UNIVERSITY OF NAIROBI

RATES AND PATTERNS OF CENTRAL DIABETES INSIPIDUS AFTER SURGERY FOR SELLAR AND PARASELLAR TUMORS AT THE KENYATTA NATIONAL HOSPITAL

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STUDENT'S DECLARATION

Dr. Ngetich Gilbert Kiprop, do hereby declare that this research thesis is my own original work and has not been presented for award of a degree in any university.

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DEDICATION

To my family, my wife, Ruth and our children, Peter, Jessica and Melissa for their abundant support, for their patience and understanding, and for their love.

To my parents and siblings, thank you for believing in me.

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LIST OF ABREVIATIONS

ADH: Antidiuretic Hormone

AVP: Arginine vasopressin

cAMP: cyclic Adenosine monophosphate

CCU: Critical care unit

CNS: Central Nervous System

CT: Computed tomography

DI: Diabetes Insipidus

D5: 5% dextrose

ICA: Internal carotid artery

ICU: Intensive care unit

KCL: Potassium chloride

KNH: Kenyatta National Hospital

MRI- Magnetic resonance imaging

PO-Per oral

RBS-Random blood sugar

RL – Ringer's lactate

SG: Specific gravity

UECs-Urea, electrolytes and creatinine

WHO- World Health Organization

ABSTRACT

Background: Central Diabetes Insipidus (DI) is a common post operative complication after procedures for sellar and parasellar tumors. It is associated with increased morbidity, mortality and prolonged hospital stay. It is diagnosed clinically by symptoms of polyuria and polydipsia and measuring serum sodium and osmolality as well as urine osmolality and specific gravity (SG). There is limited data on rates and patterns of post operative central DI for tumors in this anatomically complex region even with increasing number surgeries being done for these tumors.

Objective: To determine the rates and patterns of post-operative central Diabetes Insipidus in patients with sellar and parasellar tumors at the (Kenyatta National Hospital) KNH.

Study Design: This was a descriptive cross-sectional study.

Study Setting: The study was conducted at the KNH Neurosurgery units and critical care units.

Methodology: This study involved 24 participants following surgery for sellar and parasellar tumors. Recruitment was through convenience sampling method. Informed consent was obtained from the participants. Clinical assessment for presence polyuria and polydipsia and laboratory measurement of serum sodium and urine SG for features for central DI was done.

Data Management and Analysis: A preformed data collection sheet was used to capture relevant information. This was checked for completeness and errors prior to entry into a Microsoft Excel 2017 spreadsheet, the data was exported to the Statistical Package for Social Sciences version 23 for analysis. Data was analyzed and presented as ranges, mean, frequency and percentages.

Results

The mean age of the patients was 28.69 years, 70.8% (17) were female and 29.2% (7) were male. The most common tumor as confirmed by histology was craniopharyngioma seen in 33.3% of the patients. With regards to age craniopharyngioma, pilocytic astrocytoma and arachnoid cyst was seen in paediatric age group predominantly while meningioma and pituitary adenoma was more common in adults. Polyuria and polydipsia were the main clinical features seen post operatively in patients with Central DI. 69.2% presented with both polyuria and polydipsia, 30.8% presented with polyuria alone without polydipsia. Following laboratory evaluation, 76.9% of patients who met criteria for diagnosis of central DI had serum sodium levels of 150mmol/L or more at the time of diagnosis and 23.1% of patients had serum sodium less than 150mmol/l. 69.2% of patients with post operative central DI had urine specific gravity of 1.005 or less. 30.8% of patients with post operative central DI however, had urine specific gravity of more than 1.005 (SG range 1.010-1015). No patient with post operative central DI had urine specific gravity more than 1.015. The rate of post operative Central DI after surgery for sellar and parasellar tumors was 54.2%. The most common pattern was transient type occurring in 76.9% of the cases. Biphasic pattern was seen in 23.1%. No Triphasic and permanent patterns were seen.

Conclusion: The rate of post operative central DI after surgery for sellar and parasellar tumors as seen at KNH was 54.2%. The most common pattern was transient type seen in 76.9% of the central DI cases.

CHAPTER ONE: INTRODUCTION

Sellar and parasellar regions is anatomically complex region of the skull base (3,39). Various benign and malignant lesions occur in this region and are managed surgically (35). These can arise from the pituitary gland, infundibular stalk, hypothalamus, cranial nerves, vascular structures, leptomeninges, or skull base (25,35,39). Some common tumors in this region include pituitary adenomas, craniopharyngioma, meningiomas, germ cell tumors, pilocytic astrocytoma of optic pathway and hypothalamus, arachnoid cysts, dermoid and epidermoid tumors and metastases (3,7,19,39). These tumors comprise of 25.3% and 28.3% combined prevalence rates in one African study in Rwanda. Surgical approaches to these tumors comprise both transcranial and endoscopic or microscopic transsphenoidal routes (3,11,16).

Fluid and electrolyte disorders are common problems in post operative patients more so following sellar region tumor surgeries (21). Central Diabetes Insipidus (DI) is the most common of the disorders others being Cerebral salt wasting syndrome (CSW) and Syndrome of Inappropriate secretion of Antidiuretic hormone (SIADH) (22). Diabetes insipidus (DI) is a disturbance in water homeostasis due to deficiency of antidiuretic hormone (ADH) or Arginine Vasopressin (AVP) or resistance to receptors in the renal tubular epithelial cells leading to excretion of large volume of hypotonic urine, (13).

Central DI occurs due to disturbances in ADH secretion leading to disorders of water balance due to altered secretion of ADH with normal receptor function (12). This can be transient, biphasic, triphasic or permanent Central DI type (21,22). Central DI is a common postoperative complication in patients with sellar and parasellar lesions seen in 83% of these cases (22). The diagnosis of DI, ascertaining its type and management remains a significant challenge to many clinicians (13). Keen clinical evaluation of patients post-operatively and use of routinely available laboratory tests enables early diagnosis of central DI.

There is a wide variation in the rates of postsurgical central DI from 1 to 67% as observed by Shreckinger et al (26) and rates ranging from 9-54% as observed by Nayak et al (33). There is a wide age range, with a median age of 40 years (21). There is no data on post operative central DI in our region in relation to sellar and parasellar pathologies (29). Following pituitary surgeries as seen in KNH, transient electrolyte imbalance and DI is the commonest post operative complication seen (19).

It presents mainly with polyuria and polydipsia and features of dehydration (14). Laboratory features include increased serum osmolality and increased serum sodium with reduced urine osmolality and specific gravity (3,11). Transient DI is the most common pattern of central DI (21). The sequelae following fluid loss and hypernatremia include brain shrinkage that can cause intracranial hemorrhages, seizures and obtundation with associated poor outcomes. This causes prolonged hospital stay with increasing costs and also increased mortality rates.

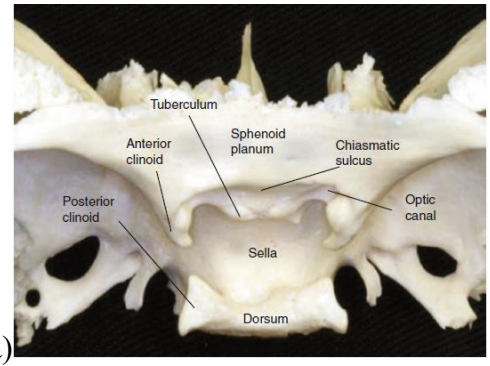
Management requires keen clinical assessment including monitoring urine output and features of dehydration and laboratory evaluation (3,34). The objective of treatment of central DI is to ensure the restoration and maintenance of osmotic homeostasis. This is individualized for each patient and depends on the type of central DI (22,24). Obtaining information on the rates and various patterns of central DI as it occurs post operatively after sellar and parasellar tumors, will help guide both clinical diagnosis and inform in focused management.

2 CHAPTER TWO: LITERATURE REVIEW

2.1.1 Anatomy of sellar and parasellar region

The sellar and parasellar regions have a complex surgical anatomy with various important neural and vascular structures confined in a small space (3,39). Whereas anatomical landmarks of the sellar region are specific, the parasellar region is not clearly delineated (3). The sellar region is located at the centre of the skull base on the sphenoid bone, with anterior limits at anterior clinoid process and tuberculum sellae, posteriorly limit includes dorsum sellae and the clivus and superior limit is diaphragma sellae. The floor comprises the sellar turcica and sphenoid sinus and contains the pituitary gland (12).

The parasellar region is part of the middle cranial fossa between the sellar region and the temporal fossa (12,25). It consists of the dural walls of the cavernous sinuses (containing cavernous segment of ICA, cranial nerves III, IV, VI and V1, V2 segments of cranial nerve V), the sphenoid sinus inferiorly, superiorly the suprasellar cistern, hypothalamus, optic nerves and optic chiasm, and ventrally the inferior third ventricle (3,5,35). It is one of the smallest areas of the skull base and has the most complex neurovascular relations in the body, (12).

a) 

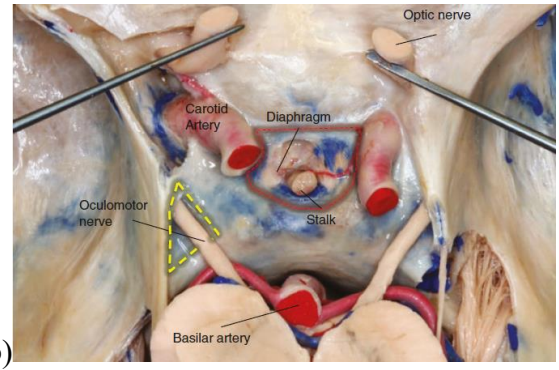
b) 

Fig. 1. Anatomy of the Sellar and parasellar region a) bony anatomy b) superior view

The hypothalamus is anatomically connected to neurohypophysis via a stalk that forms a functional unit involved in fluid and electrolyte homeostasis (6,8). The cell bodies of magnocellular neurons in the supraoptic and a smaller proportion from the paraventricular nuclei of the hypothalamus synthesize arginine vasopressin (AVP), its precursors and co-peptides, (6,14). These project into the posterior pituitary gland where the AVP is stored in the axonal terminals and released to the circulation via fenestrated capillaries (6,8).

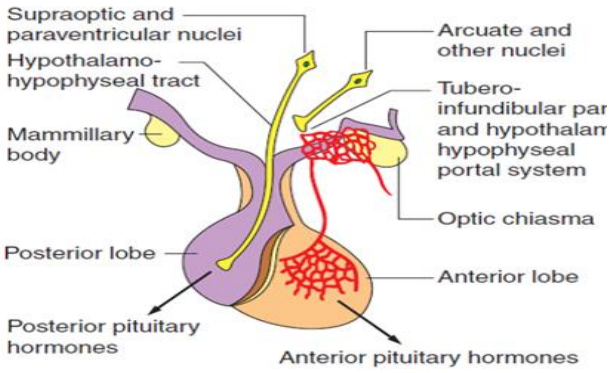
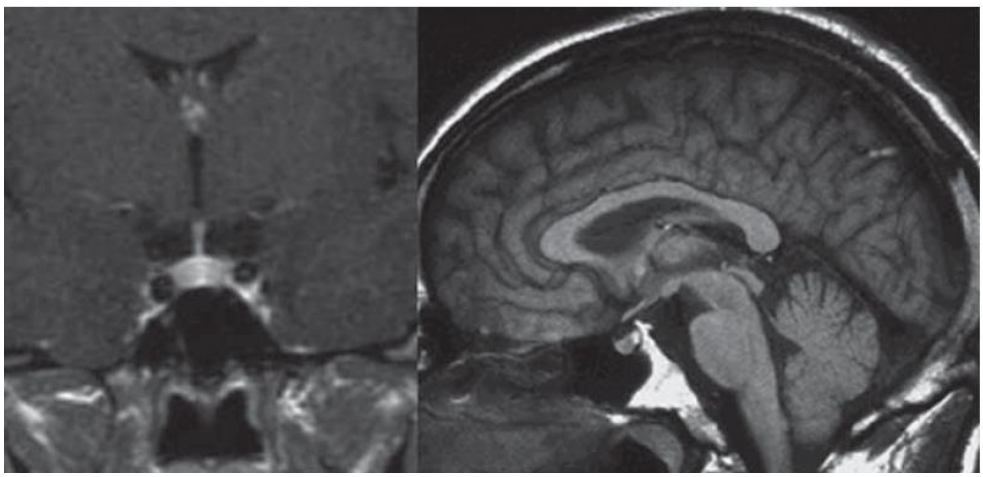


Figure 2. a) Showing anatomical relations between hypothalamus and posterior pituitary



2 b) radiological images of sellar and parasellar region in coronal and sagittal sections

Only about 15% of the vasopressin-secreting cells of the hypothalamus need to be intact to maintain fluid balance under normal conditions, (36). Simple destruction of the posterior pituitary does not cause sufficient neuronal loss to result in permanent diabetes insipidus (13,36). Central DI results from significant destruction of the hypothalamic neurons or some of the supraoptic-hypophysial axis. This could be due to direct surgical trauma or devascularization during operations for adjacent region tumors (e.g., parasellar lesions), very large tumors or lesions.

2.1.2 Physiology and role of ADH in water homeostasis

Central diabetes insipidus (DI) is due to deficiency or absence of Antidiuretic hormone (ADH) or vasopressin (AVP), a nona-peptide synthesized at the supraoptic and paraventricular nuclei and stored as a pre hormone in the intracytoplasmic granules (14,21,22). It is involved in maintaining tonicity homeostasis. Plasma osmolality is maintained between 270-290 mOsm/kg by hypothalamic osmoreceptors through modification of ADH secretion and sensation of thirst (10,14,24). Following stimulation, ADH is transported to the neurohypophysis where it is converted to active hormones and released to circulation. ADH acts on V2 receptors in the late distal renal tubular cells activating cyclic AMP (cAMP) that lead to protein kinase A (PKA) activation with insertion of aquaporin 2 channels for passive water reabsorption (6,14,22).

The stimulus for release is increased plasma osmolality (and sodium) sensed by hypothalamic osmoreceptors and also volume depletion sensed by aortic and atrial baroreceptors (6). The physiologic effect is water retention primarily via renal reabsorption, thirst triggering water intake and vasoconstriction at higher concentrations of ADH (14,22). Central DI leads to a significant shift in cellular fluid and electrolytes that increase the risk of seizures, thrombosis and tearing of the bridging veins. (24) that may result in permanent neurologic sequelae.

2.1.3 Patterns and pathophysiology of central DI

Various patterns of central DI have been described and their associated pathophysiologic mechanisms as described next.

2.1.3.1Transient diabetes insipidus

This is the most common pattern of central DI (21). It occurs at 24-48 hours post operatively and abates within 10 days. This is attributed to oedema in axonal connections between the magnocellular cells and posterior pituitary nerve terminals due to surgical trauma following manipulation at surgery and /or devascularization of the pituitary stalk, gland or hypothalamic nuclei causing axonal shock (21,22). Changes in the anatomy of sellar and parasellar regions with pathology has also been attributed to increased rates of post operative DI (20). This usually resolves when neuronal recovery occurs.

2.1.3.2 Permanent diabetes insipidus

This is seen when more than 80-90% of ADH-secreting hypothalamic neurons are damaged with subsequent degeneration of neurons. This is seen mostly when symptoms last more than 14 days. Is diagnosed in patients requiring long term desmopressin therapy more than 3 months. This is common with high stalk lesions. Kinoshita et al demonstrated 0.9% permanent DI for transsphenoidal surgeries. Craniopharyngioma is the most common tumor associated with permanent DI (3,21,22).

2.1.3.3Triphasic pattern

This is relatively uncommon with incidence rate of 1.1% in post operative patients (21). It has three consecutive phases. Initial DI phase that lasts 5-7 days characterized by polyuria and hypernatremia. This is followed by a phase of antidiuresis lasting 2-14 days, characterized by hyponatremia (21,22). This is due to uncontrolled ADH release from degenerating neurons in the posterior pituitary gland or damaged axons of the magnocellular

neurons (21). The last phase comprises DI phase that is mostly permanent due to insufficient neurons to synthesize ADH and depletion of ADH deposits. Occurs after 14 days.

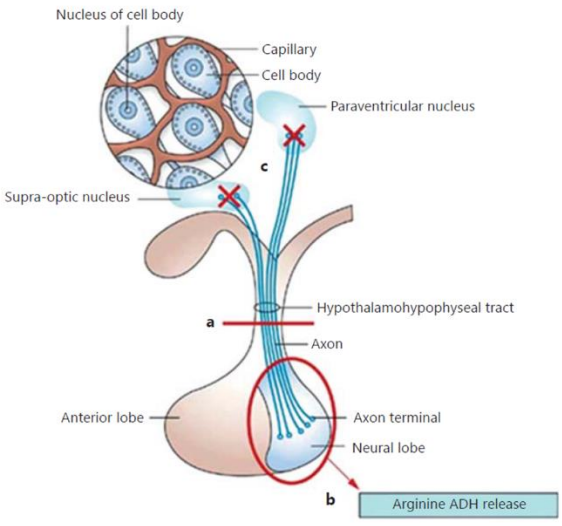
2.1.3.4 Biphasic pattern

Is characterized by the occurrence of the first two phases only. This is more common than the triphasic pattern (22). The normal fluid balance is restored after the episode of SIADH (DI-SIADH-normal fluid homeostasis).

2.1.3.5 Diabetes insipidus with adipsia or hypodipsia

Central DI may occur with associated impaired thirst due to damage to hypothalamic osmoreceptors that regulate thirst and ADH secretion (22). This is largely uncommon, but carries a high morbidity and mortality and its management is also difficult. Patients develop hypernatremia and dehydration due to this. This form is usually permanent but sometimes may improve usually within 9 months post operatively (21,22).

Fig 3. Shows areas of disruption ADH secretion at sites a, b and c



There is a wide variation in the rates of postsurgical central DI, rates ranging from 9-22% have been reported with a wide variation in some centers showing values up to 54% after surgery for sellar masses (26,33). Xin Ji et al demonstrated an incidence of 42-80% in children following surgery for sellar and parasellar tumors. Kinoshita et al, showed an overall rate of DI at 21.9% in patients undergoing transsphenoidal surgery for pituitary adenomas. In patients with craniopharyngioma, Central DI is present in 16–55% of craniopharyngioma patients preoperatively and up to 90% after surgery (4,20,33)

Following surgery for pituitary macroadenoma, Angelou et al also showed a wide variability of 11-22% depending on tumor size, location and type of surgery (3). In a retrospective cohort study, Faltado Jr demonstrated in post operative patients following pituitary surgery DI was 27.8% (11). For pituitary macroadenomas, the type of surgery influenced the development of central DI post operatively (3,11).

Following transsphenoidal surgery, the central DI rate of 3.6% compared to 66.7% for transcranial approaches most of them being transient DI (16). In his study, Islam et al showed an overall incidence of 39.4% following both endoscopic and microsurgical trans nasal resection for pituitary macroadenoma (16). The occurrence of transient DI in trans nasal microsurgical approach was 1.6- 45.6% compared to 2.5-15.2% in transnasal endoscopic approach (16). Some studies have however demonstrated similar rates for both microscopic trans nasal and endoscopic trans nasal resection. Almaliki HM et al reported 3.9 times increased risk of mortality following DI after pituitary surgery (2). According to Angelousi A et al, preoperative DI at diagnosis was found in 23.4% in patients with sellar/parasellar lesions with a variation from 10.6% -76.7% (3).

The prevalence of central DI in sellar/parasellar lesions in the post operative period remains scanty especially for most tumors other than pituitary adenomas with a prevalence of 27.8%

post-surgery for non-adenomatous sellar/parasellar lesions (3). The significant variation in central DI rates following pituitary surgery warrants a study in our set up and also to show the rates among other sellar/parasellar tumors in our set up.

In a retrospective study, Kiran Z et al found the median age to be 40 years with male predominance at 61.7% in patients following surgery for sellar, suprasellar and parasellar masses (21). Islam et al demonstrated the age range for transsphenoidal surgery for pituitary macroadenoma was 24 to 70 years with a male to female ratio of 1.5:1(16). Qari et al demonstrated a female preponderance at 61.5% and a mean age of 34 years for patients with post operative DI for sellar region tumors (34).

The sellar and parasellar regions has complex anatomy and is located in a small area of the skull base that houses several important neurovascular structures that may have similar clinical and imaging features (39). Various neoplastic and non-neoplastic lesions occur in the sellar region conditions such as infectious, inflammatory, vascular and neoplastic disorders (9, 32,39). Pituitary adenomas are the most common tumor accounting for 90% of sellar/parasellar lesions (3). Other tumors include craniopharyngiomas, germinomas, meningiomas, schwannomas, dermoid cysts, epidermoid cysts chordomas and Rathke's cleft cyst (13,25, 35,39). In a 10-year observational retrospective study conducted in Rwanda on epidemiology of Central Nervous System (CNS) tumors by Hakizimana D et al, the pediatric rates were 2.8% for sellar region tumors and 22.5% for parasellar tumors (15). In adults, sellar region tumors had a prevalence of 4.5% while parasellar tumors were 5.2%. The combined overall prevalence for sellar and suprasellar/parasellar tumors was 28.3%.

There was a female preponderance rate at 63%. Hakizimana et al showed the most common diagnoses for both adults and children were pituitary adenoma, craniopharyngioma and meningiomas (tuberculum sellae, clinoidal, and cavernous sinus) (15). Pituitary adenomas

are the most common with tumors from other cell origins accounting for about 9% of neoplasms in sellar/parasellar region (25). In a population-based study of sellar masses in Canada, Al-Dahmani K et al showed the mean age of 44.6±18 years at presentation, a female preponderance of 62% (1). The prevalence rate in the population was 0.1% with 83% being pituitary adenomas 17% had nonpituitary lesions (1). The heterogeneity of lesions in the sellar and parasellar region accounts for the broad landscape of tumours seen here and being a crossroad to vital neural structures makes surgery in this location a challenge with attendant risks of central DI.

The WHO 2021 classification of CNS tumors recognizes the tumors of the sellar region as a distinct entity whereas the parasellar tumours are not classified as a distinct group due to the different cell origins of tumors in this region (23,25). As demonstrated in various studies in KNH on brain tumors, the clear proportion and burden of sellar and parasellar tumors is still limited as most studies were generalized with no location specific information available (29). This is replicated in other studies carried out in Nigeria and Cameroon where no specific location prevalence for the tumors is available (27,31). These tumors present with a wide spectrum of manifestations due to mass effects and alteration of endocrine function. There is a considerable overlap in the clinical spectrum and this is influenced by the size, anatomical location, the biological behavior of the tumor and patient's age, (2,25). The later features in addition to the type of surgery influences the risk to developing post operative central DI, (2,34). As described by Faltado Jr. et al the location of the tumor has a relation to the development of post operative DI (11).

Magnetic resonance imaging (MRI) scan is the main diagnostic modality alongside Computerized tomography (CT) scan in characterizing the anatomical location and type of pathology (3,9,21). The unique attenuation and signal characteristics in the distinct locations as well as age and sex may help to elucidate the likely pathology radiologically (35,39).

Additional imaging for vascular studies may be requested, when necessary, especially for large lesions or suspected vascular pathologies. Preoperative features such as absence of posterior pituitary bright spot and enhancement of the pituitary stalk may occur in preoperative central DI (3,21). Histopathological evaluation helps in confirmation of the diagnosis post operatively.

Central DI develops in most patients within 24hrs (16), following trans sphenoidal surgery with 76.9% presenting in 24 hours and 23% by 48 hours post operatively (16). Faltado Jr et al found a mean time of 27.38 hours after pituitary surgery for spontaneous DI to occur (11). DI diagnosis is made by fluid balance determination. Clinical symptoms and examination are important as well measurement of the plasma and urine sodium concentration, as well as osmolality (14,34,39).

The clinical presentation includes hypotonic polyuria and polydipsia (3,14,16,18,34) as well as increased thirst. Features of dehydration such as tachycardia, dry mouth, restlessness, headache and mental state change occur as a sequela (11,14,21,22,39). Polyuria occurs with urine output of 250mls/hr for 2 or more consecutive hours or greater than 3L/24hrs or 2.5mls/kg/hr in adults. In pediatrics, polyuria occurs when urine volume is >150 ml/Kg/24 hours at birth, >100-110 ml/Kg/24 hours up to the age of 2 years, and >50 ml/Kg/24 hours in older children (3,11,14,18, 34). This is ascertained my measuring daily urine output with hourly charting.

Laboratory assessment includes urinary specific gravity and serum sodium levels (3,14,16) and serum and urine osmolality also help in the diagnosis (3,11,34). Other causes of polyuria in post operative patients have to be ruled out including diuresis of intravenous fluids administered in the perioperative period, hyperglycemia and diuretic therapy, (3,11,16). In a patient with findings of polyuria the laboratory features to fulfill for diagnosis of central DI

include serum sodium >145mmol/L, serum osmolality >300mosm/kg, urine specific gravity <1.005 and urine osmolality <300mosm/kg (3,11,16,34,39). Islam et al demonstrated that inpatients post trans sphenoidal surgery for pituitary adenoma, 92.9% of patients with serum Na+ above 145mmol/l had DI (16). Various authors have used some or all of these laboratory features depending on the availability and the urgency with which the results are obtained which varies from place to place. Faltado Jr et al showed that a change in serum sodium and urine specific gravity was significantly associated with development of post operative DI after pituitary surgery with 96% sensitivity and 50% specificity (11). Challenges in accurately making a diagnosis of DI occur due various overlapping states of polydipsia-polyuria, absence of standardized diagnostic criteria and variability in patient monitoring (2,14).

The normal serum osmolality is 275 to 295 mOsm/kg and is influenced by the concentration of the dissolved particles (30). Measurement of serum sodium and plasma osmolality is key in diagnosis of central DI (14). Hence serum sodium concentration generally corresponds to plasma osmolality (8). Plasma osmolality of >300Mosm/kg and/or serum sodium >145mmol/l or an increase of 8mmol/hr is seen in DI (3,11,14,34). The normal urine specific gravity (SG) is 1.005-1.030 in normal plasma osmolality. It is determined by number and size of osmotically active particles in urine.

This makes urine SG corelate well with urine osmolality except in presence of other particles in urine such as in glucosuria which may elevate the SG (11,14,34). This explains the utility of either SG or urine osmolality or both. Understanding the laboratory parameters and their utility guides the use in diagnosis of central DI depending on the availability of the tests.

Post operatively, following surgery for non-adenomatous sellar/parasellar lesions, transient central DI was seen in 11.6% as reported by Angelousi et al (3). Wang S et al in a retrospective study found transient DI after transcranial surgery for pituitary adenoma at 33.3% while permanent DI rates were 12.6% (38). Central DI rates as reported by Qari et al were 16-34% in patients post operatively for sellar region operations (34). Most of the cases were transient DI and were associated with increased morbidity and length of hospital stay (21,34). Islam et al reported 38.8% of the cases had transient DI and permanent DI pattern rates of up to 0.5% following pituitary gland surgery (16). Di Iorgi N et al reported that following craniopharyngioma surgery the rates were 80% for permanent DI and 13% for transient DI (8). Nayak P et al is a study following post resection of pituitary adenoma, triphasic response rates was 1.1% (33). The permanent DI rates were lower, occurring when 80-90% of the hypothalamic neurons and proximal infundibulum have been damaged (8,11), these mandates long term use of desmopressin for more than 3 months (3). Limited studies have assessed the patterns of sellar/parasellar lesions in relation to central DI with significant variance in incidence in different studies and pathologies. It is important to study the patterns to inform clinicians caring for patients following surgery for sellar/parasellar tumors and guide monitoring and duration of treatment for DI (3,34). This is particularly useful when patients are sedated, have adipsia or are unconscious and in pediatric patients. This is relevant with increasing surgeries around the sellar region in order reduce the related adverse events due to central DI (27,39).

2.2 STUDY JUSTIFICATION

The sellar and parasellar region is anatomically complex and tumors here account for a significant percentage of brain tumors and has seen increasing surgeries for tumors here. Most patients in our set up present late with very large tumors that distort normal anatomy, making surgical management a challenge with a myriad of complications including central DI. Central DI is a common condition following surgery in the sellar region and is associated with increased morbidity, long ICU/hospital stay and mortality. It is diagnosed by keen clinical evaluation and using available routine laboratory tests and requires early recognition and swift intervention.

Neurosurgical patients many of whom are sedated, may have impaired consciousness and impaired thirst mechanism which is a diagnostic challenge and mandates clinicians to be very keen to suspect and intervene appropriately. The sequelae following fluid loss and hypernatremia include brain shrinkage that can cause intracranial hemorrhages, seizures and obtundation with associated poor outcomes.

There is still limited data regarding the post operative rates and patterns of central DI following surgery for sellar and parasellar tumors and no study on the same exists in our region. There are no available local standardized diagnosis and management guidelines for central DI which can be derived from various evidence-based strategies.

2.3 Research question: What is the rate and pattern of post operative Central Diabetes insipidus in patients with sellar and parasellar tumors at the KNH?

2.4 Objectives

2.4.1 Broad objective

To determine the rates and pattens of post operative central Diabetes insipidus in patients with sellar and parasellar tumors at KNH.

2.4.2 Specific objective

1. To describe the biodemographic features of patients with sellar and parasellar tumors at KNH.
2. To determine the proportion of various histologic types of sellar and parasellar pathologies as seen at KNH
3. To assess the clinical manifestations and laboratory findings for post operative Central DI in patients with sellar and parasellar lesions at KNH.
4. To describe the rates and pattern of post operative central DI in patients with sellar and parasellar tumors at KNH.

3 CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Study Design

This study was be a descriptive cross-sectional study.

3.2 Study Setting

The study was carried out at the KNH neurosurgery unit (ward 4C and adult and pediatric neurosurgery clinics) and the critical care units (CCU) (Main CCU and 4C CCU).

3.3 Study population

The study population was be drawn from all the post operative patients with sellar and parasellar tumors that had been seen and operated at the KNH Neurosurgery unit.

3.4 Inclusion Criteria

1. All pediatric and adult post operative patients with radiologically confirmed sellar and para sellar tumors operated at KNH.
2. Patients who give informed consent to be included in the study.

3.5 Exclusion Criteria

1. Patients with preoperative DI
2. Preexisting renal disease, symptomatic lower urinary tract symptoms (LUTS), and newly diagnosed diabetes mellitus
3. Patients on diuretic therapy and mannitol therapy post operatively

3.6 Sample size

Sample size was calculated using Fisher's formula.

$$\boldsymbol{n = \frac{Z^2 P(1-P)}{d^2}}$$

$\boldsymbol{n}$ = Desired sample size

Z= value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)

P = Prevalence taken from a previous study was 27.8% from 10-year study by Hakizimana et al in Rwanda (15)

$\boldsymbol{d}$ = Precision (expected to be around 5% if disease prevalence is between 10-90%

$\boldsymbol{n = \frac{1.96^2 * 0.278(1-0.278)}{0.05^2}}$ **= 308**

In the year 2021, 41 patients had surgeries for sellar parasellar tumours in KNH from data collected from RedCap at UoN/KNH brain tumour registry.

To correct for small population size, we used the formula N* n / N+n

N=sample size obtained from Fisher's formula

n=size of the small population

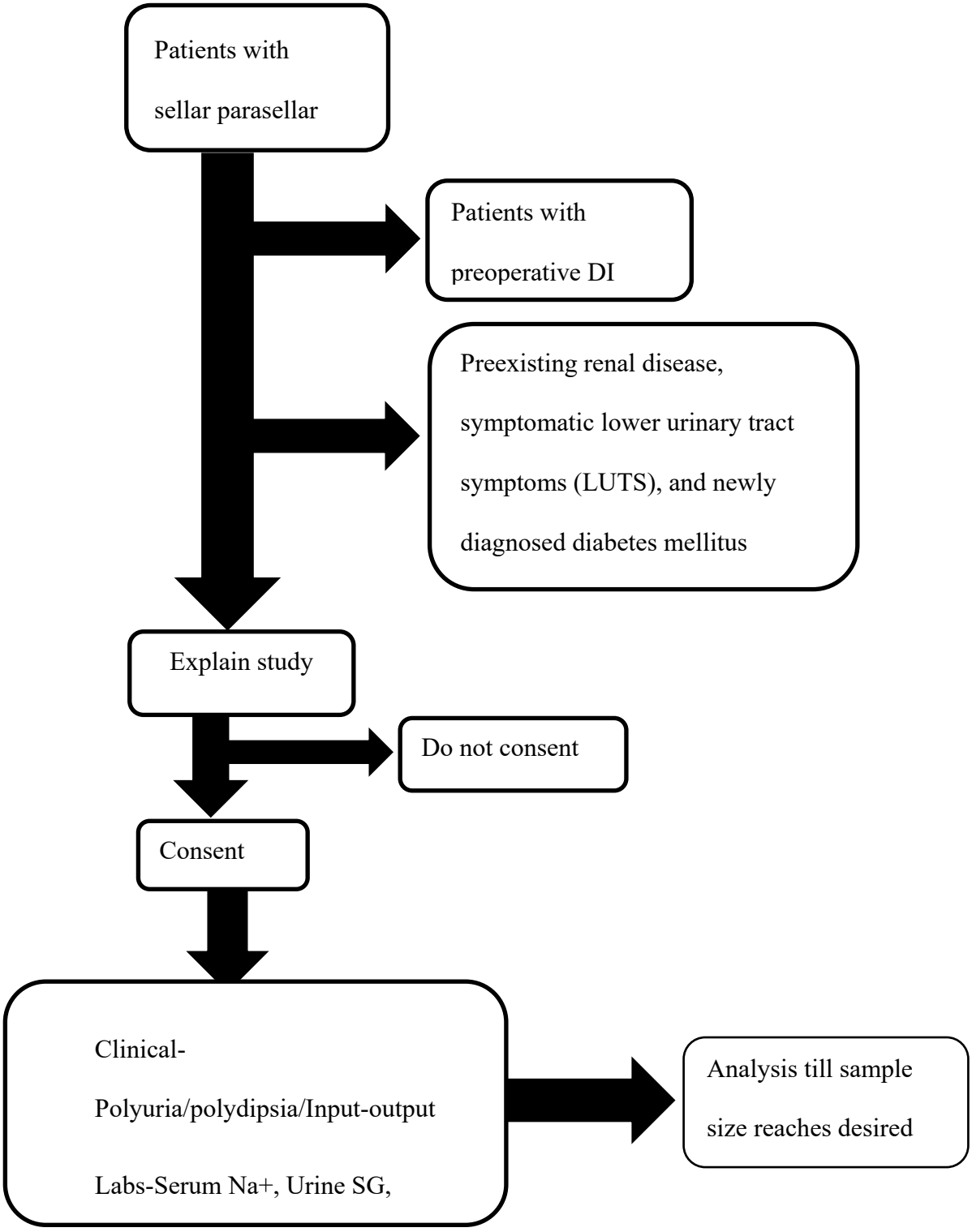
Thus= $\boldsymbol{\frac{308*41}{308+41}}$**=36.2**

hence a sample size of 36 patients was used in this study.

3.7 Sampling Method

Convenience sampling technique was employed in order to attain the desired sample size. All patients who fulfilled the criteria and consent to the study were recruited into the study.

3.8 Study recruitment procedure



3.9 Materials and equipment

The Biochemistry machine used at KNH, the Mindray BS-2000M was used to analyze serum sodium and urea electrolytes and creatinine. For random blood sugar testing, the Sinocare machine was used. Urine specific gravity was measured using human urinalysis strips, U-AQS 10.

3.11 Study procedure

The study was carried out after approval by the ethics committee. Patients were recruited at the KNH Neurosurgery ward 4C, Main CCU, 4C CCU and neurosurgery clinics after undergoing surgery for sellar and parasellar tumors. The study details were explained to all patients who meet the inclusion criteria and informed consent (appendix I) taken by the principal researcher. The patient's demographic data was collected and entered into the data collection sheet (appendix II). Clinical assessment for polyuria and polydipsia was done. The laboratory features mainly serum sodium and urine specific gravity as well as urea, electrolytes and creatinine and random blood sugar was measured. The results were collected and entered into the data collection sheet appendix II.

3.12 Data management and analysis

The findings were entered into a preformed data collection sheet. All data collection sheets were checked for completeness and errors prior to entry into a Microsoft Excel 2017 spreadsheet thereafter, exported to the Statistical Package for Social Sciences version 27 for analysis.

The rates of post operative central DI were analyzed as means, range and median with standard deviations and presented in the form of tables and charts. The various sellar and parasellar tumors presented as percentages and clinical and lab features tabulated with

frequencies provided for each parameter. The pattern of distribution of central DI was analyzed using frequencies and percentages.

3.13 Quality control

A standard data collection sheet to collect clinical information was be used. The same machine Mindray BS-2000M was be used to measure serum urea, creatinine and electrolytes which was up to date in terms of service and calibration. Glucometer Sinocare was used to measure random blood sugar using the same batch of test strips. Urine specific gravity was measured using the same U-AQS 10 strips.

3.14 Ethical consideration

The study was carried out after the approval of Kenyatta National Hospital, University of Nairobi ethics committee. Only patients who gave written informed consent were included in the study. Additional surrogate consent form for minors (less than 18years) and those unable to consent due to cognitive impairment was be provided. No extra costs were be incurred by the patients who are recruited into the study. Neither refusal nor participation in the study resulted in victimization or preferential treatment. On the study data collection sheet, no names were recorded and all patient information was kept confidential.

3.15 Covid protocol

The KNH-UoN ERC guidelines for the conduct of research during the covid-19 pandemic in Kenya (Ref no: KNH-UoN/ERC/FORM/RGCOV-19 of July 2020) was used to ensure safety of study participants and the researcher. This included appropriate personal protective equipment, hygiene measures: sanitization, hand washing; and social distance where applicable and appropriate for the level of risk.

3.16 Study results dissemination

In addition to publication in peer-reviewed journals, the results of the study will be presented at scientific meetings to the medical fraternity. The dissertation hard copies will be available at the KNH UoN Library and at the Departments of Surgery (UoN) and Neurosurgery (KNH). A soft copy of the dissertation will be available at the UoN e-repository on the UoN website (http://erepository.uonbi.ac.ke).

3.17 Study limitation

Limited understanding of criteria for diagnosis of central DI and premature institution of desmopressin therapy was a common setback. This was mitigated by clear instructions on subsequent post operative patients averting indiscriminate desmopressin use that could alter the clinical picture.

4.0 CHAPTER FOUR: RESULTS

4.1 Biodemographic data

The mean age of the patients was 28.69 years with a range of 2-71 years. There was a female preponderance with a male to female ratio of 1:2.4. This distribution is further shown in the table below and illustrated in the figures.

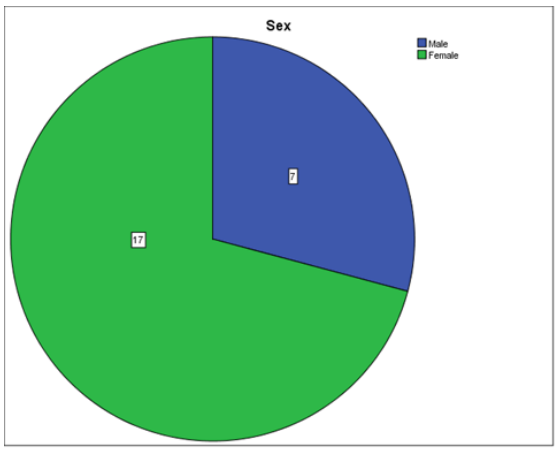
Table 1: Demographic characteristics of patients with sellar and parasellar tumors

Variable	**n (%)**
Age in years	
Mean (SD)	28.69
Median	36
Min-max	2-71
Sex	
Female	17(70.8)
Male	7(29.2)

Table 2: Frequency distribution table for age

Age of participants (years)	**Frequency (n) Valid**	**Cumulative**	**Percentage (%) Valid**
0-10	8	8	33.33
11-20	3	11	12.5
21-30	0	11	0.0
31-40	5	16	20.83
41-50	3	19	12.5
51-60	4	23	16.67
61-70	0	23	0.0
71-80	1	24	4.17
Total	24	24	100

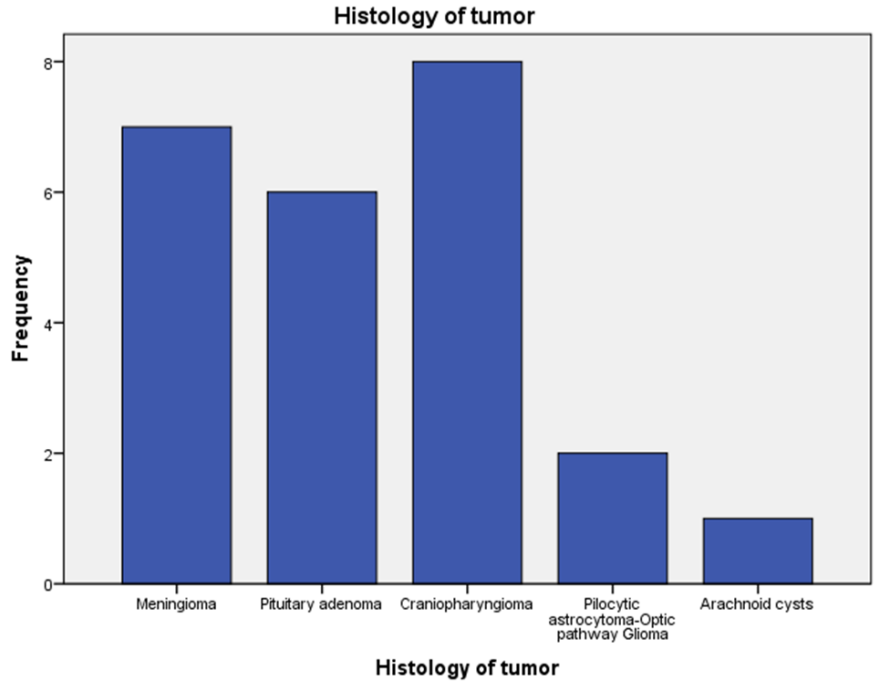
Figure 5: Pie chart showing sex distribution



4.2 Proportion of various sellar and parasellar pathologies in patients with post operative central DI

Most pathologies in the evaluated cases comprised mostly both sellar and parasellar anatomic location in 83.3% and 16.7% were located in parasellar region alone. The most common tumor as confirmed by histology was craniopharyngioma with a proportion of 33.3% of the cases. The table and figures below further demonstrate the distribution of these tumors.

Figure 6: Histology of the sellar parasellar tumor

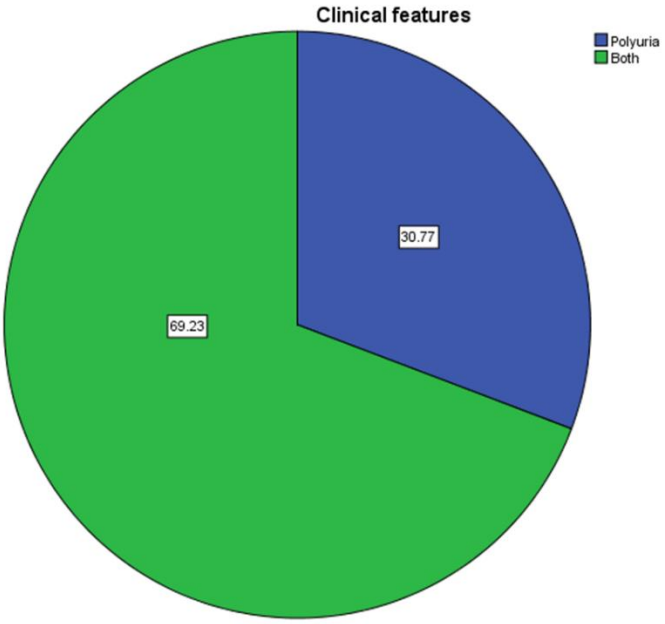


With regards to age craniopharyngioma was the commonest in pediatrics age and other histologic types seen were pilocytic astrocytoma and arachnoid cyst. Craniopharyngioma was seen between 2 to17 years old and both Pilocytic astrocytoma and arachnoid cyst occurring age group of 4yrs old and below. Meningioma and pituitary adenoma were seen in the adult patients.

4.3 The clinical manifestations and laboratory findings for post operative Central DI in patients with sellar and parasellar lesions

Polyuria and polydipsia were the main clinical features seen post operatively in patients with Central DI. 69.2% presented with both polyuria and polydipsia, 30.8% presented with polyuria alone without polydipsia. This shows that 100% of patients presented with polyuria.

Figure 7: Clinical features of central DI



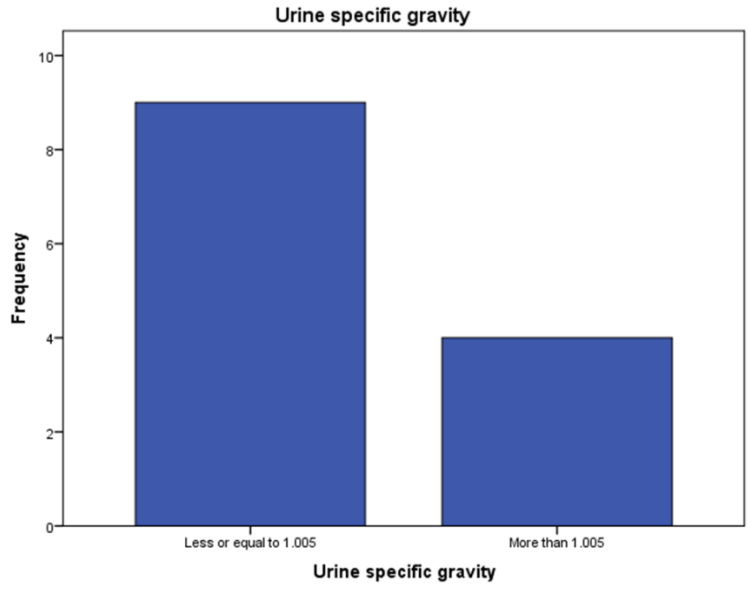
Following laboratory evaluation, 76.9% of patients who met criteria for diagnosis of central DI had serum sodium levels of 150mmol/L or more at the time of diagnosis and 23.1% of patients had serum sodium less than 150mmol/l as shown in the table below.

Table 3: Serum sodium levels in central DI

	Frequency	Percent
Less than 150mmol/L	3	23.1
More than 150mmol/L	10	76.9
Total	13	100.0

With regards to laboratory assessment of urine specific gravity, 69.2% of patients with post operative central DI had urine specific gravity of 1.005 or less. 30.8% of patients with post operative central DI however had urine specific gravity of more than 1.005 (SG range 1.010-1015). No patient with post operative central DI had urine specific gravity more than 1.015.

Figure 8: Urine specific gravity in central DI



4.4 The rate and pattern of post operative central DI in patients with sellar and parasellar tumors as seen in KNH

The rate of post operative Central DI after surgery for sellar and parasellar tumors was 54.2%. The most common pattern was transient type occurring in 76.9% of the cases. Biphasic pattern was seen in 23.1%. No cases of triphasic and permanent patterns were recorded. The time to symptom onset in 69.2% cases was between 24-48 hours. Early onset of symptoms in less than 24 hours occurred in 15.4% while also 15.4% symptom onset occurred after 48 hours.

Figure 9: Bar chart showing presence of postoperative Central DI

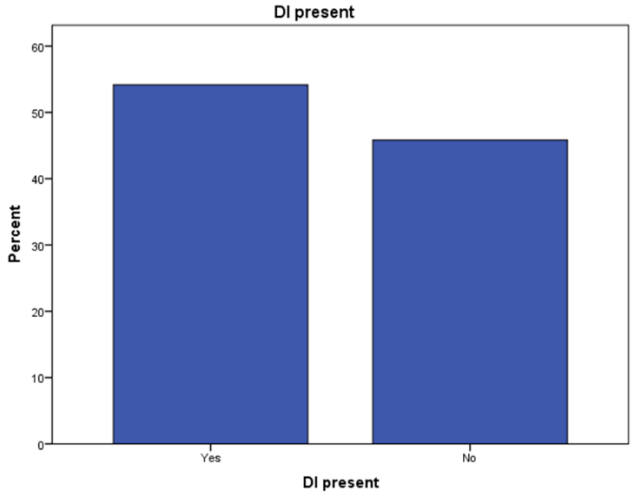


Table 4: Pattern of postoperative Central DI

	Frequency	Percent
Transient	10	76.9
Biphasic	3	23.1
Triphasic	0	0.0
Permanent	0	0.0
Total	13	100.0

Table 5: Associations of Central DI

Variable	Central Diabetes Insipidus		P value*
	Present	Absent	
Age			
<12	7 (77.8)	2 (22.2)	0.084
>12	6 (40)	9 (60)	
Sex			
Male	2 (28.6)	5 (71.4)	0.122
Female	11 (64.7)	6 (35.3)	
Type of surgery			
Endoscopic	1 (20)	4 (80)	0.131
Transcranial	11 (61.1)	7 (38.9)	
Type of tumor			
Arachnoid cyst	0 (0)	1 (100)	0.458
Craniopharyngioma	6 (75)	2 (25)	0.156
Meningioma	3 (42.9)	4 (57.1)	0.660
Pilocytic astrocytoma	2 (100)	0 (0)	0.283
Pituitary adenoma	2 (33.3)	4 (66.7)	0.239
Prior Surgery			
Yes	4 (50)	4 (50)	0.556
No	9 (56.3)	7 (43.7)	

*p values are based on Fishers exact test (level of significance $p \leq 0.05$)

There was no association between patients' age, sex, the type of surgery done and the histology of the tumor with the development of central DI.

5.0. DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1. Discussion

In terms of biodemographic features, the mean age was 28.69 years with a range of 2-71 years. The male to female ratio was 1:2.4, showing a female predominance of these sellar parasellar tumors. Prior studies (1,3, 34, 37) had shown a comparable wide age range for these tumors showing the various age predominant pathologies seen. Female predominance is also similar to prior studies that most ratios of up to 1.2-1.7: 1(3,15,16,19, 34). The M:F ratio for those with central DI was 1:9 and mirrors those following pituitary surgery as seen in prior studies (3,15,37). A similar study in Greece demonstrated 69.6% of the lesions being suprasellar (3) unlike in our case where 83.3% of the patients had tumors in both sellar and parasellar region that depicts late presentation to our neurosurgical service for intervention when tumors are very large in size.

This region has a range of neurovascular structures hence a broad tumor heterogeneity. Among the evaluated participants with sellar parasellar tumors across the age ranges, craniopharyngioma was the most common tumor comprising 33.3% of the total. Meningioma was the second most common tumor forming 29.2%. Craniopharyngioma was largely seen in pediatric age group alongside pilocytic astrocytoma seen in 8.3% of the cases. These findings are similar to the study by Hakizimana et al who showed that the most common diagnoses for both adults and children were pituitary adenoma, craniopharyngioma and meningiomas in Rwanda. Other studies also showed pituitary adenoma as the most common tumor in this region (3,20).

Among patients with central DI, craniopharyngioma was the most common tumor occurring in 46.2% of patients with DI in our study. This is similar to a study by Angelousi et al which demonstrated craniopharyngioma as the most common pathology associated with post operative central DI in 31% of the cases (3). Meningioma was the second commonest and comprised 23.1% of pathologies associated with central DI. Pilocytic astrocytoma pituitary adenoma were the least common tumors seen in post operative central DI each forming 15.4%.

Among these patients who developed post operative central DI, 84.6% had undergone transcranial surgeries while 15.4% underwent endoscopic transsphenoidal resection. Prior studies though inconsistent had associated central DI rates to be high following transcranial as compared to endoscopic surgery (2,15), the association cannot be fully drawn due to large tumors that preclude endoscopic surgery as the primary approach in our set up. Other studies

showed similar rates of central DI after resection of pituitary tumors between both endoscopic and transcranial routes (20).

The most common clinical features in patients who developed central DI was both polydipsia and polyuria which was seen in 69.2% patients. 30.8% of the patients however presented with polyuria alone. This demonstrates that polyuria is a very reliable clinical parameter in central DI patients. This confirms polyuria as a hallmark for central DI as seen in other studies (2,3,7, 15,20,26,37).

Regarding laboratory findings, 76.9% of patients diagnosed with post operative central DI had serum sodium more than 150mmol/L at the time of diagnosis. Only 23.1% had serum sodium less than 150mmol/L. Most studies have reported central DI occurring with serum sodium more than 145mmol/L in 92.9% (2, 3, 15, 37). Among those who developed post operative central DI in our study, 69.2% had urine SG less than 1.005 and 30.8% had urine SG more than 1.005 (between 1.010 to 1.015). All patients had urine SG less than 1.015 at the time of diagnosis of central DI. Most studies showed serum sodium above 145mmol/L as cut off criterion (2,15, 20,37). This demonstrates utility of both serum sodium and urine SG in diagnosis of central DI.

The rate of post operative central DI was 54.2% in our study. This was higher than that for non-adenomatous lesions that Angelousi et al found rates of 27.8% (3,15) but mirrors studies by Qari et al among pituitary surgeries (37). Our findings fall within the highly variable rates from 0-90% that has been reported by various studies (2,3,20,37,). Transient DI pattern was the most common pattern occurring in 76.9% of the patients with central DI. This similar to most studies on pituitary surgeries and sellar region tumors that demonstrate transient DI as the commonest (2, 3, 21, 25,37). Biphasic DI was seen in 23.1% of cases. No case of triphasic and permanent DI was recorded in our study.

5.2 Conclusion

In our study population, the rate of post operative central DI after surgery for sellar and parasellar tumors was 54.2%. The most common pattern type was transient DI that comprised 76.9% of the cases.

5.3. Recommendations

The use of clinical and laboratory parameters is reliable in diagnosis of central diabetes insipidus and health care workers should utilize this in patient care and to guide instituting desmopressin treatment. Post operative central DI is associated with endocrinopathy in a number of patients and a further study on post operative endocrinopathy after surgery for sellar and parasellar tumors is recommended.

Table 6: Study Timelines

Month **Activity**	**Nov-Dec 2021**	**Jan-March 2022**	**April-May 2022**	**June-August 2022**	**Sept 2022-April 2023**	**April-May 2023**	**April-May 2023**
Concept development							
Proposal writing							
Presentation							
Ethics approval							
Data collection							
Data analysis							
Presentation of results							

Table 7: Study budget

ITEM	COST (KES)
KNH-UON ERC	5,000
Stationary	30,000
Data storage	15,000
Statistician Fee	30,000
Publication Fee	10,000
Miscellaneous	50,000
TOTAL	140,000

The budget included costs for materials needed for the study e.g, stationary (paper, printer ink cartridges, pens, folders, stapler and staples, data storage device (flash disk), cost for ethics review, statistician and publication fee is also included. The total cost of the study was funded by the principal investigator.

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APPENDICES

Appendix I: Participant Information and Consent Form

TITLE OF THE STUDY: RATES AND PATTERNS OF CENTRAL DIABETES INSIPIDUS AFTER SURGERY FOR SELLAR AND PARASELLAR TUMORS IN KNH

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Introduction:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in medical research:

i) Your decision to participate is entirely voluntary.

ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal.

iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? YES / NO

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee protocol No. _____

What Is This Study About?

The researchers listed above are interviewing and collecting information on patients who undergo surgery for sellar and parasellar brain tumors. The purpose of the study is to find out the rates and patterns of Central DI after surgery for sellar and parasellar tumors. This is aimed at fostering the understanding of this condition which will help in care of patients following these types of brain tumors. The blood and urine tests done routinely post operatively after surgery together with preoperative scans and post operative clinical information will be evaluated.

There will be approximately 31 participants in this study randomly chosen. We are asking for your consent to participate in this study.

What Will Happen If You Decide To Be In This Research Study?

If you agree to participate in this study, the following things will happen:

Your post operative urine, blood and tissue biopsy test results as requested by your doctor will be analyzed as well as clinical evaluation after surgery including preoperative diagnosis. Your bio data will also be collected from you. We will ask for a telephone number where we can contact you if necessary. If you agree to provide your contact information, it will be used only by people working for this study and will never be shared with others. The reasons why we may need to contact you include clarifying details of your past medical history.

Are There Any Risks, Harms Discomforts Associated with This Study?

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being

in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be secure, so it is still possible that someone could find out you were in this study and could find out information about you.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview.

Furthermore, all study staff and interviewers are professionals with special training in these examinations. In case of an injury, illness or complications related to this study, contact the study staff right away at the number provided at the end of this document. The study staff will treat you for minor conditions or refer you when necessary.

Are There Any Benefits Being In This Study?

This information you provide will help us better understand the complications regarding central diabetes insipidus that happens after surgery. This will help in instituting treatment and guide the duration of treatment. It will help health care workers caring for other patients with similar tumors in future by providing them with relevant working knowledge. This information is a contribution to science and medicine.

Will Being In This Study Cost You Anything?

No additional costs will be incurred because of being recruited in this study beyond the tests requested by your doctors.

Will You Get Refund For Any Money Spent As Part Of This Study?

There shall be no refunds because of being recruited in this study

What If You Have Questions In Future?

If you have further questions or concerns about participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

What Are Your Other Choices?

Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice or loss of any benefits.

Consent Form

Participant's statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counsellor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential. By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study: Yes ☐ No ☐

I consent for my child/parent/spouse/sister/brother/kin to participate in this study (For unconscious, confused, sedated patients or minors)

Y ☐ N ☐

I agree to provide contact: Yes ☐ No ☐

Participant/Kin printed name: ……

Relationship ……...

Participant signature / Thumb stamp _____

Date _____

Surrogate consent (For minors and adults who cannot consent due to cognitive impairment).

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counsellor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my child/spouse/Parent or kin participation in this study is voluntary and that we may choose to withdraw any time. I freely agree to consent on behalf of my ……...(child/spouse/parent/kin-specify) to participate in this research study.

I understand that all efforts will be made to keep information and the identity confidential. By signing this consent form, I have not given up any of the legal rights that of my ……. (child/spouse/parent/kin-specify) has as a participant in a research study.

I consent for my child/parent/spouse/sister/brother/kin to participate in this study

Y ☐ N ☐

I agree to provide contact: Yes ☐ No ☐

Participant/Kin printed name: ……

Relationship ……...

Signature / Thumb stamp _____

Date _____

Researcher’s statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher ‘s Name: _____

Date: _____

Signature: _____

Role in the study: _____

IDHINI KWA KISWAHILI

FOMU YA IDHINI

Fomu hili lina sehemu tatu

I. Maelezo ya Mtafiti Mkuu na utafiti

II. Fomu ya Idhini

III. Kiapo cha Mtafiti

(i) Sehemu ya kwanza –Maelezo ya Mtafiti Mkuu na utafiti.

Mimi ni Dkt. Ngetich Gilbert Kiprop, kutoka chuo kikuu cha Nairobi, Shule ya Utabibu, Idara ya upasuaji, sehemu ya Ubongo. Ninafanya utafiti wa kubainisha “Rates and patterns of central diabetes insipidus after surgery for sellar and parasellar tumors in KNH” yani, kubainasha “viwango na mienendo ya ugonjwa wa kisukari insipidus baada ya upasuaji wa upimbe wa sellar na parasellar huko knh”.

Utafiti huu unaangalia viwango na mienendo ya ugonjwa wa kisukari insipidus baada ya upasuaji wa upimbe wa sellar na parasellar huko knh. Hili litasaidia katika matibabu ya wagonjwa wenye upimbe za sehemu hii baada ya upasuaji na kusaidia kwa kuelimisha wanaowatunza wagonjwa hao baada ya upasuaji. Hili litasaidia kupunguza wagonjwa kukaa sana hospitali baada ya upasuaji wa sehemu hii ya ubongo.

Ningependa kukuchagua kushiriki katika utafiti huu. Kukubali kwako ni kwa hiari yako. Kukataa kwako hakutadhuru matibabu unayopata wako anafaa kupata, hautakatazwa matibabu kwa sababu ya kukataa kushiriki utafiti huu.

Kushiriki utafiti huu hakutakudhuru au kudhuru mtoto wako kwa njia yoyote kwani kile kinachohitajika ni vipimo za damu na mkojo ambavyo pia ni sehemu ya vipimo zinazofanyika baada ya upasuaji kulingana na maagizo ya daktari wako.

Habari zozote zitakazokusanywa kutoka kwako zitashughulikiwa kwa usiri na hazitasambazwa kwa yeyote ila tu kwa ruhusa kutoka kwa kamiti kuu ya utafiti ya chuo kikuu cha Nairobi, hospitali kuu ya Kenyatta (KNH/UON ERC).

(ii) Sehemu ya pili– Idhini ya mgonjwa

Mimi (Jina)..... kwa hiari yangu, nimekubali kushiriki/ kushirikisha mtoto wangu katika utafiti huu ambao unafanywa na Daktari Ngetich Gilbert Kiprop.

Nimeelezewa manufaa na madhara ya utafiti huu kwa undani na nimeyaelewa.

Jina la Mgonjwa.....

Sahihi.....

Tarehe.....

Siku/Mwezi/Mwaka

ii) Idhini kwa wale wasioweza kutoa idhini kwa mujibu wa sheria (Watoto chini ya miaka 18 na wasio na ufahamu wa kutoa idhini

Ningependa kuchagua mume/mkeo/mzazi wako/ mtoto wako/ndugu yako (bainisha uhusiano) ……. katika utafiti huu. Kukubali kwako ni kwa hiari yako. Kukataa kwako hakutadhuru matibabu unayopata/ mtoto wako/jamaa wako au unayemwakilisha anafaa kupata, hatakatazwa matibabu kwa sababu ya kukataa kushiriki utafiti huu.

Kushiriki utafiti huu hakutamdhuru mtoto wako/mzazi wako/ndugu/jamaa yako kwa njia yoyote kwani kile kinachohitajika ni vipimo za damu na mkojo ambavyo pia ni sehemu ya vipimo zinazofanyika baada ya upasuaji kulingana na maagizo ya daktari wako.

Habari zozote zitakazokusanywa kutoka kwako zitashughulikiwa kwa usiri na

hazitasambazwa kwa yeyote ila tu kwa ruhusa kutoka kwa kamiti kuu ya utafiti ya chuo

kikuu cha Nairobi, hospitali kuu ya Kenyatta (KNH/UON ERC).

Mimi (Jina)..... / Mzazi/ndugu/mume/mke/ndugu Cbainisha uhusiano) wa..... kwa hiari yangu, nimekubali kushiriki/

kumshirikisha katika utafiti huu ambao unafanywa na Daktari Ngetich Gilbert Kiprop.

Nimeelezewa manufaa na madhara ya utafiti huu kwa undani na nimeyaelewa.

Jina la Mgonjwa/ Mzazi.....

Sahihi.....

Tarehe.....

Siku/Mwezi/Mwaka

Nambari ya utafiti.....

Sahihi.....

Tarehe.....

(Siku/Mwezi/Mwaka)

Unaweza kupata uchambuzi wa utafiti huu na maelezo zaidi kutoka kwa:

Katibu wa utafiti,

Hospitali kuu ya Kenyatta (KNH/UON ERC).

Sanduku la Posta 20723 00202.

KNH, Nairobi, Kenya

Nambari ya simu: 020726300-9.

Appendix II: Data Collection Tool

STUDY NUMBER ……

1.Biodata

a) Age (Years) ……. B) Sex: Male ☐ Female ☐

2.a) Preoperative radiological diagnosis …….

b) Imaging study used CT scan ☐ MRI ☐ Both ☐

3. a) Anatomical location of tumor

Sellar ☐

Parasellar ☐

Both ☐

b) Type of surgery Transcranial ☐ Endoscopic ☐

c) Histological diagnosis ……

4. Clinical features a) Polydipsia Y ☐ N ☐

Polyuria Y ☐☐

b) Vital signs BP…….PR…… Oral Mucosa Dry ☐ Moist ☐

c) Symptoms present before surgery Y ☐ N ☐

d) Electrolyte abnormalities before surgery Y ☐ N ☐

e) Prior Cranial surgeries Y ☐ N ☐

5. a) Time of onset of symptoms after surgery……

6. Urine output/24hrs

Day	0	1	2	3	4	5	6	7	8	n
Volume										

b) Post operative day of resolution of symptoms …….

7. Laboratory parameters

a) i)Sodium and Urine SG

Postop Day	0	1	2	3	4	5	6	7	8	9	10	n
Serum Na+(mmol/l)												
Urine SG												

ii) Post operative day of normalization of serum Na+ ……

ii)Post operative day of normalization of urine SG ……

c) Random Blood sugar at onset of symptoms ……...

9. Fulfills criteria for Central DI? Y ☐ N ☐

10. Pattern of Central DI

Transient ☐ Triphasic ☐ Biphasic ☐ Permanent ☐

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Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

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

Ref: KNH-ERC/A/378

28th September, 2022

Dr. Gilbert Kiprop Ngetich
Reg. No. H58/6719/2017
Dept. of Surgery
Faculty of Health Sciences
University of Nairobi

Dear Dr. Ngetich,

RESEARCH PROPOSAL: RATES AND PATTERNS OF CENTRAL DIABETES INSIPIDUS AFTER SURGERY FOR SELLAR AND PARASELLAR TUMORS IN KNH (P585/07/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P585/07/2022.** The approval period is 28th September 2022 – 27th September 2023.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://research-portal.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely,

DR. BEATRICE K.M. AMUGUNE
SECRETARY, KNH-UoN ERC

c.c. The Dean, Faculty of Health Sciences, UoN
The Senior Director, CS, KNH
The Assistant Director, Health Information Dept., KNH
The Chairperson, KNH- UoN ERC
The Chair, Dept. of Surgery, UoN
Supervisors: Dr. Peter Kitunguu, Dept. of Surgery, UoN
Dr. Michael Magoha, Dept. of Surgery UoN
Dr. Susan Karanja, Consultant Neurosurgeon, Dept. of Surgery, KNH

RATES AND PATTERNS OF CENTRAL DIABETES INSIPIDUS AFTER SURGERY FOR SELLAR AND PARASELLAR TUMORS IN KNH

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