CLINICAL PROFILE, INDICATION AND OUTCOME OF PATIENTS WHO UNDERWENT TRANSSPHENOIDAL PITUITARY SURGERY AT MUHIMBILI NATIONAL HOSPITAL AND MUHIMBILI ORTHOPAEDIC INSTITUTE

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MMed(Otorhinolaryngology) Dissertation

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COLLEGE OF MEDICINE

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CLINICAL PROFILE, INDICATION AND OUTCOME OF PATIENTS WHO UNDERWENT TRANSSPHENOIDAL PITUITARY SURGERY AT MUHIMBILI NATIONAL HOSPITAL AND MUHIMBILI ORTHOPAEDIC INSTITUTE

BY

NOEL MOSES NNYITI

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

October, 2024

CERTIFICATION

The undersigned certify that he has read and hereby recommends for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation entitled "**CLINICAL PROFILE, INDICATION AND OUTCOME OF PATIENTS WHO UNDERWENT TRANSSPHENOIDAL PITUITARY SURGERY AT MUHIMBILI NATIONAL HOSPITAL AND MUHIMBILI ORTHOPAEDIC INSTITUTE**" in (partial) fulfilment of the requirements for the Degree of Master of Medicine (Otorhinolaryngology) of Muhimbili University of Health and Allied Sciences.

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Dr. Enica Richard

(Supervisor)

Date: _____

_____

Dr. Edwin Liyombo

(Co-supervisor)

Date: _____

DECLARATION AND COPYRIGHT

I, **NOEL MOSES NNYITI,** declare that this **dissertation** is my 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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Lastly, my sincere appreciation also goes to my family and friends for their continuous support and love throughout my postgraduate training.

DEDICATION

I would love to dedicate this dissertation to my Mother for her never ending guidance, support and encouragement through my study period and the writing of this research topic.

I dedicate this to my family and Otorhinolaryngology classmates for their never-ending love, support, and encouragement.

ABSTRACT

Background: Transsphenoidal pituitary surgery is an endoscopic approach to the pituitary gland through the sphenoid sinus for removal of pituitary tumors. The aim of this surgery is to correct any pituitary hormone over secretion, eliminate the mass effect of the tumor, decompress the visual pathway, reduce the risk of tumor recurrence and get histological diagnosis of pituitary tumors. Like any other surgery, there are complications associated with it.

Objectives: To assess the clinical profile, indication and outcome of patients who underwent transsphenoidal pituitary surgery at Muhimbili national hospital and Muhimbili orthopaedic institute.

Methodology: A retrospective cross sectional study was conducted which included all the patients who underwent transsphenoidal pituitary surgery since the initiation of the approach in 2018. By using a structured checklist & accessing the patient database, demographic information, signs & symptoms at presentation, indication and outcome of the transsphenoidal pituitary surgery was acquired. All of the findings were recorded in a data collection sheet, data was analyzed using Statistical Package for Social Science software version 23, and the Chi-Square and Fisher's exact test were used to assess the association of variable. A confidence interval of 95% was used, and a P-value of <0.05 was considered significant.

Results: A total of 40 patients were enrolled in the study whereby majority were 41-50 years (30%) and females accounted for 57.5% of the patients with a female to male ratio of 1.3:1. Vision loss was the common complaint seen in 87.5% of the patients followed by headache which accounted for 85%. Some patients presented with secretory adenomas which accounted for 17.5%. The most common indication for surgery was progressive mass effect seen at 78.4% of patients followed by hormonal control seen in 13.7% of patients. Symptom relief post-surgery was seen in 85% of patients and hormonal control was seen in 71.4% of patients. Patients who developed diabetes insipidus and hypopituitarism were observed to be

12.5%, whereby, cerebrospinal fluid leak as an intra-op or early complication was seen in 7.5% of individuals and 2.5% had it as a late complication.

Conclusion: Transsphenoidal pituitary surgery is a novel/modern approach to pituitary tumors in Muhimbili National Hospital and Muhimbili Orthopedic Institute. Most patients were seen in the middle age and females accounted more than males. Patients presented with various clinical complaints whereby vision loss and headache accounted for majority of the complaints. The most common indication was due to mass effect. Majority of patients reported symptom relief and hormonal control post-surgery whereby the most common complication was diabetes insipidus and hypopituitarism. Therefore, this study helps on shedding light as well as contribute to the existing knowledge of surgeons as well as the medical community to improve outcomes of these patients.

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ABBREVATIONS

ACTH	Adenocotricotrophin Hormone
CSF	Cerebrospinal Fluid
GH	Growth Hormone
MNH	Muhimbili National Hospital
MOI	Muhimbili Orthopaedic Institute
MUHAS	Muhimbili University Of Health And Allied Sciences
TSH	Thyroid Stimulating Hormone
TSS	Transsphenoidal Sinus Surgery

DEFINITON OF TERMS

Clinical profile- this is the age, sex, symptoms and signs the patient presents with at the hospital/clinic.

Clinical Presentation – these are signs and symptoms the patient presents with.

Minimal invasive surgery- this is surgery that is done using small incisions and few to no stitches.

Operation outcome- this is the turn out of the operation which will be defined as hormonal control, symptom relief and complications post-surgery.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Endoscopic endonasal surgery has revolutionized skull base surgery. This technique was initially used for paranasal sinus procedures. These surgeries have since been expanded to include other procedures such as the resection of pituitary tumors (1). Access to practically all areas of the skull base located anterior to the foramen magnum is made possible by endoscopic endonasal surgery. Although tumors are the primary lesions, endoscopic surgery is also an option for cerebrospinal fluid (CSF) leaks from trauma or other causes, some persistent infections, and congenital deformities. The significant advancement made in recent years a huge number of anatomical studies, variations, and improvements in this "minimally invasive" surgery has sparked the increasing interest of Otorhinolaryngologists and neurosurgeons in this procedure. (1,2) Intranasal structure and function is preserved, there is less collateral tissue damage, faster recovery than with an open technique, and improved light penetration to the target area are all benefits of the endoscopic approach. (3)

Patients with primary pituitary tumors usually have presentations based on the endocrinological symptoms which are specific to the hormones secreted, space occupying/pressure effects of the tumor with surrounding structures e.g. visual disturbances, obstructive hydrocephalus, hypothalamic syndromes, cerebrospinal fluid rhinorrhea or nasopharyngeal mass. Based on the endocrinological symptoms, patients with Growth Hormone secreting adenoma may present with either; headaches, vision changes, an increase in ring or shoe size, arthritis, carpal tunnel syndrome, excessive sweating, coarse facial features, frontal bossing, enlarged nose, prognathism, enlarged tongue, and skin tags. Patients with Prolactin-secreting adenoma may present with infertility, decrease libido, and osteoporosis in both sexes. Females present with amenorrhea and galactorrhea while men present with erectile dysfunction and gynecomastia. Patients with Adenocorticotrophin hormone secreting adenoma (Cushing disease) presents with weight gain, muscle weakness, mood disorders, easy bruising, and multiple fractures, round face, facial plethora, supra-

clavicular fat, ecchymoses, and purple striae on the abdominal area and armpits. Patients with thyroid stimulating hormone secreting adenoma present with palpitations, arrhythmias, and weight loss, tremors and goiter.(4)

Indications for transsphenoidal pituitary surgery are pituitary apoplexy, progressive mass effect of the tumor, normalization of pituitary hormone hypersecretion, biopsy of sellar and suprasellar lesions, failed medical or radiotherapy treatment of pituitary tumors (2). As with any other surgeries, transsphenoidal pituitary surgery also has its complications that may be grouped as minor morbidities, major morbidities or operative mortality. These are, operative mortality that include meningitis, intracranial hemorrhage, hypothalamic injury. Major morbidities include a fresh cranial nerve palsy, meningitis, vascular injury, cerebrospinal fluid rhinorrhea necessitating additional surgery, and a fresh visual loss. Minor illnesses include new anterior pituitary insufficiency, temporary and persistent diabetes insipidus, nasal hemorrhage, transitory cranial nerve palsy, and sinusitis. Others include donor site hemorrhage, sphenoid abscess, hydrocephalus, and pneumocephalus. (2,5)

The best surgical results are achieved with microadenomas, and in these cases, anterior pituitary function can be preserved in up to 95% of patients. With established preoperative hormonal insufficiency, only 10–15% of individuals have full or partially restored endocrine function. After surgery, 85–90% of patients with non–functioning adenomas with pressure effects experience some visual improvement, with up to 40% reaching vision normalcy (2). Currently, in our settings no research study has been done to look at the demographics of the patients that come with pituitary tumors as well as the outcomes of these patient’s post-surgery, this study will bridge that gap.

1.2 PROBLEM STATEMENT

Endoscopic transanasal surgery is a relatively new technique in the Tanzanian health field. Patients with pituitary pathologies are now seen a lot more at the neurosurgical departments at MOI/Mloganzila. Previously patients were treated with an open approach (craniotomies) to access the pituitary tumors at the sellar but, with continuing advancements in technology especially in the endoscopic field, a lot more patients and neurosurgeons'/ Otorhinolaryngology surgeons are opting for endoscopic approach rather than an open approach in accessing these pituitary pathologies. Currently these endoscopic surgeries are done in collaboration between Otorhinolaryngologists and neurosurgeons.

No studies have been done so far in our settings that looked at the clinical presentations of patients who present with pituitary pathologies and require transsphenoidal pituitary surgery, as well of the outcome of such patients after they have undergone surgery. This includes recovery from symptoms or complications of the surgery.

1.3 CONCEPTUAL FRAMEWORKS

This framework is important to clearly understand the clinical profile that patients present with at the outpatient clinics as well as the outcomes of the transsphenoidal surgery. It looks at the independent and dependent variables that are stated below.

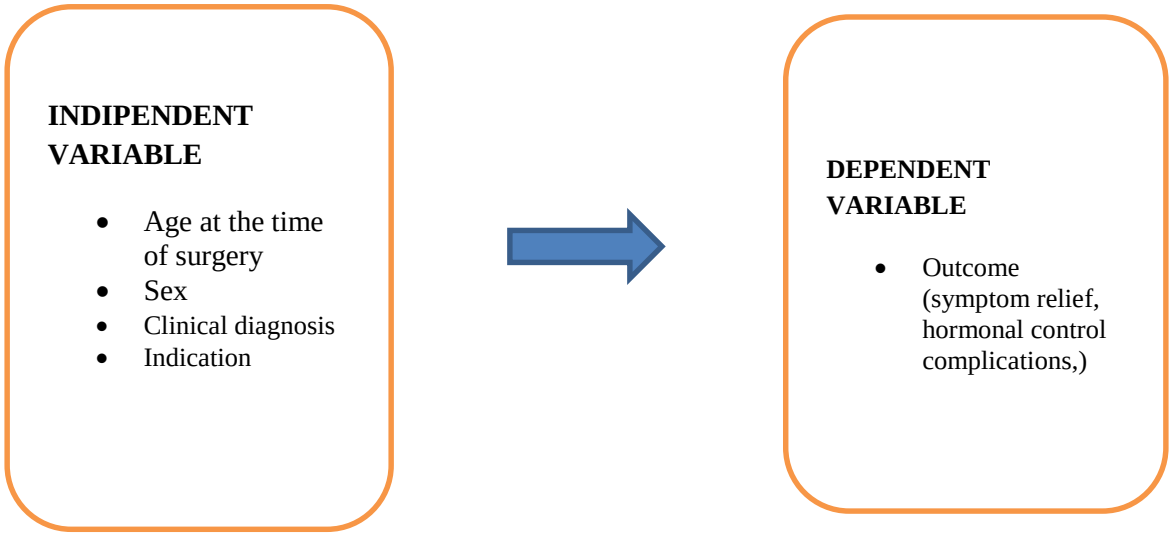


Figure 1: Conceptual framework

1.4 RATIONALE

The goal of this study was to assess the clinical presentation of patients with pituitary pathologies that require endoscopic transsphenoidal surgery. This study aimed at reviewing the indciations of transphenoidal pituitary surgery in our settings as well as to review the outcomes of the surgery.

This study also reviewed the complications as well as if these patients recovered from these surgeries. These complications could also be assesed further and used to improve on our clinical practices so as to avoid them. This study also serves as a starting point for future studies in our country

This study is also a partial fulfilment of the requirements for the award of a master in medicine degree in otorhinolaryngology at MUHAS.

1.5 RESEARCH QUESTION

What is the clinical profile, indication and outcome of patients who underwent transsphenoidal pituitary surgery at Muhimbili National Hospital and Muhimbili Orthopaedic Institute?

1.5.1 SPECIFIC RESEARCH QUESTION

1. What are the demographic characteristics of patients who underwent transsphenoidal pituitary surgery?
2. What are the clinical features among patients prior to transsphenoidal pituitary surgery at MNH and MOI?
3. What are the indications of transsphenoidal pituitary surgery among patients who underwent transsphenoidal surgery?
4. What are the outcomes of transsphenoidal pituitary surgery among patients underwent transsphenoidal surgery?

1.6 BROAD OBJECTIVES

To assess clinical profile, indication and outcome of patients who underwent transsphenoidal pituitary surgery at Muhimbili National Hospital and Muhimbili Orthopaedic Institute

1.6.1 SPECIFIC OBJECTIVES

1. To determine the demographic characteristics of patients who underwent transsphenoidal pituitary surgery
2. To determine the clinical features among patients prior to transsphenoidal pituitary surgery at MNH and MOI.
3. To determine the indications of transsphenoidal pituitary surgery among patients who underwent transsphenoidal surgery.
4. To assess outcomes of transsphenoidal pituitary surgery among patients who underwent transsphenoidal surgery.

CHAPTER TWO

2.0 LITERATURE REVIEW

Transsphenoidal sinus surgery is a surgical procedure used to treat a variety of conditions affecting the pituitary gland, such as acromegaly, Cushing's disease, and prolactinoma. It involves accessing the pituitary gland through the sphenoid bone, which is done by creating a small hole in the nasal cavity. Over the years, transsphenoidal sinus surgery has become increasingly popular as a treatment option for pituitary disorders. In addition to its efficacy, transsphenoidal sinus surgery is also considered safe. A study published in the Journal of Neurosurgery found that the complication rate for the procedure was low, with only 5% of patients experiencing postoperative complications (6).

Demographic characteristics of patients who underwent transsphenoidal pituitary surgery.

A study by Tabaee et al. found that the mean age was 51.2 years, with a range of 20-88 years. Although pituitary tumors have no sex predilection, apart from cortisol secreting adenomas, this study revealed that around 60.9% of the patients were female (7). Another study by Patra Charalampaki et al. revealed that out of the 150 patients; 70 men and 80 women had endonasal transsphenoidal surgery for the removal of sellar lesions under endoscopic guidance. These patients' ages ranged from 26 to 88 years old, with a mean age of 57. (6)

Clinical features among patients prior to transsphenoidal pituitary surgery

Several studies have reported that the most common clinical features of patients with pituitary disorders are headache, visual disturbances, and endocrine abnormalities. These symptoms are often the result of a pituitary adenoma, which is a benign tumor that can grow and compress the surrounding structures, leading to hormonal imbalances and other complications. The clinical presentation of the patient depends on the type of pituitary tumor i.e. Microadenoma versus macroadenoma or secreting versus non secreting tumor. (8)

A study done by Marta Araujo-Castro et al revealed the clinical presentations of pituitary tumors which can be divided into hormonal manifestations, mass effect manifestations, pituitary incidentaloma and pituitary apoplexy (9). Functional pituitary tumors account for 48 to 78% of all pituitary tumors and mostly present as prolactin secreting tumors, Cushing syndrome, hyperthyroidism or growth hormone secreting tumors. Patients with these tumors can present with a range of symptoms from infertility and milk production in prolactinomas to acromegaly/gigantism in growth hormone secreting tumors. (9)

Mass effect of pituitary tumors is usually caused by macroadenomas, microadenomas can cause mass effect depending on their location. The most common presentation of patients with mass effect of pituitary tumors is visual impairment which is around 13-60.8% of patients, which is described as visual hemianopia. This is due to optic nerve compression. Headache is the another common mass effect manifestation seen in 37-70% of pituitary tumors and is described as a migraine or tension-type headaches. These are believed to be caused by the stretching of the dura sheath. (9,10)

Large pituitary tumors that grow out of the sellar and extend posteriorly and superiorly may cause obstructive hydrocephalus due to involvement of the third ventricles. As a result, intracranial pressure rises, which can lead to a variety of symptoms including headache, nausea, papilledema, loss of bladder control, memory loss, poor coordination or balance, irritability, personality changes, attention deficit disorders, lethargy, or even coma (9,10). If the tumor then grows anteriorly and involves the frontal lobe of the brain then the patient may present with generalized seizures or dementia, anterior extension with nasal obstruction, nasal bleeding or rhinorrhea. If the tumor, then extends inferiorly it can cause craniocervical joint instability; and posterior extension with brainstem compression and cerebellar syndrome (8,9).

Patients with pituitary apoplexy present with headache (80%), nausea, decreased vision or field (50%), ophthalmoplegia/paresis, and altered mental status are among the symptoms. Pituitary apoplexy always starts with at least one anterior pituitary deficit. The most prevalent

and significant impairment in patients with pituitary apoplexy, affecting 60 to 80% of patients, is corticotropic deficiency.(9,11)

Indications of transsphenoidal pituitary surgery among patients who underwent transsphenoidal surgery.

The pituitary gland is a small gland located at the base of the brain that produces and secretes hormones that regulate various bodily functions, including growth, metabolism, and reproduction. Tumors in this area may cause overproduction of these hormones or can cause mass-effects that can lead to surgical removal of these tumors (5). The general and common indications for transsphenoidal pituitary surgery are pituitary apoplexy, progressive mass effect, control of hormonal hypersecretion, histological diagnosis of sellar tumors (biopsy) (2). Pituitary apoplexy is a surgical emergency and requires immediate removal of the hematoma or necrotic tissue so as to relieve the mass effect characterized by acute visual loss or cranial nerve palsies. (2,11)

The progressive mass effects of pituitary tumors usually seen in macroadenomas are also indications for transsphenoidal sinus surgery. Patients usually present with reduced visual field and acuity and surgery is done to decompress the tumor to prevent further loss of visual field (2). A study done by Mendel Castle-Kirszabaum et al revealed that 71.6% of the 304 patients in their study had a complete or partial improvement in visual field acuity after surgery (12).

‘Surgical cure’ is possible for patients who have pituitary tumors that are secretory and present with acromegaly or Cushing’s disease. This will work in tandem with medical or radiological therapy to help control and maintain the normal hormone levels in the blood. (2) A study done by Robert M Starke et al revealed that hypercortisolemia resolved in 95% of all patients after endoscopic transphenoidal pituitary surgery (13).

Outcome of transsphenoidal pituitary surgery among patients who underwent transsphenoidal surgery.

Endoscopic transsphenoidal pituitary surgery has become the treatment of choice and has shown to have good success in tumor removal with low remission. But transsphenoidal sinus surgery has also its complications. One of the indications for transsphenoidal surgery was pituitary apoplexy, a study done by Osamah J. Choudhryet al showed that the patients who had to undergo emergency surgery all recovered from the pituitary apoplexy, had gland function and improvement in visual field and other mass effect symptoms after surgery (14).

The other indication for transsphenoidal pituitary surgery is progressive mass effect which a study done by Shabin Man Joshi et al showed that in non-functioning adenomas, with pressure effects, 85–90% of patients gain some improvement in their vision following surgery, with normalisation of vision in up to 40% (2). Another indication for transsphenoidal pituitary surgery was the control of pituitary hormones. A study done by AbdMoainAbu. Dabrh et al on the outcome of transsphenoidal surgery on cortisol secreting pituitary tumors showed that it had a high remission of 76% and low recurrence rate of just 10% (15). Also a study done by Harish Babu et al revealed that 71% of the 58 patients who underwent endoscopic transsphenoidal sinus for the treatment for acromegaly were in remission after follow up (7,16).

One of the most common complications of transsphenoidal pituitary surgery is cerebrospinal fluid (CSF) leakage. A study by Youssef et al, reported a CSF leakage rate of 8.5% in 1,159 patients who underwent transsphenoidal surgery. Another study have reported leakage rates ranging from 3.6% to 20% (17). CSF leakage can lead to meningitis, intracranial abscess, and other serious infection (6). Another complication of transsphenoidal pituitary surgery is pituitary hormone deficiency. The pituitary gland produces several hormones that regulate various bodily functions, and damage to the gland during surgery can result in hormonal imbalances. A study found that 11% of patients who underwent transsphenoidal surgery developed postoperative pituitary hormone deficiency (18). Another study by Raverot et al, reported that 16.4% of patients developed hypopituitarism following surgery (7).

In addition to CSF leakage and pituitary hormone deficiency, other complications of transsphenoidal pituitary surgery include visual disturbances, vascular injury, and infection. A study by Roldan Urgoiti et al, reported that 5% of patients who underwent surgery experienced visual disturbances, such as double vision or visual field defects. Vascular injury can occur during surgery, resulting in hemorrhage and stroke. Infection is also a risk, with reported rates ranging from 0.7% to 10.8% (19). Death and disability have also been reported in cases of endoscopic transsphenoidal surgery but these are rare. A retrospective study of patients done for 25 years showed a death and disability rate of 0.26% to 1%. (20).

These tumors are usually assessed through laboratory results prior to surgery if they are secretory or non-secretory tumors and are then sent for histology after being removed by TSS to see if they are malignant or benign. Majority of pituitary tumors are benign (16,18). Ahmed Mohyeldin et al observed that the histological diagnosis of these tumors removed after surgery was corticotroph, gonadotroph, somatotroph, lactotroph, null-cell and plurihormonal tumors (21). Corticotroph (cortisol-secreting) was found to be the most common follow by gonadotroph, somatotroph and lactotroph. Null-cell and plurihormonal tumors were seen in lower amounts.(21).

In a study done by Matthew et al, complications following transsphenoidal pituitary surgery was seen more in patients with prior surgery (11.4%), preoperative vision loss (10.3%) and patients with pituitary tumor invasion (8.5%) (20). Patients with macroadenomas that extended into the suprasellar region also presented with worst complications including CSF leak, hemorrhage and even death as seen by Charalampaki et al (6). A study done by Babu et al showed that transphenoidal pituitary surgery had great effect in controlling pituitary hormones where by in 58 patients between 65-77% of the patients were in remission up-to 8years post-surgery (16). Therefore, it is seen that clinical presentation/clinical diagnosis plays a role in surgical complications but also transphenoidal surgery has been shown to help control hormone secretion and relieve symptoms.

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study area

This study was conducted at Muhimbili National Hospital which has two campuses one at Ilala district of Dar es Salaam and the other campus is Mloganzila located in Kibamba. The hospital receives referral patients from around Tanzania mainland, Zanzibar and neighboring countries. Muhimbili has 25 departments and ten specialized care units. Otorhinolaryngology is one of the 25 departments.

Transsphenoidal pituitary surgery is done at MOI which is attached to Muhimbili National Hospital. Muhimbili Orthopaedic Institute is the largest orthopaedic and neurosurgical referral center in the country. It has outpatient clinics from Monday to Saturday with private clinics being on Wednesday and Friday. The first clinic visits as well as follow up of patients is also done at the neurosurgery clinic. Around 4 to 5 transsphenoidal pituitary surgeries are done per month. The follow up is usually a monthly then 3 monthly and then 6 monthly.

3.2 Study Design

This was a hospital based retrospective cross-sectional study.

3.3 Study Duration

This study duration is 3 months.

3.4 Study Population

All patients who underwent transsphenoidal pituitary surgery at MOI and Mloganzila during the study period.

3.5 3.5 Sample size and Sampling technique

By using Slovin's formula

$$\text{Sample size } n = \frac{N}{1 + N£^2}$$

£ - this is the margin of error 5% = 0.05

N= 40, this is the number of patients who underwent transsphenoidal pituitary surgery so far

$n= 40/ (1+ (40 \times 0.05^2)) = 33$

n= 36

10% will be added to cover the patients whose files are inadequate (n=4); therefore, the minimal sample size will be **40**.

3.6 INCLUSION AND EXCLUSION CRITERIA

3.6.1 Inclusion criteria

All patients who were seen at the clinic within one month after transsphenoidal pituitary surgery.

3.6.2 Exclusion criteria

Patients who have undergone previous pituitary surgeries or open brain surgeries.

Patients with secondary/metastatic tumors to the pituitary gland.

3.7 DATA COLLECTION TECHNIQUE

By using a structured checklist, medical records of the patients were obtained from the records system from the first patient in 2018, no patient was contacted to recall initial symptoms or signs. All findings on the clinical presentation, indication, outcome of the surgery and histological diagnosis of the pituitary tumors was recorded in the data sheet. Convenient sampling method was used to collect the data.

3.8 DEFINITION OF VARIABLES

3.8.1 Independent variable

In this study the independent variables are the demographic characteristics of the patient which includes age at the time of surgery, sex

3.8.2 Dependent variable

The dependent variable is the clinical diagnosis, indication for surgery, outcome of the surgery including relief of symptoms, complications and histological diagnosis.

3.9 DATA ANALYSIS

After data collection, collected data was evaluated for accuracy, consistency and completeness then analyzed using a statistical software. Variables were analyzed and presented using frequency distribution tables and diagrams; continuous variables were calculated using mean and standard deviation. This was done with the aid of Statistical Package for Social Science version 23.

Association between clinical profile and indication of surgery with outcome of surgery was analyzed. The chi square and fisher exact t-test were used to measure association**.** The level of significance which was used is 0.05 for a 95% confidence. Hence a p-value of less than or equal to 0.05 was considered statistically significant.

3.9.1 Descriptive Analysis of Variables

Tables were used to present statistics of the measured sample and variables. Frequencies were used to evaluate the age, sex, clinical complaints, indication and outcomes of the patients. The Mean and standard deviation were used to determine the age of the participants. Association with use of chi square and fischer exact test were used to check for the association between age and sex and the indication, outcomes of the patients.

3.10 3.10 Ethical issues

The Muhimbili University of Health and Allied Sciences (MUHAS) ethical committee and MNH research publication department approved for the study to be conducted. The Muhimbili Orthopedic Institute granted permission for accessing the data.

3.10.1 The waiver of consent

This study was conducted using secondary data from the system held in the hospital archive under the custody of MNH and MOI. The data that was accessed included presenting symptoms and signs, indication and outcome of the transsphenoidal pituitary surgery, therefore this research carried not more than minimal risk to the subjects as private /personal information wasn’t accessed. Also loss to follow-up and death would affect the results if informed consent was to be sought for each subject. Given the factors stated above the consent was waived in this research.

3.10.2 Confidentiality

No names of the patients were taken and recorded. Each subject was given an unidentifiable serial number so as to keep their data confidential. All other identifying information was kept secret and away from the results. Only investigators had access to this information and was only used for the purpose of the study.

3.11 Study Limitations

Endoscopic transsphenoidal pituitary surgery is a relatively new technology in our settings, very few patients had undergone such surgeries. Therefore, findings from this study may not represent the outcomes of patients in the future as expertise increases and technology advances. The collection of data relied on good documentation in the system, this is therefore prone to bias where there's poor documentation.

CHAPTER FOUR

4.0 RESULTS

4.1 Demographic characteristics of patients who have undergone transsphenoidal pituitary surgery

A total of 40 patients who underwent transsphenoidal pituitary surgery at MNH and MOI were enrolled into the study. Majority of the patients were females and accounted for 57.5% (n=23). Males accounted for 42.5% (n=17) of the patients with a female to male ratio of 1.3:1. The participants age ranged from 25 to 69 years of age with a mean age of 49.9 years. The age group of 41-50 years accounted for 30% (n=12) of all participants and was followed by 31-40, 51-60 and more than 61years which accounts for 22.5% (n=9) each. The least common age group was 21-30 which accounted for 2.5%(n=1). Males were found to be more in the age of 41-50 years 41.1% (n=7) followed by the age group of 51-60 at 29.4% (n=5). Females were found more in the age group of >61 at 34.8% (n=8), followed by the age group of 31-40 at 26.1% (n=6). [Table 1]

Table 1: Demographic characteristics of study participants

		AGE GROUPS(years)					
SEX		**21-30 n(%)**	**31-40 n(%)**	**41-50 n(%)**	**51-60 n(%)**	**>61 n(%)**	**Total (%)**
	Male	1(5.9)	3(17.6)	7(41.1)	5(29.4)	1(5.9)	**17 (42.5)**
	Female	0(0)	6(26.1)	5(21.7)	4(17.4)	8(34.8)	**23 (57.5)**
	Total(%)	**1(2.5)**	**9(22.5)**	**12(30)**	**9(22.5)**	**9(22.5)**	**40 (100)**

4.2 Clinical features among patients prior to transsphenoidal pituitary surgery

The most common presenting clinical feature was due to mass effect where by vision loss was the most common chief complaint accounting for 87.5% (n=35), followed by headache which accounted for 85% (n=34). The least common clinical finding observed was papilledema 5% (n=2). [Figure 1]. Of the 40 participants, 17.5% of the pituitary adenomas were secretory. All the patients found to have hormonal effect also presented with mass effect. [Table 2]

Figure 2: Clinical features due to mass effect

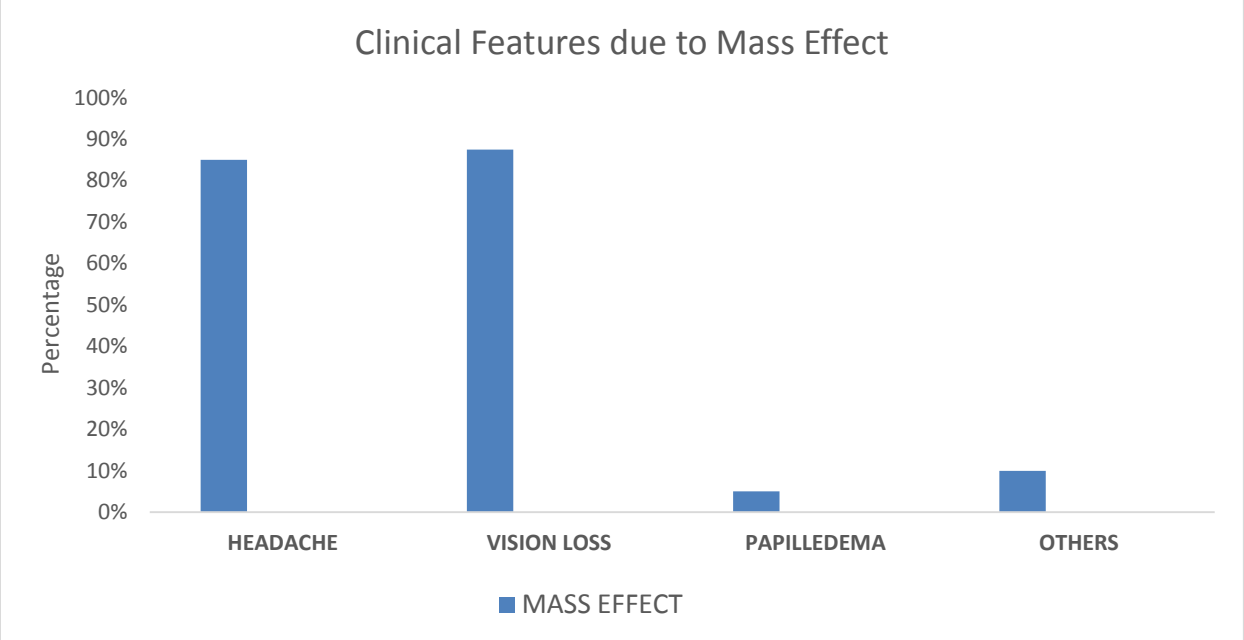


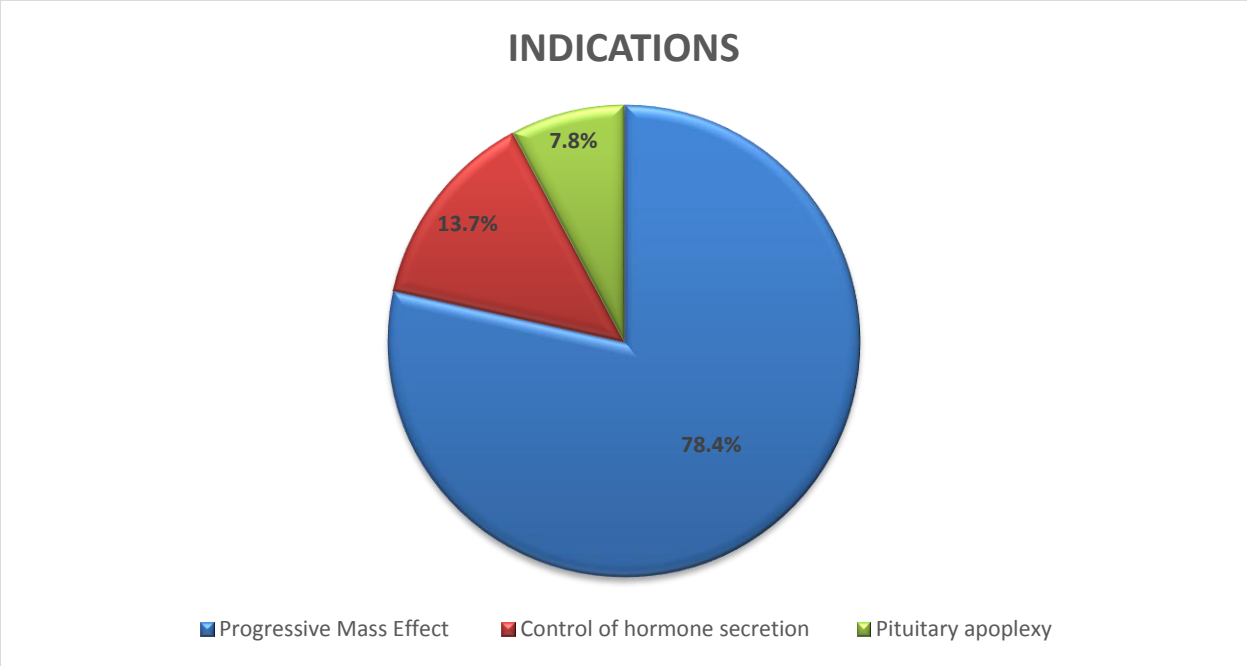
Table 2: Hormonal effect of pituitary tumors

		Frequency (%)
HORMONAL EFFECT	**Secretory**	**7 (17.5)**
	Non-secretory	**33 (82.5)**
	Total	**40 (100)**

4.3 Indications of transsphenoidal pituitary surgery among patients who underwent transsphenoidal surgery.

Among the 40 patients who underwent transsphenoidal pituitary surgery they had 3 main indications where by progressive mass effect accounted for the majority of the indications 78.4% (n=40) followed by control of hormone secretion at 13.7% (n=7) and the least being pituitary apoplexy 7.8% (n=4). [Figure 3]

Figure 3: Indications of transsphenoidal pituitary surgery



As shown in table 3, all patients presented with progressive mass effect. The age group found to have the highest indication for hormonal control was 31-40 years (33%) followed by 41-50 years (25%) and the age groups 21-30 years and 51-60 years had no patient with indication for hormonal control. However, this difference is not statistically significant as Fischer's Exact test was found to be 0.405. The age group which presented with pituitary apoplexy as an indication was seen mostly in 31-40 years whereby 22.2% had pituitary apoplexy, followed by ages >61 years whereby 11.1 % had pituitary apoplexy. No patient with pituitary apoplexy was seen in the age groups of 21-30 and 51-60 years. However, this difference is not statistically significant as Fischer's Exact test was 0.729. [Table 3]

Table 3: Association between indication and age of patients undergoing transsphenoidal surgery

		PROGRESSIVE MASS EFFECT	CONTROL OF HORMONE		TOTAL(%)	P value	PITUITARY APOPLEXY		TOTAL(%)	P value
			YES n(%)	NO n(%)			YES n(%)	NO n(%)		
AGE GROUP (years)	**21-30**	1	0(0)	1(100)	1(2.5)	0.405	0(0)	1(100)	1(2.5)	0.729
	31-40	9	3(33.3)	6(66.7)	9(22.5)		2(22.2)	7(77.8)	9(22.5)	
	41-50	12	3(25)	9(75)	12(30)		1(8.3)	11(91.7)	12(30)	
	51-60	9	0(0)	9(100)	9(22.5)		0(0)	9(100)	9(22.5)	
	>61	9	1(11.1)	8(88.9)	9(22.5)		1(11.1)	8(88.9)	9(22.5)	
	TOTAL	**40**	**7(17.5)**	**33(82.5)**	**40(100)**		**4(10)**	**36(90)**	**40(100)**	

As seen in table 4, all patients presented with progressive mass effect. Females were found to have the highest indication for surgery due to hormonal control whereby 21.7% of them had an indication for hormonal control and 11.8% in males. This was not statistically significant as Fischer's Exact test was 0.677. Pituitary apoplexy was found to be the most common indication for surgery in male patients with 11.8% and female patients had 8.7%. However, this was statistically not significant as the Fischer exact test was 1.000. [Table 4]

Table 4: Association between indications and sex of patients undergoing transsphenoidal surgery

		PROGRESSIVE MASS EFFECT	HORMONAL CONTROL		TOTAL	P value	PITUITARY APOPLEXY		TOTAL	P Value
			YES n(%)	NO n(%)	n(%)		YES n(%)	NO n(%)	n(%)	
SEX	**MALE**	17	2(11.8)	15(88.2)	17(42.5)	0.677	2(11.8)	15(88.2)	17(42.5)	1.000
	FEMALE	23	5(21.7)	18(78.3)	23(57.5)		2(8.7)	21(91.3)	23(57.5)	
	TOTAL	**40**	**7(17.5)**	**33(82.5)**	**40(100)**		**4(10)**	**36 (90)**	**40(100)**	

4.4 Outcome of transsphenoidal pituitary surgery among patients who underwent transsphenoidal surgery

As shown in table 5, of the patient who underwent transsphenoidal pituitary surgery 85% (n=34) had a relief of progressive massive effect symptoms, 71.4% (n=5) had hormonal control post tumor surgery and only 2.5% (n=1) had no relief of symptoms or control of hormone secretion. Some of the patients had complications linked to the surgery which were divided into early and late complications. The most common early complication was diabetes insipidus 12.5% (n=5) which was followed by CSF leak 7.5% (n=3), there was no reports of worsening or new visual loss as well as any early infection signs seen. The most common late complications was hypopituitarism 12.5% (n=5) followed by meningitis 5% (n=2) and the least reported late complication was CSF leak 2.5 % (n=1). No patient was seen with early signs of infection. One patient was reported to have died as an outcome of these complications [Table 5]

Table 5: Post-operative outcomes of patients who underwent transsphenoidal surgery

OUTCOME		Frequency (%)
POSITIVE OUTCOMES	**Symptom relief (n=40)**	**34 (85)**
	Hormonal control (n=7)	**5 (71.4%)**
	No relief/hormone control (n=40)	**1 (2.5)**
	Total	**40 (100%)**
COMPLICATIONS (n=40)		Frequency (%)
EARLY <7days	**Bleeding**	**1 (2.5)**
	CSF leak	**3 (7.5)**
	Diabetes insipidus	**5 (12.5)**
	Pneumocephalus	**1 (2.5)**
	Meningitis	**2 (5)**
LATE >7 days	**Hypopituitarism**	**5 (12.5)**
	CSF leak	**1 (2.5)**

As seen in table 6, of the patients who underwent transsphenoidal pituitary surgery in the age groups of 21-30 and 31-40 100% of them had complete symptoms relief, followed by ages of 41-50 (91.7%). Patients in the age groups of >61 had the highest percentage with no symptom relief at 44.4%. However, this different was not statistically significant (Fischer's Exact Test= 0.108). Majority of males had symptom relief 94.1% (n=16) and the female sex had 78.3% (n=18). This difference was not statistically significant (Fischer's Exact Test = 0.216). [Table 6]

Table 6: Relationship between symptoms relief with age and sex

		SYMPTOM RELIEF			
		Yes n(%)	**No** n(%)	**Total** n(%)	
AGE GROUPS (years)	**21-30**	1(100)	0 (0)	1(2.5)	P Value 0.108
	31-40	9(100)	0 (0)	9(22.5)	
	41-50	11(91.7)	1(8.3)	12(30)	
	51-60	8(88.9)	1(11.1)	9(22.5)	
	>61	5 (55.6)	4(44.4)	9(22.5)	
	TOTAL	**34 (85)**	**6 (15)**	**40(100)**	
SEX	**MALE**	16(94.1)	1(5.9)	17(42.5)	P Value 0.216
	FEMALE	18(78.3)	5(21.7)	23(57.5)	
	TOTAL	**34 (85)**	**6 (15)**	**40(100)**	

As seen in table 7, of the patients who presented with hormonal symptoms, the age group of 31-40 had 100% hormonal control post-surgery followed by the age group of 41-50 (66.7%). The age group of >61, 100% (n=1) of the patients had no hormonal control. This difference is not statistically significant (Fischer's Exact Test = 0.204). Hormonal control was seen in 13% (n=3) of the female patients and 11.8% (n=2) of the male patients. This difference is seen to be statistically insignificant (Fischer's Exact Test = 1.00). [Table 7]

Table 7: Relationship between hormonal control with age and sex

		HORMONAL CONTROL			
		Yes	**No**	**Total**	
AGE GROUP	**21-30**	0 (0)	0 (0)	0 (0)	P Value 0.204
	31-40	3(100)	0 (0)	3(43)	
	41-50	2(66.7)	1(33.3)	3(43)	
	51-60	0 (0)	0(0)	0(0)	
	>61	0 (0)	1(100)	1(14)	
	TOTAL	**5 (71.4)**	**2(28.6)**	**7 (100)**	
SEX	**MALE**	2(100)	0(0)	2(28.6)	P Value 1.000
	FEMALE	3(80)	2(40)	5(71.4)	
	TOTAL	**5(71.4)**	**2(28.6)**	**7(100)**	

As seen in table 8, age group with the most complications was seen in 41-50, 50% followed by the age group of 31-40, 51-60, >61 44.4%. The age group of 21-30 was seen to have no complications. This difference is not statistically significant (Fischer's Exact Test = 0.325). The female sex had 61.1% (n=11) complications post-surgery and 38.9% (n=7) of the male sex had complications post-surgery. This is not statistically significant (Fischer's Exact Test = 0.425). [Table 8]

Table 8: Association between complications with age and sex

		COMPLICATIONS			
		Yes	**No**	**Total**	
AGE GROUP	**21-30**	0(0)	1(100)	**1(2.5)**	P Value 0.325
	31-40	4(44.4)	5(55.6)	**9(22.5)**	
	41-50	6(50)	6(50)	**12(30)**	
	51-60	4(44.4)	5(55.6)	**9(22.5)**	
	>61	4(44.4)	5(55.6)	**9(22.5)**	
	TOTAL	**18 (100)**	**22(100)**	**40(100)**	
SEX	**MALE**	7(38.9)	10(58.8)	**17(42.5)**	P Value 0.425
	FEMALE	11(61.1)	12(52.2)	**23(57.5)**	
	TOTAL	**18(45)**	**22(55)**	**40(100)**	

CHAPTER FIVE

5.0 DISCUSSION

Transsphenoidal pituitary surgery is increasingly preferred mode of surgery around the world as an approach to pituitary tumors. It is now considered as the first-line treatment of most pituitary adenomas. It provides an access to the pituitary gland that is cosmetic with less blood loss and equal outcomes if not better to that of an open approach.(4,8,22) Very few studies have been done in our setting showing the clinical characteristics of these patients, the common indication and the outcome of these patients.

A total of 40 patients were enrolled, whereby the youngest was aged 25 and the oldest aged 69 with a mean age of 49.9 years. The female to male ratio was 1.3:1. These findings are similar to a study done in China, India and Senegal (4,22,23). Majority of the patients seen were in the age group of 41-50 which accounted for 30% and this can be explained with majority of the patients with pituitary adenoma were seen between the age of 30-55. These findings are similar to a study which was done in Kenya (8).

Among the 40 patients the common presenting symptom was due to mass effect of the pituitary tumor. This is described as increase in size of the tumor resulting in invasion of near structures like the optic nerve, ventricles blocking the flow of the cerebrospinal fluid and causing increased intracranial hypertension. Vision loss due to mass effect was seen in 87.5% of all complaints reported by the patients. This is seen in similar studies in Kenya, China, Senegal, India (8,22–24). Most of the patients with vision loss presented with bi-temporal hemianopia due to compression or invasion of the optic chiasma (9). Similar findings were also seen in Saudi Arabia (12).

The second most common complaint by patients due to mass effect was headache. This is explained by a compressive effect of the mass into the ventricles and cranial space causing increase in the intracranial pressure. This was seen in 85% of the patients. Increase in intracranial pressure also showed signs of papilledema which was seen in 5% of patients. Other mass effects seen as a result of increased intracranial pressure and also craniocervical

joint instability which was seen in 10% of patients. These findings are similar to studies done in Senegal, Kenya, USA and India (1,8,22,24,).

Pituitary tumors are also described as secretory (secreting hormones) and non-secretory. In the 40 patients that were enrolled in the study, only 17.5% (n=7) of these patients presented with secretory tumors, whereby higher than normal levels of hormones were found in the blood as well as presenting with symptomatic effects of these hormones. These were cortisol secreting adenomas, prolactinomas and growth hormone secreting adenomas. These are similar findings seen by Marta Araujo-Castro et al (9,23).

For the patients to have undergone transsphenoidal pituitary surgery, tumors of the pituitary gland had to be accessible from the sphenoid sinus and removed completely through TSS and this was for all the 40 patients. The indications for these patients to undergo surgery were due to progressive mass effect, for hormonal secretion control and if a patient presented with pituitary apoplexy which is in an emergency. Progressive mass effect was seen as the most common indication accounting for 78.4%, followed by control of hormone secretion at 13.7% and pituitary apoplexy was seen in 7.8% of all indications. These findings are similar to those seen in India, Senegal , China and South Africa (8,11,14,22). Also similar findings were reported by Araujo-Castro et al (9).

The age group of 31-40 years was found to have the highest percentage (33.3%) of patients with indication of surgery for hormone control and was also found to be more in females (21.7%) indication for hormonal control. This is similar to the study seen in Senegal (23), but in this study it was not found to be statistically significant (p value of 0.405 and 0.677 respectively).

Pituitary apoplexy is a surgical emergency whereby there's sudden onset of hemorrhage in the tumor resulting in sudden loss or deterioration of vison loss, convulsions or loss of consciousness. This was seen more in the age group of 31-40 years and was found more in the male sex 11.8% compare to the female 8.7%. Similar findings were seen in a study done in the USA and South Africa (11). But these differences between the age and sex are not statistically significant (p value of 0.729 and 1.000 respectively).

The outcome of transsphenoidal pituitary surgery can be divided into positive outcomes (symptom relief, hormonal control) or complications. In this study, 34 patients reported to have had symptom relief post-surgery which accounted for 85%. These included improvement in vision, less headaches and no signs of increased intracranial pressure. This finding is similar to multiple studies seen in USA, Senegal, Saudi Arabia, India and South Africa (4,10,12,23). Hormonal control was seen in 5 patients of the 7 that had an indication for surgery secondary to hormonal control, whereby this accounts for 71.4%. These findings were seen in a similar meta-analysis done in USA (6,26).

Intermittent/reversible diabetes insipidus was the most reported early complication seen within the first 1week post-surgery. It was reported in 12.5% of patients and these patients recovered from this. These findings are much lower than a study done in Senegal whereby 47.4% of those patients developed diabetes insipidus (23), but these findings are also much higher than seen in studies done in the USA whereby percentages of less than 6% were reported (20,26). Also, Shabin et al saw lower rates of diabetes insipidus of up to 2-3% (2). These findings could be explained with the large sample sizes observed in these studies.

Vascular injury was seen in 2.5% of patients in this study which is similar findings reported by Shabin et al (2). Also a study done in Germany found the occurrence of vascular injury within the same range 2-4% (6).Cerebrospinal fluid leak is one of the commonest reported complaint post transsphenoidal sinus surgery. In this study it was seen in 7.5% of patients as an intra-op or early complication and only 1 (2.5%) patient reported a later/persistent complaint more than 1 week. These findings are lower than studies done in Senegal and Brazil whereby 11.6% and 9% (23,27), but these findings are much higher than studies done in the USA, Europe whereby CSF leak occurrence was less than 4% (6,7). These findings could be explained with the large sample sizes observed in these studies.

Meningitis was seen in 5% of the patients in this study. These reported findings are higher than those seen in the West whereby most studies report an occurrence of 1-3% (2,6,7).Hypopituitarism or hypo-function of the pituitary axis after surgery is also a common complaint or outcome post-surgery whereby, 12.5% were seen with pituitary hypo-function.

These findings were actually found to be similar to those observed in the USA, Europe as well as Brazil whereby pituitary axis hypo-function was seen to range from 9-15% (6,7,20,27).

Death was seen in 1 patient which accounted for 2.5%. These findings are lower than those seen in Senegal whereby 7.4% of the patients were reported to have died (23). These findings are similar in range to a study done in Brazil whereby death was observed in 1-2% (27). But mortality reported studies done in USA was seen to be <1% (6,7).

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATION

6.1 CONCLUSION

Transsphenoidal pituitary surgery is a novel/modern approach to pituitary tumors in Muhimbili National Hospital and Muhimbili Orthopedic Institute. Most patients were seen in the middle age and females accounted more than males. Patients presented with various clinical complaints whereby vision loss and headache accounted for majority of the complaints. The most common indication was due to mass effect. Majority of patients reported symptom relief and hormonal control post-surgery whereby the most common complication was diabetes insipidus and hypopituitarism. Therefore, this study helps on shedding light as well as contribute to the existing knowledge of surgeons as well as the medical community to improve outcomes of these patients.

6.2 RECOMMENDATIONS

Transsphenoidal pituitary surgery is still a relative new approach in MNH/MOI. As we have seen, there's minimal complications observed in this approach. Variety of inidcations were seen and all were managed by this approach. Patient's presented with symptom relief and hormonal control post-surgery. This shows that this approach is the best option and more coverage is needed for Otorhinolaryngology surgeons as well as Neurosurgeons. This should be the main modality for approaching pituitary tumors. Therefore, further studies should be done on this approach as well as the patients who undergo this procedure.

7.0 REFFERENCES

1. Verillaud B, Bresson D, Sauvaget E, Mandonnet E, Georges B, Kania R, et al. Endoscopic endonasal skull base surgery. Eur Ann Otorhinolaryngol Head Neck Dis [Internet]. 2012;129(4):190–6. Available from: http://dx.doi.org/10.1016/j.anorl.2011.09.004

2. Joshi SM, Cudlip S. Transsphenoidal surgery. Pituitary. 2008;11(4):353–60.

3. Moses Penduka, Semple P, Lubbe D. Endoscopic transsphenoidal (ETSS) pituitary surgery tecnique. Open Access Atlas Otolaryngol , Head Neck Oper Surg [Internet]. 2008;1–12. Available from: www.entdev.uct.ac.za

4. Yadav YR, Sachdev S, Parihar V, Namdev H, Bhatele PR. Endoscopic endonasal trans-sphenoid surgery of pituitary adenoma. Vol. 3, Journal of Neurosciences in Rural Practice. 2012. p. 328–37.

5. Miller BA, Ioachimescu AG, Oyesiku NM. Contemporary indications for transsphenoidal pituitary surgery. World Neurosurg [Internet]. 2014;82(6):S147–51. Available from: http://dx.doi.org/10.1016/j.wneu.2014.07.037

6. Charalampaki P, Ayyad A, Kockro RA, Perneczky A. Surgical complications after endoscopic transsphenoidal pituitary surgery. J Clin Neurosci [Internet]. 2009;16(6):786–9. Available from: http://dx.doi.org/10.1016/j.jocn.2008.09.002

7. Tabaee A, Anand VK, Barrón Y, Hiltzik DDH, Brown SM, Kacker A, et al. Endoscopic pituitary surgery: A systematic review and meta-analysis: Clinical article. J Neurosurg. 2009;111(3):545–54.

8. Kiboi J., Kitunguu P., Musau C., Mwang'ombe N. AJNS – African Journal of Neurological Sciences | » CLINICAL EXPERIENCE AND OUTCOME OF PITUITARY SURGERY IN KENYAN PATIENTS AT THE KENYATTA NATIONAL HOSPITAL. African J Neurol Sci [Internet]. 2010;31(2):200–50. Available from: https://ajns.paans.org/clinical-experience-and-outcome-of-pituitary-surgery-in-kenyan-patients-at-the-kenyatta-national-hospital/

9. Araujo-Castro M, Berrocal VR, Pascual-Corrales E. Pituitary tumors: epidemiology and clinical presentation spectrum. Hormones. 2020;19(2):145–55.

10. Suri H, Dougherty C. Clinical Presentation and Management of Headache in Pituitary Tumors. Curr Pain Headache Rep. 2018;22(8).

11. Semple PL, De Villiers JC, Bowen RM, Lopes MBS, Laws ER. Pituitary apoplexy: Do histological features influence the clinical presentation and outcome? J Neurosurg. 2006;104(6):931–7.

12. Castle-Kirszbaum, M., Wang, Y.Y., King J et al. Predictors of visual and endocrine outcomes after endoscopic transsphenoidal surgery for pituitary adenomas. J

Neurosurg [Internet]. 2021;45(1):843–53. Available from: https://link.springer.com/article/10.1007/s10143-021-01617-y

13. Starke RM, Reames DL, Chen CJ, Laws ER, Jane JA Jr. Endoscopic transsphenoidal surgery for cushing disease: techniques, outcomes and predictors of remission. N 2013 F-7; discussion 247. doi: 10. 1227/NEU. 0b013e31827b966a. P 23149974. TSS as a cure for Cushings Disease.

14. Choudhry OJ, Choudhry AJ, Nunez EA, Eloy JA, Couldwell WT, Ciric IS, et al. Pituitary tumor apoplexy in patients with Cushing's disease: Endocrinologic and visual outcomes after transsphenoidal surgery. Pituitary. 2012;15(3):428–35.

15. Dabrh AMA, Ospina NMS, Al Nofal A, Farah WH, Barrionuevo P, Sarigianni M, et al. Predictors of biochemical remission and recurrence after surgical and radiation treatments of cushing disease: A systematic review and meta-analysis. Endocr Pract. 2016;22(4):466–75.

16. Babu H, Ortega A, Nuno M, Dehghan A, Schweitzer A, Bonert HV, et al. Long-Term Endocrine Outcomes Following Endoscopic Endonasal Transsphenoidal Surgery for Acromegaly and Associated Prognostic Factors. Neurosurgery. 2017;81(2):357–66.

17. Bharadwaj, S., Kasaliwal, R., Sankhe, S. S., Lila, A. R., Budyal, S. R., Bhadada, S. K. & M. Postoperative CSF leakage in endoscopic endonasal transsphenoidal surgery for pituitary adenoma and the efficacy of the preventive use of a nasoseptal flap. J Neurosurg Anaethesiology. 2015;27:350–1.

18. Buchfelder, M., Schlaffer, S. M., Lin, F., & Willenberg HS (2017). Pituitary function before and after pituitary surgery for nonfunctioning pituitary adenoma. Eur J Endocrinol [Internet]. 189(2):217–24. Available from: https://doi.org/10.1093/ejendo/lvad104

19. Dusick, J. R., Esposito, F., Malkasian, D., Kelly, D. F., & Hamilton BE (2015). Avoidance of postoperative cerebrospinal fluid leaks following anterior skull base surgery. J Neurosurg [Internet]. 2015;944–50. Available from: https://doi.org/10.3109/00016489.2013.793821

20. Agam MS, Wedemeyer MA, Wrobel B, Weiss MH, Carmichael JD, Zada G. Complications associated with microscopic and endoscopic transsphenoidal pituitary surgery: Experience of 1153 consecutive cases treated at a single tertiary care pituitary center. J Neurosurg. 2019;130(5):1576–83.

21. Mohyeldin A, Katznelson LJ, Hoffman AR, Asmaro K, Ahmadian SS, Eltobgy MM, et al. Prospective intraoperative and histologic evaluation of cavernous sinus medial wall invasion by pituitary adenomas and its implications for acromegaly remission outcomes. Sci Rep [Internet]. 2022;12(1):1–13. Available from: https://doi.org/10.1038/s41598-022-12980-1

22. Fan Y ping, Lv M hui, Feng S yan, Fan X, Hong H yu, Wen W ping, et al. Full Endoscopic Transsphenoidal Surgery for Pituitary Adenoma-emphasized on Surgical Skill of Otolaryngologist. Vol. 66, Indian Journal of Otolaryngology and Head and Neck Surgery. 2014. p. 334–40.

23. Demba D, Mané DI, Maguette M, Djiby S, Mody NF, Assane NM, et al. Profile of Pituitary Adenomas in Senegal: Epidemiological, Clinical and Therapeutic Aspects about 241 Collected Cases. Vol. 13, Open Journal of Internal Medicine. 2023. p. 144–54.

24. Patel PN, Stafford AM, Patrinely JR, Smith DK, Turner JH, Russell PT, et al. Risk Factors for Intraoperative and Postoperative Cerebrospinal Fluid Leaks in Endoscopic Transsphenoidal Sellar Surgery. Otolaryngol - Head Neck Surg (United States). 2018;158(5):952–60.

25. Wass GN& JA. Epidemiology, clinical presentation and diagnosis of non-functioning pituitary adenomas Pituitary. J Pituit Surg. 2018;21:111–8.

26. Seltzer J, BA, Wedemeyer MA, MD. Outcomes following transsphenoidal surgical management of incidental pituitary adenomas a series of 52 patients over a 17-year period in Journal of Neurosurgery Volume 130 Issue 5 (2018) Journals. Journal of Neurosurgery JNS; 2018.

27. Gondim JA, Almeida JP, De Albuquerque LAF, Gomes E, Schops M, Mota JI. Endoscopic endonasal transsphenoidal surgery in elderly patients with pituitary adenomas. J Neurosurg. 2015;123(1):31–8.

8.0APPENDICES

8.1 APPENDIX 1: Data Collection sheet

A. General information

i. Number ……
ii. Age …..
iii. Sex …... 1. Male □ 2. Female □

B. Clinical Features Patient presented with

		1. YES	2. NO
i.	Mass effect		
i.	Headache	□	□
ii.	Vision loss	□	□
iii.	Papilloedema	□	□
iv.	Seizures	□	□
v.	Nasal obstruction	□	□
vi.	Nasal bleeding	□	□
vii.	Rhinorrhea	□	□
viii.	Craniocervical joint instability	□	□
ix.	Others……..		

If the patient presents with hormonal effects proceed with (ii) according to the hormone found in excess; if no hormonal effect, continue to part C

ii. Hormonal effect

i. Prolactinoma Lab Reading…….

1.	Infertility	□	□
2.	Decrease libido	□	□
3.	Amenorrhea	□	□
4.	Galactorrhea	□	□
5.	Erectile dysfunction	□	□
6.	Gynaecomastia	□	□
7.	Others……..		

ii. Growth hormone secreting tumor Lab Reading……..

1.	Increase in ring or shoe size	□	□
2.	Joint pain	□	□
3.	Excessive sweating	□	□
4.	Coarse facial features	□	□
5.	Frontal bossing	□	□
6.	Enlarged nose	□	□
7.	Prognathism	□	□

8. Enlarge tongue □ □
9. Sleep disorder □ □
10. Others…….

iii. Corticotrop secreting adenoma Lab Reading…….

1. Weight gain □ □
2. Muscle weakness □ □
3. Mood disorders □ □
4. Easy bruising □ □
5. Round face □ □
6. Facial plethora □ □
7. Supra-clavicular fat □ □
8. Echymoses □ □
9. Purple striae □ □
10. Others……..

iv. Thyrotroph adenomas Lab Reading…..

1. Anterior neck mass (goitre) □ □
2. Palpitaions □ □
3. Weight loss □ □
4. Heat intolerance □ □
5. Others……

C. Indications for Transphenoidal Pituitary surgery 1. YES 2. NO

i. Progressive mass effect □ □
ii. Control of hormonal hypersecretion □ □
iii. Pituitary apoplexy □ □

D. Outcome of Transsphenoidal pituitary surgery 1. YES 2. NO

i. Symptom relief □ □
ii. Hormonal control □ □
iii. Complications

i. Early (within 7 days)

1. Bleeding/vascular injury □ □
2. CSF leak…. □ □
3. Visual disturbances… □ □
4. Infection… □ □
5. Death □ □
6. Others……..

ii. Late (7-30days)

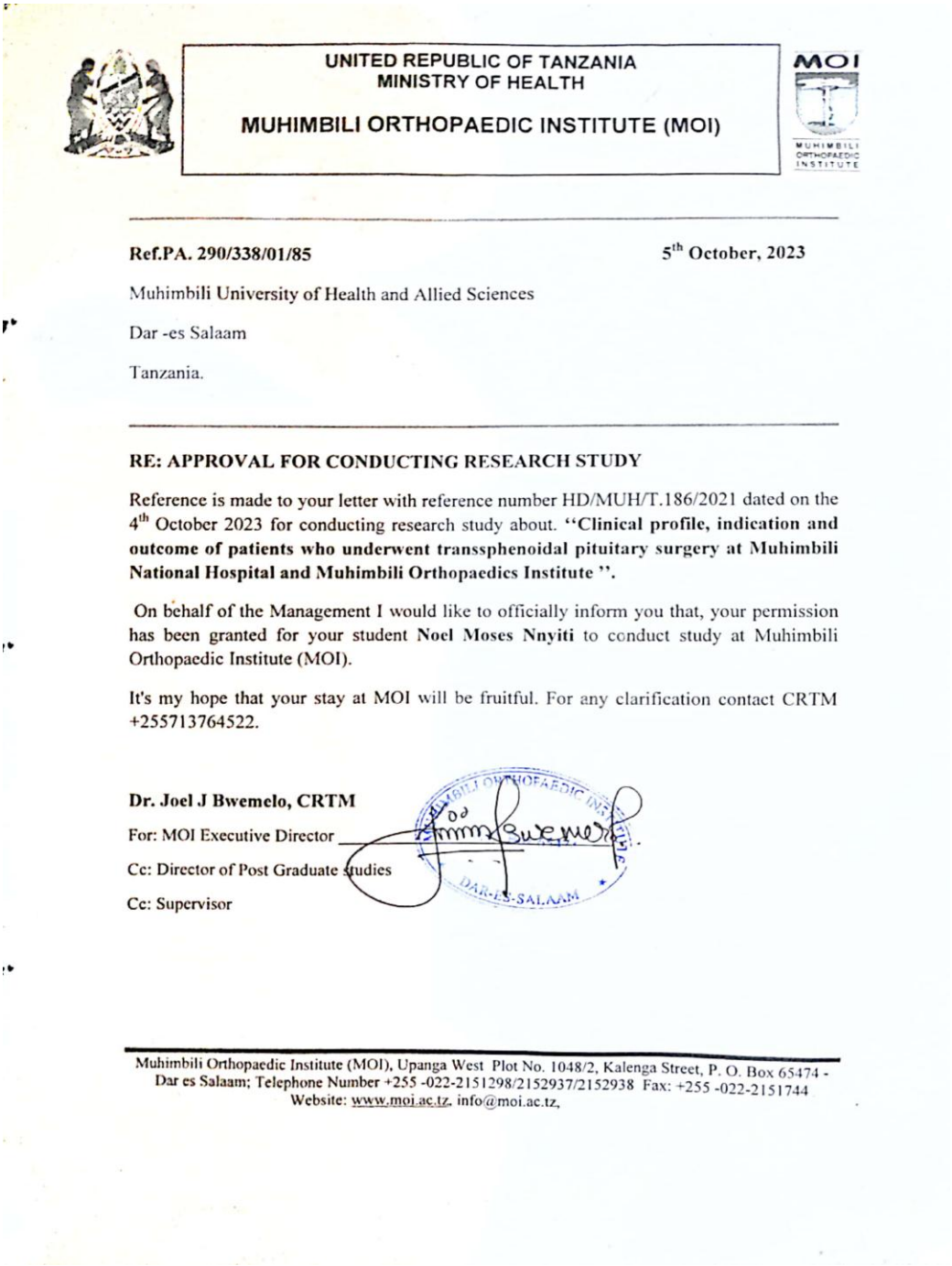
1. Meningitis…. □ □

2. Inctracranial abscess… □ □
3. Brain Absecesss □ □
4. Hypopituitarism… □ □
5. Others……

E. Histological Diagnosis

i. Prolactinoma □ □
ii. Throtroph adenoma □ □
iii. Corticotroph secreting adenoma □ □
iv. Growth hormone secreting adenoma □ □
v. Others…….

8.2 APPENDIX 2: CLEARANCE AND CERTIFICATES



UNITED REPUBLIC OF TANZANIA
MINISTRY OF HEALTH

MUHIMBILI ORTHOPAEDIC INSTITUTE (MOI)

Ref.PA. 290/338/01/85 **5th October, 2023**

Muhimbili University of Health and Allied Sciences

Dar -es Salaam

Tanzania.

RE: APPROVAL FOR CONDUCTING RESEARCH STUDY

Reference is made to your letter with reference number HD/MUH/T.186/2021 dated on the 4th October 2023 for conducting research study about. **''Clinical profile, indication and outcome of patients who underwent transsphenoidal pituitary surgery at Muhimbili National Hospital and Muhimbili Orthopaedics Institute ''.**

On behalf of the Management I would like to officially inform you that, your permission has been granted for your student **Noel Moses Nnyiti** to conduct study at Muhimbili Orthopaedic Institute (MOI).

It's my hope that your stay at MOI will be fruitful. For any clarification contact CRTM +255713764522.

Dr. Joel J Bwemelo, CRTM

For: MOI Executive Director

Cc: Director of Post Graduate Studies

Cc: Supervisor

Muhimbili Orthopaedic Institute (MOI), Upanga West Plot No. 1048/2, Kalenga Street, P. O. Box 65474 - Dar es Salaam; Telephone Number +255 -022-2151298/2152937/2152938 Fax: +255 -022-2151744
Website: www.moi.ac.tz, info@moi.ac.tz,

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/1889 Date: 31/08/2023

MUHAS-REC-08-2023-1889
DR NOEL MOSES NNYITI
SCHOOL OF MEDICINE
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: CLINICAL PROFILE, INDICATION AND OUTCOME OF PATIENTS WHO UNDERWENT TRANSSPHENOIDAL PITUITARY SURGERY AT MUHIMBILI NATIONAL HOSPITAL AND MUHIMBILI ORTHOPAEDIC INSTITUTE

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: 31/08/2023
EXPIRATION DATE OF APPROVAL: 31/08/2024

STUDY DESCRIPTION:
Purpose:
The purpose of this hospital based retrospective cross-sectional study is To assess the clinical profile, indication and outcome of patients who have undergone transsphenoidal pituitary surgery at MNH and MOI.

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-%2014380.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



UNITED REPUBLIC OF TANZANIA
MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY
MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
OFFICE OF THE DIRECTOR – POSTGRADUATE STUDIES

In reply quote;
Ref. No. HD/MUH/T.186/2021

04th October, 2023

The Executive Director,
Muhimbili National Hospital,
P.O. Box 65000,
DAR ES SALAAM

Re: INTRODUCTION LETTER

We would like to inform you that the bearer of this letter is Noel Moses Nnyiti with Reg. No. HD/MUH/T.186/2021 is a student at Muhimbili University of Health and Allied Sciences (MUHAS) "pursuing MMed. Otorhinolaryngology.

As part of his studies, he will be doing an elective research titled: "**Clinical Profile, Indication and Outcome of Patients Who Underwent Transsphenoidal Pituitary Surgery at Muhimbili National Hospital and Muhimbili Orthopaedic Institute."** he is being supervised by Dr. Enica Richard from MUHAS and Dr. Edwin Liyombo from MNH.

The research has been approved by the Chairman of University Senate.

Kindly provide him the necessary assistance to facilitate the conduct of his research.

We thank you for your cooperation.

Ms. Victoria Mwamlwa
For: DIRECTOR, POSTGRADUATE STUDIES

c.c Noel Moses Nnyiti

9 United Nations Road; Upanga West; P.O. Box 65001, Dar Es Salaam: Tel. G/Line: +255-22-2150302/6; Ext. 1015; Direct Line:+255-22-2151378;Telefax:+255-22-2150465;E-mail:dpgs@muhas.ac.tz;Web:https://www.muhas.ac.tz