CLINICOPATHOLOGICAL FEATURES AND STAGE AT DIAGNOSIS OF HYPOPHARYNGEAL TUMORS AMONG ADULT PATIENTS ATTENDING OTORHINOLARYNGOLOGY DEPARTMENT AT MUHIMBILI NATIONAL HOSPITAL

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MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
COLLEGE OF MEDICINE
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CLINICOPATHOLOGICAL FEATURES AND STAGE AT DIAGNOSIS OF HYPOPHARYNGEAL TUMORS AMONG ADULT PATIENTS ATTENDING OTORHINOLARYNGOLOGY DEPARTMENT AT MUHIMBILI NATIONAL HOSPITAL

By

Pamela D. Mosha (MD)

A Dissertation Submitted in (Partial) Fulfillment of the Requirements for the Degree of Master of Medicine (Otorhinolaryngology) of Muhimbili University of Health and Allied Sciences

October 2024

CERTIFICATION

The undersigned certify that he has read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences, a dissertation entitled "**Clinicopathological features and stage at diagnosis of hypopharyngeal tumors among adult patients attending Otorhinolaryngology department at Muhimbili National Hospital,**" in (partial) fulfillment of the requirements for the Degree of Master of Medicine (Otorhinolaryngology) of Muhimbili University of Health and Allied Sciences.

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Date:

DECLARATION AND COPYRIGHT

I, **Pamela Donati Mosha,** declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature …… **Date** ……...

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ACKNOLEDGEMENT

I would like to thank the Almighty God for his enduring grace and protection that he bestowed upon me and giving me the opportunity to achieve my goal.

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Finally, I would like to express my gratitude to the participants of this study, without whom this research would not have been possible. Their willingness to participate has enriched this work and contributed to the advancement of knowledge in this field.

DEDICATION

This study is wholeheartedly dedicated to my beloved parents who are so dear and close to my heart, who have been my source of inspiration and have given me strength and willpower when I thought of giving up, who continually provide their unconditional love and support which has enabled me to achieve my goals.

To my son, I thank him for the patience and understanding he has shown me when I was not fully present for him during this study.

ABSTRACT

Background: Diagnosis of hypopharyngeal tumors continues to be a significant challenge due to symptomatology resemblance to other benign diseases of the upper aerodigestive tract. Studies indicate that majority of patients with hypopharyngeal tumors are diagnosed in late stages, which have a poor five-year survival rate. Therefore, it is imperative to have a clear understanding of the clinical presentation of these tumors in order to attain early diagnosis for a timely treatment initiation.

Objective: To determine the clinicopathological features and stage at diagnosis of hypopharyngeal tumors among adult patients attending Otorhinolaryngology department, Muhimbili National Hospital.

Methodology: This was a hospital based cross-sectional study conducted for a period of 6 months from September 2023 to March 2024, among adult patients aged 18 years and above who were diagnosed with hypopharyngeal tumor who attended Otorhinolaryngology department at Muhimbili National Hospital. This study utilized a pretested data collection tool to gather information on demographic characteristics, symptoms and signs, histology results and stage at the time of diagnosis. Data obtained in this clinical survey form was entered in Statistical Package for Social Sciences version 24 for analysis. Descriptive statistics was employed and statistical significance was determined by Fisher Exact Test whereby P value of ≤ 0.05 was considered statistically significant.

Results: This study involved 61 patients with Hypopharyngeal tumors with the age range of 35 to 69 years and the median age of 57 years (53,63). Majority were male who contributed (59.0%), with a male to female ration of 1.4:1. The age group of 51-60 years had the majority of cases (49.18%). The leading clinical feature was difficulty in swallowing contributing (98.3%) while the least common was coughing blood (19.7%). The commonest histological type of hypopharyngeal tumors of all patients (n=61) was squamous cell carcinoma. Majority of patients were diagnoses in advanced stage IVA (39.3%).

Conclusion: This study confirms what other literatures indicate which is that majority of hypopharyngeal cancer patients are males, the most common presentation is difficulty swallowing, Squamous cell carcinoma is the commonest histological type of HPC and majority of patients are diagnosed in late stage disease.

TABLE OF CONTENTS

CERTIFICATION i
DECLARATION AND COPYRIGHT ii
ACKNOLEDGEMENT iii
DEDICATION iv
ABSTRACT v
LIST OF TABLES x
LIST OF FIGURES xi
LIST OF ABREVIATIONS xii
DEFINITION OF TERMS xiii
1.0 INTRODUCTION 1
1.1 Background information 1
1.2 Problem statement 4
1.3 Rationale of the study 4
1.4 Research questions 5
1.5 Objectives of the study 5
1.5.1 Broad objective 5
1.5.2 Specific objectives 5
1.6 Conceptual framework 6
2.0 LITERATURE REVIEW 7
2.1 Clinical features of hypopharyngeal tumors among adult patients. 7
2.2 Histological types of hypopharyngeal tumors among adult patients. 8
2.3 Clinical stage at diagnosis of hypopharyngeal tumors among adult patients. 8
3.0 METHODOLODY 10
3.1 Study area 10
3.2 Study design 10
3.3 Study duration 10
3.4 Study population 10
3.5 Sample size calculations 11

3.6 Sampling Technique 11
3.7 Inclusion and exclusion criteria 12
3.7.1 Inclusion criteria 12
3.7.2 Exclusion criteria: 12
3.8 Data collection technique 12
3.9 Pre-testing of the study instruments 13
3.10 Tools and measurement 13
3.10.1 Clinical survey form 13
3.11 Data analysis plan 13
3.12 Recruiting and training research assistant 13
3.13 Ethical consideration 14
3.14 Study limitations 14
4.0 RESULTS 15
4.1 Distribution of age by sex of the studied population 15
4.2 Clinical features of hypopharyngeal tumors among adult patients with hypopharyngeal tumor. 16
4.3 Histological types among adult patients with hypopharyngeal cancer. 17
4.6 Clinical stage at diagnosis among adult patients with hypopharyngeal cancer 17
4.7 Distribution of clinical stage at diagnosis among adult patients with hypopharyngeal cancer according to age 18
5.0 DISCUSSION 20
6.0 CONCLUSION AND RECOMMENDATIONS 22
6.1 Conclusion 22
6.2 Recommendations 22
REFERENCES 23
APPENDENCES 27
Appendix I: Informed Consent – English Version 27
Appendix II: Informed Consent – Swahili Version 29
Appendix III: Clinical survey form 31

Appendix IV: Ethical Clearance 33
Appendix V: Permission to Collect Data at MNH..... 35

LIST OF TABLES

Table 1: Distribution of age by sex of the studied population.....15
Table 2: Clinical stage at diagnosis among adult patients with hypopharyngeal tumor according to age.....18
Table 3: clinical stage at diagnosis among adult patients with hypopharyngeal cancer according to sex.....19

LIST OF FIGURES

Figure 1: Distribution of clinical features among adult patients ith hypopharyngeal tumor.....16
Figure 2: Distribution of clinical stages at diagnosis among adult patients with hypopharyngeal cancer.....17

LIST OF ABREVIATIONS

AJCC	American Joint Committee on Cancer
CT	Computed Tomography
CM	Centimeter
ENE	Extra Nodal Extension
ENT	Ear, Nose and Throat
GERD	Gastro Esophageal Reflux Disease
HPC	Hypopharyngeal cancer
HPV	Human Papilloma Virus
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
ORL	Otorhinolaryngology
TNM	Tumor size, Lymph Node, Metastasis
SCC	Squamous Cell Carcinoma

DEFINITION OF TERMS

Aerodigestive tract – Combined organs and tissues including nose and paranasal sinuses, oral cavity, pharynx, larynx, salivary glands and upper part of the esophagus.

Carcinoma in situ – Is the presence of a group of abnormal cells found in the place they first formed.

Dysphagia – Is described as difficulty swallowing.

Globus pharyngeus – Is a non-painful sensation of a lump or foreign body in the throat.

Mortality – Is defined as number of deaths in a population in a specific period.

Odynophagia – Is defined as painful swallowing.

Tumor – Abnormal proliferation of cells, which may be either benign or malignant.

Hypopharyngeal tumor – Is an abnormal growth of malignant cells in the hypopharynx.

1.0 INTRODUCTION

1.1 Background information

Hypopharynx extends from the hyoid bone to lower border of cricoid cartilage with three anatomical subsites namely pyriform sinus, post cricoid region and posterior pharyngeal wall. Among the subsites of hypopharynx, pyriform cancers are commonest with estimated 85%, while 20% affects the posterior pharyngeal wall and 15% in post cricoid region. The hypopharynx also known as laryngopharynx, is an important structure for ensuring swallowing, breathing and speech thus tumors situated at this anatomical structure can affect breathing and swallowing due to the effect of the mass for larger tumors or by the lymphatic invasion induced edema(1–3).

Globally, 84254 people suffer from hypopharyngeal cancer with mortality rate estimated to be about 38,599 of all patients with hypopharyngeal cancer diagnosis. There is evidence that HPC have a low rate of five year survival of only 52% for early localized stage of the cancer with a five year survival rate of 23% for metastatic cancers(4,5).

The majority of hypopharyngeal cancer patients have a preponderance of elderly male who have a record of tobacco and alcohol abuse. The amount of alcohol consumed and its concentration both directly affect the likelihood of developing hypopharyngeal cancer. In addition, other risk factors include gastroesophagial reflux disease, Plummer Vinson Syndrome, poor nutrition, HPV and immunodeficiency such as HIV. It occurs in men more often than women with age of onset being between 50 to 70 years and rare in young population. Plummer Vinson Syndrome is linked to post cricoid cancer characterized by dysphagia and iron deficiency anemia. There is still minimal evidence of involvement of HPV in oncogenesis of HPC. Prolonged and strong occupational exposure to wood dust, paint fumes, chemicals used in metalworking, construction, petroleum and textile industries have been shown to increase the probability of acquiring HPC(1,6,7).

Early stage disease symptoms resemble those of other benign disorders of aerodigestive tract such as upper respiratory tract infections and GERD, which can be misdiagnosed, and lead to

delayed diagnosis of HPC. Tumors involving depth of pyriform sinuses are usually asymptomatic until they invade the larynx whereby manifests as upper airway obstruction. However, early stage symptoms are usually nonspecific, globus pharyngeus or sore throat can be early presentations. As the tumor grows, progressive dysphagia and referred otalgia while swallowing could exist. Noticeable weight loss is often a result of dysphagia. Another clinical feature of HPC is the presence of neck mass, comparatively to tumors of the posterior pharyngeal wall and post-cricoid region, tumors of the pyriform sinus have a higher rate of neck metastasis of approximately more than 75%. Hoarseness of voice can be indicative of a more advanced stage HPC(1).

For the best possible outcome when treating HPC, an early clinical diagnosis and precise staging are crucial. An intricate patient history including the clinical features and thorough physical examination including head and neck is recommended. Indirect mirror laryngoscopy or a fiber optic examination or even a direct laryngoscopy under general anesthesia should be performed in order assess the main site of the tumor. A contrast enhanced computed tomography scan is crucial for demonstrating the breadth of tumor invasiveness. However, a magnetic resonance imaging with contrast is superior for soft tissue invasion. Distant metastatic radiological work up including a chest CT scan or PET/CT scan is essential. A histopathology examination following a biopsy taken during endoscopic examination is a key method which gives a diagnosis with exactitude(1,2,6).

Histologically squamous cell carcinoma is the commonest about 95% of all histological types often presented as poorly differentiated while the remaining are adenocarcinoma, papillary squamous cell carcinoma and lymphoepithelial-like carcinoma have been recorded(2).

Hypopharyngeal cancer staging adapts TNM staging classification according to the American Joint Committee on Cancer (AJCC) 8th edition, Whereby T stands for primary tumor categorized into TX, Tis, T1 up to T4 with two subdivisions in T4 (T4a and T4b). N stands for lymph node also categorized into NX, N0, N1, N2 which is further subdivided into N2a, N2b and N2c and N3. Furthermore, M which stands for metastasis is categorized in M0 and M1. With regard to this AJCC TNM classification HPC is classified into four stages, stage I, II, III, with three sub

stages in stage four (stage IVA, IVB, IVC) basing on severity of cancer spread and metastasis(1,2,6,8).

In TX cannot evaluate primary tumor, Tis is cancer in situ, T1-tumor with a maximum size of 2cm or less which is restricted to one subsite of the hypopharynx, T2-tumor has invaded more than one subsite, a neighboring site, or is bigger than 4cm withour fixing the hemilarynx. In T3, the largest dimension of the tumor is greater than 4cm and it may fix the hemilarynx or extend to mucosa lining of esophagus. T4a-thyroid gland, hyoid bone, esophageal muscle, prelaryngeal strap muscles and subcutaneous fat can be invaded by the tumor. T4b-Prevertebral fascia is invaded, carotid artery or mediastinal tissues are affected by the tumor(8).

In Nx cannot evaluate regional lymph nodes, N0-Lymph node metastasis is absent. N1 is same side lymph node metastasis that is ENE absence, 3cm or less in maximum diameter, N2a-3cm or less in maximum diameter and ENE presence in a single, one side node. N2b is multiple same side nodes not more than 6cm in maximum diameter and absent ENE. While in N2c, involvement of more than one node on both sides have maximum size of not bigger than 6cm and ENE absence. In N3a, presence of a node bigger than 6cm in size and absent ENE and N3b has Metastatic to one node on same side greater than 3cm in diameter and ENE presence or more than one, same side or both sides nodes ENE presence or one node on opposite side any variable size with ENE presence. Distant metastases M0 indicates absence metastatic spread to distant sites while M1 symbolizes presence of distant metastases(8).

According to AJCC TNM staging, stage I HPC is T1N0M0, stage II when there is T2N0M0. Stage III includes T3N0M0, T1/T2/T3N1M0. Stage IVA involves T4AN0M0, T4aN1M0, and T1/T2/T3/T4a N2M0. Any T, N3M0 or T4bAnyNM0 is staged as stage IVB HPC while presence of any T, any N and M1 is regarded as stage IVC(8).

1.2 Problem statement

Hypopharyngeal cancer makes up about 3-5% amongst head and neck malignancies. A previously done research claimed hypopharyngeal cancer contributes about 0.41% deaths in Tanzania and it ranks 27th cause of cancer related mortality(2,9).

The clinical presentations often mimic those of other benign upper aerodigestive tract conditions such as upper respiratory tract infections, GERD and pharyngitis, which lead to misdiagnosis of hypopharyngeal cancer owing to a lack of knowledge and result to late stage diagnosis and therefore increase mortality.

There is limited data in Tanzania on clinicopathological features and clinical stages at the time of diagnosis of hypopharyngeal cancers. Thus, there is lack of awareness of hypopharyngeal cancer among health care providers.

1.3 Rationale of the study

This study is a step towards increased index of suspicion among health care providers on early diagnosis of hypopharyngeal cancer, which will lead to appropriate, and timely management hence improve survival rate and reduce mortality attributable to hypopharyngeal cancer.

In addition, the study will be done for the partial fulfillment of master of medicine in Otorhinolaryngology of Muhimbili University of Health and Allied sciences.

1.4 Research questions

- What are the clinical features of hypopharyngeal tumors among adult patients attending ORL department, MNH?
- What are the histological types of hypopharyngeal tumors among adult patients attending ORL department, MNH?
- What are the clinical stages at diagnosis of hypopharyngeal tumors among adult patients attending ORL department, MNH.

1.5 Objectives of the study

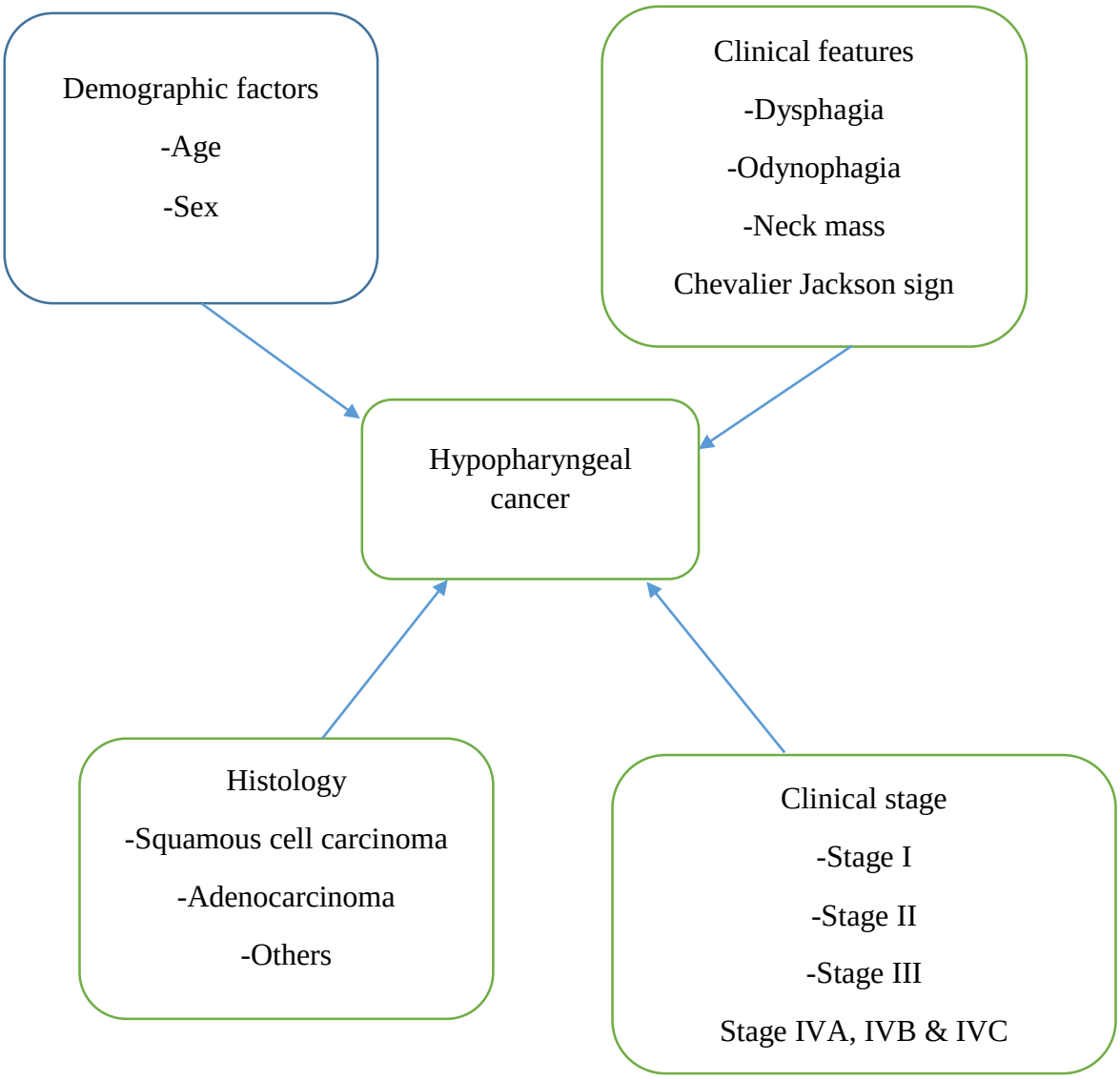
1.5.1 Broad objective

To determine clinicopathological features and stage at diagnosis of hypopharyngeal tumors among adult patients attending ORL department, MNH.

1.5.2 Specific objectives

1. To assess clinical features of hypopharyngeal tumors among adult patients attending ORL department, MNH.
2. To determine histological types of hypopharyngeal tumors among adult patients attending ORL department, MNH.
3. To determine clinical stage at diagnosis of hypopharyngeal tumors at diagnosis among adult patients attending ORL department, MNH.

1.6 Conceptual framework



2.0 LITERATURE REVIEW

2.1 Clinical features of hypopharyngeal tumors among adult patients.

Patients with hypopharyngeal tumors present with varying symptoms that are nonspecific such as sore throat, which can mimic upper respiratory tract infections, which are commonly managed by antibiotics and antihistamines without addressing the primary cause, which can be hypopharyngeal cancer. In advanced stages, patients may present with hoarse voice, dyspnea, neck mass, ear pain and in some cases coughing blood commonly indicating adjacent tissues infiltration, neural invasion and lymphatic spread of tumor(10,11).

Non-respiratory tract symptoms are not uncommon, a study conducted in Pakistan found out dysphagia as the commonest symptom among all patients who attended Otorhinolaryngology clinic with final diagnosis of hypopharyngeal tumor. While in Doumbia et al, 100% patients who were diagnosed with hypopharyngeal cancer, the main reason for consultation to the health care provider was dysphagia(3,12).

The National Health Institute as among the commonest symptom that made patients seek for care reported progressive dysphagia. Dysphagia is also associated with obstructive symptoms and encroachment to the adjacent structures translating into poor prognosis. As a result, due to complicated feeding and cancer spread, patient will have a significant weight loss in association with aerodigestive system symptoms, which also signify the advanced stage of the disease(2,13). However patients with HPC may present with unexplained ear pain as an early symptom unlike hoarseness of voice which is a presentation of much advanced stages(10)

A common complaint among patients, globus pharyngeus accounts for 3-4% new referrals to the ORL clinic. Cervical lymphadenopathy is the commonest finding during physical examination by the health care provider, indicating lymphatic metastasis as HPC tend to have nodal metastases therefore it is crucial to perform a complete head and neck exam and take note on whether or not there are enlarged lymph nodes, their number, size and distribution. In addition, loss of laryngeal crepitus, a sign elicited by loss of mobility of laryngopharynx during palpation of the anterior neck may be indicative of a larger tumor. In addition, pooling of saliva

in the pyriform sinus can be noted during indirect mirror laryngoscopy or flexible fiber optic nasopharyngoscopy, a sign known as Chevalier Jackson's sign(10,14).

2.2 Histological types of hypopharyngeal tumors among adult patients.

Histologically, 95% of all HPC are squamous cell carcinoma. The United Kingdom National Multidisciplinary guidelines reveal that squamous cell carcinoma affects greater than 90% of patients with survival rate being less than 30%. Other frequent histological types of HPC have also been documented in literature including verrucous carcinoma, spindle cell carcinoma, basaloid carcinoma and undifferentiated squamous cell carcinoma. In Netherlands, HPC are labeled as squamous cell carcinoma cancer because of high preponderance of this histological type among all other types which were seen in a twenty years cohort study period(2,15,16).

In, Tanzania, squamous cell carcinoma is the most common histological type of head and neck malignancies summing up to 74% of all histological types. In addition, invasive advanced stage squamous cell carcinoma has been reported as an atypical hypopharyngeal tumor in a patient who presented with thyroid abscess. Therefore, of all available literatures, squamous cell carcinoma is the leading histological type while less than 10% are adenocarcinoma, sarcoma, verrucous sarcoma, and undifferentiated cancers(14,17).

2.3 Clinical stage at diagnosis of hypopharyngeal tumors among adult patients.

Patients with HPC present to the health care providers at different stages. Stage of HPC at the time a diagnosis is made is linked to tumor clinical variability, different health-seeking behaviors, accessibility to specialized Otorhinolaryngology services and degree of suspiciousness by the health care provider. A Carvalho et al. found strong association between patient delay to seek medical care and advanced clinical stage of HPC. About 70%-85% of hypopharyngeal cancers are discovered in patients late stage III or stage IV among them 60% - 75% have regional cervical lymph nodes (N1 – N3)(10,18).

According to Otorhinolaryngology standards in the United Kingdom, the majority of patients with HPC are diagnosed in stage III or IV and their risk of distant metastasis is higher than that of other head and neck malignancies. In Malaysia, a case report study shows preponderance of

late stages III and IV which can reflect the common trend of the hypopharyngeal cancers(13,19–21).

Studies also show that more than 75% of new diagnoses present in stage III or IV among which 60 – 85% have squamous cell carcinoma which poses a risk for poor prognosis(13,16).

In Belgian, a study reveal about 91.3% of hypopharyngeal cancer receive a stage III or IV diagnosis with majority being in stage IV that is even higher at 91.5% when pathological staging is done. A study done in Brazil had shown that compared to other aerodigestive tract cancers, HPC was diagnosed in more advanced stages III and IV with ultimate poor prognosis during and after treatment. In Tanzania, a study done on pattern of head and neck cancer, which includes HPC, was highlighting the histological profiles of these cancers. Therefore, in general there is a dearth of evidence on the clinical features and clinical stages at the time of diagnosis of hypopharyngeal cancers in Tanzania(14,18,22).

3.0 METHODOLODY

3.1 Study area

The study was conducted at Otorhinolaryngology department at MHN in Ilala District, Dar es Salaam region in Tanzania. MNH is a tertiary hospital in Tanzania, which receives referral patients from Tanzania mainland, Tanzania Island and neighboring countries.

The otorhinolaryngology unit is under the department of surgical services at the MNH. The department host about 50 beds, 2 theatre rooms with modern equipment and 7 clinic rooms which run 6 days a week. Health attendants, nurses, general practitioner doctors (GP), resident doctors, ENT surgeons compose the staffing of otorhinolaryngology unit.

About 38 patients with head and neck tumors are attended monthly, this number includes both admitted and outpatients. Following management, those who do not require admission are discharged home or as follow-up patients at ORL clinic, majority fall on the admitted group.

3.2 Study design

The study was a cross-sectional study that applied a quantitative research method to collect and analyze data.

3.3 Study duration

This study was conducted for a period of 6 months from September 2023 to March 2024

3.4 Study population

The study was done among adult patients 18 years and older who had a working diagnosis of hypopharyngeal tumor who attended ORL department, Muhimbili National hospital.

3.5 Sample size calculations

Calculation of sample size was done using Yamane formula (23) which is employed in the non-probability sampling method to determine sample size.

Sample size n

$$n = \frac{N}{(1+N£^2)}$$

Whereby:

N=Estimated sample size

£=Margin of error at 5% (0.05)

N=72 (Estimated 6 months' population of adult patients with hypopharyngeal tumors according to MNH records.

$$n = \frac{72}{(1+72\ (0.05^2))}$$

$$= 61.01 \sim 61$$

$$n = 61$$

Therefore, 61 participants were recruited to participate in this study.

3.6 Sampling Technique

The study was hospital based, recruited all adult patients diagnosed with HPC who were attending Otorhinolaryngology department, MNH. A non-probability convenient sampling technique was employed in this study. In this technique, each patient who met the study's inclusion criteria was recruited as a study participant. Recruiting was done throughout the study duration.

3.7 Inclusion and exclusion criteria

3.7.1 Inclusion criteria

Adults 18 years of age and above diagnosed with hypopharyngeal tumor who provided a consent for participation in the study.

3.7.2 Exclusion criteria:

Patients with hypopharyngeal cancer who were debilitated and could not comprehend the questionnaire.

Patients who had hypopharyngeal cancer as an extension from adjacent structures.

3.8 Independent and Dependent variables

3.8.1 Independent variables

In this study independent variables were demographic data, symptoms, signs, clinical stage at the time of diagnosis and histology of hypopharyngeal tumors.

3.8.2 Dependent variables

In this study dependent variables include hypopharyngeal tumors.

3.8 Data collection technique

By using a clinical survey form, demographic information as well as symptoms were enquired from the study participants. All participants were subjected to a physical examination where they were examined for signs of neck mass and laryngeal crepitus. Endoscopic examination by the use of rigid indirect laryngngoscope or fiber optic nasopharyngolaryngoscope at ENT clinic was done, Chevalier Jackson's sign findings were acquired. At a subsequent time, patients underwent a direct laryngoscopy procedure under general anesthesia at theater where biopsy was taken for histological studies and tumor extension was well observed. All participants were subjected to a CT scan of neck in order to ascertain the degree of tumor spread, and a chest X-ray for metastatic work up. All information gathered was recorded in the data collection sheet by the principal investigator, staff working at ENT department and ENT residents.

3.9 Pre-testing of the study instruments

Pre testing whether the clinical survey tool was well understood, 5 research assistants were invited to participate in the piloting of the tool one week before commencing data collection. Piloting the study helped to estimate the time for the interview and refining the clinical survey form before implementation began**.**

3.10 Tools and measurement

3.10.1 Clinical survey form

A clinical survey form was used for data collection; both sociodemographic characteristics, clinical features, histological types and stage at diagnosis were obtained from the study participants. The lead researcher and research assistants documented each finding in the data-collecting sheet.

3.11 Data analysis plan

Descriptive analysis was done using Statistical Package for Social Sciences (SPSS) for windows version 23. The collected information was checked for consistency as well as accuracy. Statistical tables and figures have been used to display sociodemographic information, clinical features, histological types and clinical stage of hypopharyngeal tumors. Descriptive statistics data were organized, summarized, and interpreted based on table summaries and their respective frequencies. Using a Fisher exact test, a P-value of less than 0.05 was considered statistically significant.

3.12 Recruiting and training research assistant.

Two study assistants were hired, educated about the study's goals and ethical considerations. They were oriented on data collection tool before being involved in data collection. The research assistants were medical personnel who were willing to take part and had the skills necessary to contribute to the data collection process.

3.13 Ethical consideration

Ethical approval for the study's execution was requested from MUHAS ethical committee and MNH research publication committee. Permission for patient interviews was requested from the executive director and head of research and training at MNH. Participants were informed about the study verbally and requested to participate. It was conveyed to the participants that partaking was by one's own will and failure to comply would not bear any consequences for them. Participants who provided a written consent were recruited.

3.14 Study limitations

This study involved patients who attended Otorhinolaryngology department at Muhimbili National Hospital in a period of six months therefore the sample size cannot be representative of all patients with hypopharyngeal cancer in Dar es Salaam.

4.0 RESULTS

4.1 Distribution of age by sex of the studied population

This study involved 61 patients with the age range of 35 to 69 years and the median age of 57 years (53,63). Majority were males who contributed (59.0%), with a male to female ratio of 1.4:1. The age group of 51-60 years had the majority of cases (49.18%). Table 1.

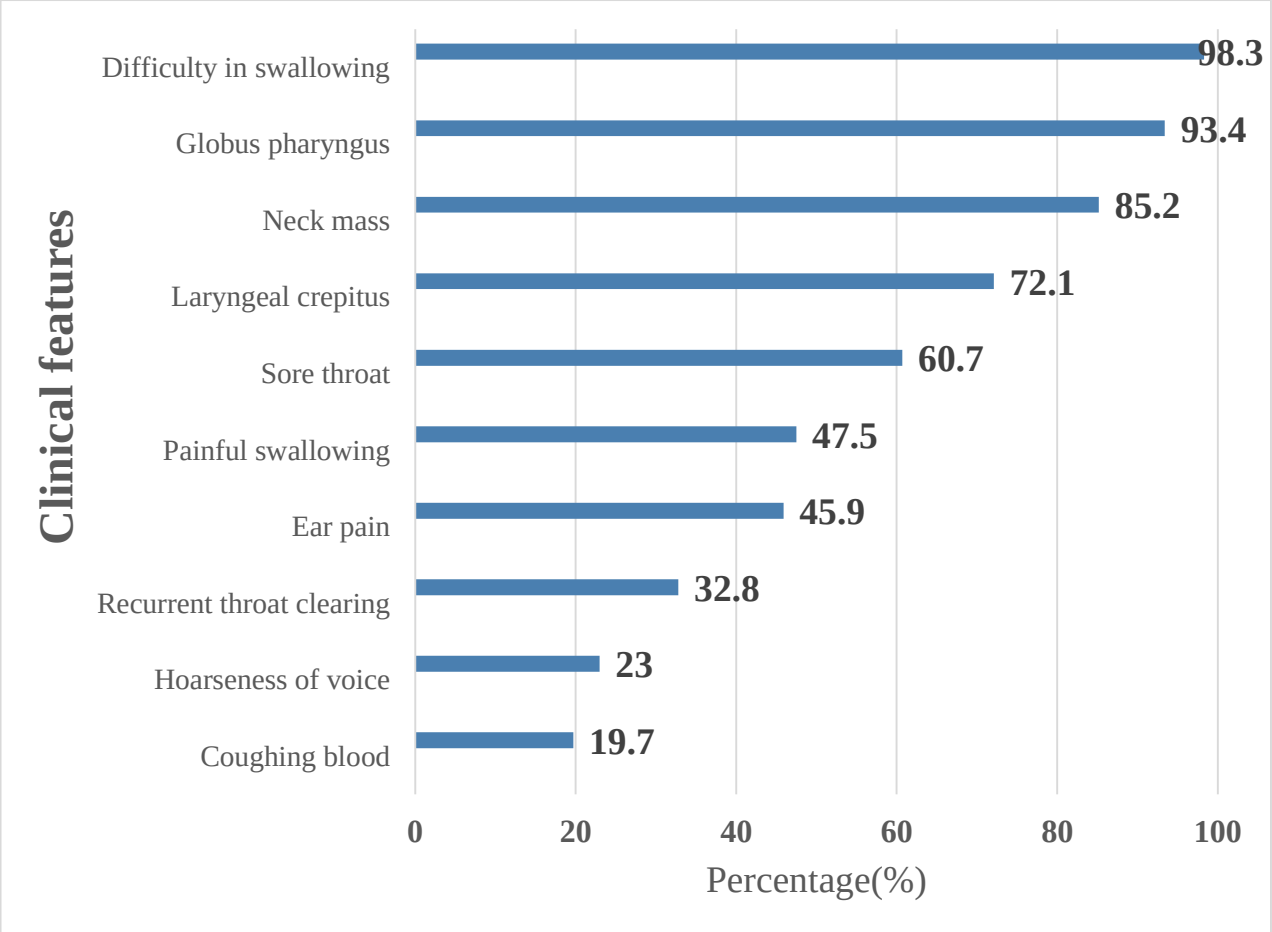
Table 1: Distribution of age by sex of the studied population

Age groups Years	**Sex**		
	MALE	**FEMALE**	**Total N(%)**
30-40	0(0.0%)	2(100.0%)	2(3.28%%)
41-50	1(14.3%)	6(85.7%)	7(11.48%)
51-60	19(63.3%)	11(36.7%)	30(49.18%)
61-70	16(72.7%)	6(27.3%)	22(36.07%)
Total N(%)	**36(59.0%)**	**25(41.0%)**	**61(100.0%)**

4.2 Clinical features of hypopharyngeal tumors among adult patients with hypopharyngeal tumor.

Among all study participants (n=61), difficulty swallowing was the commonest clinical feature (98.3%) while coughing blood was least common (19.7%).

Figure 1: Distribution of clinical features among adult patients ith hypopharyngeal tumor.



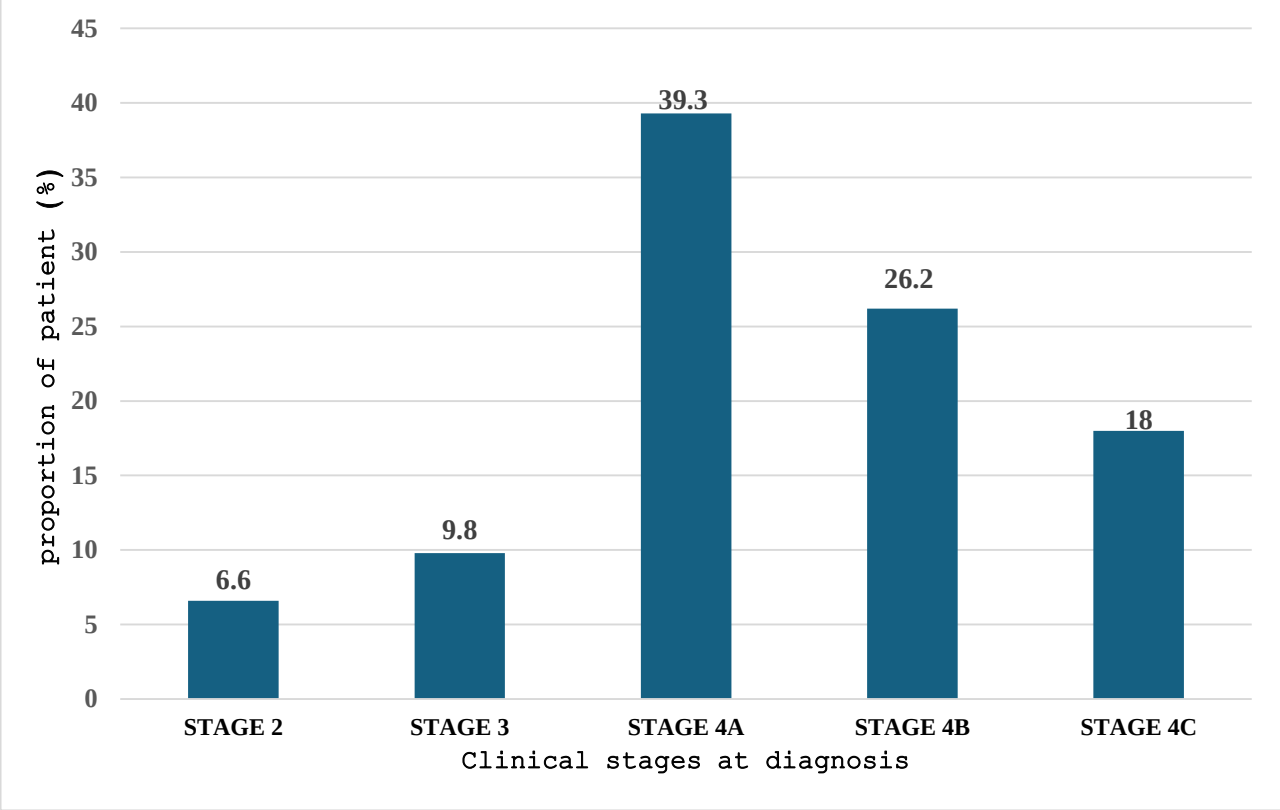
4.3 Histological types among adult patients with hypopharyngeal cancer.

In this study, the histological type of all hypopharyngeal tumors (100%) was found to be squamous cell carcinoma.

4.6 Clinical stage at diagnosis among adult patients with hypopharyngeal cancer

Majority of patients were diagnosed in stage IVA (39.3%). The least common diagnosed stage was stage II (6.6%) while stage I cancer was not found.

Figure 2: Distribution of clinical stages at diagnosis among adult patients with hypopharyngeal cancer.



4.7 Distribution of clinical stage at diagnosis among adult patients with hypopharyngeal cancer according to age

In patients who belong to age group 30-40 (n=2), most common stages were stage III and stage IVA. Those in age group 41-50, majority had stage IVA (42.90%) and least common stage in this age group was stage II (14.30%) and III (14. 30%) equally. In age group 51-60 majority had stage IVA (33.30%) and least common stage was stage II (6.70%). Majority of participants in age group 61-70 had stage IVA (45.50%) and least common stage in this age group was stage II (4.50%). The difference in disease stage across all age groups was not statistically significant with a p-value of 0.659.

Table 2: clinical stage at diagnosis among adult patients with hypopharyngeal tumor according to age

Age groups (years)	**Stage of hypopharyngeal tumor**					**Total n%**	**P value**
	STAGE II	**STAGE III**	**STAGE IVA**	**STAGE IVB**	**STAGE IVC**		
30- 40	0(0.00%)	1(50.00%)	1(50.00%)	0(0.00%)	0(0.00%)	2(3.28%)	0.659
41-50	1(14.30%)	1(14.30%)	3(42.90%)	2(28.60%)	0(0.00%)	7(11.48%)	
51-60	2(6.70%)	3(10.00%)	10(33.30%)	7(23.30%)	8(26.70%)	30(49.18%)	
61-70	1(4.50%)	1(4.50%)	10(45.50%)	7(31.80%)	3(13.60%)	22(36.07%)	
Total	**4(6.60%)**	**6(9.80%)**	**24(39.30%)**	**16(26.20%)**	**11(18.00%)**	**61(100.00%)**	

4.8 Distribution of stage of hypopharyngeal cancer at diagnosis according to sex

In this study, majority of male patients were diagnosed in late stage IVA and IVB (36.10%) equally. Likewise, Majority of females were diagnosed in stage IVA (44.00%). The difference of stage of cancer across all genders was found to be not statistically significant with a p-value of 0.128.

Table 3: clinical stage at diagnosis among adult patients with hypopharyngeal cancer according to sex

Sex	**Stage of hypopharyngeal tumor**					**Total**	**P value**
	STAGE II	**STAGE III**	**STAGE IVA**	**STAGE IVB**	**STAGE IVC**		
MALE	1(2.80%)	2(5.60%)	13(36.10%)	13(36.10%)	7(19.40%)	36(59.01%)	0.128
FEMALE	3(12.00%)	4(16.00%)	11(44.00%)	3(12.00%)	4(16.00%)	25(41.0%)	
Total	**4(6.60%)**	**6(9.80%)**	**24(39.30%)**	**16(26.20%)**	**11(18.00%)**	**61(100.00%)**	

5.0 DISCUSSION

This study included a total number of 61 participants with age range from 35 to 69 median age 57 years whereby majority of patients with hypopharyngeal tumors were males with a male to female ratio of 1.4:1 and majority of the participants with hypopharyngeal tumors were seen in the 5th decade of life. These results are consistent with the findings of a study done in Pakistan whereby out of 75 patients 43 were males and 32 were females with a male to female ratio 1.34:1. A study done in Denmark found a male preponderance whereby among 138 study participants, 100 were males and 38 were females. Furthermore, In Bamako - Mali, a study of 35 patients revealed that those aged 51 to 60 years were largely affected. (3,24,25).

However, this study differs from one which was done in Tanzania which found that patients over the age of 60 years had the highest incidence of HPC. This could be due to a recent up rise in variety of high risk behaviors. There has been a surge in popularity of electronic cigarettes, vaping and shisha smoking all which have been established to cause cancers due to their carcinogenic properties. A study done in London found a positive association between shisha smoking and squamous cell carcinomas (26,27).

Additionally, an increase in some sexual behaviors such as homosexuality, orogenital practices and prostitution highly predispose individuals to Human Papilloma Virus which is a risk factor for HPC. Evidently, in Sweden a study found that 3.7% of the 82 patients with hypopharyngeal carcinoma had tumors that tested positive for HPV16 DNA. Furthermore, Heck et al found that sexual behaviors have been linked to increased risk of cancers of head and neck sub sites that have been previously linked to HPV infection. However, the sample size for this study was comparatively smaller than that of the other study conducted in Tanzania. All these variables may account for the dissimilarity between this study's finding which showed HPC peak in the 5th decade of life and the one done in Tanzania which found HPC to be more prevalent in the 6th decade of life (26,28,29).

In this study, the most prevalent clinical feature was dysphagia (98.3%) followed by globus pharyngeus ((93.4%), neck mass (85.2%) while coughing blood was the uncommon feature among all participants (19.7%). In the United Kingdom a study has similar findings of dysphagia, globus sensation, neck mass and odynophagia to be the most common clinical presentations while coughing blood was the least frequent. Fahad et al reported that the main clinical feature was dysphagia (92%). In addition, a study in China revealed that the most common symptoms of HPC were globus pharyngeus, sore throat, dysphagia, neck mass, otalgia. In support of findings of this study, a study in India also found that the most common symptoms were painful swallowing, difficulty swallowing, hoarseness, ear pain, neck mass and globus sensation (1–3,10,19).

In this study, the most prevalent histological type of HPC was squamous cell carcinoma (100%). This is in concurrence with available literature around the world. In Pakistan a study reported squamous cell carcinoma to be the leading histological type (97.33%). Likewise, in United Kingdom, China and Kenya squamous cell carcinoma was found to be the most prevalent. (1,3,15,30).

Majority of participants in this study had advanced stage IV HPC at the time of diagnosis. This finding is similar to that of a study by Bradley et al whereby most patients were diagnosed in late stage III and IV. Furthermore, in Bamako, a study found that more than half the patients (54%) were diagnosed at the T3N2Mo stage, which corresponds to advanced stage disease. In United Kingdom, it is reported that more than 80% of patients are diagnosed in advanced stage III and IV. The reason behind is due to its spacious anatomy, there is typically significant tumor growth in the pyriform fossa prior to onset of noticeable symptoms. Thus greater number of patients with HPC are diagnosed at advanced stages (10,15,24).

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

In this study, HPC was found to be most prevalent among male population in their 5th decade of life. The proportion of HPC was found to increase as the age increased. The most common clinical feature was dysphagia. The commonest histological type of hypopharyngeal cancer was found to be squamous cell carcinoma and majority had well differentiated characteristic. Most patients presented in late stage IV disease with a preponderance of stage IVA however, there was no statistically significant difference in terms of age and sex. Therefore, high degree of suspicion from patients' clinical presentations by a healthcare provider is crucial for early intervention.

6.2 Recommendations

In this study, HPC was found to be most prevalent among male population in their 5th decade of life. The proportion of HPC was found to increase as the age increased. The most common clinical feature was dysphagia. The commonest histological type of hypopharyngeal cancer was found to be squamous cell carcinoma and majority had well differentiated characteristic. Most patients presented in late stage IV disease with a preponderance of stage IVA however, there was no statistically significant difference in terms of age and sex. Therefore, high degree of suspicion from patients' clinical presentations by a healthcare provider is crucial for early intervention.

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APPENDENCES

Appendix I: Informed Consent – English Version

No…… Date……

I am Dr. Pamela Mosha, a student at MUHAS undertaking Masters of Medicine in Otorhinolaryngology. I am researching the clinicopathological features and stage at diagnosis of hypopharyngeal tumors among adult patients attending Otorhinolaryngology department at Muhimbili National Hospital, Dar -es-Salaam. As one of the patients diagnosed or with features suggestive of hypopharyngeal cancer, I would like you to participate in the study.

Aim of the Study: Is to assess clinicopathological features and determine stage at diagnosis of hypopharyngeal tumors among adult patients attending otorhinolaryngology department at MNH. I will conduct this study under my supervisor.

Participation: Your role in this research is to answer a few questions regarding your symptoms and you will be examined physically for any signs. It will take me between 10 to 20 minutes to evaluate you and there will not be any invasive procedures. Participation is fully voluntary; you may choose to revoke your contribution at any time without any repercussions.

Confidentiality: Only your cell phone number will be recorded, your name will not appear anywhere. All details from the questionnaire will be entered into computers in designated numbers. The research will be executed in a discreet manner.

Risks and benefits This Study will not have any negative risks to the participants. You will not receive any immediate advantages but the entire research is going to make plain and improve hypopharyngeal cancer awareness among health care providers.

In the course of this research, you can get in touch with the following in case of any queries or worries:

Contacts: For queries and worries about the study, you can get in touch with principal Investigator: Dr. Pamela Mosha P.O.BOX 65001 Dar Es Salaam mobile: +255 789267198 or

Research supervisors: Dr Daudi Ntunaguzi, Mobile phone: +255687365208 or

Dr. Aslam Nkya, Mobile phone: +255769228424

In case you have any concerns about your rights as a participant please contact Dr. Nahya Salim, Director of Research and Publication (DRP) of MUHAS, P.O. Box 65001, Dar es Salaam, Tanzania. Tel: +255-713-250074, Email drp.muhas.ac.tz.

I, the signatory, voluntarily agree to take part in this study. My understanding of nature and purpose of the research is complete. I am aware that details acquired are for this research only.

Participant signature……... Mobile …….

Lead investigator/assistant investigator signature…….

Appendix II: Informed Consent – Swahili Version

Namba…… Tarehe……

Kichwa: Utafiti wa viashiria, dalili, aina za kihistolojia na hatua za ugonjwa wa saratani ya koo aina ya hypopharyngeal.

Utangulizi:

Habari, naitwa Dr. Pamela Mosha, ninasoma ngazi ya uzamili katika fani ya utaalamu wa magonjwa ya Sikio, Pua na Koo Katika Chuo Kikuu cha Afya na Sayansi Shirikishi Muhimbili Dar Es Salaam.

Ninaomba kwa utayari wako na idhini yako ushiriki katika utafiti tajwa kwenye kichwa cha habari hapo juu.

Lengo la huu utafiti: Lengo kuu ni kuchunguza dalili, viashiria, hatua na aina za kihistolojia za ujongwa ya saratani ya hypopharyngeal baina ya wagonjwa wanaopata matibabu katika hospitali ya taifa ya Muhimbili, Dar es salaam.

Kushiriki kutahusisha nini: Kukubali kushiriki katika utafiti huu, tutakuuliza maswali kuhusiana dalili za ugonjwa wa saratani ya hypopharyngeal pia utafanyiwa uchunguzi wa unaohusiana na ugonja huu wa saratani ya hypopharyngeal. Kushiriki kwako ni kwa hiari na utapata huduma zote stahiki hata kama hutashiriki kwenye utafiti, pia kama baadae ukiamua kujitoa kwenye utafiti bado utaendelea kupata huduma kikamilifu.

Usiri wa taarifa: Taarifa zote zitakazopatika na katika utafiti huu zitabaki kuwa ni siri. Tutatumia namba ya hospitali na namba ya utambulisho ya utafiti kwaajili ya kuwatambua washiriki wa utafiti, hakuna majina ya takayo tumika katika utafiti huu au katika machapisho yoyote yakiutafiti yatakayotokana na utafiti huu hapo baadaye. Majina yataonekana kwenye hii fomu ya ridhaa tu, ambayo itatunzwa na mtafiti, mbali na fomu nyingine za washiriki.

Faida na Madhara ya Utafiti: Hakutakua na faida za moja kwa moja kwako lakini kushiriki kwako kutawapa watoa huduma uwezo wa kugundua ugonjwa huu mapema Zaidi. Kwa kushiriki kwenye utafiti huu hautapata madhara yoyote.

Kwa maelezo Zaidi kuhusu utafiti huu, wasiliana na mtafiti mkuu Dr. Pamela Mosha, , S.L.P. 65001 Dar es Salaam. Simu +255789267198 au wasimamizi wa utafiti Dr. Daudi Ntunaguzi +255687365208 au Dr. Aslam Nkya +255769228424.

Ikiwa unahitaji maelezo yoyote kuhusu haki zako na menendo wa kimaadili wasiliana na:

Mkurugenzi wa Kamati ya Tafiti na Machapisho wa Chuo Kikuu cha Afya na Sayansi Shirikishi Muhimbili, Dr. Nahya Salim, S.L.P 65001, Dar es salaam, Tanzania. Tel: +255-713250074. Barua pepe: Email: drp.muhas.ac.tz.

Tamko la ridhaa

Mimi …… nimesoma na kuelezwa yaliyomo kwenye hii fomu ya ridhaa. Maswali yangu yote yamejibiwa na ninakubali bila kushurutishwa kuwa mshiriki wa utafiti huu.

Saini ya mshiriki ……. Simu: …….

Saini ya mtafiti mkuu/ mtafiti msaidizi ……..

Appendix III: Clinical survey form

A. GENERAL INFORMATION

Identification number……

Age…… Sex……

B. CLINICAL FEATURES OF THE STUDY PARTICIPANT.

Select symptoms of hypo pharyngeal cancer by ticking on the check box **(√)**

		Yes	No
1.	Sore throat	☐	☐
2.	Globus pharyngeus	☐	☐
3.	Difficulty swallowing	☐	☐
4.	Painful swallowing	☐	☐
5.	Recurrent throat clearing	☐	☐
6	Hoarseness of voice	☐	☐
7	Coughing blood	☐	☐
8	Ear pain	☐	☐
9	Neck mass	☐	☐

C. SELECT SIGNS BY TICKING IN THE RIGHT BOX

Select signs of hypopharyngeal cancer by ticking on the check box **(√)**

		YES	NO
10.	Neck mass	☐	☐
11.	Chevalier Jackson's sign	☐	☐
12.	Laryngeal crepitus	☐	☐

13. Other presentations…….

D. HISTOLOGICAL TYPE OF HYPOPHARYNGEAL TUMOR

Circle the histological type of hypopharyngeal cancer of the study participant

1. Squamous cell carcinoma
2. Other types ……

E. HISTOLOGICAL GRADING

1. Grade 1 (Well differentiated)
2. Grade 2 (Moderately differentiated)
3. Grade 3 (Poorly differentiated)
4. Grade 4 (Undifferentiated)

F. STAGE AT DIAGNOSIS

Circle the clinical stage at diagnosis of hypopharyngeal tumor of the study participant

1. Stage I
2. Stage II
3. Stage III
4. Stage IVA
5. Stage IVB
6. Stage IVC

Appendix IV: Ethical Clearance

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR – RESEARCH, PUBLICATIONS AND INNOVATION

Ref. No.DA.282/298/01.C/1913 Date: 18/09/2023

MUHAS-REC-09-2023-1913
PAMELA DONATI MOSHA
SCHOOL OF MEDICINE
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: CLINICOPATHOLOGICAL FEATURES AND STAGE AT DIAGNOSIS OF HYPOPHARYNGEAL TUMORS AMONG ADULT PATIENTS ATTENDING OTORHINOLARYNGOLOGY DEPARTMENT AT MUHIMBILI NATIONAL HOSPITAL.

Reference is made to the above heading,
I am pleased to inform you that the Chairman has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 18/09/2023
EXPIRATION DATE OF APPROVAL: 18/09/2024

STUDY DESCRIPTION:
Purpose:
the purpose of this cross-sectional study is to determine clinicopathological features and stage at diagnosis of hypopharyngeal tumors among adult patients attending OTORHINOLARYNGOLOGY DEPARTMENT AT MUHIMBILI NATIONAL HOSPITAL.

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided:
https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%2014844.pdf and in the MUHAS archives.

The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain data transfer agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain material transfer agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country,
8. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
9. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
10. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.

Dr. Nahya Salim Masoud,

Chairperson, MUHAS Research and Ethics Committee

Muhimbili University of Health and Allied Sciences
DIRECTOR
Research, Publications & Innovations
Box 65001

Appendix V: Permission to Collect Data at MNH

THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

MUHIMBILI NATIONAL HOSPITAL

In reply please quote;

Ref. No.: MNH/CRTCU/Perm/2023/508 Date: 26th September, 2023

Head Department,
Otorhinolaryngology
Muhimbili National Hospital

RE: PERMISSION TO COLLECT DATA AT MNH.

Name of Student	**Pamela Donati Mosha**
Title	**"Clinicopathological Features and Stage at Diagnosis of Hypopharyngeal Tumour Among Adults Patients Attending Otorhinolaryngology Department at MNH".**
Institution	Muhimbili University of Health and Allied Sciences
Supervisor	Dr. Daudi Ntunaguzi (MUHAS)
Co - Supervisor	Dr. Aslam Nkya (MNH)
Period	26th September, 2023 to 30th December, 2023

Approval has been granted to the above mentioned student to collect data at MNH. **A final study report should be lodged with Clinical Research, Training and Consultancy Unit.** Dissemination of study findings to MNH stakeholders shall be overseen by **Dr.** Aslam Nkya (MNH) Co – supervisor.

Kindly ensure that the student abide to the ethical principles and other conditions of the research approval.

Yours Sincerely,

Dr. Deus Buma
For: Head of Clinical Research, Training and Consultancy Unit

c.c DSS
c.c Dr. Aslam Nkya
c.c **Pamela Donati Mosha**

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