Odhiambo Department of Diagnostic Imaging and Radiation Medicine University of Nairobi

### INTRODUCTION:

My name is Dr Josephine Achieng Aywak, I am a postgraduate student in the Department of Diagnostic Imaging and Radiation Medicine. I am carrying out the above study. I am requesting you to participate in this study. The aim of this consent form is to assist you in deciding whether to be included in the study or not. Kindly read through this form and feel free to ask any questions about this study. The principal investigator will be available to answer all and any questions that you may have at any point in this study and thereafter.

### STUDY BACKGROUND

This study involves undertaking an ultrasound examination of the thyroid, that is found in the front of the neck, and documenting the results followed by collection of a tissue sample from any swellings seen during the ultrasound.

### STUDY OBJECTIVE

The goal of the study is to evaluate if a standardized ultrasound report that categorizes any swellings encountered is comparable to the final diagnosis got from the samples collected.

### STUDY PROCEDURES

Prior to the examination one will be required to answer a few questions mainly based on their bio data. The examination is short and minimal pain will be experienced. It requires one to extend their neck, while an ultrasound probe is used for the examination and during the tissue sample collection. The thyroid ultrasound results will then be correlated with the results of the Fine needle aspirate cytology. The Fine needle aspirate will be examined by a qualified histopathologist after collection.

**VOLUNTARINESS OF PARTICIPATION**

Enrollment in the study is purely voluntary and you are free to withdraw from the study at any point during the study without injustice or fear of repercussions.

**CONFIDENTIALITY**

Confidentiality will be observed within the extent allowed by law as all your information will be encoded and all recorded data obtained will be secured.

**BENEFITS OF THE STUDY.**

The examination will aid the primary physician in making decisions as regards to appropriate management and follow up of one's condition. No additional cost will be incurred apart from what has been recommended by the primary physician.

**RISKS OF THE STUDY**

There is a risk of experiencing temporary mild to moderate pain during the tissue sample collection, however this will be alleviated by use of analgesics after the procedure.

**RIGHT OF WITHDRAWAL**

You are free to decline to give consent and to withdraw from participating in this study at any juncture. There will be no repercussions to my person, nor will it affect my medical care.

**APPENDIX II: CONSENT CERTIFICATE**

My name is Dr Josephine Achieng Aywak, a postgraduate student in the department of Diagnostic Imaging and Radiation Medicine at the University of Nairobi.

I hereby confirm that the above named doctor has explained the study to me in a language that I can understand and the benefits and risks have been explained to me.

I understand that my participation is voluntary, and I have not been forced or coerced to participate.

I understand that I can refuse to participate or opt out of the study at any point without any effect to my medical care

I understand that I will not receive neither I am entitled to any compensation monetary or otherwise for taking part in this study.

I understand that all personal information availed for purposes of this study will be kept confidential.

I do hereby consent to take part in the above study.

Patient number _____ Signature _____

Date _____

I certify that the patient has understood and consented to participate in the study.

Dr Josephine Achieng Aywak

Signature _____ Date_____

## CONTACTS

### Researcher

Dr Josephine Achieng Aywak

Department of Diagnostic Imaging and Radiation Medicine

University of Nairobi

2nd Floor, Old Kenyatta National Hospital

Telephone Number: 0720562653,

Email: joaywak@gmail.com.

### Supervisor

Dr Caroline Kebuka

Department of Radiology

Kenyatta National Hospital

Ground Floor next to Casualty Department KNH

Telephone Number: 254722475372

Email: kebukac@gmail.com

### KNH-UON SECRETARIAT

Kenyatta National Hospital and University of Nairobi.

Ethics and Research Committee

College of Health Sciences

Telephone Number: (254- 020) 2726300 EXT 44355

Email: uonknh_erc@uonbi.ac.ke

## APPENDIX III: HATI YA HABARI YA MGONJWA

## KICHWA CHA UTATIFI: UTUMIZI YA MTAMBO WA ACR TIRADS KULINGANISHWA NA FNAC KATIKA UTAFITI WA UVIMBE YA THYROID

Mtafiti mkuu/ taasisi wa ushirka: Dr Josephine Achieng Aywak. University of Nairobi

Wasimamizi/ taasisi wa ushirka:
1. Dr Caroline Kebuka. Kenyatta National Hospital
2. Dr Alfred Odhiambo. Department of Diagnostic Imaging and Radiation Medicine University of Nairobi

### KAULI YA UTAFITI

Jina langu ni Dr Josephine Achieng Aywak, mwanzafunzi wa uzamili katika Chuo Kikuu ya Nairobi, Idara ya Radiologia na Dawa Mionzi.

Utafiti huu unaangalia utumizi wa mtambo ya ACR TIRADS na kulinganisha maajibu yake na yale ya FNAC katika ukaguzi wa uvimbe ya thyroid.

Ningependa kuomba ushiriki wako katika utafiti huu.

Lengo la fomu hii la idhini ni kukusaidia kuamua kama ungekubali kujishiriki au la. Nakusihi kusoma fomu hii kwa makini.

Uko huru kuuliza maswali yoyote kuhusu utafiti huu. Mtafiti ataweza kujibu maswali haya wakati wa utafiti au baada ukamilishaji wa utafiti.

### MHUTASARI:

Utafiti huu, utatumia kipimo cha ‘ultrasound’ kuchunguza kiungo cha thyroidi, inayopatikana katika shingo.

Matakeo ya hiyo uchunguzi yataandikwa na kufuatiliwa na kuchukuliwa kwa sampuli ya uvimbe yeyote katika kiungo cha thyroidi.

Matokeo ya ultrasound yatalinganishwa na yale ya FNAC, ambayo yatakaguliwa na muuguzi maalum.

### LENGO KUU:

Lengo la utafiti huu ni kutathmini kama utumizi wa ripoti malalum ya ultrasound yakilinganishwa na majibu ya FNAC yataweza kusaidia daktari kutambua wale watakayohitaji kupima kutumia FNAC..

**UTARATIBU WA UTAFITI:**

Kabla ya uchunguzi huu, wahusika wataulizwa maswali kuhusu ukoo wao. Matokeo ya ultrasound yatalinganishwa na yale ya FNAC, ambayo yatakaguliwa na muuguzi maalum.

**KUSHIRIKI KWA HIARI**

Kushiriki kwako ni kwa hiari. Hakuna malipo juu ya yale yatakayoandikishwa na muuguzi wa kwanza.

**FAIDA YA UTAFITI HUU**

Utafiti huu utawezesha madaktari kupanga mwelekeo ya matibabu ya wagonjwa wa shida ya thyroid.

**HATARI YA UTAFITI:**

Mhusika atahisi uchungu kidogo wakati sampuli inachukuliwa kutoka uvimbe wa thyroid. Uchungu huu utamializwa kwa kutumia madawa ya uchungu.

**SIRI KWENYE UTAFITI:**

Haki zako zitalindwa kamili, habari utakayo toa or itakayopatikana itawekwa siri wakati wote, na kutumia kwa utafiti huu pekee.

**UHURU WA KUTOSHIRIKI AU KUJIONDOA**

Una uhuru wa kutoshiriki au kujiondoa kutoka utafiti huu wakati wowote bila sababu. Hamna adhabu wala upotezi wa faida au haki zako wakati unapojiuzulu.

## APPENDIX IV: KIBALI CHA KUSHIRIKI KWA UTAFITI

Jina langu ni Josephine Achieng Aywak, mwanafunzi wa uzamili katika Chuo Kikuu cha Nairobi Idara ya Radiologia na Dawa Mionzi.

Ninathibitisha ya kwamba daktari amenieleza kwa lugha ambalo ninaelewa kuhusu utafiti huu.

Ninakiri kuwa nimepewa nafasi ya kuuliza maswali kuhusu utafiti huu na nimeridhka.

Ninaelewa kuwa ushiriki wangu katika utafiti huu ni kwa hiari yangu mwenyewe. Sijalazimishwa wala sijapendekezwa kujijumushia.

Ninafahamu ya kwamba ninaweza kubadilisha nia langu wakati wowote kuhusu ushiriki wangu bila athari kwangu .

Ninaelewa kuwa sitapata fidia yoyote iwe kifedha au vinginevyo nitakaposhiriki katika utafiti huu.

Ninafahamu ya kwamba taarifa zangu kibinafsi zitakuwa siri

Ninatoa idhini yangu kushiriki katika utafiti huu

Nambari ya mgonjwa _____

Sahihi _____

Tarehe _____

Nimekubali ya kuwa nimemweleza mshirika kikamilifu kuhusu uchunguzi hii na amekubali kushirika

Dr Josephine Achieng Aywak

Sahihi _____ Tarehe _____

**MAWASILIANO**

**Mtafiti**

Dr Josephine Achieng Aywak

Mwanafunzi wa uzamili katika fani ya radiologia

Idara ya Radiologia na Dawa Mionzi

Chuo Kikuu cha Nairobi

Nambari ya simu: 0720562653,

Barua pepe: joaywak@gmail.com.

**Msimamizi**

Dr Caroline Kebuka

Idara ya Radiologia

Hospitali kuu ya Kenyatta

Nambari ya Simu: 254722475372

Barua pepe: kebukac@gmail.com

**KNH-UON SECRETARIAT**

Hospitali kuu ya Kenyatta / Chuo Kikuu cha Nairobi

Ethics and Research Committee

Nambari ya simu: (254- 020) 2726300 EXT 44355

Barua pepe: uonknh_erc@uonbi.ac.ke

**APPENDIX V: QUESTIONAIRE: DATA COLLECTION FORM**

FORM NO: DATE:

DEPARTMENT NUMBER:

Please tick where appropriate:

1. AGE

   18- 28 □

   29-39 □

   40-50 □

   51-61 □

   62-72 □

   73-83 □

   >84 □

2. GENDER :

   MALE □ FEMALE □

3. NUMBER OF NODULES

1 □

2 □

3 □

>3 □

3. SONOGRAPHIC FINDINGS

Size right lobe: ____ cm height X ____ cm width X ____ cm length

Size left lobe: ____ cm height X ____cm width X ____cm length

Size isthmus: ____ cm length

Overall texture: Homogenous, Heterogenous

Estimated total number of nodules ≥1cm: _____

| NODULE NUMBER | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| LOCATION | | | | |
| COMPOSITION (Score) | | | | |
| Cystic 0 | | | | |
| Spongiform 0 | | | | |
| Mixed solid-cystic 1 | | | | |
| Solid 2 | | | | |
| ECHOGENICITY (Score) | | | | |
| Anaechoic 0 | | | | |
| Hyperechoic 1 | | | | |
| Isoechoic 1 | | | | |
| Hypoechoic 2 | | | | |
| Markedly hypoechoic 3 | | | | |
| SHAPE (Score) | | | | |
| Wider than tall 0 | | | | |
| Taller than wide 3 | | | | |
| MARGIN (Score) | | | | |
| Smooth 0 | | | | |
| Ill defined 0 | | | | |
| Lobulated/ Irregular 2 | | | | |
| Extrathyroid extension 3 | | | | |
| ECHOGENIC FOCI (Score) | | | | |
| None 0 | | | | |
| Large comet tail artefact 0 | | | | |
| Macrocalcifications 1 | | | | |
| Rim calcification 2 | | | | |
| Punctate echogenic foci 3 | | | | |
| TOTAL SCORE | | | | |
| ACR TIRADS | | | | |
| FNA CATEGORY | | | | |

## APPENDIX VI: ETHICAL APPROVAL LETTER


UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/446

19th November, 2019

Dr. Josephine Achieng Aywak
Reg. No.H58/87365/2016
Dept of Diagnostic Imaging & Radiation Medicine
School of Medicine
College of Health Sciences
University of Nairobi

Dr. Aywak

**RESEARCH PROPOSAL: CHARACTERIZATION OF THYROID NODULES USING ACR 2017 TIRADS CLASSIFICATION SYSTEM AND CORRELATION WITH THE BETHSEDA FNAC SYSTEM AT KENYATTA NATIONAL HOSPITAL (P707/08/2019)**

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 19th November 2019 – 18th November 2020.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to discover

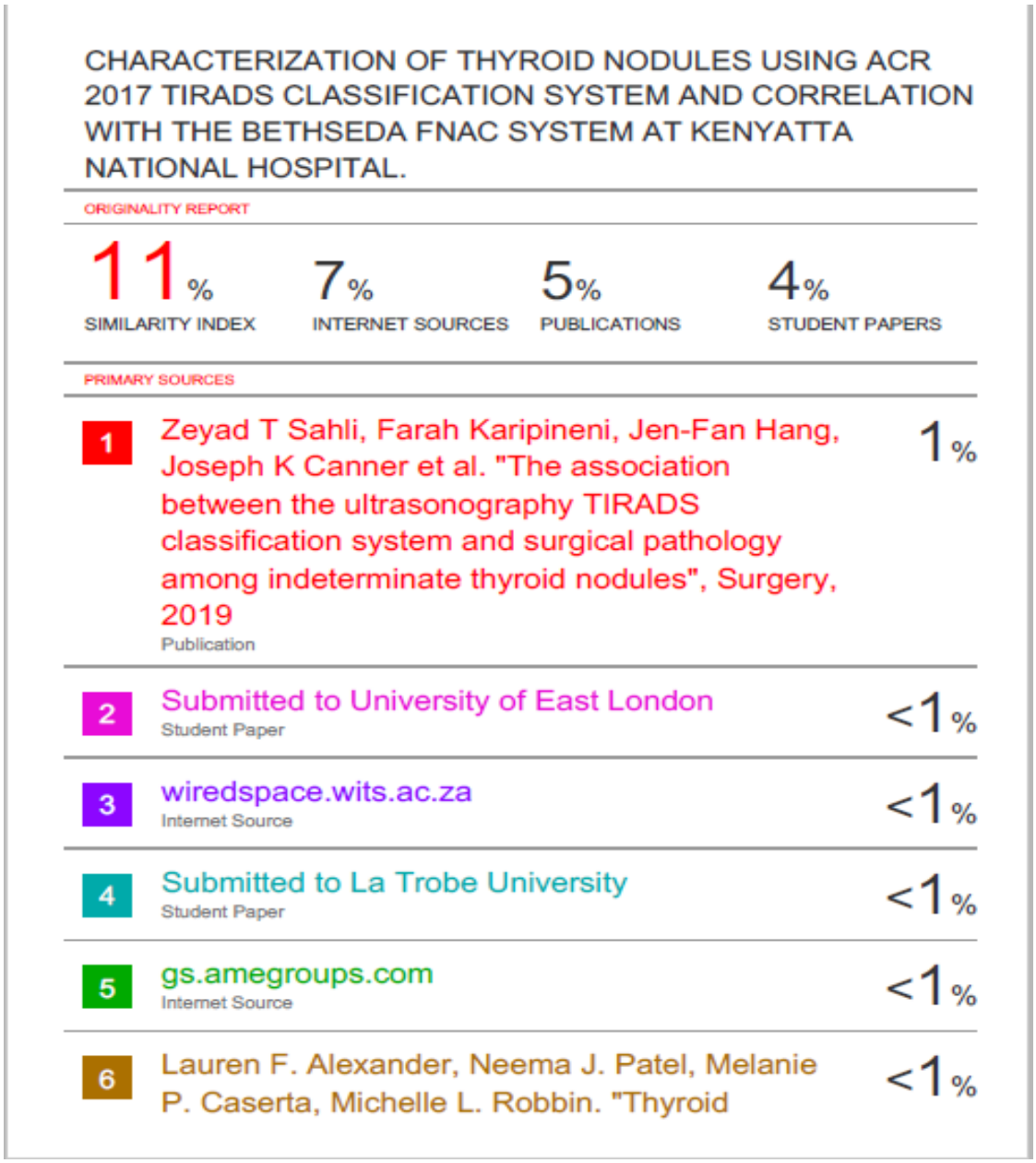
For more details consult the KNH- UoN ERC website**http://www.erc.uonbi.ac.ke**

Yours sincerely,

**PROF. M. L. CHINDIA**
**SECRETARY, KNH-UoN ERC**

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Diagnostic Imaging and Rad. Medicine, UoN
Supervisors: Dr. Caroline Kebuka, Dept. of Radiology, KNH
Dr. Alfred Odhiambo, Dept.of Diagnostic Imaging and Rad. Medicine, UoN

**APPENDIX VII: ANTIPLAGUARISM REPORT**



CHARACTERIZATION OF THYROID NODULES USING ACR 2017 TIRADS CLASSIFICATION SYSTEM AND CORRELATION WITH THE BETHSEDA FNAC SYSTEM AT KENYATTA NATIONAL HOSPITAL.

ORIGINALITY REPORT

| 11% | 7% | 5% | 4% |
|---|---|---|---|
| SIMILARITY INDEX | INTERNET SOURCES | PUBLICATIONS | STUDENT PAPERS |

PRIMARY SOURCES

| | | |
|---|---|---|
| 1 | Zeyad T Sahli, Farah Karipineni, Jen-Fan Hang, Joseph K Canner et al. "The association between the ultrasonography TIRADS classification system and surgical pathology among indeterminate thyroid nodules", Surgery, 2019<br>Publication | 1% |
| 2 | Submitted to University of East London<br>Student Paper | <1% |
| 3 | wiredspace.wits.ac.za<br>Internet Source | <1% |
| 4 | Submitted to La Trobe University<br>Student Paper | <1% |
| 5 | gs.amegroups.com<br>Internet Source | <1% |
| 6 | Lauren F. Alexander, Neema J. Patel, Melanie P. Caserta, Michelle L. Robbin. "Thyroid | <1% |