COMPARISON OF COMPUTED TOMOGRAPHY AND HISTOPATHOLOGICAL FINDINGS AMONG PATIENTS WITH NASOPHARYNGEAL TUMORS AT MOI TEACHING AND REFERRAL HOSPITAL, KENYA.

TOO SHARON CHEROTICH

THESIS SUBMITTED TO MOI UNIVERSITY, SCHOOL OF MEDICINE IN PARTIAL FULFILLMENT FOR THE AWARD OF A MASTER OF MEDICINE IN RADIOLOGY AND IMAGING

DECLARATION

Student's Declaration:

I declare that this thesis is my original work, and that it has not been presented elsewhere for academic purposes or otherwise to the best of my knowledge. The research work was carried out while pursuing my Master of Medicine in Diagnostic Radiology and Imaging course at the Moi University, School of Medicine. No part of this work may be reproduced without permission of the author and/ or Moi University.

Dr. Too C. Sharon
SM/PGR/05/18

Signature……...Date……

Supervisors Declaration

This thesis has been submitted for consideration with our approval as supervisors

Dr. T. M Sisenda,

Consultant ENT surgeon & Senior Lecturer, Moi University

Signature……. Date……

Dr. David K. Chumba

Pathologist, Senior Lecturer, Department of Human Pathology, Moi University

Signature……...Date……

Dr. Daniel Chepsiror

Diagnostic and Interventional Radiologist, Moi Teaching and Referral Hospital

Signature……...Date……

DEDICATION

I would like to dedicate this work to the Almighty God for the gift of life. To my family for their motivation and steady support. To all the radiology registrars and friends for their daily words of encouragement.

To you all, I am truly grateful.

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ABBREVIATIONS

ACP	Antrochoanal Polyps
CSR	Corporate social responsibility
CT	Computed Tomography
EBV	Epstein - Barr virus
ENT	Ear Nose and Throat
FDG	Fluoro-deoxy glucose
GOK	Government of Kenya
H&E	Hematoxylin and Eosin
HLA	Human Leukocyte Antigen
ICCC	International Classification of Childhood Cancer
IREC	Institutional Research and Ethics Committee
JNA	Juvenile Angiofibroma
KNH	Kenyatta National Hospital
MDCT	Multidetector Computed Tomography Scan
MES	Managed Equipment Services
MTRH	Moi Teaching and Referral Hospital
MUSOM	Moi University School of Medicine

NHL	Non-Hodgkin's Lymphoma
NPC	Nasopharyngeal Carcinoma
NPAC	Nasopharyngeal adenocarcinoma
PPS	Parapharyngeal space
RMS	Rhabdomyosarcoma
RNE	Rigid Nasoendoscopy
SCC	Squamous Cell Carcinoma
WHO	World Health Organization

OPERATIONAL DEFINITION OF TERMS

Nasopharyngeal tumor	Is a mass/lesion arising from the primary tissues of the nasopharynx. They can either be benign (non-cancerous) or malignant (cancerous).
Secondary nasopharyngeal tumor	Is a tumor that arise as a result of direct or distant spread from a primary site elsewhere
Benign	This is a tumor that does not invade nearby tissues or other parts of the body.
Malignant	This is a tumor characterized by rapid abnormal cell growth, invasiveness and metastasis
Sensitivity	It is the ability of a test (CT) to correctly classify an individual as diseased as compared with the gold standard (histopathology)
Specificity	The ability of a test (CT) to correctly classify an individual as disease free

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ABSTRACT

Background: Nasopharyngeal tumors are lesions arising from the tissues of the nasopharynx. They can either be benign or malignant, with the latter being the most common. Clinically, they often present late and they tend to be locally advanced by the time of diagnosis. This causes serious morbidity and mortality to the patients and subsequently a burden to the health care system. Early detection is imperative via Computed tomography (CT) scan which is currently widely available and is essential in assessment of extent of the disease as well as guiding further evaluation including biopsy. Biopsy and histopathology are the gold standard for confirmation of nature of lesion. However, histopathology services are limited to referral hospitals, private laboratories and institutions. This study will increase awareness among radiologists and clinicians on the high index of suspicion for nasopharyngeal malignancies especially where histopathology services are limited.

Objective: To describe the accuracy of CT scan in the diagnosis of nasopharyngeal masses using histopathology as the gold standard among patients at Moi Teaching and Referral Hospital (MTRH).

Methods: This was a descriptive cross-sectional study carried out from September 2021 to August 2022 at MTRH, Eldoret, Kenya. Census study method was used to enroll a total of 87 consecutive patients. CT scan images were acquired from MTRH CT centres. Histopathology results were obtained from the histopathology laboratory. Data was collected using structured interviewer administered questionnaire with a checklist of demographics, CT neck and histopathological findings. Continuous variables were analyzed using means, standard deviation and categorical variables were summarized in frequency tables, percentages and bar graphs. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were determined using a 2x2 table. An exact McNemar's test and Kappa test were used to determine any statistically significant difference between CT and histopathology.

Results: The age of the participants ranged between 6 to 77 years with a mean age of 36 years. Males were more affected at 56.3%. On CT evaluation, 84(96.6%) were suspected malignant lesions while 3(3.4%) were benign. Primary involvement was seen in 65(74.7%) patients while 22(25.3%) were of secondary involvement. Most lesions were of soft tissue density 49(56.3%) and heterogenous enhancement pattern 73(83.9%). Histopathologically, 77(88.5%) of the lesions were malignant while 10 (11.5%) were benign. The sensitivity of CT in the diagnosis of nasopharyngeal tumours was 97.4%, specificity of 10%, positive predictive value of 89.3% and negative predictive value of 33.3%.

Conclusion: Malignant tumors were the most common in both radiological and histopathological findings, with nasopharyngeal carcinoma being the most prevalent histological type. Suspicious CT features that correlated with histopathological diagnosis of nasopharyngeal carcinoma were; soft tissue density, heterogenous enhancement, neck spaces and nodal involvement, central skull base, intracranial and vertebral invasion. CT had a high sensitivity but a low specificity in diagnosis of nasopharyngeal lesions. The high sensitivity means that CT can be used for preliminary investigation and screening while a low specificity denotes that it is not a good tool on its own in the diagnosis of nasopharyngeal tumors.

Recommendation: Generally, CT scan can be used for accurate diagnosis of nasopharyngeal tumors as it provides high diagnostic yield. To radiologists, subtle features like asymmetric nasopharyngeal mucosal thickening and enhancement on CT imaging should be considered suspicious to enable early detection in combination with histopathology and prompt management. To clinicians, any patient with persistent rhinological & related symptoms should be advised to have neck imaging.

CHAPTER ONE: INTRODUCTION

1.1 Background of the study

The nasopharynx is the uppermost part of the pharynx and aero-digestive tract. It lies behind the nasal cavity under the skull base. It represents an intersection between the nasal choanae, oropharynx, the deep facial spaces, intracranial cavity and the skull base*(Dubrulle et al., 2007)(Otol & Laryngol, 2015)*

The nasopharynx extends from the clivus and floor of the sphenoid sinus, inferiorly to the level of the junction of the hard and soft palates. The anterior border is formed by the posterior margin of choanal area and the posterior bony septum representing the vomer. The superior border is composed of the clivus and the upper two cervical vertebrae and the superior constrictor muscle, which is bound to the prevertebral fascia*(Weber et al., 2003).*

The anterior, posterior, and inferior walls of the nasopharynx are lined by stratified squamous epithelium. The roof and nasal choanae are lined by respiratory epithelium. The remaining areas have mixtures of squamous and respiratory or intermediate (transitional) epithelium. Abundant lymphoid tissue is present in the nasopharynx which is particularly seen at the rim of eustachian tube opening. This is functionally equivalent to that of gastrointestinal tract or Mucosal Associated Lymphoid Tissue, MALT*(Tan & Loh, 2010)*

The nasopharyngeal surfaces are divided into three subsites: the postero-superior wall, lateral walls, and the postero-superior surface of the soft palate. Laterally, the pharyngeal wall is elevated by the torus tubarius, a cartilaginous structure constituting the distal end of the eustachian tube. Inferior to the torus tubarius is the slit-like opening of the

eustachian tube that ventilates the middle ear airspace and secures pressure equilibrium between the pharyngeal air space and tympanic cavity. The fossa of Rosenmüller or lateral recess, is situated posterior to the torus at the junction between the lateral and posterior walls. This groove and surrounding area are a frequent site for the origin of NPCs. The superior constrictor and the buccopharyngeal fascia envelop the mucosa. Superiorly, the buccopharyngeal fascia unites with the pharyngobasilar fascia, which is attached to the skull base*(Weber et al., 2003).*

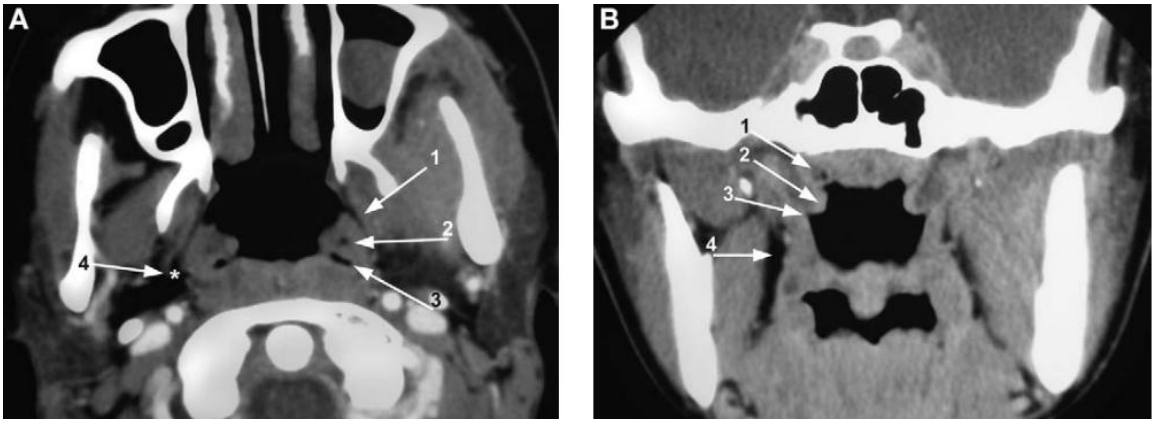


Figure 1: Normal anatomy of the nasopharynx.

(A) Axial CT section: **(1)** Eustachian tube opening**, (2)** Torus tubarius, **(3)** Fossa of Rosenmuller, **(4)** and PPS *

(B) Coronal CT section: **(1)** Fossa Rosenmuller, **(2)** Torus tubarius, **(3),** Eustachian tube opening, and **(4)** PPS

Images adopted from *(Weber et al., 2003)*

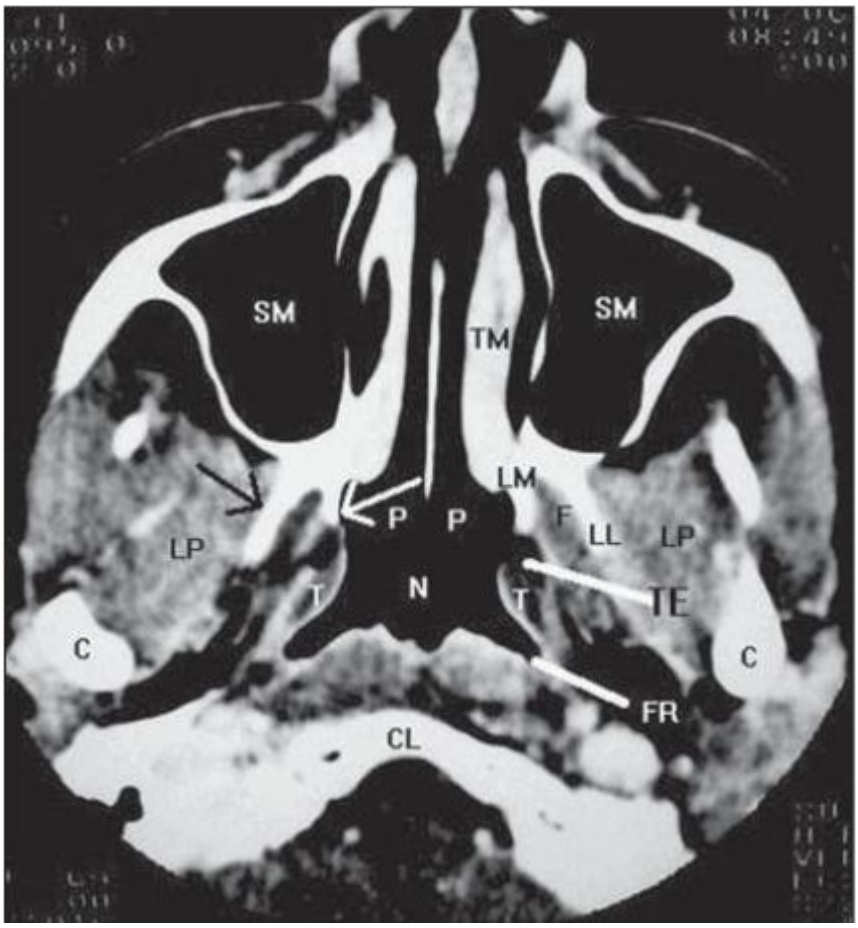


Figure 2: Contrast-enhanced CT axial view: normal anatomy.

SM-maxillary sinus; **TM**-middle turbinate; **P**-posterior choana; **N**-nasopharynx;

LM-medial pterygoid lamina **(white arrow); F**, pterygoid fossa;

LL-lateral pterygoid lamina (**black arrow); LP**-lateral pterygoid muscle;

TE-auditory tube (Eustachian tube); **T**-torus tubarius;

FR-pharyngeal recess (Rosenmuller's fossa); **CL**-clivus; **C**-mandibular condyle

Images adopted from *(Weber et al., 2003)*

The pharyngobasilar fascia originates from the medial pterygoid plate, coursing postero-laterally between the levator palatini medially and tensor veli palatini laterally to the anterior margin of the carotid foramen. It forms the medial boundary of the parapharyngeal space (PPS) together with the buccopharyngeal fascia of the superior constrictor muscle.

The PPS is a triangular-shaped fibrofatty space bounded laterally by the pterygoid muscles and the parotid sheath and extends from the base of the skull inferiorly to the level of the hyoid bone. The PPS is divided by the styloid process into a pre-styloid and post-styloid compartment. The PPS is the most common site for NPC invasion*(Weber et al., 2003).*

The anterior, posterior, and inferior walls of the nasopharynx are lined by stratified squamous epithelium and by respiratory epithelium at the roof and nasal choanae. The remaining areas have mixtures of squamous and respiratory or intermediate (transitional) epithelium. Plenty lymphoid tissue is present, particularly at the rim of eustachian tube opening, which is functionally equivalent to that of gastrointestinal tract or mucosal-associated lymphoid tissue*(Duarte et al., 2013).*

A nasopharyngeal tumor is a growth that forms in the nasopharynx. A tumor in the nasopharynx may be either benign, malignant and congenital or developmental in children. Secondary nasopharyngeal tumors are very rare but occur as a result of secondary infiltration of salivary, parotid and tonsillar neoplasms. Nasopharyngeal tumors that are malignant may spread to surrounding tissue and other parts of the body*(Duarte et al., 2013).*

The patient's age and sex are important in the differential diagnosis of a nasopharyngeal mass. In the pediatric population, differential diagnoses of nasopharyngeal masses include inflammatory lesions, malignant tumors, and congenital masses. The rareness of pediatric nasopharyngeal masses and the diversity of possible pathologies make a clinical diagnosis difficult. In the pediatric age group, adenoidal hypertrophy is the most common benign tumor, whilst Juvenile Angiofibroma (JNA) is strongly considered in teenage males having a nasopharyngeal mass. In adults, the default diagnosis for masses in this area is nasopharyngeal malignancy, as adenoid hypertrophy would have usually regressed*(Duarte et al., 2013).*

Most nasopharyngeal neoplasms are malignant tumors. Squamous cell carcinoma of undifferentiated type is the most common form of malignancy accounting for up to 98% of all nasopharyngeal malignancies in the Orient. The highest incidence rates are found in Southern China especially Guangdong Province, Hong Kong and the southern rim of the Mediterranean, but low incidence reported in the Western countries of Europe and North America*(Dubrulle et al., 2007).*

In as much as NPC appears to be less frequent amongst all body cancers, it is a prominent malignancy amongst head and neck cancers. In the USA, NPC is the 4th most common head and neck cancer accounting for 0.25% of all malignancies in the United States. It also accounts for 10–20% of childhood malignancies in Africa*(Abdel et al., 2012).* Head and neck cancers inclusive of nasopharyngeal cancers constitute about 5.7% of the cancer burden in Kenya*(Kalebi. A et al., 2019).* The nasopharynx is the third most common site for head and neck cancer in Kenya. In Tanzania, it is the second most common aero-

digestive tract whereas in Uganda, Senegal and Sudan, it has been reported as the most common site for upper respiratory cancer*(Onyango & Macharia, 2006).*

The nasopharyngeal region has a diverse array of tissues in which a wide variety of cancers could arise from. Epithelial malignancies include nasopharyngeal carcinoma, nasopharyngeal papillary adenocarcinoma and salivary gland-type carcinomas. Amongst Haemato-lymphoid tumors, non-Hodgkin lymphomas (NHL) are the commonest with Hodgkin's disease contributing a small proportion of cases. Diffuse large B cell and extranodal NK/T cell lymphomas are the commonest NHLs. Mesenchymal cancers include chondrosarcoma, osteosarcoma and chordoma. The commonest histological type are carcinomas arising from the mucosa, with squamous cell carcinoma being very predominant at 95%*(Muhammad, 2017).*

According to the WHO, grading of nasopharyngeal neoplasms and all other tumors is based on histopathological characteristics under light microscopy. WHO acknowledges three histopathological types of NPC based on the degree of differentiation. Type I is keratinizing squamous cell carcinoma (SCC), similar to other head and neck cancers. Type II is non-keratinizing carcinoma which are divided into differentiated and undifferentiated tumors and Type III is basaloid squamous*(Y. P. Chen et al., 2019).*

The clinical presentation of a nasopharyngeal tumor is variable ranging from ear, nasal, and throat symptoms to neck masses and cranial nerves palsies. Painless, enlarged cervical lymph nodes, nasal obstruction, epistaxis, sore throat and headache, diminished hearing, tinnitus, recurrent otitis media and cranial nerve dysfunction are some of the signs and symptoms of nasopharyngeal neoplasms *(W. C. S. Cho, 2007)*

Since the nasopharynx is a deep-seated clinically silent area, the symptoms generally arise late and the first presentation maybe with distant metastasis or cervical nodal involvement. Therefore, they can reach significant sizes before presentation because of the diagnostic inaccessibility of the nasopharyngeal area. A high index of suspicion on clinicians' part is paramount for successful recognition of early lesion*(Muchiri, 2008) (Lee et al., 2012)*

Radiological imaging plays a big role in accurate tumor detection and mapping of tumor extension especially to the deep facial spaces and the skull base. CT scan imaging in addition to Magnetic Resonance Imaging (MRI) are imperative in assessment of extent of disease, associated bone destruction and staging of the disease*(Abdel et al., 2012)(V. F.H. Chong & Ong, 2008).* Tissue biopsy and subsequent histopathology are required for confirmation of nature of lesion.

The availability and accessibility of CT scan services across counties in Kenya has been improved by the National Government project of Managed Equipment Services (MES) launched in 2013(*Govt. Managed Equipment Service Rise Capacity for Screening Illnesses – MINISTRY OF HEALTH*, n.d.) and the Universal Health Coverage (UHC) under the Big Four Agenda. This has enabled CT scan to be used as one of the primary imaging modalities for nasopharyngeal tumors.

In Africa, there's paucity of data on CT scan characteristics in comparison to histopathological diagnosis of nasopharyngeal tumors. This study therefore endeavours to compare CT scan characteristics with histopathological findings of nasopharyngeal tumors in Kenya and specifically at Moi Teaching and Referral Hospital, Eldoret.

1.2 Problem Statement

Early detection of nasopharyngeal neoplasms continues to be a great challenge to clinicians. Their late presentation is owed to their relatively silent growth with no characteristic macroscopic features and the difficulty in visualizing the nasopharynx. This allows for significant spread of the disease before diagnosis and consequently, poor prognosis *(Muchiri, 2008) (Otol & Laryngol, 2015).*

In addition to their disease burden, poor prognosis when diagnosed late and great strain on health resources, they are associated with psychological stress to the clinicians, patients and relatives. The strain is more evident in developing countries such as Kenya, where individuals and families bear the cost of health bills since health insurance benefits has not been fully realized *(Ologe et al., 2005).* CT scan imaging is a non-invasive diagnostic tool and is of great importance in early diagnosis and staging of the disease. It is the standard imaging modality for determining skull-base erosion and intracranial spread *(Hoover, 2015).* This characterization helps in early referral for specialist care and the management and ultimate outcome of the patient.

The gold standard for diagnosis of nasopharyngeal lesions is histopathological examination of tissue biopsy. This procedure is expensive, invasive and associated with increased morbidity*(Simo et al., 2016).* Moreover, the number of ear, nose and throat specialist services and histopathological laboratories is limited to the referral hospitals and major private hospitals. Consequently, this causes delays in the definitive management of such patients.

Comparison of CT scan and histopathology in the diagnosis of nasopharyngeal tumors has not been studied in Kenya. Reporting of neck CT scan is varied with most reports indicating a suspicious mass as the tentative diagnosis without specifying if it's cancerous or non-cancerous lesion. Therefore, more work needs to be done on reporting in conjunction with histopathology results to come up with a comprehensive way of reporting the neck CTs. This informs the need for a standardized way of reporting the CT neck scan results with accuracy in MTRH.

There needs to be improvement in the ability to determine the prognosis of a given nasopharyngeal neoplasm on the basis of its imaging findings. This would allow the radiologists to add more value to the management of a newly diagnosed nasopharyngeal cancer patient.

This study therefore endeavors to assess the level of agreement of CT scan findings in comparison with the gold standard histopathologic findings of nasopharyngeal tumors. This will generate information on the local findings and prevailing spread patterns of nasopharyngeal tumors vis-a-vis histopathology findings. This will help radiologists to further understand the patterns, abnormal mucosal thickness, contrast uptake of these tumors to obtain better CT reports and quick recommendation for ENT specialist's review. It will also be a guide to clinicians for early referral of patients presenting with ear-pain, discharge, neck swelling to the ENT department. Furthermore, the information obtained from this study will be used to recommend the use of CT scan in peripheral facilities without histopathology and interventional radiology services in the management of patients with nasopharyngeal neoplasms resulting in better outcomes and less complications for patients.

With installation of CT centres in County Referral hospitals in Kenya, this will be the imaging modality of choice in early diagnosis and referral for nasopharyngeal pathologies.

1.3 Justification

Cancer is the leading cause of morbidity and mortality in developing countries *(Kanavos, 2006*). Nasopharyngeal neoplasms specifically are not suspected clinically until late into the disease process. The cost of treatment is high and is associated with poor prognosis when diagnosed late. This requires general medical providers to have a basic understanding of their diagnosis and management *(Hoover, 2015)*.

At the time of clinical presentation, the extent of disease by radiological assessment is usually greater than assessment by clinical examination(*Abdel et al., 2012)*. With the evolution of CT scanners to high resolution multi-detector scanners, very subtle features suspicious of nasopharyngeal lesions can be detected. The management of patients with nasopharyngeal neoplasms depends on the initial imaging findings on CT scan. To gain further insight into the nature and patterns of nasopharyngeal tumors, radiological studies are paramount in diagnosis*(K. S. Cho et al., 2012)*. Therefore, there's need to generate accurate information in regards to the congruency between the CT features and the final histopathology diagnosis to develop comprehensive CT scan reports.

In Kenya, the National Government through the MES program has installed CT scan centres in county referral hospitals (*Govt. Managed Equipment Service Rise Capacity for Screening Illnesses – MINISTRY OF HEALTH*, n.d.). This has improved the diagnostic capacity of county hospitals after training of specialists, has decongested national referral hospitals and reduced the turn-around time between diagnosis and management of

patients with nasopharyngeal neoplasms. In addition, it is relatively cheaper and safe compared to surgery and histopathological examination.

This study therefore, aims to provide data that will be used by clinicians and radiologists for diagnosis, characterization and early referral of nasopharyngeal tumors. Additionally, it will provide data that will be useful in staging and treatment planning. It will also recommend the use of CT scan in peripheral facilities without histopathology and interventional radiology services for early referral and management of patients with nasopharyngeal neoplasms resulting in better outcomes and less complications for patients.

Currently, there's paucity of data on the congruency of CT scan vs histopathology in diagnosis of nasopharyngeal tumors, thus the need for this study in MTRH which serves as a referral centre to specialist, general and private hospitals in the South Rift and Nyanza region. The data from this study, when available, will have the potential of being used as a guide to radiologists in developing a standardized way of reporting neck CT scan images. It will also be used as a guide and evidence on policy development in regards to care, diagnosis and management of patients with nasopharyngeal tumors in MTRH and Kenya at large.

1.4 Research Questions

This study aims to answer the following question:

1. What is the comparison between CT scan and histopathology findings among patients with nasopharyngeal tumors at MTRH?

   What CT scan features correlate with the histopathology findings in the diagnosis of nasopharyngeal tumors at MTRH?

1.5 Objectives

1.5.1 Broad Objective

To compare CT scan and histopathology findings of nasopharyngeal tumors at MTRH

1.5.2 Specific Objectives

1. To describe the CT scan findings among patients with nasopharyngeal tumors at MTRH
2. To describe the histopathological findings among patients with nasopharyngeal tumors at MTRH
3. To compare the radiological findings seen on CT scan with histopathologic findings among patients with nasopharyngeal tumors at MTRH

CHAPTER TWO: LITERATURE REVIEW

2.1 Epidemiology

Nasopharyngeal tumors may be either benign or malignant. Primary and secondary nasopharyngeal tumors are uncommon with the latter being very rare. In the pediatric population, nasopharyngeal masses are quite uncommon, and the majority of these are benign. Adenoidal tissue, Antrochoanal polyp (ACP), and Juvenile Nasopharyngeal Angiofibroma (JNA) are some of the benign tumors. Benign adenoidal hypertrophy is by far the most common mass in the nasopharynx in children. A recent meta-analysis in Europe, Brazil and Mexico showed the prevalence of adenoid hypertrophy among children and adolescents was at 34.46%*(Pereira et al., 2018)*. In Nigeria, the prevalence among children attending a private hospital was found to be 1.3% with male predominance*(Chinawa et al., 2015)*. In adolescence, juvenile nasopharyngeal angiofibromas should be a highly suspected especially in the males. Sarcomas and lymphomas are more common in younger children, whereas carcinoma of the nasopharynx (NPC) has a fondness for adolescents and teenagers*(Duarte et al., 2013).*

Adenoidal tissue consists of lymphoid tissue that can enlarge over time leading to symptoms of nasal airway obstruction. Adenoid hypertrophy has no predilection of any gender or racial group. Prevalence of adenoid hypertrophy has been noted to decrease age increases and lowest among children from high socioeconomic class*(Chinawa et al., 2015).*

ACP is a benign lesion that arises from the mucosa of the maxillary sinus. It grows into the maxillary sinus and may pass into the choanae and nasopharynx. One of the most

common associated complaints is nasal obstruction. ACPs are usually unilateral and appear in childhood. They account for 4–6% of nasal polyps, and 90% are solitary.

Nasal polyps are polypoidal masses arising from the mucous membranes of the nose and paranasal sinuses leading to overgrowth of the mucosa. Nasal polyps often recur due to persistence of causative factors, such as allergic rhinitis. In comparison to ACPs, nasal polyposis is frequently seen in adults*(Duarte et al., 2013)*

JNA is the most common benign tumor of the nasopharynx and accounts for 0.05% of all neoplasms of the head and neck*(Sennes et al., 2003).* It is a slow growing, vascular neoplasm that occurs in prepubertal and adolescent males*(Wheat et al., 2016).* The exact site of origin of JNA remains controversial. The blood supply to these benign tumors is often from the internal maxillary artery, but they may also be supplied by the external carotid artery, common carotid artery, internal carotid artery or ascending pharyngeal artery*(Wu et al., 2011)*. JNAs classically present with unilateral nasal obstruction, epistaxis, and nasopharyngeal mass in adolescent males, with an average age of onset of 15 years*(Duarte et al., 2013).*

Less frequently seen benign nasopharyngeal masses in the pediatric population include fibromas, rhabdomyomas, chordomas and chondromas. A fibroma is a localized pedunculated mass, usually less than 1 cm in size. Chordomas are believed to originate from the notochord during development. Chordomas have been reported to recur as high-grade spindled cell sarcomas. Rhabdomyomas are benign neoplasms of striated muscle, based on histologic features they are divided into fetal and adult types.

A chondroma is a benign cartilaginous tumor that occurs in two forms, solitary and multiple, and is hard to differentiate from a malignant chondrosarcoma *(Mohanty et al., 2013).*

Congenital midline nasal masses include nasal dermoids, nasal gliomas, and encephaloceles. These form part of secondary tumors of the nasopharynx. These congenital anomalies are estimated to occur in 1 out of 20,000–40,000 births. Despite being rare, these lesions are clinically important because of their potential for communicating with the central nervous system. A dermoid cyst is a midline lesion that can present as a mass on the dorsum of the nose or totally intranasally. They often have a pit or sinus tract opening on the nasal dorsum and discharge or purulence or sebaceous material. It has been reported to extend intracranially and cause central nervous system infections, such as meningitis*(Duarte et al., 2013).*

Nasal gliomas are firm masses which are non-pulsatile and tend to arise from the lateral nasal wall and may extend to the nasopharynx. What distinguishes these lesions from others is their lack of enlargement with bilateral compression of the internal jugular veins. Contrary to nasal gliomas, encephaloceles are blue colored, pulsatile lesions that arise from the nasal bridge and can lead to nasal broadening. They are compressible and can be transilluminated on exam. Additionally, they can enlarge with bilateral compression of the internal jugular veins or crying. Intranasal encephaloceles are usually seen arising from the cribriform plate*(Duarte et al., 2013)*

Other rarely seen congenital lesions that have been reported in the pediatric nasopharynx include teratomas, Thornwaldt’s cysts, craniopharyngiomas, hamartomas and hemangiomas. Teratomas, also known as hairy polyp of nasopharynx, are derived from

pluripotent tissues composed of all three germinal layers and are often diagnosed in the neonatal or infancy periods. The lesion can be sessile or pedunculated and can be commonly seen protruding into the mouth. Teratomas are associated with intracranial anomalies such as palatal fissures, hemicranias, anencephaly, and polyhydramnios and with elevated alpha fetoprotein levels*(Duarte et al., 2013).*

A craniopharyngioma is a type of pituitary adenoma and is of cystic nature. It is a benign epithelial tumor of the central nervous system that is found as a sellar or suprasellar mass. It has been reported to recur after excision, and rarely does it undergo malignant change.

Thornwaldt's cyst is a fairly rare lesion located in the posterior wall of the nasopharynx. Most are small and asymptomatic, but some can cause nasal obstruction, postnasal drip, eustachian tube dysfunction or occipital headache.

A hamartoma is a simple congenital malformation derived from local tissue and often appears polypoid but does not infiltrate the surrounding tissue.

Globally, nasopharyngeal malignancies are uncommon in most regions of the world both in the paediatric and adult population. Malignancies of the pediatric nasopharynx include rhabdomyosarcomas, nasopharyngeal carcinomas (NPCs), and lymphomas. Malignant tumors of the nasopharynx are rare in children, and their histology generally varies with the age of the patient at presentation. Soft tissue sarcomas and lymphomas are more frequently diagnosed in younger children, whereas NPC has a predilection for adolescents and teenagers*(Liu et al., 2014)(Duarte et al., 2013).*

NPC is primarily a disease of adults and its incidence in children varies with geographic location. In China, where NPC is endemic, less than 1% of NPC occurs in children under 14 years of age. Comparatively, 10–20% of NPC in Tunisia, Uganda, Kenya, Nigeria,

and Sudan occur in children. In the United States there are reports of higher prevalence of NPC in African Americans, but the relationship of ethnicity to NPC in children is uncertain*(Stambuk et al., 2005).*

Rhabdomyosarcomas are most commonly seen in the nasopharynx, orbit, middle ear, mastoid, nose or paranasal sinuses. Rhabdomyosarcomas are diagnosed at age 12 or younger in 75% of patients. These tumors are hardly found in teenagers, adults or the elderly. Eighty-five percent of rhabdomyosarcomas comprise of the embryonal subtype, including botyroides variant. Survival varies by site: the orbit at 90%, nose, paranasal sinuses and nasopharynx at 45%, other head and neck subsites at 75%*(Duarte et al., 2013).*

Nasopharyngeal malignancies are infrequent all over the world. Nasopharyngeal carcinoma is the predominant tumor type in both endemic areas and regions with low incidence. NPC is the 23rd most common cancer worldwide and is the 18th most commonly occurring cancer in men and 22nd most commonly occurring cancer in women. It accounts for 1.2% of the global cancer burden. According to the International Agency for Research on Cancer in 2018, they were 129,000 new cases (in men 1.7 per 100,000; in women, 0.7 per 100,000) *(Ferlay et al., 2019) (Yousefi et al., 2018)* (Y. P. Chen et al., 2019)

NPC accounts for 5% of all pediatric head and neck malignancies and about one-third of all cancers of the upper airway. It is very rare in children younger than 10 years of age but increase in incidence is seen from 0.8 to 1.3 per million per year in children of ages 10 to 14 and in children of ages 15 to 19, respectively*(Siegel et al., 2016).*

The incidence of NPC is characterized by geographic and racial variations with well-defined ethnic groups exhibiting endemic distribution, as seen in in North Africa and Southeast Asia. In the United States, NPC is seen more in black children when compared with other malignancies. It is endemic in Southern China, Hong Kong, Taiwan and Singapore with the highest incidence is found in Guangdong province in Southern China. The reported incidence of NPC among men and women in Hong Kong is 20–30 per 100 000 and 15–20 per 100 000, respectively *(Wei & Sham, 2005).*

The cancer is generally found in patients over 40 years of age and is uncommon, <1% in childhood. In low incidence areas like Europe, Japan and United States of America (USA) or intermediate; North Africa, the Middle East, Turkey, Greece, Southern Italy, two frequency peaks have been observed, the first between 10 and 20 years of age and the second between 40 and 60 years*(Daoud et al., 2003)*. In high incidence areas, the prevalence of nasopharyngeal carcinoma rises after the age of 30 years and peaks at 40-60 years of age*(Bray et al., 2008).*

In a retrospective study done in Tunisia in patients 16 years or younger, one peak was seen arising in young adolescents of ages between 15 and 20 years and a second peak between 50 and 55 years of age. Seven to 18% of NPCs were found to occur in children*(Hasnaoui et al., 2020)*

In low incidence areas, bimodal age distribution with first peak in late adolescence or young adults (15-24 years) and second peak late among the elderly (65-79 years) were demonstrated.

The mean age reported in Ghana is 36.7 years and the peak is 10-19 years. In Morocco, the mean age is 43 years with a range of 6-91 years*(Ferlay et al., 2019) (Raissouni et al., 2013)*

In Africa, Nasopharyngeal carcinoma is largely seen among Arab populations in North Africa and in 'hotspots' in East Africa like the Kenyan highlands*(Tamura, 2008)*. It is also seen in Western North Africa (Morocco, Algeria and Tunisia) and in North America within the artic circle(Feng et al., 2009). Kenya, Tunisia and Algeria have higher incidences than non-Mongolian races*(Muchiri, 2008)*. The worldwide distribution of NPC in 2018 estimated the age-standardized incidence rates of Kenya, Uganda and Tanzania were more or equal to 1.5 per 100,000 (Y. P. Chen et al., 2019).

In North Africa, NPC constitutes 5–10% of childhood tumors. NPC is strongly linked with Epstein-Barr virus (EBV) infection. Three histologic subtypes of nasopharyngeal carcinoma are recognized by the World Health Organization (WHO): type 1 is squamous cell carcinoma; type 2 is non-keratinizing squamous cell carcinoma; and type 3 is undifferentiated carcinoma*(Cheuk et al., 2011)*

Children with NPCs are more likely to have WHO type 2 or type 3 tumors. Undifferentiated NPC is typically associated with a more advanced locoregional stage and with frequent distant metastases than in the adult. However, the overall survival rates of children and adolescents with NPC has improved over the last four decades with 5-year survival rates in excess of 80%*(Stambuk et al., 2005).*

A prospective study on NPC was done in the United States using the surveillance, epidemiology, and end results (SEER) data. The epidemiology, clinical features, and outcome between paediatric and adult patients was compared. 6,014 patients diagnosed

with NPC were actively followed over a period of 18 years. Only 129 children and adolescents were identified representing 2% of the studied population. The median age of these patients was 16 years, range of 7–19 years. The incidence for children and adolescents was 0.5 per million person-years. The age-adjusted incidence in adults was 8.4 per million person-years with the highest incidence above the age of 60 years (16.8 per million person-years). No bimodal age distribution was observed.

Male predominance was seen with no difference in gender distribution between children and adolescents and adults. Blacks represented 34.9% of children and adolescents with NPC, while they represented only 9.1% of adults(P<0.001). Children and adolescents were more likely to have WHO types II and III, while type I was the most frequent type in adults (P<0.001)*(Stevens et al., 2008)*

In contrast to other head and neck cancer and epithelial malignancies, a unique feature of NPC is its strong association with Epstein Barr virus (EBV) especially in the pathogenesis of NPC types II and III. EBV primary infection takes place in childhood and is always accompanied by seroconversion and harboring of virus in dormant state for life. Higher EBV antibody titers, especially of IgA class couple with presence of EBV DNA or RNA in all tumor cells, are observed in most NPC patients*(Li & Wang, 2018).* Latent EBV infection is identified in cancer cells of virtually all cases of NPC in endemic regions. (Y. P. Chen et al., 2019).

Non-Hodgkin’s lymphoma (NHL) accounts for 60% of all lymphoma cases. It is associated with T-cell deficiencies. They are often bulky lesions that affect multiple sinuses and nasal cavity, with extension into nasopharynx. The 5-year survival is 55% for

stage I/II. The different histological subtypes include NK/T cell, diffuse large B cell, and peripheral T cell; mantle cell lymphoma is most commonly seen in the nasopharynx*(Laskar et al., 2006)*

A retrospective review of clinical and histological records of adult head and neck cancer was done at Kenyatta National Hospital, Kenya. A total of 793 cases were reviewed and the nasopharynx was found to be the third most common site (12.5%) for head and neck cancers*(Onyango & Macharia, 2006).*

In one study done in Nigeria, 89 cases of head and neck cancers in adults over a five-year period were reviewed. The nasopharynx was reported as the third most overall site (11.3%), but the second most common aero-digestive site for head and neck cancer. Squamous cell carcinoma was found to be the most common type*(Ologe et al., 2005).*

A demographic study on the epidemiology of nasopharyngeal carcinoma was done in China. They found that independent of race or ethnicity, rates of NPC are higher in men than women with a male: female ratio at 2–3:1 for most populations. For most low-risk populations, NPC incidence rises conspicuously with age. In contrast, among high-risk Southern Chinese of both sexes, incidence of NPC increases with age until it peaks between 45 and 54 years, then it shows a definite decline at older ages*(Yuan, 2002).*

In Hong Kong, NPC incidence is at 20 to 30 per 100,000 inhabitants a year *(Simo et al., 2016).* The highest incidence is found among the Southern Chinese, around 25 to 30 per 100,000 persons per year, especially those of Cantonese origin. Southern Chinese immigrants also have a higher risk of NPC as compared to the local Western population. Independent of race or ethnicity, men are 2 to 3 fold more frequently affected than women *(Lo et al., 2001)*

In another demographic study of NPC done in KNH, a total of 125 patients were reviewed. The male to female ratio was found to be 2.3:1. Subject ages ranged from 13-85 years. Those in ages of 31-40 years recorded the highest numbers. She reported that most patients were noticed to come from the highland areas of Rift Valley (Kericho), Western Kenya and Mt. Kenya region*(Muchiri, 2008)*

In another study done in North Western Nigeria, a total number of 30 cases were reviewed. The age range was from 14 to 60 years. The mean age was 39.1 years with the 4^{th} decade of life (31–40years) recording the highest number of 16 cases (53.3%), whilst lowest frequency of 3.3% was recorded in the 3rd decade of life. Male patients were 22 (73.3%) and 8 (27.7%) were females with a male to female ratio of 2.8:1*(Iseh et al., 2009)*

The histological diagnosis in the study by Iseh et al were squamous cell carcinoma 23 cases (76.7%), non-Hodgkin's lymphoma 3 cases (10%), plasmacytoma 2 cases (6.7%), rhabdomyosarcoma one case (3.3%) and Kaposi's sarcoma one case (3.3%). Squamous cell carcinoma was predominantly seen at 85% of all malignant tumors of the nasopharynx while other types constituted the rest.

A retrospective study conducted in the ENT department of Tahar Sfar hospital in Tunisia, included all patients with a primary diagnosis of NPC. A total of 80 patients were reviewed. 18 pediatric patients (22.5%) and 62 adults (77.5%) were identified. The mean age was 13 years for pediatric patients with a range of 10 to 16 years and 51.5 years for adults, range of 20 to 76 years. Male predominance was seen, with a male to female ratio of 3:1. There was no difference in gender distribution between pediatric and adult patients ($p>.05$) *(Hasnaoui et al., 2020).*

A study done in the UK reported that the annual incidence of NPC is 0.25 per million (age standardized age of 0–14 years), 0.1 per million at age 0–9 years and 0.8 per million at age 10–14 years. On the basis of England and Wales cancer registry data, the assumption that at least 80% of nasopharyngeal cancers at age 15–19 years are carcinomas was made. This suggested an incidence of 1 to 2 per million for NPC at age 15–19 years. In comparison with other countries like Tunisia, Southern China and South East Asia, the incidence in the UK is low *(Brennan, 2006).*

With regards to Non-Hodgkin's lymphoma (NHL), the head and neck is the second most common site of disease. NHL is most frequently found in the Waldeyer's ring which is an extranodal–lymphatic region. It may arise as a primary, secondary or disseminated disease. The nasopharynx is the second most common site of disease after the tonsil within Waldeyer's ring (WR). Non-Hodgkin's lymphoma (NHL) accounts for 60% of all lymphoma cases. It is associated with T-cell deficiencies. They are often bulky lesions that affect multiple sinuses and nasal cavity, with extension into nasopharynx. The 5-year survival is 55% for stage I/II. The different histological subtypes include NK/T cell, diffuse large B cell, and peripheral T cell; mantle cell lymphoma is most commonly seen in the nasopharynx*(Laskar et al., 2006)(King et al., 2003)*

In Western countries, less than 10% of NHL cases involved the WR (WR-NHL), while 10–18% of NHL cases were WR-NHL in Asian countries. Among WR-NHL, about 35–37% of cases were at the nasopharyngeal site, and no difference of incidence between Western and Asian countries was noted. Epstein–Barr virus (EBV) is known to be related to lymphoma pathogenesis. EBV-associated viral proteins were found to play crucial roles in the genesis of lymphomas. The expression of EBV-encoded small RNAs (EBER)

is common in NK/T cell lymphoma (NKTCL), while EBER positivity is still contentious in Diffuse large B cell lymphoma (DLBCL). Some studies report that EBER-positive patients have a poorer prognosis than EBER-negative patients*(Hsueh et al., 2019).*

Rhabdomyosarcoma (RMS) is an aggressive malignant soft tissue tumor that arises from rhabdomyoblasts which are primitive striated muscle cells. It is the most common soft tissue malignant tumor in children and accounts for about 5–8% of childhood cancers. It most commonly arises in the head and neck region (the nasal cavity and paranasal sinuses) but can arise from almost anywhere in the body. The head and neck region accounts for 35–40% of cases and is often seen in younger children. In childhood, a bimodal distribution pattern is seen. One peak occurring during the first decade of life and the other peak during adolescence. The age-group distribution is 1% in <1yearof age; 35% in 1–4 years of age; 25% for 5–9 years of age; 20% for 10–14 years of age; and 13% for more than 15 years of age *(Mondal et al., 2009)(Radzikowska et al., 2015).*

In the United States, approximately 350 new cases are diagnosed each year, and the annual incidence in children, adolescents, and young adults under the age of 20 is 4.3 cases per one million. Diagnosis is made in two-thirds of cases in children younger than six years of age. There is a small male predominance of M:F ratio between 1.3 and 1.5. The incidence in Black patients is higher than in White, especially in those 15 to 19 years. Lower incidence is seen in Asian (Indian sub-continent and West Indian ethnic origin) when compared with predominantly White populations(*SEER Report: Childhood Cancer by the ICCC, CSR 1975-2015*, 2015).

Rhabdomyosarcoma is an uncommon neoplasm of the adult head and neck. In the adult head and neck, rhabdomyosarcomas tend to occur before the age of 40. In adults, it usually spares the head and neck and mostly affects the extremities. It is commonly seen in the paranasal sinuses and tumors of the nasopharynx are seen but rarely. Histologically, adult rhabdomyosarcomas tend to be of a pleomorphic variety especially in the extremities and in the nasopharynx, the alveolar rhabdomyosarcomas are predominantly seen *(Kanagalingam et al., 2002)(Mondal et al., 2009)*

In a study done by Mondal et al, the most common age group for rhabdomyosarcoma is before the second decade (83.3%). A male preponderance was noted their study (66.6%) and its incidence in adults in the head and neck in the region was uncommon(Mondal et al., 2009).

Adenoid cystic carcinoma ordinarily affects patients during middle age and there is no sex predilection reported. Patients with adenoid cystic carcinomas hardly present with cervical lymphadenopathy unlike patients with NPC. This tumor has a greater tendency for perineural spread than does NPC*(K. S. Cho et al., 2012).*

Extramedullary plasmacytoma is an uncommon malignant soft-tissue tumor. Eighty percent of these tumors occur in the head and neck and the nasopharynx is a common site. It has an 80% male predilection and is most typically seen in the sixth and seventh decades. In 20 to 30% of cases, the tumor degenerates into a multiple myeloma. The lesion may present as a submucosal homogeneous and enhancing polypoid nasopharyngeal mass of several centimeters in diameter, with or without bone destruction*(Otol & Laryngol, 2015)(Abdel et al., 2012).*

Table 1: Differential diagnoses of benign and malignant nasopharyngeal tumors
The tables below are adopted from *(Tan & Loh, 2010)(Abdel et al., 2012)(Vincent F H Chong et al., 2019)*

CHILDHOOD BENIGN TUMORS	
Developmental	**Mesodermal**
Thornwaldt's cyst	Juvenile angiofibroma
Hairy polyp	Fibromyxomatous polyps
Teratomas (varied origin)	Choanal polyps
	Osteomas
Ectodermal	Fibrous dysplasia
Papilloma	Craniopharyngioma
Adenomatous polyps	Solitary fibrous tumor
	Desmoid fibromatosis
	Schwannoma
	Benign Salivary Gland Tumors
	Pleomorphic adenoma
	Monomorphic adenoma

CHILDHOOD MALIGNANT TUMORS	
Epithelial	**Malignant Salivary Gland Tumors**
Nasopharyngeal cancer (NPC)	Adenoid cystic carcinoma
Undifferentiated carcinoma	Mucoepidermoid carcinoma
	Acinic cell carcinoma
Lymphoid	Adenocarcinoma
Lymphoma	
Mesodermal	**Metastatic tumors**
Hemangiopericytoma	Adenocarcinoma
Malignant fibrous histiocytoma	Papillary carcinoma
Rhabdomyosarcoma	

ADULT MALIGNANT TUMORS

Epithelial	**Malignant Salivary Gland Tumors**
Nasopharyngeal cancer (NPC)	Adenoid cystic carcinoma
Undifferentiated carcinoma	Mucoepidermoid carcinoma
	Acinic cell carcinoma
	Adenocarcinoma
Lymphoid	
Lymphoma	**Metastatic tumors**
	Adenocarcinoma
Mesodermal	Papillary carcinoma
Rhabdomyosarcoma	Malignant melanoma
Carcinosarcoma	Malignant meningioma
Chondrosarcoma	Malignant macroadenoma
Plasmacytoma	

2.2 Histology of nasopharyngeal malignancies

NPC is a squamous cell carcinoma that develops from the epithelium of the nasopharynx. WHO acknowledges three histopathological types of NPC based on the degree of differentiation.

a) Type I is keratinizing squamous cell carcinoma (SCC), similar to other head and neck cancer.
b) Type II is non-keratinizing carcinoma which are divided into differentiated and undifferentiated tumors
c) Type III is basaloid squamous

Different prevalent histologic types of NPC are found in endemic and non-endemic regions. In endemic areas such as Southern China, WHO Type III accounts for more than 97%, while keratinizing SCC is more common in the Western countries at 75%*(Raman et al., 2015)*

The keratinizing subtype accounts for less than 20% of cases worldwide, and is relatively rare in endemic areas such as southern China. The non-keratinizing subtype constitutes most cases in endemic areas (>95%) and is predominantly associated with Epstein Barr virus (EBV) infection. Alternative pathogenic processes of EBV- negative NPC, especially WHO Type I from Western populations may be involved (Y. P. Chen et al., 2019).

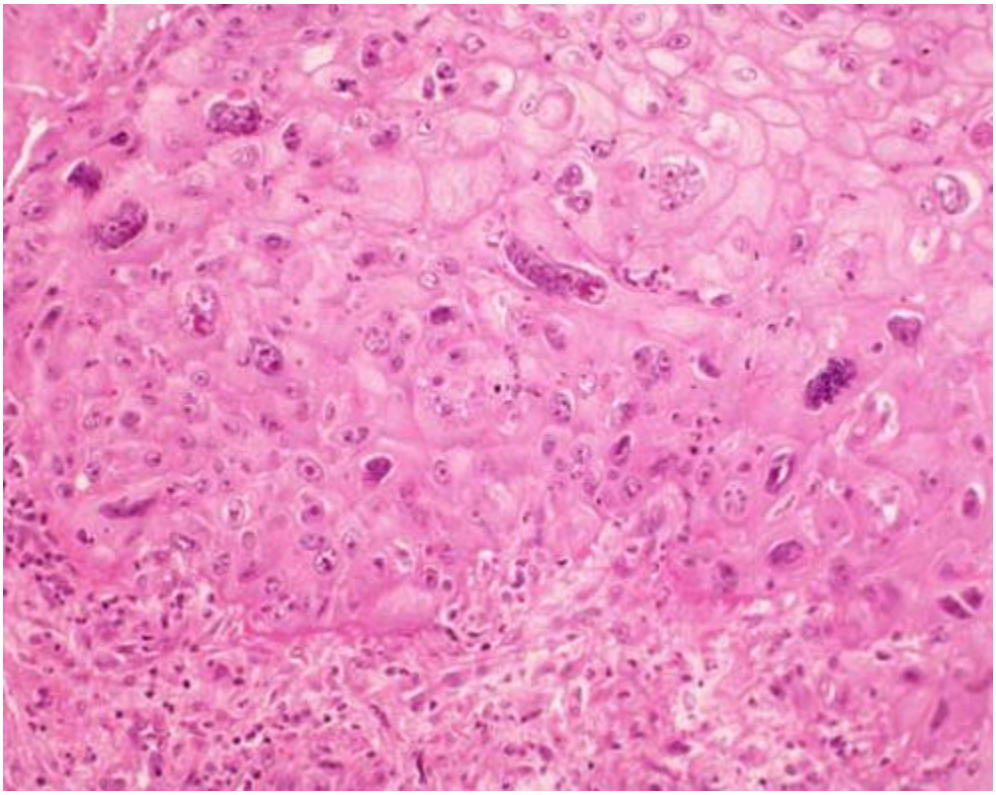


Figure 3: This squamous cell carcinoma shows prominent intercellular bridges, keratinization and an infiltrative growth pattern. The tumor is classified as keratinizing squamous cell carcinoma. Images as adopted from *(Thompson, 2007)*

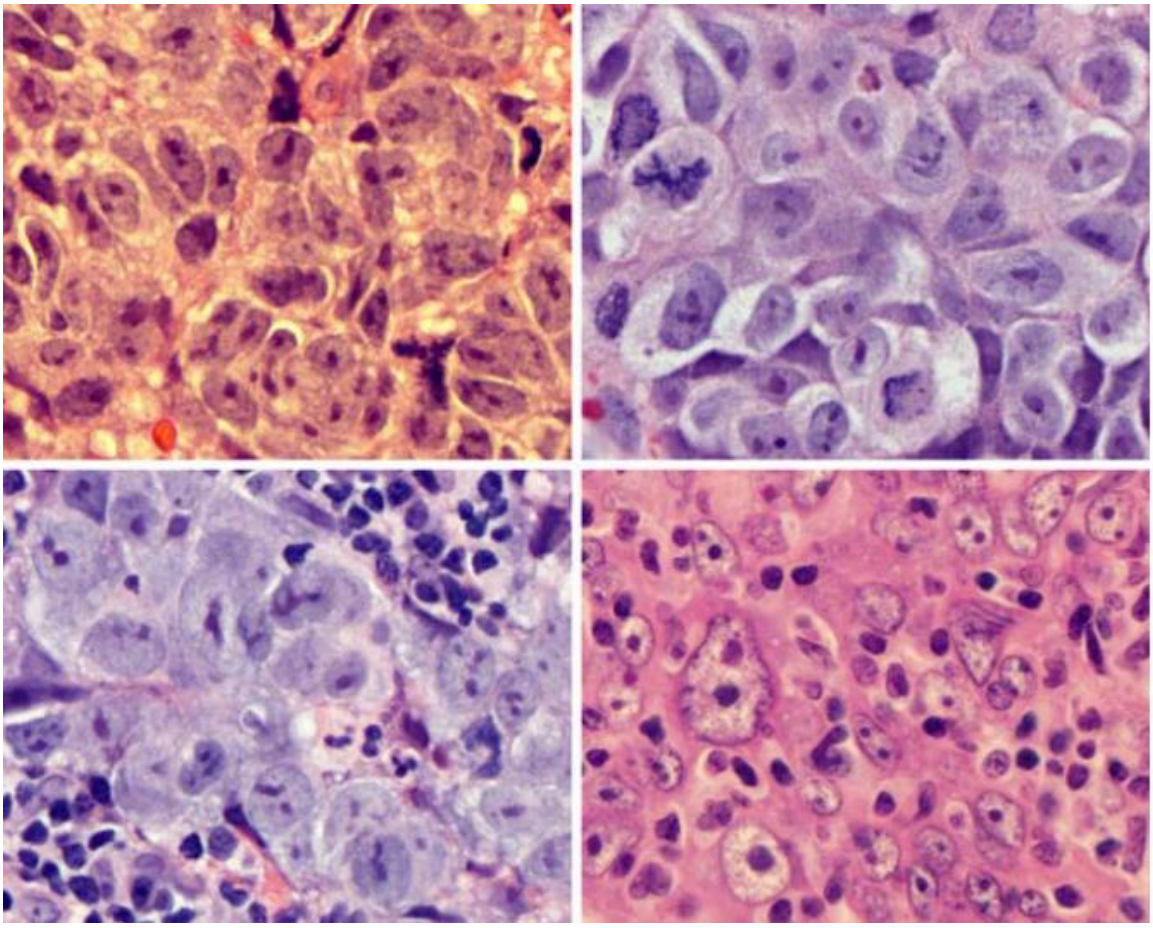


Figure 4: This quartet of non- keratinizing carcinoma show a spectrum of cytologic features. The nuclei range from vesicular to lightly granular. Nucleoli are prominent. There is a high nuclear to cytoplasmic ratio. Inflammatory cells are identified within the syncytium of tumor cells. Images adopted from *(Thompson, 2007)*

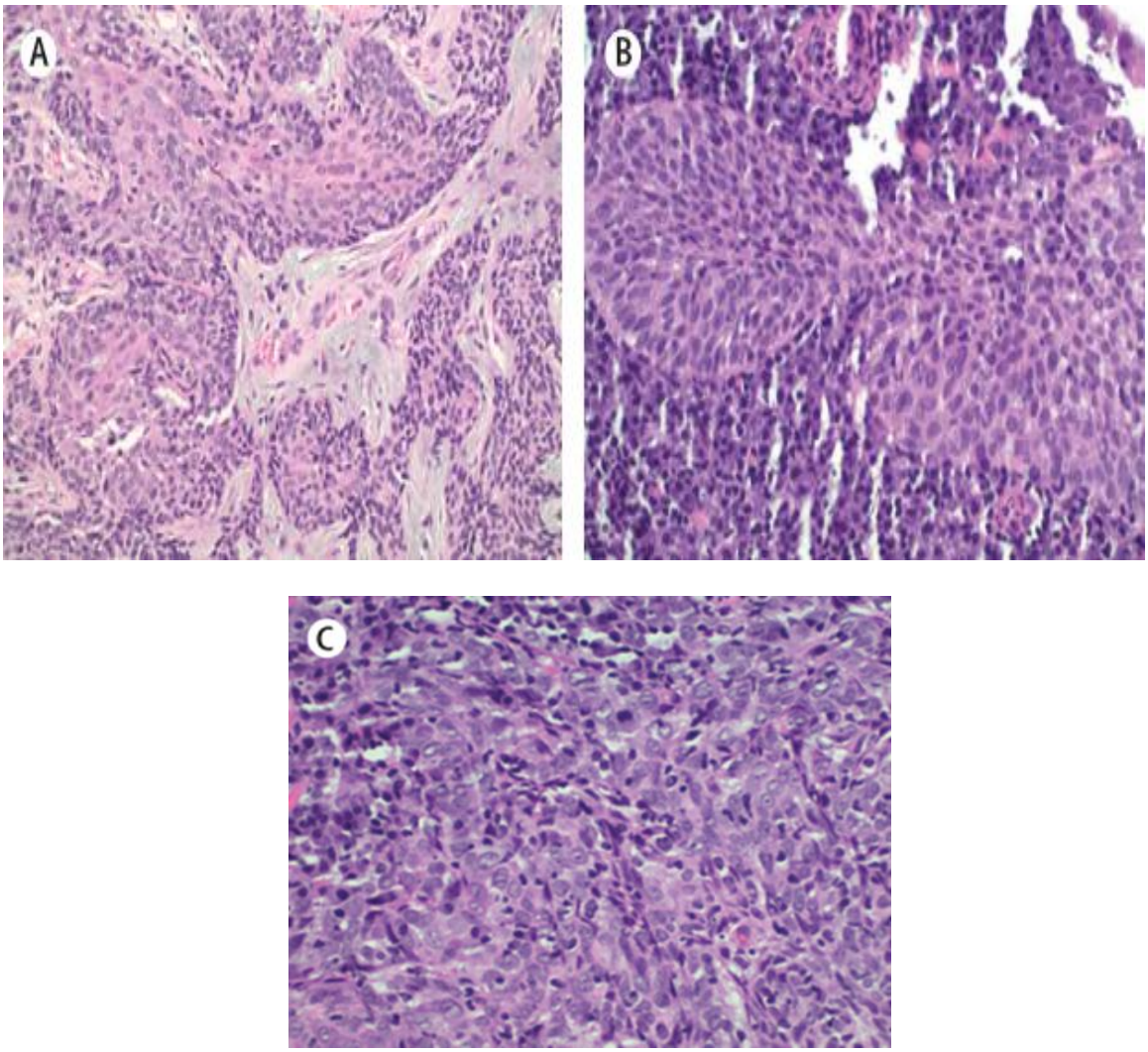


Figure 5: Light microscopic appearance of nasopharyngeal carcinoma

(A) Keratinizing squamous cell carcinoma; hematoxylin and eosin (H&E) stain, magnification 200×

(B) Non- keratinizing carcinoma, differentiated subtype; H&E stain, magnification 400×.

(C) Non-keratinizing carcinoma, undifferentiated subtype; H&E stain, magnification 400×.

Images adopted from *(Thompson, 2007)*

Rhabdomyosarcoma is highly malignant neoplasm derived from primitive mesenchymal tissue expressing myogenic (skeletal muscle) differentiation and is thought to arise from striated muscle progenitor cells. The Intergroup Rhabdomyosarcoma Studies (IRS) Committee and WHO recognizes four major histological subtypes of RMS. The Embryonal botryoid, Spindle cell (leiomyomatous)type, Alveolar RMS and Undifferentiated sarcoma. These are important both prognostically and therapeutically. The most common subtype is the embryonal type and it has an intermediate prognosis. The less common variants of this subtype are the botryoid and spindle cell (leiomyomatous) RMS. These two variants generally have a superior prognosis. Alveolar RMS and undifferentiated sarcoma are both accompanied with a relatively poorer prognosis. The embryonal type is the most frequent form of RMS of the head and neck region and seldom involve regional lymph nodes*(Healy & Borg, 2010)(Mondal et al., 2009).*

Typically, tumors from mucosal surfaces are predominantly of the alveolar subtype. The botryoid variety has a grossly grape-like appearance since its actually an embryonal tumor arising in the submucosal location. Generally, the embryonal variant is the commonest type of RMS arising in the nose, nasopharynx and paranasal sinuses. It is frequently seen in younger children while adolescents have the alveolar type. Histologically, adult rhabdomyosarcomas tend to be of a pleomorphic variety and are commonly found in the extremities. In the nasopharynx, alveolar type tend to be prevalent *(Kanagalingam et al., 2002).*

Histologically RMS is composed of small, round, blue cells that resemble fetal skeletal muscle before innervation. Combined use of transmission electron microscopy, histologic

analysis and assays for muscle specific transcription factors like the MyoD family are essential in the definitive diagnosis of this poorly differentiated tumor. The presence of sarcomeres, myosin, actin and thick filaments lined by ribosomes on electron microscopy are diagnostic for RMS*(Mondal et al., 2009)(Kanagalingam et al., 2002).*

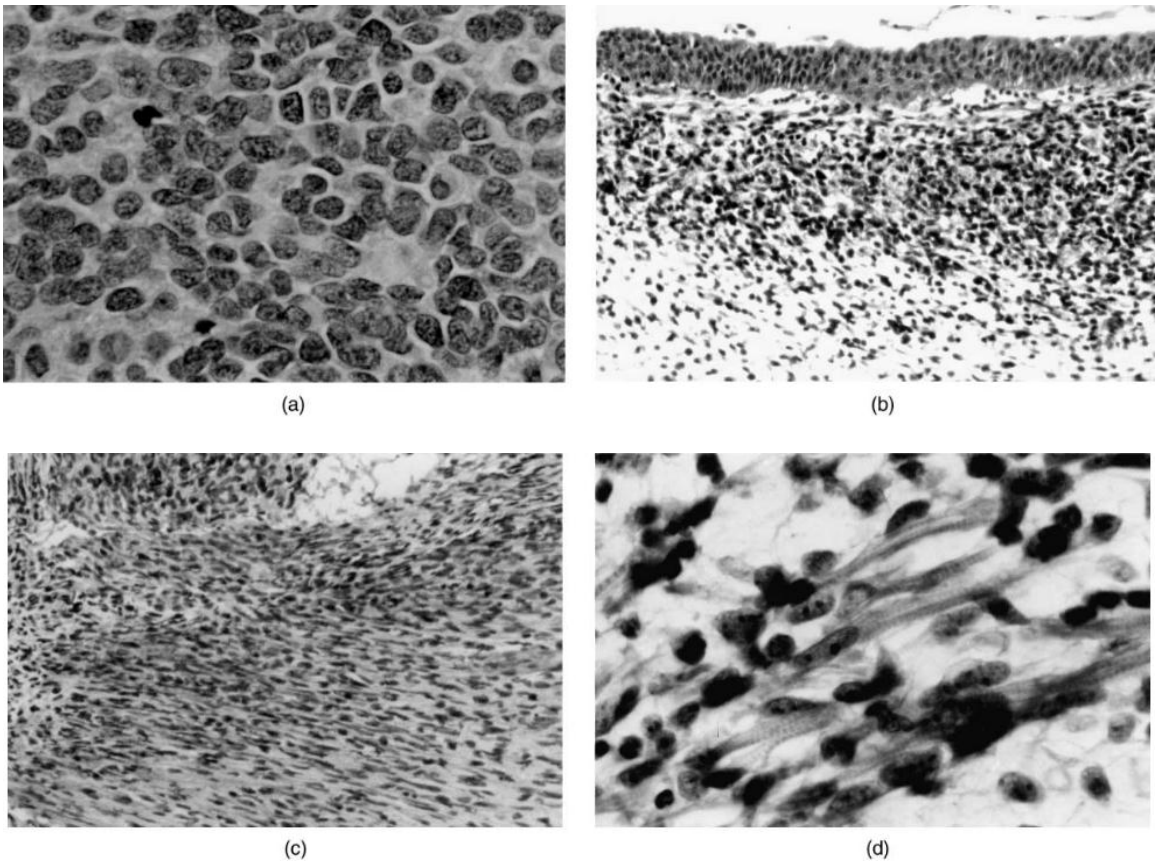
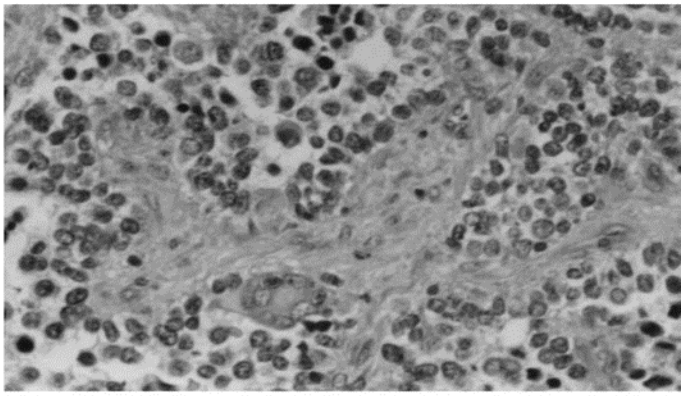
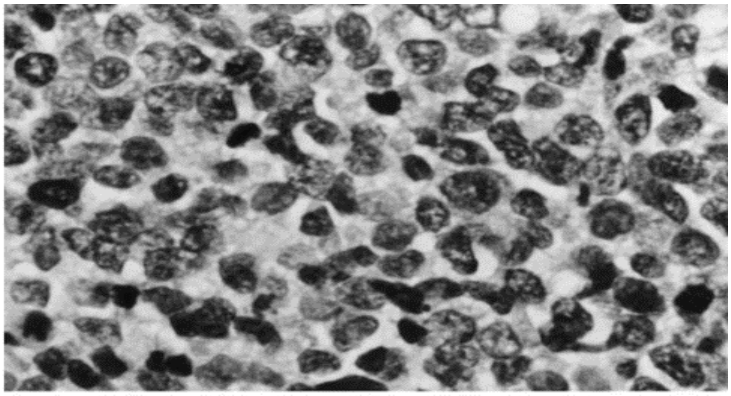


Figure 6: Embryonal Rhabdomyosarcoma: histopathologic appearance. **(A)** embryonal rhabdomyosarcoma NOS; **(B)** botyroid embryonal rhabdo- myosarcoma; **(C)** spindle cell rhabdomyosarcoma; **(D)** strap cells with striated myofilament

Images adopted from *(Radzikowska et al., 2015)*



(a)



(b)

Figure 7: Alveolar Rhabdomyosarcoma: histopathologic appearance. **(A)** Classic alveolar rhabdomyosarcoma with fibrovascular septa, ‘‘alveolar-like’’ spaces, and occasional giant tumor cells.

(B) Solid variant of alveolar rhabdomyosarcoma with large angulated, irregular nuclei and subtle spaces separating tumor cells respectively.

Images adopted from *(Radzikowska et al., 2015)*

Nasopharyngeal adenocarcinoma (NPAC), is an uncommon pathological type of NPC. It is histologically characterized by the presence of a glandular structure and production of mucus. According to WHO classification, NPAC can be divided into common type and salivary gland type, which can be further sub-divided into several varieties of each type. Common types; Acinic cell, papillary, tabular adenocarcinomas and Salivary gland types; Adenoid cystic, mucoepidermoid and malignant mixed tumour*(Guo et al., 2009) (Kuan et al., 2017)*

Histological examination of malignant melanoma is characterized by marked cytological and architectural polymorphism. The presence of intracytoplasmic melanin pigment can be detected by the affinity for Fontana stain. Findings such as surface deviation, pigmentation pagetoid spread, and necrosis giant-cell formation, spindle-shaped, peritheliomatous, solid-sheet, or meningothelial growth pattern can be seen. Immunohistochemistry using a panel of markers: protein S100 and melanocytic markers (HMB45,Melan-A,tyrosinase,MITF) are used for confirmation of the diagnosis*(Gilain et al., 2014)(Sanderson & Gaylis, 2007).*

Histologically, extramedullary plasmacytoma (EMP) is composed of monomorphic plasmacytoid-appearing cells of different degrees of differentiation involving a single extramedullary site. No appreciable admixture of lymphocytes and no bone marrow involvement should be seen. Immuno-positivity to certain leukocyte cell surface markers such as CD79a, CD138, CD38, MUM-1 and CD56, but lack immunoreactivity to pan-CK (AE1/AE3), CD20, CD21 and EBERs are seen*(Du et al., 2015)(Padhi & El-Behery, 2020)*

Of the lymphoid malignancies, NHL is the most commonly seen in the head and neck region. On histology of NHL, more than 60 different histological subtypes exist, but NHL is broadly grouped into mature B-cell neoplasms and mature T-cell and natural killer (NK)–cell neoplasms, or commonly grouped as Diffuse large B cell lymphoma (DLBCL) and NK/T cell lymphoma (NKTCL. Other uncommon types of NHL include; MALToma: extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue, Small lymphocytic lymphoma, Mantle cell lymphoma and PTLD: post-transplant lymphoproliferative disorder.

Epstein–Barr virus (EBV) is related to lymphoma pathogenesis therefore antibodies to EBV are seen microscopically. Histologically, nasopharyngeal lymphomas show diffuse proliferation of variable sized atypical lymphoid cells and the neoplastic lymphoid cells will be positive for characteristic phenotypes such as CD20,CD3 and CD56*(Hsueh et al., 2019)*

2.3 Clinical presentation of malignant nasopharyngeal tumors

There are variable clinical presentations of nasopharyngeal malignancies, ranging from ear, nasal, and throat symptoms to neck masses and cranial nerves palsies. Patients can present with signs and symptoms from one or more of four categories. The categories consist of;

1. Presence of tumor mass in the nasopharynx (epistaxis, nasal obstruction, and discharge)
2. Dysfunction of the eustachian tube, associated with the latero-posterior extension of the tumour to the parapharyngeal space (Audiological problems like tinnitus, deafness and otitis media with effusion, OME)

3. Skull-base erosion and palsy of the fifth and sixth cranial nerves, associated with the superior extension of the tumour (headache, diplopia, facial pain and numbness)
4. Neck lumps and swellings, usually appearing first in the upper neck. This is due to cervical lymph node metastasis on the upper levels of the neck and are often bilateral due to the midline lymphatic drainage of the tumor*(Li & Wang, 2018) (Tabuchi et al., 2011)*

About 70% of NPC patients present with neck masses initially. Neck masses are usually observed in the upper neck. T1 tumors, confined to the nasopharynx, may be clinically occult, and also may be difficult to differentiate from the normal mucosa on a CT scan. However, such small tumors are usually readily evident by their less enhancement with contrast than the normal nasopharyngeal mucosa*(Tabuchi et al., 2011)*

Adenoidal hypertrophy is usually associated with cervical and to a lesser degree retropharyngeal lymphadenopathy in the normal pediatric population*(Stambuk et al., 2005).*

Systemic manifestations such as such as anorexia, weight loss, difficulty in breathing may be present and distant spread should be suspected when such symptoms are present. Unfortunately, because of the non-specific nature of the nasal and aural symptoms and the difficulty in clinical examination of the nasopharynx, most patients with malignant disease are diagnosed only when the tumour has reached an advanced stage (stages III and IV).

The most common presenting symptoms for nasopharyngeal RMS are nasal obstruction, rhinorrhea, and recurrent otitis media. These can cause nasal, aural or sinus obstruction with or without a mucopurulent or sanguineous discharge. Persistent pain, cranial nerve

palsies or sero-sanguineous discharge indicate a serious cause of the symptoms and the tumor often attains a fairly large size at initial diagnosis*(Mondal et al., 2009)*. Nasopharyngeal RMSs have a tendency to grow rapidly and invade adjacent structures by hematogenous or lymphatic spread. Initially, nasopharyngeal malignancies may remain asymptomatic for months, presenting a significant risk of tumour extension at the time of diagnosis. This can include extension into central nervous system or the skull base. The anatomic boundaries to prevent tumour extension are absent in nasopharyngeal tumors, allowing tumor spread and limiting the role and extent of surgery in these cases as distinct from other sites. This pattern of rapid growth, tumour extension and asymptomatic period distinguish nasopharyngeal RMSs from other parameningeal RMSs. Death often occurs via intracranial spread or distant metastasis*(Healy & Borg, 2010)*

Signs and symptoms of nasopharyngeal lymphoma are the same in patients with any nasopharyngeal mass e.g., neck mass, epistaxis, hearing loss, nasal discharge and obstruction. Therefore, it is important to differentiate nasopharyngeal lymphomas from other nasopharyngeal tumors. The key difference is that some patients with nasopharyngeal lymphomas may have constitutional symptoms (B symptoms) including weight loss, night sweats, and fevers, which are less common in patients with other nasopharyngeal tumors. Nonetheless, some patients may be asymptomatic at diagnosis. Nevertheless, the only method for a definite diagnosis is a biopsy-based histopathological analysis*(Hsueh et al., 2019).*

A retrospective analysis of 4768 patients identified symptoms of nasopharyngeal carcinoma at presentation as neck mass (76%), nasal dysfunction (73%), aural dysfunction (62%), headache (35%), diplopia (11%), facial numbness (8%), weight loss (7%), and trismus (3%). The physical signs present at diagnosis were enlarged neck node (75%) and cranial nerve palsy (20%). The cranial nerves most commonly affected were the third, fifth, sixth, and 12th nerves *(Wei & Sham, 2005)*

A prospective analysis of 125 patients at ENT department of KNH identified the most common symptoms were neck swelling (85%), unilateral nasal blockage 71%, epistaxis 44.8% and unilateral hearing loss 36.6%. Most patients had a multiplicity of symptoms. Many patients (48%) had symptoms for between 4-7 months before seeking any medical attention. 89% of the patients had cervical node involvement mainly involving levels II and III. Conductive hearing loss was noted in 36% of patients out of whom 22.2% also had otitis media with effusion (OME). A total of 42 patients had cranial nerve (CN) involvement. The most involved CN was trigeminal nerve *(Muchiri, 2008).*

A retrospective study was done in Tunisia of 40 patients under 17 years of age. Neck mass was the most common presenting complaint in 36 patients (90%), followed by blocked nose (35%), headache (35%) and hearing loss at 20% of the cases *(Zrafi et al., 2017).*

158 NPC patients younger than 20 years old were studied in Beijing by Weixin et al. They found that neck mass (32.3%), headache (21.5%) and nasal obstruction (15.2%) were the most common chief complaints. 36 patients (22.8%) were observed to have cranial nerve palsies, the trigeminal nerve (V) and abducent nerve (VI) were the most commonly involved*(Liu et al., 2014).*

In a study done by Mondal et al, cheek swelling, nasal obstruction and discharge and were the common symptoms among all the patients. A nasal mass, upper jaw or maxillary swelling and were the commonest signs *(Mondal et al., 2009)*

2.4 Imaging of Nasopharyngeal Tumors

Clinical examination (including endoscopic examination) can provide valuable information about mucosal involvement and tumour extension into the nasal fossae and oropharynx, but deep extension, skull-base erosion, or intracranial spread cannot be assessed. In some instances, the differentiation of benign from malignant processes may be difficult. Imaging plays a crucial role in characterizing and assessing the extent of nasopharyngeal lesions. CT and MRI are useful tools for the assessment of tumor location, size, nature, extent, and invasion. They have revolutionized and improved the effectiveness of treatment for nasopharyngeal malignancies in coming to a correct staging of the lesion. Multidetector CT demonstrate the neck and cranium in unparalleled detail both in coronal and horizontal planes. Data reconstruction of sagittal and oblique projections can also be done with multiplanar reconstruction*(Manavis et al., 2005).*

In malignant diseases, imaging is useful in detecting metastatic spread and in following response to treatment. Additionally, imaging may be used to guide fine-needle aspiration (FNA) or needle biopsy*(Lloyd & McHugh, 2010)*

The evaluation of the potential extension into adjacent regions impacts therapeutic planning, particularly in cases with the involvement of the anterior and middle cranial fossa, pterygopalatine fossa and infratemporal fossa (masticator and parapharyngeal space). CT is particularly important in assessing the tumor growth pattern into adjacent

bone, tumor homogeneity, lesion margins, internal signal intensity and contrast enhancement pattern. It is also crucial in delineating calcification.

Intralesional calcifications have been observed in some malignancies such as adenocarcinoma. Bone invasion characteristic patterns help predict the tumor histology. High grade malignancies demonstrate extensive bony destruction, whereas low grade tumors show permeative invasion and lack of bony destruction. Low-grade malignancies and benign lesions may cause bony expansion due to their slow and expansile growth.

By defining soft tissue structures, CT makes it possible to see the relationship of tumor to mucosal surfaces and musculofascial planes. Orbital and sinus extension and alterations in bone density or attenuation are readily appreciated. Contrast enhancement demonstrates tumor vascularity, intracranial extension nodal involvement and vascular involvement *(Otol & Laryngol, 2015)*

Contrast-enhanced CT is indispensable for the identification of the feeding artery (because of its high spatial resolution) and for the diagnosis of hypervascular tumors

Aggressiveness of nasopharyngeal processes is determined by the presence or absence of intracranial spread. Intracranial spread from the nasopharynx occurs by four primary pathways, namely;

1. Posterior lateral spread via the foramen lacerum along the carotid artery to the cavernous sinus and middle cranial fossa
2. Posterior lateral metastasis to the highest jugular node to the jugular fossa and posterior cranial fossa
3. Spread laterally through the pterygoid venous plexus and directly through the floor of the middle cranial fossa

4. Anterior lateral spread into the infratemporal fossa through the sphenopalatine foramen. This passage is then continuous through the inferior orbital and superior orbital fissure to the middle cranial fossa*(Hoover, 2015).*

In regards to staging, CT imaging identifies paranasopharyngeal extension as one of the most common modes of extension of nasopharyngeal carcinomas and has shown perineural spread through the foramen ovale to be an important route of intracranial extension. Perineural spread through the foramen ovale also accounts for the CT evidence of cavernous sinus involvement without skull-base erosion *(Wei & Sham, 2005)*

For distant metastases, imaging using isotope bone scan and CT of the chest and upper abdomen are considered for node positive patients*(Chan et al., 2012)*

CT is also used for radiotherapy planning i.e. in three-dimensional (3D) radiotherapy planning because it provides the superior spatial accuracy and electron density information necessary for heterogeneity corrections in dose calculation *(Wang et al., 2009).*

In some centers, it is used together with PET CT using 18F-FDG. PET/CT has been shown to be of value in nasopharyngeal malignancy staging, where the main advantage is for the detection of distant metastasis. It is also used for monitoring patients after therapy and detecting recurrence (Y. P. Chen et al., 2019) It has proven to be the most specific, sensitive and accurate diagnostic method*(Chan et al., 2012)*

Using PET CT, tumour areas with considerable metabolic activity can be identified and the radiation dose can be modulated to deliver a higher daily dose to these areas compared to the remaining target areas, using conformal or Intensity Modulated

Radiotherapy (IMRT) techniques. This is based on CT scan simulation and computerized field definition.

This allows the delivery of high doses of radiation without damaging adjacent normal organs. The precision of imaging of the tumor and the adjacent anatomical structures with CT scan or MRI combined with the imaging of the tumor metabolic activity provide a crucial tool to identify viable residual disease demanding booster radiation doses or to recognize recurrent disease at an early stage of development, which is essential for the successful outcome of re-irradiation of nasopharyngeal cancers*(Manavis et al., 2005)*

CT is useful to detect early skull base erosion. The CT evident skull base erosion has been proved to be a remarkable independent prognostic factor for the regional control and distant metastasis in NPC *(Yi et al., 2016)*

In children, certain radiographic features of the primary tumor can be useful in differentiating NPC from other tumors. Contrary to other masses, the configuration of NPC is generally asymmetric. Local spread of the tumor outside the confines of the nasopharynx is dictated in large measure by the local anatomy. The pharyngobasilar fascia acts as a barrier to local spread of the tumor and tends to direct the advancing tumor towards the central skull base (clivus). Therefore, skull base invasion is frequently seen with locally advanced tumors. CT imaging depicts invasion of the skull base and widening of the petroclival fissure due to infiltration by tumor especially on CT bone windows. Extension to the pterygopalatine fossa causing widening is easily detected on CT *(Stambuk et al., 2005).*

In antrochoanal polyps (ACP), the Holman-Miller sign (also called antral sign), which is described as anterior bowing of the posterior wall of the maxillary antrum can be seen on CT imaging.

On CT or MRI, teratomas may demonstrate cystic areas together with solid areas with bone and tooth formation*(Duarte et al., 2013)*

On CT, adenocarcinomas appear as a soft-tissue mass and periodically exhibit areas of calcification, which reflect the mucin content. High-grade adenocarcinomas often show bone destruction while nasopharyngeal lymphomas typically show both infiltrative or permeative bony invasion and exhibit varying degrees of regional bony destruction.

Extramedullary plasmacytomas typically appear as well-defined, polypoid soft-tissue masses, which exhibit homogenous enhancement. Large tumors may show areas of necrosis, destruction of the adjacent bone, infiltration of the adjacent structures, and vascular encasement*(Kawaguchi et al., 2017)(K. S. Cho et al., 2012).*

On CT, RMSs appear as an isodense or slightly hypodense mass and show homogeneous enhancement on contrast-enhanced CT. Intratumoral calcification and hemorrhage hardly occur in RMS*(Mondal et al., 2009)(Abdel et al., 2012)*

Hilda et al did a retrospective study on 11 patients under the age of 18 years with untreated NPC. All the patients had a nasopharyngeal mass. Central skull base invasion was noted in 10 (91%). Patients. The petroclival fissure was widened in 8 (73%) patients; all except one patient had accompanying skull base invasion. Tumor extension into the adjacent parapharyngeal space was seen in 6 (55%), the pterygopalatine fossa in 2 (18%), and the masticator space in 2 (18%)*(Stambuk et al., 2005)*

A prospective analysis of 125 patients at ENT department of KNH identified 26.6% of patients had evidence of skull bone erosion while 13.8% had evidence of intracranial extension on CT scan *(Muchiri, 2008).*

A retrospective review of CT examinations of 70 patients with histologically proved lesions of the nasopharynx was done by L Hoover et al. He found that 81% of the malignant lesions demonstrated invasion of one or more of the paranasopharyngeal fascial planes. The percentage rose to 100% for all primary malignant neoplasms. Intracranial extension occurred in 53% of the primary malignant neoplasms and 14% of the secondary malignant neoplasms affecting the nasopharynx.

They also found that benign tumors showed a lower incidence, 30% of intracranial spread. Benign tumors such as Juvenile Angiofibromas, inflammatory conditions in the immunosuppressed such as Mucormycosis, aggressive Aspergillosis and Wegener's granulomatosis showed obliteration of the lateral low-density fascial planes, expanding in a rounded growth pattern leaving some low-density fatty margins at the periphery of the tumors.

Less aggressive diseases such as adenoiditis demonstrated no invasive appearance on CT examination. Clinically, these relatively benign inflammatory processes appear quite suspicious on visual examination. Therefore, CT scanning is of great help in such unsettling clinical situations to yield further information regarding spread to the paranasopharyngeal fascial planes. Furthermore, this can prevent the patients from having to undergo an invasive procedure*(Hoover,* 2015).

CHAPTER THREE: STUDY METHODOLOGY

3.1 Study site

This study was conducted at the Radiology directorate and histopathology lab of the Moi Teaching and Referral Hospital, Eldoret.

The hospital is a level 6B hospital located in Eldoret town, Uasin Gishu County which is 310 kilometers North West of Nairobi, the capital city of Kenya. The hospital is a teaching and referral hospital and serves as a teaching hospital for Moi University School of Medicine, Nursing, Public Health, Dentistry, Physiotherapy and Mental Health. Other institutions that use this hospital for teaching purposes include University of East Africa, Baraton School of Nursing and Kenya Medical Training Center (KMTC) Eldoret.

MTRH is also a training center for medical, clinical and nursing officer interns. It serves as the main referral hospital for the Western part of Kenya and North Rift region and has a catchment population of approximately 13 million people. The radiology directorate has the following units: CT centres, Magnetic Resonance Imaging, Ultrasound and Interventional Radiology, Digital General X-ray and the Digital mammography units. Apart from Radiology and imaging, the facility has several other directorates including Histopathology, Internal Medicine, Surgery, Pediatrics and Child Health, Obstetrics and Gynecology, Mental health, General Surgery and Anaesthesia, Orthopedic surgery, Radio-oncology and many other subspecialities.

3.2 Study design

The study was a hospital-based prospective cross-sectional study that was conducted for a period of 12 months. Recruitment was done at the CT scan room where patients presented for neck imaging. CT scan images and reports of patients with nasopharyngeal tumors was then matched with their histopathological diagnosis.

3.3 Study Population

The study population included all patients with nasopharyngeal tumors who were referred by a clinician for CT scan evaluation and histopathology after biopsy.

3.4 Study Period

This study was conducted for a period of 12 months between month of September 2021 and August 2022

3.5 Eligibility Criteria

Those eligible to take part in the study fulfilled the following eligibility criteria.

3.5.1 Inclusion criteria

All patients presenting at MTRH CT units for neck CT examination with clinically suspected nasopharyngeal tumor and consented for the study

3.5.2 Exclusion Criteria

Patients with known diagnosis of nasopharyngeal tumor and are on treatment and follow up.

3.6 Sampling Techniques

3.6.1 Sample size determination -The main aim of the study was to compare CT scan and histopathological findings of nasopharyngeal lesions, using histopathological findings as the gold standard. According to the Cancer Registry at MTRH, the number of patients diagnosed with nasopharyngeal neoplasms in 2017,2018 and 2019 was 67, 103 and 98 cases respectively. A census study was done based on the small numbers. Every patient with a CT scan diagnosis of nasopharyngeal tumor and requires confirmatory histopathological diagnosis for the tumor was recruited into the study.

3.6.2 Sampling procedure - Because of the small numbers, consecutive sampling was used to recruit patients to this study. Patients who met the inclusion criteria were recruited into the study.

3.6.3 Study Procedure- The staff and technicians at the CT scan centres were sensitized about the study and trained on data collection. Patients with suspected nasopharyngeal tumour underwent neck CT scan at the CT Centre in Radiology and Imaging Department of MTRH. Biopsy was then done via RNE or image guided biopsy (for those inaccessible by RNE) at the ENT and Interventional Radiology Department and the biopsy samples were taken to the histopathology lab for a confirmatory diagnosis.

3.6.3.1 Neck CT Scan protocol for MTRH Radiology and Imaging Department

After patient preparation and signage of consent, CT scan images were acquired with a helical technique from the three CT centres at MTRH. The Neusoft 128 slice machine, the 64 slice Phillips machine and the 32 slice Siemens machine operated by 2 qualified radiographers. Scanograms of the skull base, nasopharynx, and neck were then acquired.

During CT scan, patients were immobilized in head-first, supine position with a thermoplastic face mask. Scanning was taken in craniocaudal direction from the external auditory meatus to aortic arch. The imaging parameters were: 120 kVp, 250-300 mAs, slice thickness of 2.5mm and 70cc of IV contrast (Omnipaque) was used for adults at a rate of 2cc per second. For children, a slice thickness of 3mm was used with Low Molecular Weight, LMW IV Omnipaque at 1cc per kg of body weight with a maximum of 100cc and at a rate of 2cc per second.

Multiplanar reconstructions was performed in all cases using a bone window and soft tissue window. The CT images generated were interpreted by the primary investigator and then verified by two independent consultant radiologists.

3.6.3.2 Biopsy Technique and Percutaneous needle biopsy protocol at MTRH

During EUA, RNE of the nasopharyngeal tumors was done, and Image guided Interventional radiology (IR) biopsies of those tumors inaccessible via RNE was also done. The biopsy procedure was explained to the patient the benefits, risks, possible complications that may arise and informed consent was sought to carry out the procedure. As part of assessment, the patient underwent ultrasound guidance to confirm the location of the mass, the access technique to be used, the equipment and medications needed and the laboratory work ups required prior to the biopsy.

The pre-procedural lab works for image-guided biopsy required were FHG, UECs, coagulation profile, COVID Test and Triple Serology. The appropriate biopsy gun and coaxial needles and premedications analgesics e.g., Morphine, local anaesthetic agent e.g., Lignocaine (for procedure use), formalin for biopsy tissue preservation and oral antibiotics and analgesics for post-procedure infection prophylaxis.

The skin of the area to be biopsied was washed with antiseptic and draped. A fine needle was used to give local anesthetic to numb the area for biopsy. Under ultrasound guidance, the coaxial needle was gently inserted into the node and the semi-automatic biopsy gun was used to obtain adequate samples. After the samples were taken, preservation in formalin solution in a clearly labelled container was done and accompanied with a well written request form to be taken to the histopathology lab. Ultrasound was then done to check for any immediate complications; bleeding, hematoma. The biopsy area was pressed for a few minutes and then dressed. The patient was then put in the observation room for two hours to monitor any other complications.

3.7 Histopathology for nasopharyngeal tumor biopsy

The biopsy samples from the Interventional Radiology and ENT Departments were preserved in a formalin solution in a clearly labelled container and a well elaborated laboratory request form. The samples were then handled by two qualified pathologists who prepared the specimens and viewed them under the microscope. I and the respective pathologists concluded on the findings and if they were in keeping with the possible CT diagnosis. Those biopsy specimens that brought about inconclusive results were taken for further studies such as immunohistochemistry to confirm the final diagnosis.

3.8 Enrollment flow chart

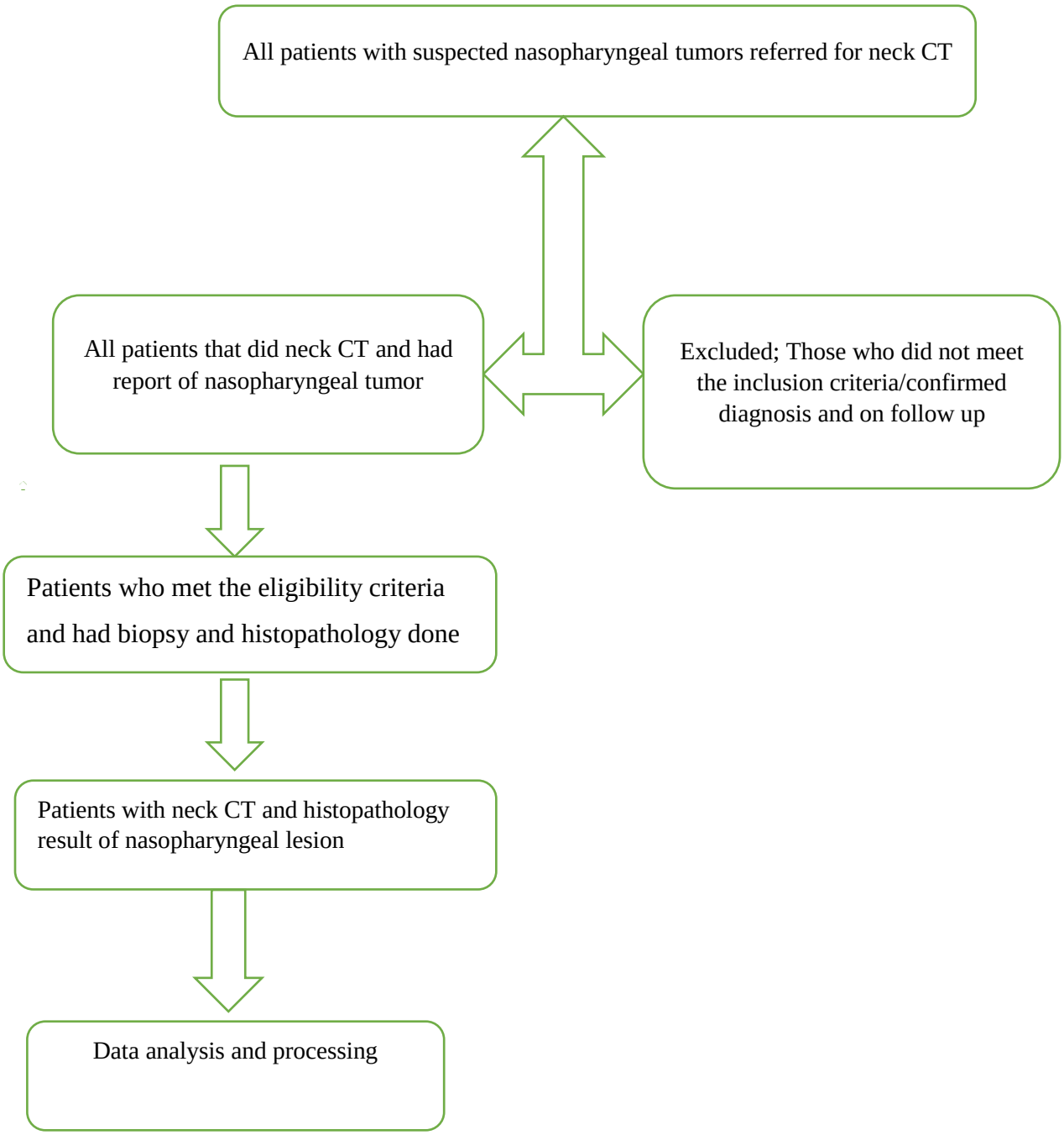


Figure 8: Enrollment flow chart

3.9 Data Collection

Data was collected using a data collection tool in form of a questionnaire. All consenting patients were awarded special numbers. A data sheet was used for data collection. The Principal Investigator was the main data collector. Comprehensive data including patient's age, gender, nasopharyngeal tumor type and CT scan findings were obtained. Imaging findings were recorded after detailed review by both radiologists. The histopathological findings from the biopsies were also recorded after obtaining results from a qualified pathologist at the histopathology laboratory. Information gathered was then entered into a computer database.

3.10 Data Analysis and interpretation

Data was imported into STATA version 16 where coding, cleaning and analysis was done. Descriptive statistics such as mean and corresponding standard deviation, the median and the corresponding interquartile range was used to summarize the continuous data such as age. Frequencies and corresponding percentages were used to summarize categorical data such as sex of patients. A p-value of <0.05 was considered statistically significant. The data was then presented in form of charts, tables, graphs and prose form.

Objective 1: To describe the CT scan findings frequencies and percentages was used.

Objective 2: To describe the histopathological findings frequencies and percentages was used.

Objective 3: To compare the radiologic features with histopathological findings. Measures of level of agreement like Kappa coefficient and McNemar tests were used to compare tumor grading based on radiologic and histologic findings.

3.11 Data Quality and Security

Data was double entered into a computer to ensure accuracy. The entry screen included check codes to minimize errors. The computers were password protected and access was allowed only for authorized persons. Databases obtained were stored electronically; copies of filled questionnaires were stored in a locked shelf located in the principal investigators office. Backups for the database were created in remote disks and flash drives and kept in different safe locations to guard against loss of information.

3.12 Ethical Considerations

Prior to the commencement of the study, ethical approval and permission was sought from Moi University Institutional Research Ethics Committee (IREC) and Permission was obtained from the MTRH administration. A consent form explaining the rationale and benefits of the study to the public health system (appendix 2) was used to seek informed consent from potential study participants. Informed consent to participate in the study was obtained from all conscious adult patients and guardians. All patients or guardians were informed about the study and the procedures involved in the study and the possible benefits and harm. Consent will be sought from the parents/guardians of the children and assent from children above 7 years.

Participation in the study was on a voluntary basis and respect for autonomy was considered by giving all the necessary information as well as freedom to withdraw from the study at any point, without any need for justification. There were no incentives for participating. The interviews were conducted in a confidential manner; participant names were not be recorded. No study participant was identified by name in any report or

publication derived from information collected for the study. Data collected was stored in lockable cabinets, databases created was password protected to avoid unauthorized access**.**

CHAPTER FOUR: RESULTS

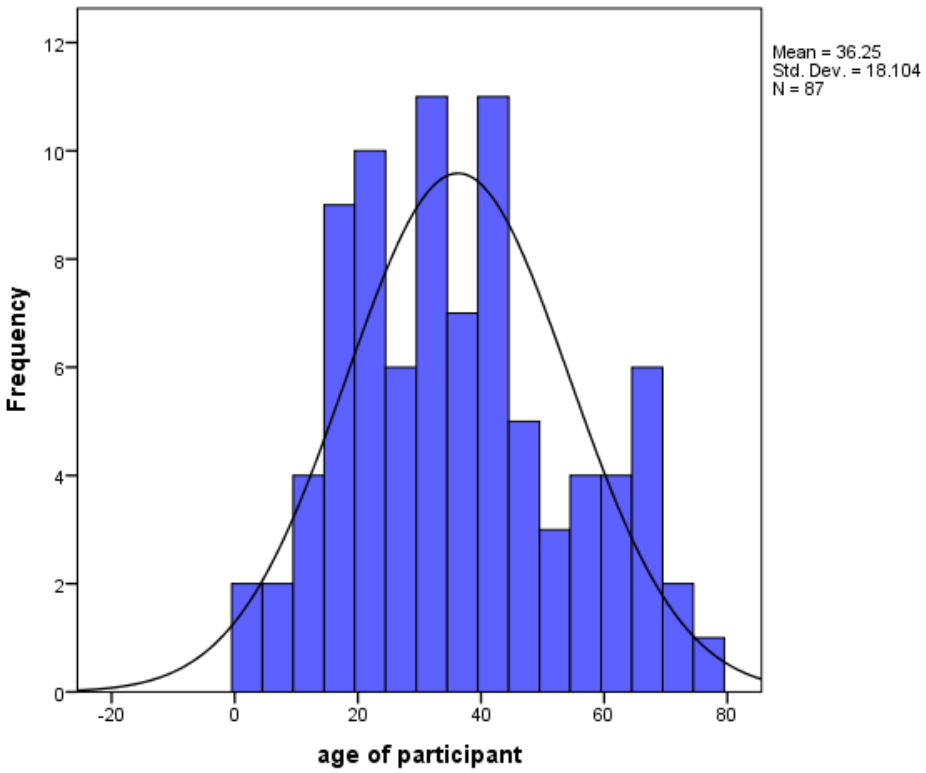


Figure 9: Participant's age

The Mean age of the participants was 36.3 years (SD=18.1). The youngest was 2 years while the eldest participant was 77 years old. **(Figure 9).**

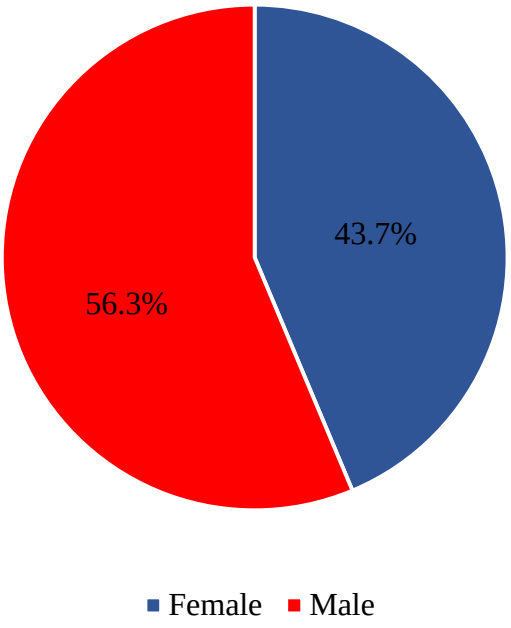


Figure 10: Participants' gender

More than half of the 87 participants, 49 (56.3%) of the participants were males while 38 (43.7%) were female. **(Figure 10)**

4.1 Clinical Features

Of the 87 participants, 77 (88.5%) had neck swellings of which 63 (81.8%) were painless while the rest were painful. Most, 58 (75.3%) were unilateral while 19 (24.7%) were bilateral. More than half, 50 (64.9%) were solitary while 27 (53.1%) had multiple neck swellings. Most (61; 70.1%) participants had nasal blockage of which 36 (59.0%) were unilateral while 24 (49.0%) were bilateral. A total of 39 (44.8%) had nasal discharge, 25 (64.1%) Unilateral and 14 (35.9%) bilateral.

Epistaxis was reported in 15 (17.2%), being posterior in 12 and anterior in 3 participants. A total of 51 (58.6%) had ear pain, 40 (78.4%) unilateral and 11 (21.6%) bilateral Only 15 (17.2%) had ear discharge, 13 unilateral and 2 bilateral. A total of 17 (19.5%) had hearing loss, 16 unilateral and 1 bilateral. Among the participants, 49 (56.3%) had headache, 71 (81.6%) neck pain, 18 (20.7%) cranial nerve palsy, and 67 (77.0%) fever of unknown origin**. (Table 2).**

Table 2: Patients' clinical presentations

Clinical Feature	Frequency (n)	Percent (%)
Neck swelling		
Present	77	88.5
Absent	10	11.5
Neck pain (n=77)		
Painless	63	81.8
Painful	14	18.2
Side of the neck swelling		
Unilateral	58	75.3
Bilateral	19	24.7
Number of swellings (n=77)		
Solitary neck swelling	50	64.9
Multiple neck swelling	27	35.1
Presence of nasal blockage		
Present	61	70.1
Absent	26	29.9
Side of the nasal blockage (n=61)		

Unilateral	36	59.0
Bilateral	25	41.0
Presence of nasal discharge		
Present	39	44.8
Absent	48	55.2
Side of nasal discharge (n=39)		
Unilateral	25	64.1
Bilateral	14	35.9
Epistaxis		
Yes	15	17.2
No	72	82.8
Location of epistaxis (n=15)		
Anterior	3	20.0
Posterior	12	80.0
Ear pain		
Present	51	58.6
Absent	36	41.1
Side of the ear pain (n=51)		
Unilateral	40	78.4
Bilateral	11	21.6
Ear discharge		
Present	15	17.2
Absent	72	82.8
Side of ear discharge (n=15)		
Unilateral	13	86.7
Bilateral	2	13.3
Hearing loss		
Present	17	19.5
Absent	70	80.5
Side of hearing loss (n=17)		
Unilateral	16	94.1
Bilateral	1	5.9
Presence of headache		
Yes	49	56.3
No	38	43.7
Presence of neck pain		
Yes	71	81.6
No	16	18.4
Cranial nerve palsy		
Yes	18	20.7
No	69	79.3
Fever of unknown origin		
Yes	67	77.0
No	20	23.0

Other clinical features included aerodigestive symptoms (28;32.2%) including Obstructive sleep apnoea symptoms, airway obstruction, dysphagia, on and off cough and Odynophagia and drooling; eye symptoms (5; 5.7%) including right orbital swelling, bulging of the left eye, large swelling and pain on the right eye, loss of vision of the right eye and loss of vision of the right eye; night sweats (5;5.7%) **(Table 3).**

Table 3: Other clinical symptoms

Other clinical symptoms (n=47)	**Frequency (n)**	**Percent (%)**
Aerodigestive symptom	28	32.2
Eye symptoms	5	5.7
Excessive sweating	1	1.1
Left cheek swelling	1	1.1
Left facial swelling	1	1.1
Mouth swelling	1	1.1
Pain around the right submandibular region	1	1.1
Weight loss	2	2.3
Night sweats	5	5.7
Right cheek mass	1	1.1
Upper back pain	1	1.1

4.2 Radiological Findings

All the 87 participants had lesions in the nasopharynx. Most, 65 (74.7%) had primary involvement while 22 (25.3%) had secondary involvement. Most, 40 (46.2%) of the primary lesions were <3cm in size, 35 (40.2%) were 3-5cm while 12 (13.8%) were greater than 5 cm. **(Table 4).**

Table 4: Radiological findings

Radiological findings	Frequency (n)	Percent (%)
Location of lesion		
Lesion in nasopharynx	87	100
Involvement		
Primary involvement	65	74.7
Secondary involvement	22	25.3
Primary lesion size		
<3cm	40	46.0
>5cm	12	13.8
3-5cm	35	40.2
Secondary lesion size		
<3cm	10	11.5
>5cm	6	6.9
3-5cm	7	8.0
None	64	73.6
Lesion classification		
Solitary lesion	76	87.3
Multiple lesions	11	12.6
Unilateral lesion	68	78.2
Bilateral lesions	19	21.84
Diffuse (Bilateral tumor with local invasion)	58	66.7
Lesions crossing the midline	52	59.8
Contours		
Lobulated contour	3	3.4
Multilobulated contours	4	4.6
Infiltrative contours	80	92.0
Margins		
Distinct tumour margins	31	35.6
Indistinct tumour margins	56	64.4
Appearance		
Cystic lesion	1	1.1
Solid lesion	49	56.3
Mixed lesion	37	42.5
Calcified lesion	0	
Mucosal thickening		
No	84	96.6
Yes	3	3.4

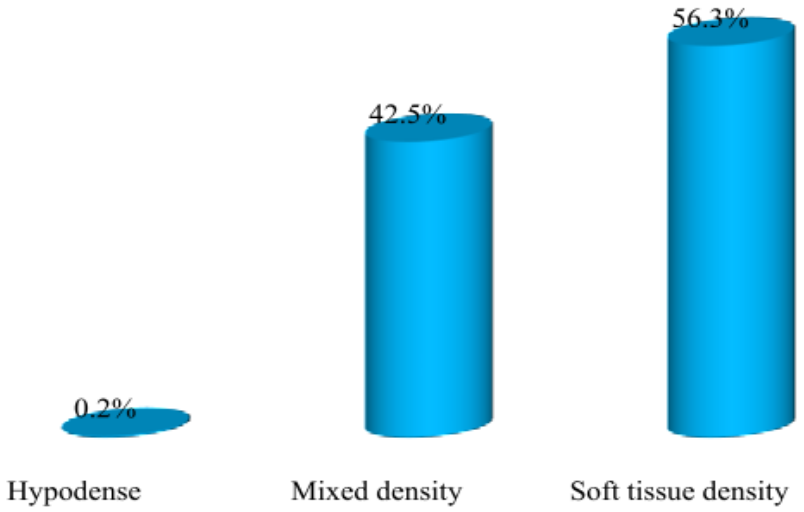


Figure 11: Density of lesion

On density of lesion to muscle without contrast, 49 (56.3%) had soft tissue density, 37 (42.5%) mixed density while 1 (0.2%) were hypodense. **(Figure 11).**

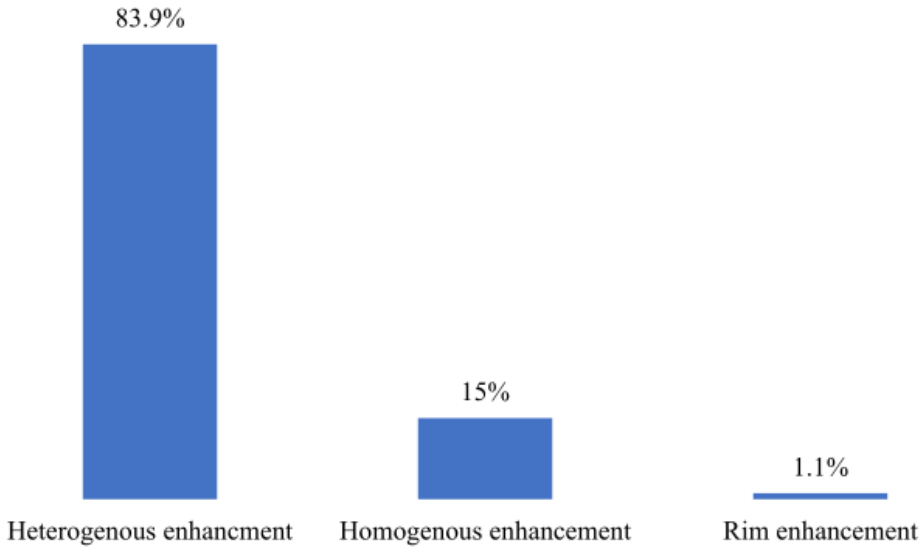


Figure 12: Enhancement

Most, 73 (83.9%) had heterogenous enhancement, 13 (15%) homogenous enhancement while 1 (1.1%) had rim enhancment. **(Figure 12).**

4.3Neck Space Involvement

Most, 52 (59.8%) had ipsilateral neck space involvement while 32 (36.7%) had bilateral neck space involvement. Parapharyngeal space was the most commonly affected 64 (73.6%) **(Table 5)**

Table 5: Neck space involvement

Neck space involvement	Frequency (n)	Percent (%)
Bilateral involvement	32	36.7
Unilateral involvement	52	59.8
None (localized to the nasopharynx)	3	3.4

4.4 Nodal Involvement

Table 6: Nodal Involvement

Nodal involvement	Frequency (n)	Percent (%)
Yes	83	95.4
No	4	4.6

Most of the lesions (83; 95.4%) had nodal involvement with 80 (92%) of bilateral multilevel pattern (more than 2 levels). Levels II and III were the most commonly affected

Table 7: Patterns of nodal involvement

Bilateral Multilevel	**80**	**92.0**
Bilateral single level	4	4.5
Unilateral	3	3.4

4.5 Intracranial Spread

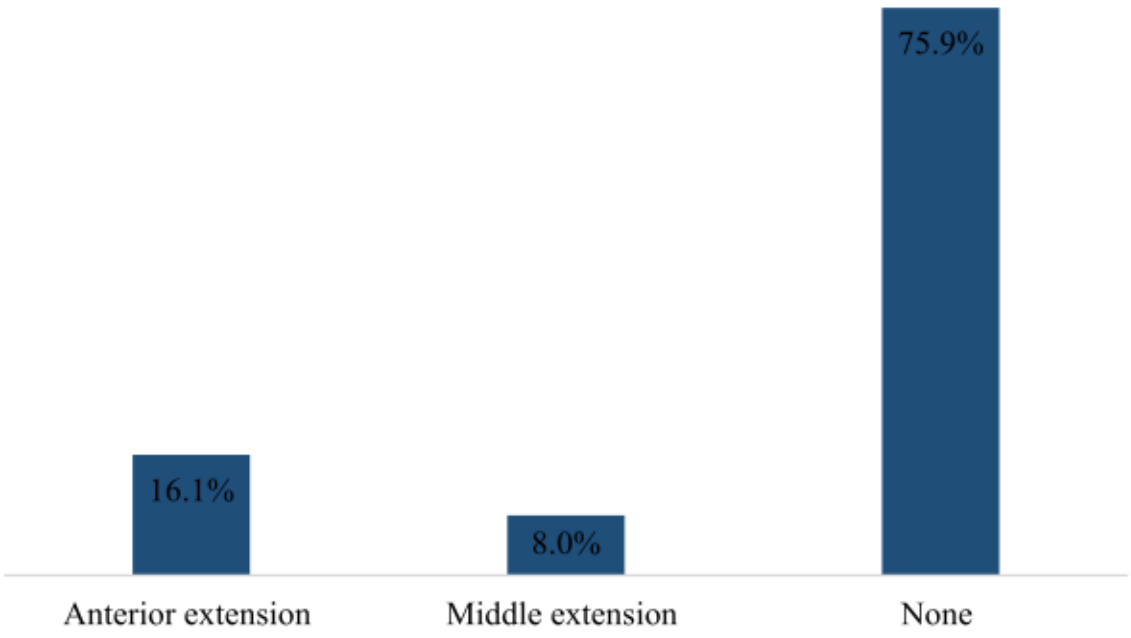


Figure 13: Intracranial spread

A total of 14 (16.1%) had anterior cranial fossa extension intracranial spread while 7 (8.0%) had middle cranial fossa extension**. (Figure 13).**

4.6 Osseous involvement

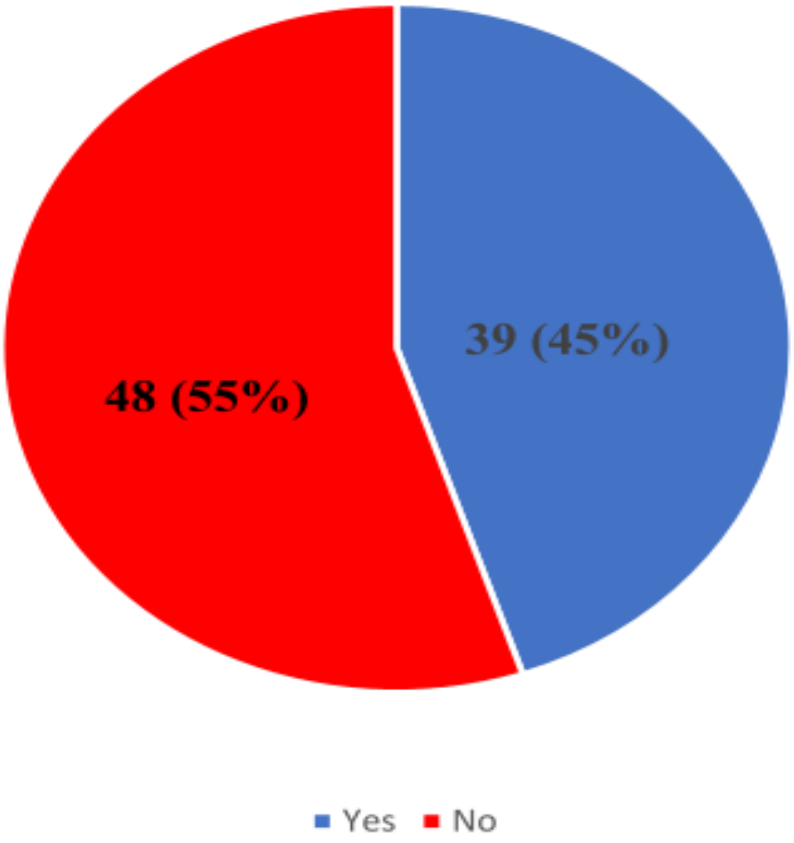


Figure 14: Osseous involvement

There was osseous involvement in 39 (44.8%) of the cases. **(Figure 14).** The bones involved included sphenoid bone, vertebral, maxillary, ethmoid, nasal and facial bones.

4.7: Other radiological features

Most of the lesions 68 (78.2%) demonstrated eustachian tube involvement, 60 (69.0%) had features of otitis media. There was Oto-mastoiditis in 36 (41.4%) of which 31 were unilateral and 5 bilateral (**Table 8).**

Table 8: Other radiological features

Other radiological features	**Frequency (n)**	**Percent (%)**
Mass effect	68	78.2
Eustachian tube involvement	68	78.2
Features of otitis media	60	69.0
Feature of mastoiditis (n=60)		
Bilateral mastoiditis	2	3.3
None	56	93.3
Unilateral mastoiditis	2	3.3
Oto-mastoiditis	36	41.4
Features of oto-mastoiditis (n=36)		
Bilateral oto-mastoiditis	5	13.9
Unilateral oto-mastoiditis	31	86.1

4.8 CT diagnosis

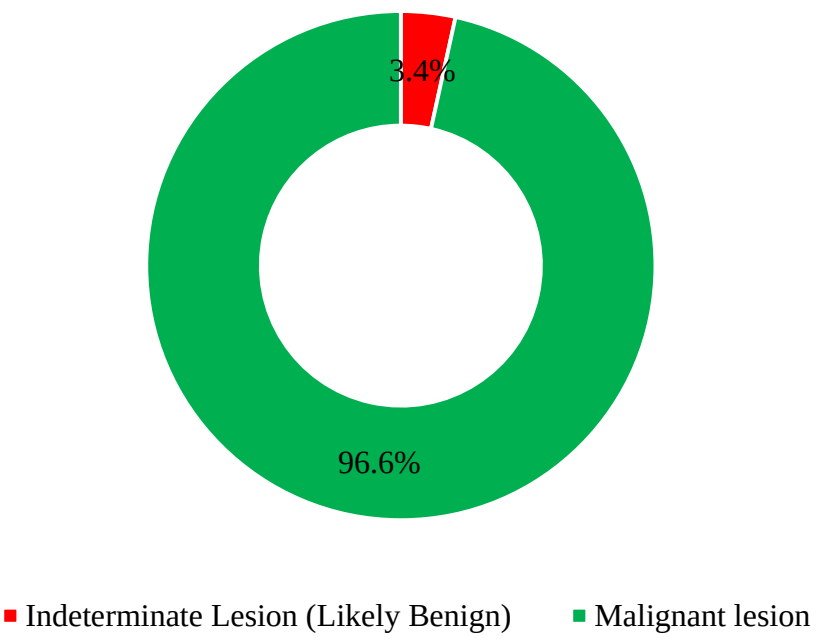


Figure 15: CT diagnosis

On CT diagnosis, 84 (96.6%) were malignant lesions while 3 (3.4%) were indeterminate lesions, likely benign**. (Figure 15).**

4.9 Histopathology findings

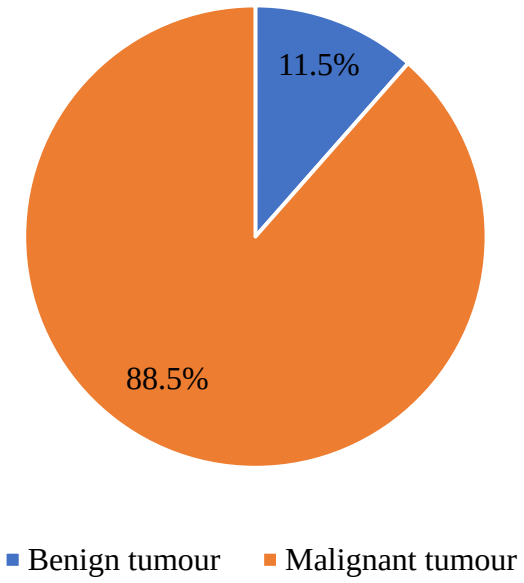


Figure 16: Histopathology findings

On histopathology, 77 (88.5%) of the lesion were malignant while 10 (11.5%) were benign. **(Figure 16).**

4.9.1 Final histopathological diagnosis

On histopathology diagnosis, 66 (76.7%) patients had squamous cell carcinoma, 7 (8.1%) lymphomas and 4 (4.7%) had rhabdomyosarcoma. Among the 66 with squamous cell carcinoma, 46 (69.7%) were anaplastic, 15 (22.7%) moderately differentiated, 4 (6.1%) poorly differentiated and 1 (1.5%) was well differentiated. Of the 7 with lymphomas, 4 (57.1%) were Hodgkin lymphoma while 3 (42.9%) were non- Hodgkin lymphoma.

Benign lesions were 10 (10.5%) with infective lesions e.g TB being the most common, 5 (50.0%), Inflammatory lesions 3 (30%), squamous papilloma 1 (10%) and Atypical angiofibroma 1 (10%)

Table 9: Histopathological diagnosis

Histopathological diagnosis (N=87)	**Frequency (n)**	**Percent (%)**
Squamous cell carcinoma	66	76.7
Lymphomas	7	8.1
Rhabdomyosarcoma	4	4.7
Squamous cell carcinoma grouping (N=66)		
Well differentiated	1	1.5
Moderately differentiated	15	22.7
Poorly differentiated	4	6.1
Anaplastic	46	69.7
Types of lymphoma (N=7)		
Hodgkin lymphoma	4	57.1
Non- Hodgkin lymphoma	3	42.9
Benign lesions (N=10)		
Infectious lesions	5	50
Inflammatory lesions	3	30
Squamous papilloma	1	10
Atypical angiofibroma	1	10

4.9.2 Comparison of the radiological features seen on CT scan with histopathologic findings among patients with nasopharyngeal tumors at MTRH

An exact McNemar's test determined that there was a no statistically significant difference in the proportion of those with malignant lesion between the gold standard histopathology test and CT diagnosis, p = 0.065. **(Table 10).**

Cohen's κ was run to determine if there was agreement between histopathology and CT findings. There was low agreement between the histopathology and CT findings, which was not statistically significant, κ = .1.6, p =0.227. **(Table 10).**

Table 10: Comparison of the radiological features seen on CT scan with histopathologic diagnosis

	Histopathology findings		**McNemar's Test P-Value**	**Kappa value (κ)**	**Kappa P value**
CT FINDINGS	**Malignant**	**Benign**			
Malignant	75 (97.4%)	9 (90.0%)	0.065	0.106	0.227
Benign	2 (2.6%)	1 (10.0%)			
Total	77	10			

Using histopathology as gold standard, CT had a sensitivity of 97.4% specificity of 10%, positive predictive value of 89.3% and negative predictive value of 33.3% in the diagnosis of nasopharyngeal tumours.

Sensitivity=number of true positives/(number of true positives + number of false negatives

75/ (75+2)=75/77= 97.4%

Specificity=number of true negatives/(number of true negatives+ number of false positives)

1/(1+9)= 1/10= 10.0%

Positive predictive value= Positive/(true and false positive)

75/ (75+9) =75/84= 89.3%

Among those who had a malignant tumor on CT screening, the probability of having a malignant tumor was 89.3%

Negative predictive value= 1/(1+2) = 1/3= 33.3%

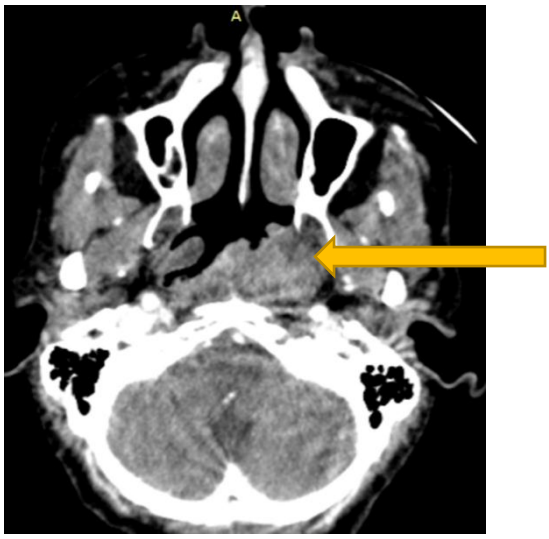
Among those who had a benign tumour on CT screening, the probability of having benign tumor was 33.3%

Table 11: The distribution of cases according to osseous involvement, intracranial spread and contrast enhancement pattern in relation to the histological type

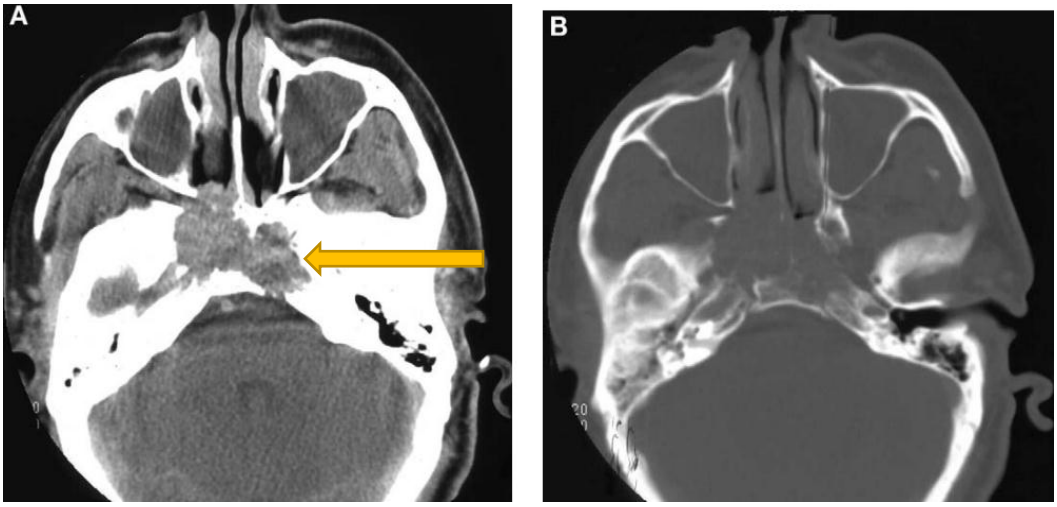
	Final histological diagnosis				Total	
	Anaplastic SCC	Moderately differentiated SCC	Poorly differentiated SCC	Well, differentiated SCC		**Likelihood ratio P value**
Osseous involvement						
Yes	**29 (85.3%)**	4 (11.8%)	2 (2.9%)	0 (0.0%)	34 (100%)	0.023
No	16 (51.6%)	11 (35.5%)	3 (9.7%)	1(3.2%)	31 (100%)	
Total	45 (69.2%)	15 (23.1%)	5 (6.2%)	1 (1.5%)	66 (100%)	
Intracranial spread						
Yes	**15 (78.9%)**	3 (15.8%)	2 (5.3%)	0 (0.0%)	20 (100%)	0.629
No	30 (65.2%)	12(26.1%)	3 (6.5%)	1 (2.2%)	46 (100%)	
Enhancement pattern						
Heterogenous enhancement	**38 (67.9%)**	13 (23.2%)	5 (7.1%)	1 (1.8%)	57 (100%)	0.659
Homogenous enhancement	7 (77.8%)	2 (22.2%)	0 (0.0%)	0 (0.0%)	9 (100%)	

Squamous cell carcinoma was the most common histopathological type, 66 (76.7%) with anaplastic subtype being the commonest, 46 (69.7%). On the distribution of cases according to histopathological sub-type, anaplastic SCC had the highest likelihood for osseous involvement and intracranial spread and heterogenous enhancement pattern as tabulated on Table 11.

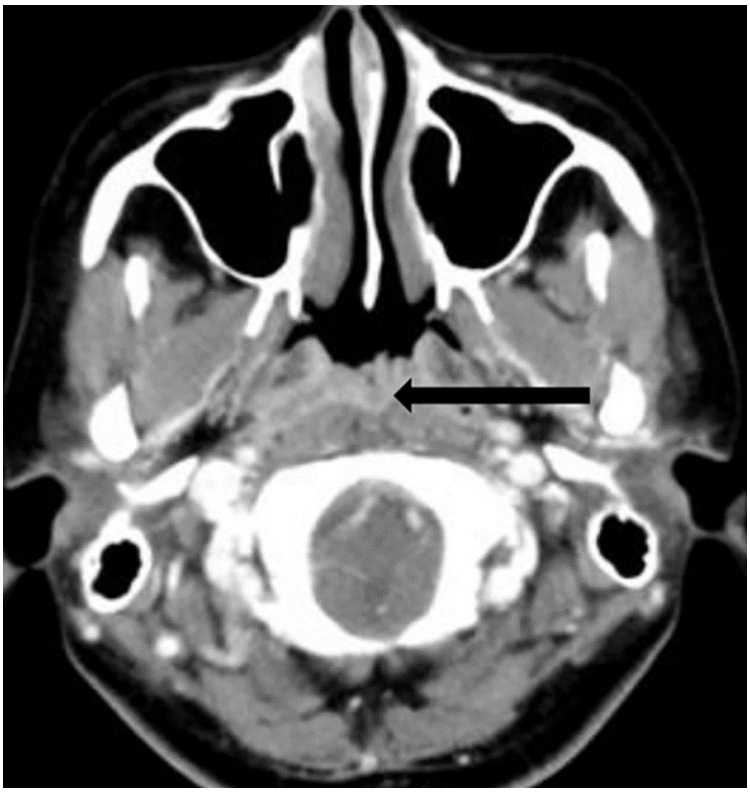
4.9.3 SAMPLE IMAGES



Sample 1- Axial neck CT image of a 60-year-old female showing a left nasopharyngeal mass obliterating the ipsilateral Eustachian tube and crossing the midline. Size was <3cm. Final diagnosis of NPC- Anaplastic subtype



Sample 2- (A) Axial contrast CT, soft tissue window, reveals a soft tissue mass in the central nasopharynx
(B) Axial bone window CT, demonstrates a large area of bone destruction involving the clivus and left petrous apex.



Sample 3- A heterogeneously enhancing soft tissue mass in the nasopharynx, obliterating the bilateral fossa of Rosenmüller and extending inferiorly to the upper part of the oropharynx**.** Final diagnosis of nasopharyngeal tuberculosis was made.

CHAPTER FIVE: DISCUSSION

5.1 Summary of findings

The Mean age of the patients with nasopharyngeal tumors was 36.3 years (SD=18.1). More than half (56.3%) were males. Among the patients, 77 (88.5%) had neck swellings, 61 (70.1%) had nasal blockage, 51 (58.6%) had ear pain, 15 (17.2%) had ear discharge, 17 (19.5%) had hearing loss, 49 (56.3%) had headache, 71 (81.6%) neck pain, 18 (20.7%) cranial nerve palsy, and 67 (77.0%) fever of unknown origin.

Most of the lesions, 65 (74.7%) had primary involvement while 22 (25.3%) had secondary involvement. Most, 40 (46.2%) of the primary lesions were <3cm in size, 35 (40.2%) were 3-5cm while 12 (13.8%) were greater than 5 cm.

On CT diagnosis, 84 (96.6%) were malignant lesions while 3 (3.4%) were indeterminate lesions, likely benign. On histopathology, 77 (88.5%) of the lesion were malignant while 10 (11.5%) were benign. Most, 66 (76.7%) patients had squamous cell carcinoma, 9 (10.5%) had benign lesions, 7 (8.1%) lymphomas and 4 (4.7%) had rhabdomyosarcoma. CT had a sensitivity of 97.4%, but a lower specificity of 10.0%. An exact McNemar's test determined that there was a no statistically significant difference in the proportion of those with malignant lesion between the gold standard histopathology test and CT diagnosis, $p = 0.065$.

5.2 Demographic information

Most of the patients with Nasopharyngeal tumours were young adults with a mean age of 36 years indicating that these tumours are more prevalent in young adult population locally. A nearly similar mean age was found in the study in Ethiopia among patients with NPC where the mean age of the patients was 37.3 ±16.2 years (Amal et al., 2020). This is way younger than the mean age of 53.85 years among patients with NPC in Saudi Arabia *(Alsafadi et al., 2020).* However, this was not different from a previous Kenyan study among NPC patients where majority of the patients were found to have age of between 31-40 years *(Muchiri, 2008).*

More than half (56%) of the patients with nasopharyngeal tumours were males demonstrating its high prevalence in this gender compared to females. As was the case in this study, NPC has been found to be more predominance among males) *(Stevens et al., 2008),* even in Kenyan studies as was the case in a study done at KNH where male to female ratio of NPC patients was 2.3:1*(Muchiri, 2008).*

Similarly, a study on imaging patterns of Nasopharyngeal carcinoma in Ethiopia found male-to-female ratio of 2:1 *(Amal et al., 2020).* This is an indicator that Nasopharyngeal tumours are more likely among males than females.

5.3 Clinical features

Most patients had multiple clinical presentations at the time of diagnosis. Among patients with nasopharyngeal tumours, symptoms of the neck, nose, ear, eyes, and throat are common. Nasal obstruction symptoms such as nasal discharge, congestion and bleeding and hearing changes linked to the blockage of the eustachian tube are also likely *(Paulino 2021).*

Neck swelling was a common presentation in the patients with nasopharyngeal tumors in this study (88.5%). Concurrence to this study findings, neck swelling has been found to be the common presentation, especially among patient's with NPC, which is the main type of nasopharyngeal tumours. This was the case in a study in Ethiopia with 81.3% of the NPC patients having neck swellings *(Amal et al., 2020)* and in another study in Malaysia where 80.8% of the NPC patients had neck swelling symptoms *(Tiong et al., 2005).*

Similarly, a previous study among young Chinese patients 9-20 years with nasopharyngeal cancer found 63% to have neck swelling *(Sham et al., 1990).* As was the case in this study where majority (75%) of the neck swellings were unilateral, the study in a referral facility in Addis Ababa Ethiopia found majority of such swelling in the NPC patients to be unilateral, occurring in 57.5% of the 80 patients evaluated *(Amal et al., 2020).*

Besides, nasal obstruction was also common, occurring in 70.1% of the patients. This was similar to experiences from previous studies with one study having found nasal obstruction and discharge in 78% of the young patients with nasopharyngeal cancer

(Sham et al., 1990). However, in the study in Addis Ababa Ethiopia, only 40% of the NCP patients had nasal obstruction *(Amal et al., 2020).*

While headache was also a common symptom in 56.3% of the cases, this proportion was less than 61% among Chinese young nasopharyngeal cancer patients *(Sham et al., 2015).* However, in the Ethiopian study, headache was only reported in 23.8% of the NPC patients (*Amal et al., 2020).*

Similarly higher proportion of the patients in the Chinese study (73%) had ear symptoms *(Sham et al., 1990).* Unlike in this study where only 58.6% had ear pain. Hearing complaints were less common (18.8%) among NPC patients in a facility in Addis Ababa Ethiopia *(Amal et al., 2020).*

As was the case in this study where only a small proportion (20.7%) had cranial nerve involvement, in the study in a referral facility in Addis Ababa Ethiopia, only 5% *(Amal et al., 2020).*

Generally, there was variation in the prevalence of the symptoms from one study and setting to another. This might be due to the differences in the condition epidemiology from one setting to another. Besides, a small proportion of our participants had non-malignant tumors unlike the other studies which mainly included those with malignant nasopharyngeal tumors and this might be the reason for the observed slight variation.

5.4 OBJECTIVE 1: To describe the CT scan findings of nasopharyngeal tumors among patients at MTRH

From this study, of the 87 participants, 84 (96.6%) had malignant lesions while 3 (3.4%) had benign lesions on CT. This compares with a study done by Hoover et al in the US who found 97.4% patients with malignant tumors and 2.6% with benign*(Hoover, 2015)*

This study contrasted with Garg et al who found 94.6% non-neoplastic lesions and 5.4% neoplastic lesions *(Garg & Mathur, 2014)*

From this study, 83.9% had heterogenous enhancement, 14.9% had homogenous enhancement while 1.1% had rim enhancment. In agreement to this study Nour et al in Addis Ababa found 60% with heterogenous enhancement pattern *(Nour Amal, 2020).*

In this study, 56.3% of the lesions were of soft tissue density, followed by 42.5% were of mixed density and 0.2% were hypodense. This is in contrast with Alcianu et al who found all his studied nasopharyngeal tumors were heterogenous (mixed density) *(Ălcianu, 2019)* This is because Alcianu focused only on squamous cell carcinoma of the nasopharynx.

From this study, asymmetric mucosal thickening was found in n=3 (3.4%) of the patients. Compares with King et al who found mild mucosal thickening in 7% of his patients *(King et al., 2003)*

From this study, neck space involvement was seen in 97.7% and the parapharyngeal space was the most commonly affected. 60.9% had ipsilateral neck space involvement while 36.8% had bilateral neck space involvement, 2 (2.3%) were localized to the nasopharynx.

Compares with S. Raissouni et al in Morocco who found 46% had parapharyngeal neck space involvement *(Raissouni et al., 2013)*

Multilevel nodal involvement was seen in n=79 (95.2%) of the lesions in this study. This agrees with Stambuk et al who found 94% of her participants had multilevel cervical lymphadenopathy*(Stambuk et al., 2005)*. Muchiri in KNH also found 80% of the patients had cervical node involvement *(Muchiri, 2008)*

This also compares with Rudresha et al who found 90% had nodal metastasis with only 27.9% having unilateral nodal disease *(Haleshappa et al., 2017)*

This study contrasted with that of Yabuuchi et al in Japan who found 77% with lymphadenopathy *(Yabuuchi et al., 2002).* In his study he got a lower value because of a small sample size (n=13)

In a Moroccan study by Raissouni et al, 79% of the subjects presented with cervical lymphadenopathy *(Raissouni et al., 2013)*. This contrasted with this study because he focused only on nasopharyngeal carcinoma as a subset of malignant tumors.

This study also contrasts with Guo et al who found only 45% presented with cervical metastasis. This is because he focused on nasopharyngeal adenocarcinoma as a subset of malignant tumors*(Guo et al., 2009).*

In this study, osseous involvement was seen in 44.8% of the cases. Central skull base invasion was most commonly seen. This agrees with Ho et al who found osseous involvement in 30.3% *(Ho et al., 2008)* and Roh et al who found central skull invasion in 38.6% of 119 patients *(Roh et al., 2004).*

This is in contrast with Stambuk et al who found (91%) had central skull base invasion *(Stambuk et al., 2005)* This is because the study had a small sample size (n=11), and only focused on pediatric patients and NPC as a subset of malignant tumors.

In this study, anterior cranial fossa extension was found in 16.1% while 8.0% had middle cranial fossa extension. This is in agreement with Muchiri in KNH who found 13.8% had intracranial involvement *(Muchiri, 2008)*

S. Raissouni et al in Morocco also found 20% with intracranial involvement*(Raissouni et al., 2013).*

5.5 OBJECTIVE 2: To describe histopathological findings among patients with nasopharyngeal tumors at MTRH

In this study, 88.5% were malignant lesions while 11.5% were benign lesions

This is in accordance with Mostafa et al found malignant lesions at 48.75% and 51.25% benign of the study population *(El Taher et al., 2017)*

This was in contrast with Biswas et al who found 40% were malignant and 60% were benign masses. This is because of a small sample size n=30 and likely due to early diagnosis of malignant lesions in developed countries *(Biswas et al., 2002)*

Berkiten et al also found benign disease in 97.4% of his patients *(Berkiten et al., 2014)* .

Benign lesions constituted 11.5% with nasopharyngeal tuberculosis being the commonest at 50%. This compares with a study by Tse et al. in Hong Kong who found 55.6% had nasopharyngeal TB *(Tse et al., 2003).*

Atypical angiofibroma comprised 10% of benign lesions in this study. This contrast with Sanjeev et al in India who found 62.5% of his participants had angiofibroma *(Mohanty et al., 2013)*

Squamous cell carcinoma accounted for 76.7% of the malignant lesions in my study. This compares with Muhammad in Nigeria who found squamous cell carcinoma (89.3%) as the most frequent histologic type *(Muhammad, 2017).*

As was the case in this study where undifferentiated non-keratinizing nasopharyngeal carcinoma was the most commonly diagnosed histopathological subtype, a study in Addis Ababa Ethiopia found non-keratinizing undifferentiated to be the most common diagnosis accounting for 70% of the cases *(Nour Amal, 2020).*

Reffai et al also found undifferentiated nasopharyngeal carcinomas as the most common histological type affecting 96.12% of patients *(Reffai et al., 2021)*

As reported by Glastonbury et-al, non-keratinizing NPC is the most common form, accounting for nearly 75% of the cases, with the undifferentiated type being nearly 4 times more common compared to the differentiated type *(13 Glastonbury, and Salzman, 2013).*

This was also the case in the study by BS Alabi et al where 70% of the NPC cases in the study conducted in Nigeria Ilorin were non-keratinizing undifferentiated subtype in Ilorin, Nigeria *(Alabi et al., 2010).*

Haleshappa et al also found 84% of cases had the WHO Type 3 histology while only 16% of cases had the WHO type 2 histology. None of the cases had well‑differentiated keratinizing squamous cell carcinoma (SCC) *(Haleshappa et al., 2017)*

In this study, lymphoma was the 2ndmost common tumor at 8.1% with Hodgkin lymphoma subtype at 57.1% and non- Hodgkin lymphoma at 42.9%.

This contrasts with Dinesh et al who found NHL at 1.78%. He had a small sample size of n=56 *(Garg & Mathur, 2014)*

In this study, the third commonest tumor was rhabdomyosarcoma at 4.7%. This compares with J. Hicks et al in Texas who found 6% of the study participants with rhabdomyosarcoma *(Radzikowska et al., 2015)*

This is in contrast with Dinesh et al who found leiomyosarcoma at 1.78% of his participants. He had a small sample size n=56 *(Garg & Mathur, 2014)*

5.6 OBJECTIVE 3: To compare CT scan and histopathologic findings among patients with nasopharyngeal tumors at MTRH

The sensitivity and specificity CT scan in diagnosis of nasopharyngeal tumors in this study was 97.4% and 10% respectively

These findings were similar to a study in China by Wang F et. al, that had a sensitivity of 96.9% *(Wang et al., 2009)*

This is in contrast with Chen in China who found sensitivity of 71.4% *(Y. K. Chen et al., 2006).* This is likely because Chen's participants were both pre and post-treatment.

In this study, the positive predictive value of CT was 89.3% and negative predictive value of 33.3%. This compares with Martino et al who had positive predictive value of 86% and negative predictive value of 43% *(Di Martino et al., 2000)*

In this study, the anaplastic SCC sub-type demonstrated osseous involvement, intracranial spread and heterogenous enhancement of the patients in 85.3%, 78.9% and 77.9% respectively.

These findings were similar to a study by who found 81.4% with osseous involvement and 74.7% with heterogenous enhancement had anaplastic SCC *(Ălcianu, 2019)*

5.7 Study limitations

This study was a hospital-based study, done at one facility and only clinically symptomatic patients presenting at the CT center were recruited therefore, this was not a representation of the general population.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

Malignant tumors were the most common in both radiological and histopathological findings, with nasopharyngeal carcinoma being the most prevalent histological type. Suspicious CT features that correlated with histopathological diagnosis of nasopharyngeal carcinoma were; soft tissue density, heterogenous enhancement, neck spaces and nodal involvement, central skull base and intracranial invasion. CT had a high sensitivity but a low specificity in diagnosis of nasopharyngeal lesions. The high sensitivity means that CT can be used for preliminary investigation and screening while a low specificity denotes that it is not a good tool on its own in the diagnosis of nasopharyngeal tumors.

6.2 Recommendations

The use of CT scan in the accurate diagnosis of nasopharyngeal tumours as it provides a high diagnostic yield for early detection and to guide patient management. This is applicable in health facilities in Kenya with CT services but with limited histopathological and ENT specialist services.

To radiologists, subtle features like asymmetric nasopharyngeal mucosal thickening and enhancement on CT imaging should be considered suspicious enabling early detection in combination with histopathology.

There is need for multidisciplinary discussions and re-evaluation among clinicians, radiologists and pathologists on patients with discordant imaging and histopathological findings.

Further studies with larger sample size should be conducted on clinical, radiological and histopathological features of nasopharyngeal tumours in Kenya.

Further epidemiological, histochemical and gene mapping studies to characterise NPC in our region would help understand the disease further and work towards identifying a screening test in our region.

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APPENDICES

Appendix I: Consent Form
English Version

Investigator: My name is Dr. Too Sharon Cherotich. I am a qualified doctor, registered by the Kenya Medical Practitioners and Dentists Board. I am currently pursuing a Master's degree in Radiology and Imaging at Moi University. I would like to recruit you into my research which is to study the comparison of radiological features and histopathological features of malignant nasopharyngeal tumors in MTRH, Eldoret.

Purpose: This study will seek to understand the relationship of these two findings and help improve patient care.

Procedure: All the patients in the CT centre with suspected malignant nasopharyngeal tumors will be guided by the researcher to fill the informed consent and details entered into a questionnaire. The questionnaires will be kept in a locked cabinet in the office of the principal investigator during the study period. The radiological features and histopathological diagnosis will be analyzed to seek the diagnostic accuracy of CT scanning.

Benefits: There will be no direct benefits of participating in this study. Study subjects will be accorded same quality of management as non-study subjects

Risks: There are no anticipated risks to the participants attributable to this study.

Confidentiality: All information obtained in this study will be treated with utmost confidentiality and shall not be divulged to any unauthorized person

Rights to Refuse: Participation in this study is voluntary, prospective participants have freedom to decline enrollment or withdraw at any point during the study. This study has

been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

Sign or make a mark if you agree to take part in the study

Name of participant: …… Investigator…….....

Date……. ……. And Time……..

Swahili Consent Form

Mtafiti: Jina langu ni Dkr Too Sharon Cherotich. Mimi ni daktari aliyefuzu na nakusajiliwa na Mimi ni daktari aliyehitimu na kusajiliwa na bodi ya Kenya ya Madaktari na Madaktari wa meno. Kwa sasa natafuta shahada ya uzamili katika Radiology na Imaging katika Chuo Kikuu cha Moi. Ningependa kukuhusisha katika utafiti ninaofanya kujua picha za ndani ya pua zinazofanywa za uvimbe zinaambatana na aina ya histologia

Kusudi: Utafiti huu utatafuta kuelezea kama kuna uhusiano wa matokeo ya CT na ya histologia ya wagonjwa walio na uvimbe ya undani wa pua

Utaratibu: Watu wenye umri wa miaka kumi na nane na juu wataelekezwa na mtafiti kujaza fomu za utafiti baada ya kukubali kufanyiwa utafiti. Matokeo ya CT na za histologia itatumika kuchunguza uhusiano kati yao. Data zitakusanywa kwenye fomu za ukusanyaji data. Hifadhi zitakazotumika katika ukusanyaji wa data zitawekwa katika kabati iliyofungwa na mpelelezi mkuu katika kipindi cha utafiti.

Faida: Hakutakuwa na faida ya moja kwa moja ya kushiriki katika utafiti huu. Wanaofanyiwa utafiti watakuwa na haki na kupewa matibabu sawa na wale ambao hawatahusishwa na utafiti huu.

Hatari: Hakuna hatari inayotarajiwa kwa washiriki inayotokana na utafiti huu.

Usiri: Habari zote zitakazopatikana katika utafiti huu zitawekwa kwa usiri mkubwa na wala hazitatolewa kwa mtu yeyote asiyehusika na utafiti.

Haki za Kuepuka: Kushiriki katika utafiti huu ni kwa hiari yako, kuna uhuru wa kukataa kusajiliwa au kutoka wakati wowote. Utafiti huu umepitishwa na Utafiti wa Taasisi na Kamati ya Maadili (IREC) ya Chuo Kikuu cha kufundishia Moi na Hospitali ya Rufaa.
Tia sahihi au kufanya alama kama unakubali kushiriki katika utafiti

Mgonjwa: .....Mpelelezi: ..... Tarehe: .....

Appendix II: Assent Form

English version

Information

This informed assent form is for patients above 7 years of age who have clinical diagnosis of nasopharyngeal malignancy and are scheduled for neck CT scan

What is medical research?

Medical research is when doctors collect information to get new knowledge about disease or illness. This helps doctors find better ways of treating diseases and helping children or people who are sick.

What is this research study about?

A study will be conducted on children below 18 years of age in clinical evaluation of nasopharyngeal malignancies where the participant's CT scan findings will be compared to histopathology findings. This information will be useful in early diagnosis and management of pediatric nasopharyngeal tumors.

Who is doing this research?

My name is Dr Too Sharon Cherotich and I'm a medical doctor. I'm currently studying for my second degree (Masters in Medicine) in Radiology & Imaging at Moi University.

What will happen to me in this study?

I will invite you to be part of this study. If you agree to participate in this study, your CT scan and histopathology report will be reviewed and findings recorded. You will then be followed up and treatment initiated.

There are no risks or benefits of participating in this study and you will be given the same medical care as the children who are not in the study. You can choose whether or not you

would like to participate in the study. I have discussed this with your parent(s)/ guardian(s) and they know we are asking for your permission to be part of the study. In case you refuse to be part of the study you will not be forced to even if your parents agreed for you to participate.

In case of any questions, feel free to ask, I will be happy to assist.

Certificate of assent

Do you understand this research study and are willing to take part in it?

Yes: ……... No: ……...

Has the researcher answered all your questions?

Yes: ……... No: ……...

Do you understand that you can pull out of the study at any time?

Yes: ……. No: …….

I agree to take part in the study.

OR

I do not wish to take part in the study and I have not signed the assent below. _____

Only if child assents:

Name of child _____

Child's thumb print: 

Date: _____

Kiswahili version

Fomu hii ya idhini ni ya watoto walio umri wa miaka chini ya kumi na nane ambao wameonwa na daktari na ugonjwa wa ndani ya pua kugundulika.

Utafiti wa matibabu ni nini?

Utafiti wa matibabu ni wakati madaktari wanapopata taarifa ili kupata ujuzi mpya kuhusu magonjwa. Hii husaidia madaktari kupata njia bora za kutibu magonjwa na kusaidia watoto au watu ambao ni wagonjwa.

Utafiti huu unahusu nini?

Utafiti huu unahusisha watoto walio na ugonjwa wa dani ya pua. Katika utafiti huu, ugonjwa wa pua kwenye picha ya CT scan utafananishwa na matokeo ya histolojia ili kuamua usawa wake. Hii itakuwa ya manufaa kwa watoto kujua ni ugonjwa upi haswa na kupata matibabu mapema.

Nani atafanya utafiti huu?

Jina langu ni Dkt. Too Sharon Cherotich na mimi ni daktari aliyehitimu. Kwa sasa ninajifunza kwa shahada yangu ya pili (Masters in Medicine) katika Radiolojia & Imaging katika Chuo Kikuu cha Moi.

Nini kitatokea kwangu katika utafiti huu?

Nitakualika kushiriki katika utafiti huu. Iwapo utakubali, matokeo yako ya CT scan na histolojia yataangaliwa na kurekodiwa. Baada ya huu utafiti matibabu yataanzishwa katika ward ya watoto.

Hakuna hatari au faida za kushiriki katika utafiti huu na utapewa huduma sawa ya matibabu kama watoto ambao hawatashiriki kwenye utafiti. Unaweza kuchagua kama ungependa kushiriki katika utafiti huu. Nimezungumza na mzazi na/au mlezi wako na anajua tunaomba ruhusa yako kushiriki katika utafiti. Ikiwa unakataa kuwa sehemu ya utafiti huwezi kulazimishwa hata kama wazazi wako walikubali kushiriki.

Ukiwa na maswali yoyote, jisikie huru kuuliza, nitafurahia kusaidia.

Hati ya kukubali

Je unaelewa utafiti huu na uko tayari kushiriki?

Ndio: _____ La: _____

Je, mtafiti alijibu maswali yako yote?

Ndio: _____ La: _____

Je unaelewa kwamba unaweza kuondoka kwa utafiti huu wakati wowote?

Ndio: _____ La: _____

Nakubali kushiriki katika utafiti huu

AU

Sitaki kushiriki katika utafiti huu na sijasaini idhini hii _____

Ikiwa mtoto pekee ataidhinisha:

Jina la mtoto: ……...

Alama ya kidole cha mtoto:

Tarehe: _____

Appendix III: Data Collection Form

Instructions:

1. All sections should be filled accordingly
2. Writings should be clear and legible
3. The form is to be filled in by the principal investigator or assistant once the patient has given consent to be part of the study

IP/OP NUMBER …….....

SERIAL NUMBER ……

DATE …….

SECTION A: DEMOGRAPHIC DATA

AGE/DOB …….

GENDER ……...

COUNTY OF RESIDENCE ……

CONTACT NUMBER …….

SECTION B: What was the clinical presentation of the patient with nasopharyngeal tumor?

Clinical Features (tick as appropriate)

1.	NECK SWELLING	Tick as appropriate
	Painless	
	Painful	
	Unilateral	
	Bilateral	
	Solitary	
	Multiple	
2.	**NASAL BLOCKAGE**	
	Unilateral	
	Bilateral	
3.	**NASAL DISCHARGE**	
	Unilateral	
	Bilateral	
4.	**EPISTAXIS**	

5.	EAR PAIN	
	Unilateral	
	Bilateral	
6.	**EAR DISCHARGE**	
	Unilateral	
	Bilateral	
7.	**HEARING LOSS**	
	Unilateral	
	Bilateral	
8.	**HEADACHE**	
9.	**NECK PAIN**	
10.	**CRANIAL NERVE PALSY**	
	Site	
11.	**FEVER OF UNKNOWN ORIGIN**	
12.	**OTHERS, SPECIFY**	

SECTION C: CT Imaging: What radiological features were present on the images?

Radiological Features (tick as appropriate)

1.	**LOCATION OF LESION**		**Tick as appropriate**
	Nasopharynx		
	Parapharyngeal		
	Retropharyngeal		
	Intracranial		
	Other neck spaces, specify		
	Solitary		Multiple
	Unilateral	Right	
		Left	
	Bilateral		
	Crossing the midline		
	Diffuse		
2.	**NUMBER OF LESIONS**		
	Primary in location	Solitary	
		Multiple	
	Secondary in location	Solitary	
		Multiple	

3.	**SIZE OF LESIONS**		**Tick as appropriate**
	Primary	<3cm	
		3-5cm	
		>5cm	
	Secondary	<3cm	
		3-5cm	
		>5cm	
4.	**CONTOUR**		
	Lobulated		
	Multilobulated		
	Infiltrative		
5.	**TUMOUR MARGINS**		
	Distinct		
	Indistinct		
	Clear		
6.	**APPEARANCE OF LESION**		
	Cystic		

	Solid	
	Mixed	
	Calcified	
7.	**MUCOSAL CHARACTERISTICS**	
	Mucosal thickening	

8.	**DENSITY OF LESION TO MUSCLE**		**Tick as appropriate**
	Without contrast	Hyperdense	
		Hypodense	
		Isodense	
		Heterogenous	
	With contrast	Nil enhancement	
		Mild	
		Moderate	
		Vivid	
		Heterogenous	

9.	**AUXILLARY FINDINGS**		
	Extension to other neck spaces, specify		
	Bone involvement, specify		
	Muscle involvement, specify		
	Mass effect	Present	
		Absent	
	Eustachian tube involvement	Present	
		Absent	
	Features of Otitis Media	Present	
		Absent	

	Nodal involvement	Ipsilateral	
		Contralateral	
		Bilateral	
		Multilevel	
	Visualized lung involvement, specify findings		
10.	Other findings		

SECTION D: Final CT diagnosis

1.	**CT DIAGNOSIS**		**Tick as appropriate (specify)**
	Benign tumor		
	Malignant tumor	Primary	
		Secondary	

SECTION E: Histopathological Results

1.	**HISTOPATHOLOGICAL DIAGNOSIS**	**Tick as appropriate (specify)**
	Benign tumor	
	Malignant tumor	

Appendix IV: Time Plan

ACTIVITY	START	END
PROPOSAL CONCEPT DEVELOPMENT	March 2020	April 2020
PROPOSAL WRITING	May 2020	December 2020
IREC APPROVAL	May 2021	May 2021
DATA COLLECTION	September 2021	August 2022
DATA ANALYSIS	September 2022	October 2022
THESIS WRITING	November 2022	December 2022

Appendix V: Budget

ITEM	QUANTITY	UNIT PRICE(KSHS)	TOTAL(KSHS)
Laptop	1	50,000	50,000
Printing and photocopying	-	12,500	12,500
Research Assistant	2	15,000	30,000
Stationery	-	5,000	5,000
Storage Devices	50	20	1,000
Statistical Consultation	-	15,000	15,000
Internet services and	-	10,000	10,000
Publication	-	50,000	50,000
Follow-up expenses	70	300	2500
GRAND TOTAL	-	-	180,000

Appendix VI:IREC Approval

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/2021/53
Approval Number: 0003940
29th July, 2021

Dr. Too Sharon Cherotich,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Too,

COMPARISON OF COMPUTED TOMOGRAPHY AND HISTOPATHOLOGICAL FINDINGS AMONG PATIENTS WITH MALIGNANT NASOPHARYNGEAL TUMORS AT MOI TEACHING AND REFERRAL HOSPITAL, KENYA

This is to inform you that ***MTRH/MU-IREC*** has reviewed and approved your above research proposal. Your application approval number is ***FAN: 0003940.*** The approval period is **29th July, *2021- 28th July, 2022.***
This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, Material Transfer Agreements (MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by ***MTRH/MU-IREC***.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to ***MTRH/MU-IREC*** within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to ***MTRH/MU-IREC*** within 72 hours.
v. Clearance for export of biological specimens must be obtained from ***MOH at the recommendation of NACOSTI*** for each batch of shipment.
vi. 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.
vii. Submission of an executive summary report within 90 days upon completion of the study to ***MTRH/ MU-IREC.***

Prior to commencing your study; you will be required to obtain a research license from the National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and other relevant clearances from study sites including a written approval from the CEO-MTRH which is mandatory for studies to be undertaken within the jurisdiction of Moi Teaching & Referral Hospital (MTRH) and its satellites sites.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
29 JUL 2021
APPROVED
P. O. Box 4606-30100 ELDORET

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc CEO - MTRH Dean - SOP Dean - SOM
Principal - CHS Dean - SON Dean - SOD

Appendix VI: Hospital Approval (MTRH)

An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone :(+254)053-2033471/2/3/4
Mobile: 722-201277/0722-209795/0734-600461/0734-683361
Fax: 053-2061749
Email: ceo@mtrh.go.ke/directorsofficemtrh@gmail.com

Nandi Road
P.O. Box 3 – 30100
ELDORET, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

30th July, 2021

Dr. Too Sharon Cherotich
Moi University
School of Medicine
P.O. Box 4606-30100
ELDORET-KENYA

COMPARISON OF COMPUTED TOMOGRAPHY AND HISTOPATHOLOGICAL FINDINGS AMONG PATIENTS WITH MALIGNANT NASOPHARYNGEAL TUMORS AT MOI TEACHING AND REFERRAL HOSPITAL, KENYA

You have been authorised to conduct research within the jurisdiction of Moi Teaching and Referral Hospital (MTRH) and its satellites sites. You are required to strictly adhere to the regulations stated below in order to safeguard the safety and well-being of staff, patients and study participants seen at MTRH.

1. The study shall be under Moi Teaching and Referral Hospital regulation.
2. A copy of MTRH/MU-IREC approval shall be a prerequisite to conducting the study.
3. Studies intending to export human bio-specimens must provide a permit from MOH at the recommendation of NACOSTI for each shipment.
4. No data collection will be allowed without an approved consent form(s) to participants unless waiver of written consent has been granted by MTRH/MU-IREC.
5. Take note that **data** collected must be treated with due confidentiality and anonymity.

The continued permission to conduct research shall only be sustained subject to fulfilling all the requirements stated above.

MOI TEACHING AND REFERRAL HOSPITAL
CEO
APPROVED
30 JUL 2021
SIGN.....
P.O. Box 3-30100, ELDORET

30/07/2021

DR. WILSON K. ARUASA, *EBS*
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

c.c. - Senior Director, Clinical Services
- Director of Nursing Services
- HOD, HRISM