

CASE REPORT/CAS CLINIQUE

CLINICAL EXPERIENCE AND OUTCOME OF PITUITARY SURGERY IN KENYAN PATIENTS AT THE KENYATTA NATIONAL HOSPITAL

EXPÉRIENCE ET RÉSULTATS DE LA CHIRURGIE HYPOPHYSIAIRE CHEZ DES PATIENTS KENYANS AU KENYATTA NATIONAL HOSPITAL

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ABSTRACT**Introduction**

Surgical extirpation of pituitary lesions and can be performed by craniotomy or trans-sphenoidal hypophysectomy. This could be for pituitary ablation, excision of pituitary adenomas, craniopharyngiomas, suprasellar meningiomas and other types of tumors of the sellar region. Despite this being a common neurosurgical procedure there is a paucity of data on the local Kenyan experience and outcomes following pituitary surgery.

Study Design and Site

A retrospective study at the Kenyatta National Teaching and Referral Hospital.

Objectives

To evaluate the clinical presentation, management and outcome of patients undergoing surgery for pituitary lesions at the Kenyatta National Hospital.

Patients and Methods

Following ethical approval, patients' records were retrieved and assessed for clinical and radiologic features of pituitary lesions, surgical treatment and post operative outcome. All the data was coded and analysed using Statistical Package for Social Sciences (SPSS) version 16.0.

Results

Sixty five patients, 39 (60%) female and 26 (40%) male patients were included. The mean age was 36.88 years (+14.689). The most common presentation were visual disturbances reported by 57 (87.7%) of the patients having reduction in visual acuity, while 37 (56.9%) had bitemporal hemianopia. Sixty two (95.4%) patients were operated during the study period and of these 28 (45.2%) by the transphenoidal approach as opposed to 34 (54.85%) by craniotomy. The pterional trans-sylvian approach was the most prevalent of transcranial hypophysectomies accounting for 17 (50%) patients, while 15 patients (44.1%) were operated by the subfrontal approach and two patients were operated via midline trans-callosal approach. Majority (96.4%) of trans-sphenoidal hypophysectomies were by sub-labial incision. Fifty (76.9%) of the patients had good functional outcome while 11 (16.9%) and 4 (6.2%) suffered moderate and severe disability respectively. Patients' age ($p=0.0029$), duration of symptoms prior to surgery ($p=0.0018$) and surgical management versus conservative ($p=0.001$) significantly affected patient outcome. There was no statistically significant difference in outcome between patients of different sex ($p=0.058$) or the type of operation performed ($p=0.191$).

Conclusion

Transsphenoidal and trans-cranial approaches are effective and safe treatment strategies for pituitary lesions with low morbidity, mortality and recurrence rates.

INTRODUCTION

Pituitary adenomas account for 10 to 15 % of all intracranial tumors and in addition to suprasellar tumors such as craniopharyngiomas, meningiomas, germinomas and low grade gliomas, account for a significant portion of the surgical workload of any neurosurgical practice³⁰. Tumors of the suprasellar region assume importance because of their anatomical proximity to the anterior visual apparatus and neuroendocrine structures (the pituitary gland and hypothalamus) which influences their clinical presentation and progression.

Surgical extirpation is the treatment of choice for pituitary adenomas and other types of tumors of the sellar region and clivus. Pituitary and sellar mass lesions presenting with chiasmatic syndrome, ophthalmoplegia, pituitary apoplexia or endocrine derangement can undergo successful surgical removal³⁴. Access to the pituitary may be achieved by craniotomy via subfrontal, pterional and sub-temporal approaches. In addition, the transsphenoidal route is widely accepted as the approach of choice for intrasellar lesions and some centers have also advocated the transsphenoidal route for tumors with subdiaphragmatic origin and subsequent suprasellar extension⁹. These subdiaphragmatic lesions are thought to be more easily removed by a transsphenoidal approach because the expanded sella provides a widened aperture to the suprasellar compartment and also diaphragmatic protection from pial invasion²⁶. Further, the transsphenoidal approach has a number of variations, including the sublabial transseptal, transnasal endoscopic, endonasal rhinoseptoplasty, and transnasal septal displacement^{26, 37}.

However, despite the major advances, reported success rates and low morbidity and mortality, there is a paucity of local data regarding the Kenyan experience and outcomes of this popular procedure. Kenyatta National Hospital is a teaching and referral hospital with a bed capacity of over 2000 patients. Through this centre the majority of neurosurgical referrals are managed. We reviewed the records of patients who were treated for pituitary tumors in the neurosurgical unit.

METHODS

Following ethical approval, the records of patients who presented to the Kenyatta National Hospital and underwent surgery for pituitary lesions from June 2000 to June 2010 were retrieved and reviewed. Patient biodata, type and duration of symptoms, hormonal profile and management modalities were recorded in a pre-formed questionnaire. A data entry interface was created through which codified data was entered and data analysis carried out using Statistical Package for Social Sciences (SPSS) version 16.0. Frequencies and means were computed for description of the various variables and presented in prose form and as pie charts and graphs. The association between categorical variables was calculated using Chi-square test while comparison of mean values was performed using the one-way analysis of variance test (ANOVA).

RESULTS

Biodata and Clinical Presentation A total of 65 patients fit the inclusion criteria during the study period and their files were retrieved and reviewed. There were 39 (60%) female as compared to 26 (40%) male patients (Figure 1).

The mean age was 36.88 (+ 14.689) with a range from 2 years and 6 months to 72 years. Majority of the patients (55%) were aged between 26 and 45 years whereas pediatric patients (aged less than 13 years) and elderly patients (over 61 years) accounted for 5% each (Figure 2).

The most common presentation were visual disturbances reported with 57 (87.7%) of the patients having reduction in visual acuity, while 37 (56.9%) had bitemporal hemianopia on confrontational and formal perimetry. Fundoscopy findings were reported for 39 patients with 24 (61.5%) of these being normal and optic atrophy and papilledema being reported for 29% and 9.5% respectively. The right and left eyes were each affected in 8 cases (12.3%) with bilateral involvement in 41 (63.1%) and 8 patients had no ocular involvement. Forty eight patients (73.8%) reported headaches while only 6% and 5% reported vomiting or convulsion respectively.

Amenorrhea and primary infertility were the presenting complaint of 11 (16.9%) patients while 14 (21.5%) and 8 (12.3%) had galactorrhea and gynecomastia respectively. Ten patients (15.4%) had acromegalic features of hypergnathia and enlarged hands and feet. In addition, 9 (13.8%) patients had erectile dysfunction, while 4 (6.2%) had atrophic testes with gynoid habitus and female hair distribution (Figure 3).

One patient aged two years and six months presented with features of precocious puberty. She had progressive breast development since eight months of age and at presentation was at tanner stage IV with growth of pubic hair from 11 months of age. In addition she experienced monthly mensrual-like flow from 1 year of age and had a post-pubertal uterus on ultrasound. She was however reported to have a normal growth rate.

Admission blood pressures were measured and recorded for all the patients and were classified using the World Health Organisation-International Society of Hypertension guidelines. Majority of the patients (65%) had optimal blood pressures while 7.5% and 5% had moderate and severe hypertension (figure 4). Also recorded were admission random blood sugars, of which 49 (75%) were normoglycemic and 12.5% each were glucose intolerant and within diabetic range each (Figure 5).

Data of the hormonal profile was also retrieved where available. Prolactin levels were recorded for 47 patients with 22 (46.8%) of them having hyperprolactinemia as compared to 21 (44.7%) and 4 (8.5%) having normal and low levels respectively. Majority of the patients were euthyroid (72.4%) while 10.3% and 17.3% were hyperthyroid and hypothyroid respectively. Cortisol levels were recorded for 41 patients of whom 4 had hypercortisolemia levels and 9 had normal with 8 patients having low levels (Table 1).

With regards to imaging, all the patients included in the study had a CT scan done while a further 8 (12%) and 5 (7.7%) had an MRI and 4-vessel angiography done respectively. The location of the lesion was described as completely intrasellar 15 (23.1%), sellar with suprasellar extension 40 (61.5%), suprasellar 5 (7.7%) or sellar with supra-, infra- and parasellar extension 5 (7.7%) (Figure 6).

Sixty two (95.4%) patients were operated during the study period, of these 28 (45.2%) by the transsphenoidal approach as opposed to 34 (54.85%) by craniotomy. In addition, there were 2 patients who had initially undergone transsphenoidal hypophysectomy who were re-operated transcranially for recurrences at 2 years and 4 years. The three patients who were not operated are included in the table below:

The pterional trans-sylvian approach was the most frequent of transcranial hypophysectomies accounting for 17 (50%) of these operations. Further, 15 patients (44.1%) were operated by the subfrontal approach with frontal lobe retraction and two patients were operated via midline trans-callosal approach. With regards to the 28 patients operated trans-sphenoidally, majority 27 (96.4%) were by sub-labial incision with blunt dissection up to the maxilla and nasal crest. Septal mucosa was then stripped up to the vomer which was excised. The ostia of the sphenoid were then identified, the body of sphenoid nibbled and the floor of the sella turcica opened. The tumor was then exposed, biopsied and removed by curette and suction.

One 37 year old patient who developed progressive blindness, erectile dysfunction and general weakness for 2 years had a pituitary tumor on CT and MRI with a sellar component, suprasellar extension, sphenoid bone erosion obliterating the sphenoid sinus and extension to both cavernous sinuses. He was scheduled for endonasal endoscopic biopsy as he was a poor anaesthetic risk for general anaesthesia due to persistent hypotension secondary to adrenocortical insufficiency.

Fifty (76.9%) of the patients in this series had good functional outcome with marked improvement in visual function, normalised post-operative hormone levels and regression of symptoms while 11 (16.9%) and 4 (6.2%) suffered moderate and severe disability respectively. There was no early post-operative mortality among this cohort. There was no statistically significant difference in outcome between patients of different sex ($p=0.058$). However, patients' age was a significant indicator of outcome. Pediatric patients in this series had good functional outcome in comparison to patients above 61 years who developed severe disability ($p=0.0029$). In addition, the duration of symptoms prior to surgery significantly affected patient outcome ($p=0.0018$). Majority of the patients (24) who presented within 6 months had good outcome compared to none of the patients who presented after 5 years of symptoms. Findings on fundoscopy had a significant on visual outcome as patients in whom optic atrophy was reported had a higher incidence of blindness and thus severe disability in comparison with those in whom the fundoscopy was normal. Patients who were operated

had a higher incidence of good functional outcome as compared to those managed conservatively ($p=0.001$) irrespective of the type of operation performed ($p=0.191$).

Transient fluid-electrolyte imbalance and diabetes insipidus (DI) was the most common postoperative complication (7.7% of the patients) in the present series. Hypothyroidism occurred in 6.2% of the patients as the second most common complication. In addition 2 patients has recurrences of tumor with clinical and radiological evidence at 2 and 4 years and had to undergo craniotomy and excision. Post-operative rhinorrhea was reported in 6.2% of the patients and was managed conservatively.

DISCUSSION

Although pituitary tumors are the most commonly encountered intracranial neoplasms, their true incidence has not been established with certainty. In literature, the prevalence of these tumors in autopsy series is reported to be 5-20%^{7, 27, 32} while most recent series estimate the prevalence of clinically apparent pituitary lesions to comprise approximately 10-15 % of all intracranial lesions^{10, 18}. Improvement in radiographic imaging, biochemical detection of hormonal abnormalities, and microsurgical techniques have raised the number of surgical procedures, and in some series pituitary adenomas represent approximately 25% of surgically resected intracranial neoplasms; however, this may reflect a bias that reflects the interests of the surgeon or institution.

In the current study, there is a slight majority of 39 (60%) female as compared to 26 (40%) male patients. Previous studies report that pituitary tumors tend to afflict both sexes equally^{3, 5, 18}. In addition, the mean age was 36.88 years (+ 14.689) with most of the patients (55%) were aged between 26 and 45 years and fewer patients at both extremes of age. There is a wide range of reported mean ages in literature ranging from 39.8 years⁴⁰ to 50.4 years¹⁰. Reported incidence rates demonstrate an increase with age for both clinically apparent and autopsy diagnosis of pituitary tumors. In this regard, autopsy analyses and imaging studies report that more than 30% of people 50 - 60 yr of age harbor clinically undetected tumors^{5, 7, 28, 31}. Further, it is widely reported that pituitary adenomas are infrequent in childhood accounting for only about 3.5- 8.5% of pituitary adenomas which are diagnosed before the age of 20 yr^{23, 33}. Childhood tumors exhibit a female preponderance, and it has been suggested that they are smaller, less invasive, and less aggressive than tumors of adults²³.

Patients with pituitary tumors present with signs and symptoms related to mechanical effects of an expanding tumor within the sella turcica (headaches, visual disturbances and cranial nerve palsies), excessive or impaired hormone production³. The most common presentation in this series, were visual disturbances reported by 57 (87.7%) of the patients with reduction in visual acuity. Chang¹⁰ reported that in an American population, over one half of patients presented with visual disturbance while other studies have reported a prevalence rate of up to 90%^{19, 39}. The classic bitemporal field loss is found in chiasmatic compression and was described by 37 (56.9%) of the patients. These patients frequently complain of bumping into objects on one or both sides of the contracted visual field, reflecting both unilateral and bitemporal field loss. However, early compression may lead to upper quadrantic defects secondary to inferior chiasmatic fiber compression.

Central vision may be affected by direct compression of the intracranial optic nerve. This may present as a blurring of vision or scotomatous central field defects. This is more common in individuals with a "post-fixed" chiasm - an anatomical variation where the chiasm is situated further back, thus exposing more optic nerve to the compressive effects of an expanding adenoma²⁵. If compression has been longstanding, funduscopy may reveal optic atrophy which was observed in 10% of the current population. In our study, 50 (87.7%) the patients had improved visual function following surgery. The reported results in literature of visual outcome after surgical management of pituitary and sellar tumors vary considerably among studies, with improvement rates ranging from 36 to 80%^{2, 4, 20, 21, 24, 25}. Hypertension is an important complication of pituitary tumors and contributes to the increased morbidity and mortality of this condition. In the current study, 12.5% of the patients had moderate and severe hypertension. Bondanelli⁶ reported that the prevalence of hypertension in acromegalic patients is about 35%, ranging from 18 to 60% in different clinical series, while Chanson¹¹ reported a range of 20% to 50% of patients. The exact mechanisms underlying the development of hypertension in pituitary lesions are still not clear but may include several factors including chronic hypervolemia (the plasma volume is 10% to 40% above normal due to increased renal sodium reabsorption at the distal tubule level)^{12, 22}. In addition, hypertension can also result from endothelial dysfunction²⁹ and it has been postulated that insulin resistance and diabetes may also play a role in the onset of hypertension¹³. Recent studies indicate that an increased sympathetic tone could play an important role in

development and maintenance of elevated blood pressure⁶. With regards to surgical approaches, 28 (45.2%) patients were operated by the transsphenoidal approach as opposed to 17 (45.83%). 15 (37.5%) and 2 patients by pterional, subfrontal and midline trans-callosal approaches respectively. However, as the current study was retrospective in nature the indications for choice of approach were not accurately captured in data. When analysed over time, more of the recent surgeries were increasingly via of the transsphenoidal route. This notwithstanding, there was gradual shift towards the transsphenoidal route likely guided by an increase in proficiency and the reported lower morbidity in other populations.

The choice for transphenoidal approach as opposed to craniotomy is determined by a number of factors including degree of suprasellar extension, cavernous sinus invasion, tumor consistency, brain invasion and cerebral edema as well as encasement of the optic apparatus⁴¹. Tumors with significant suprasellar extension, especially through the plane of the hypothalamus and floor of the third ventricle, have been correlated with significantly worse postoperative outcomes^{14, 35}. As such, particular features of suprasellar extension that mandate additional consideration prior to an operation are intraventricular extension, displacement or edema of the hypothalamus, displacement/compression of the proximal branches of the ACA, and involvement of the perforating arteries off the ICA and ACA^{1, 15, 17, 38}.

Firm tumor consistency creates an inherent limitation in the ability to completely deliver the suprasellar tumor component via any transsphenoidal approach. Tumor consistency remains one of the most important, yet elusive, factors in the consideration of an trans-sphenoidal versus open craniotomy for skull base tumors. If a tumor's consistency is known to be fibrotic ahead of time (as in some cases of reoperation), thus making it less amenable to suction, dissection and gross total resection, this should provide added support for consideration of an open approach. On the contrary, a primarily cystic or hemorrhagic appearance on MR imaging, especially a fluid-fluid level, can often lend support to selecting a less invasive approach for sellar region tumors¹⁶. In the future, a priori knowledge of tumor consistency may lend major support to the selection of a skull base approach from above versus below and warrants further research. Although cavernous sinus invasion is by no means a contraindication to selecting a transsphenoidal approach, its presence is known to limit the extent of tumor resection⁴². In addition, the anatomical relationship of the tumor to the optic chiasm, the degree of circumferential encasement of the optic nerve, and invasion of the optic foramina each require careful preoperative consideration. In the majority of suprasellar pituitary adenomas, the plane between the tumor pseudocapsule and arachnoid membrane is preserved, and the tumor can be safely debulked or removed in its entirety from below. If visual loss is the major indication for surgery, the surgeon must be satisfied that the transsphenoidal approach can safely and effectively decompress the optic nerve and chiasm. Otherwise, the patient may be better served by an open craniotomy with direct visualization of these structures, such as a frontoorbital or supraorbital subfrontal eyebrow craniotomy³⁶.

CONCLUSION

In conclusion, key advances have been made to improve the ability to safely treat patients with larger and increasingly complex tumors of the anterior and middle skull base since the re-emergence of the transsphenoidal approach. Nevertheless, patient selection remains of paramount importance in guiding the decision to perform a particular surgical approach for a given tumor, and it remains clear that, for the time being, some patients with large sellar and parasellar region tumors are better served by performing one of many variations of an open craniotomy (such as a pterional, frontoorbital, subfrontal, or interhemispheric approach)⁸. This study highlights the experience and outcomes following pituitary surgery in a Kenyan referral hospital. It demonstrates that good surgical outcomes can be achieved by both the trans-sphenoidal and craniotomy approaches based on the indications and tumor characteristics. There is a need to carry out a prospective study with closer assessment of hormonal profile and response to surgery as well as perioperative management and longer follow-up for outcome. It however, demonstrates the current clinical status and lays a foundation for further inquiry of this subject that is central to neurosurgical practice.

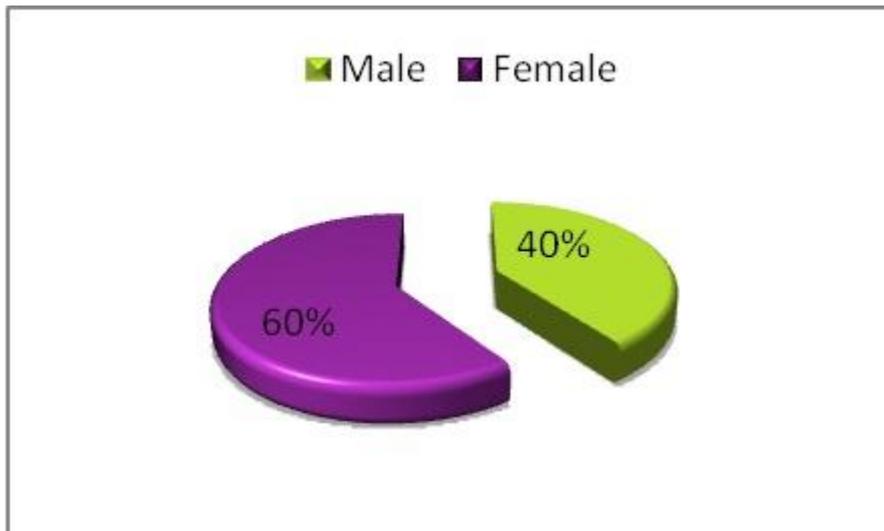


Figure 1: Illustration of the patient distribution by sex

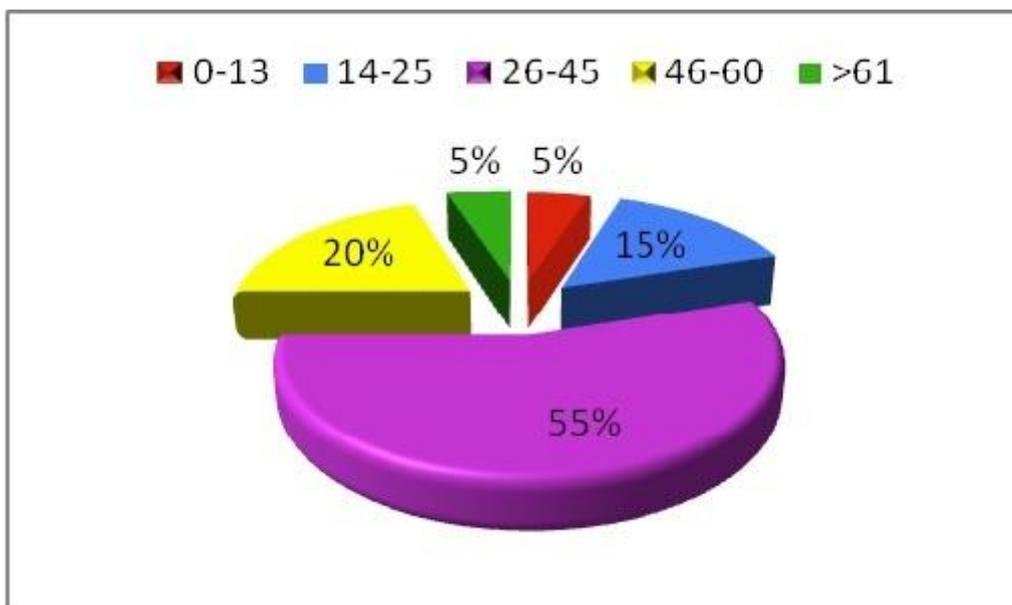


Figure 2: A pie chart demonstrating the distribution by age of patients with pituitary tumors managed at the neurosurgical unit. The majority of the patients were aged between 26-45 years.

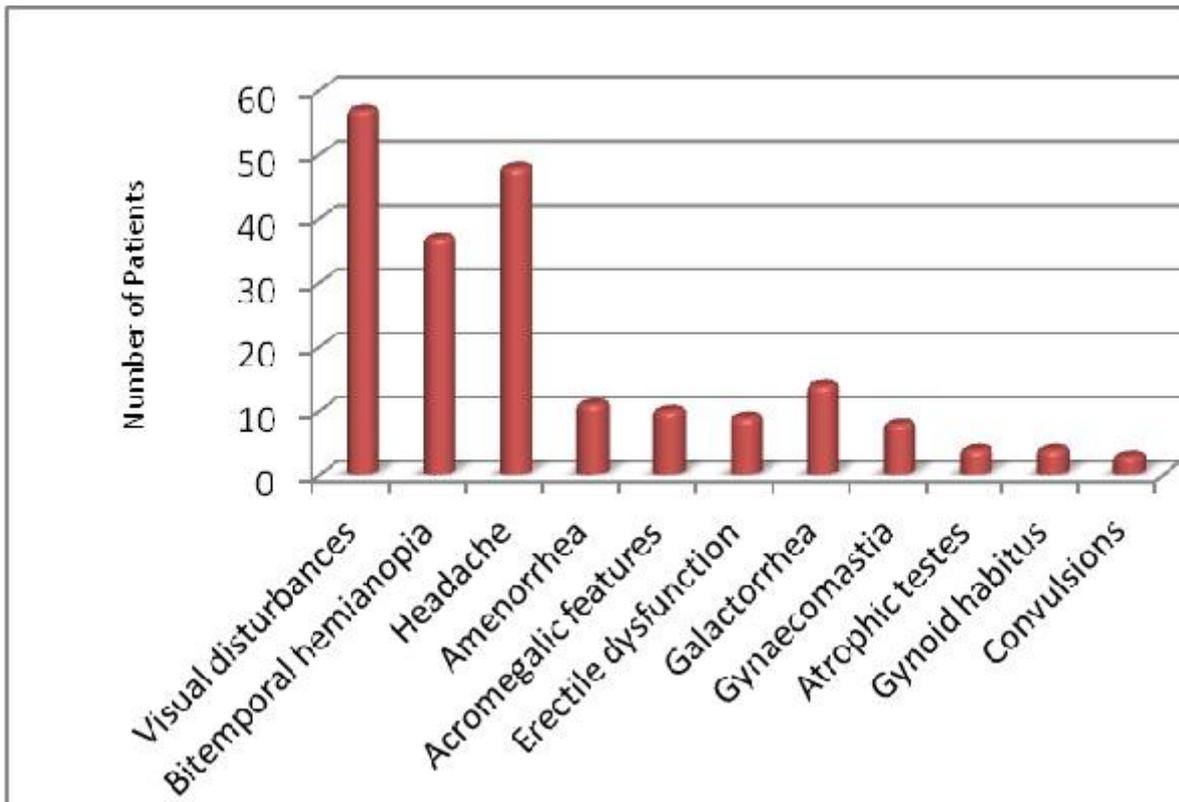


Figure 3: A bar graph showing the frequency of common presentations of patients with pituitary lesions

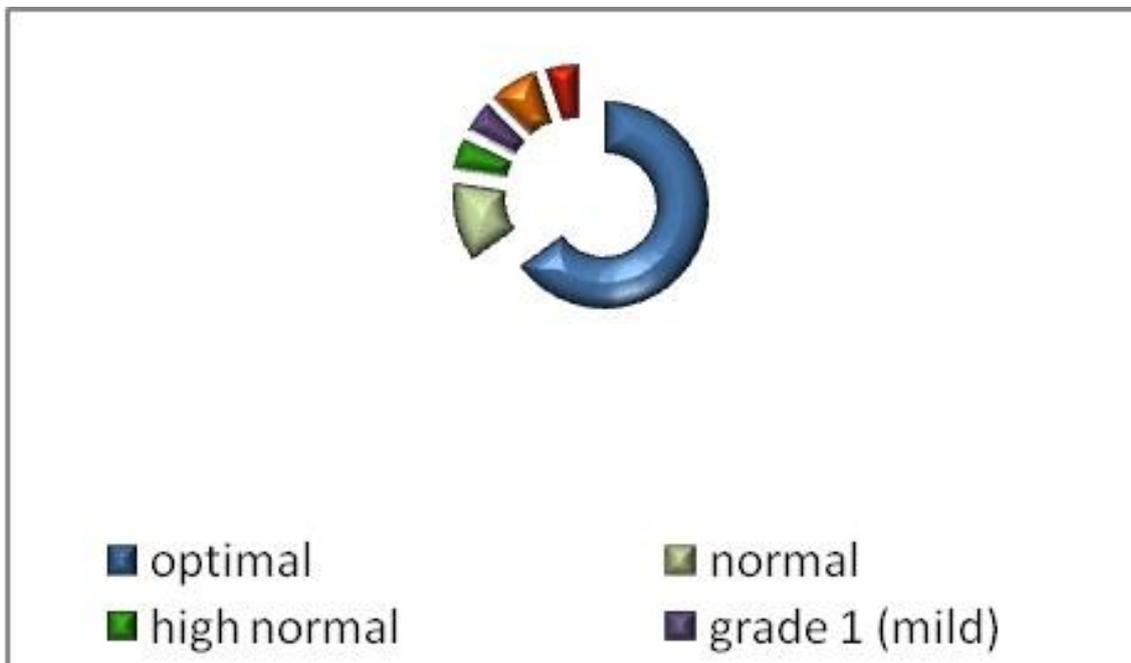


Figure 4: An illustration of the distribution of admission Blood Pressure according to the World Health Organisation-International Society of Hypertension guidelines. Grades 1, 2 and 3 refer to the severity of hypertension

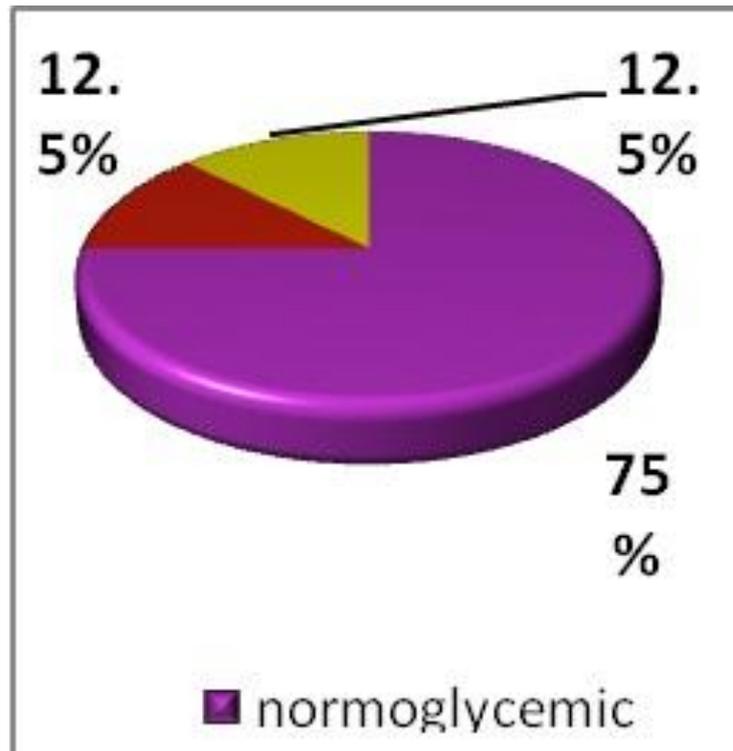


Figure 5: A pie chart representing the proportions of with the various blood sugar levels. Where normoglycemic refers to random blood sugars ≤ 6.9 mmol/L, glucose intolerance (7-11 mmol/L) and diabetes (≥ 11.1 mmol/L).

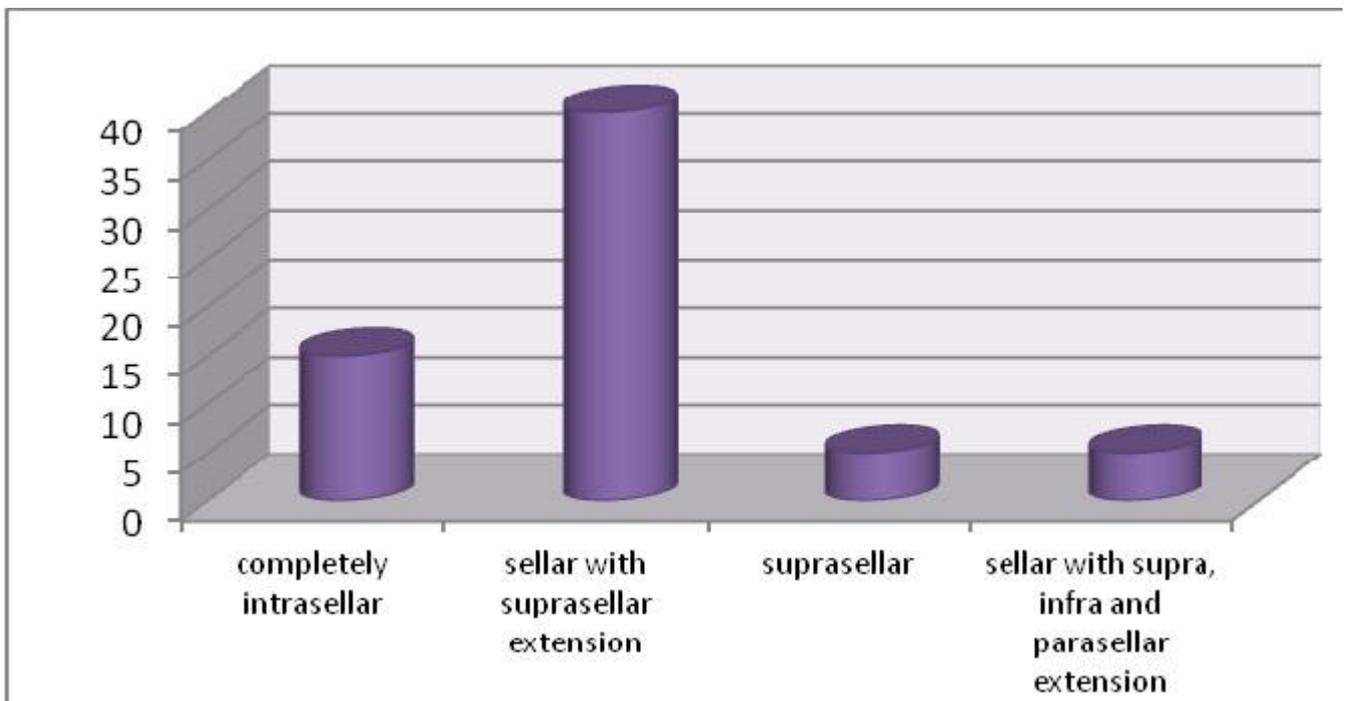


Figure 6: Location of pituitary lesions as seen on CT scan

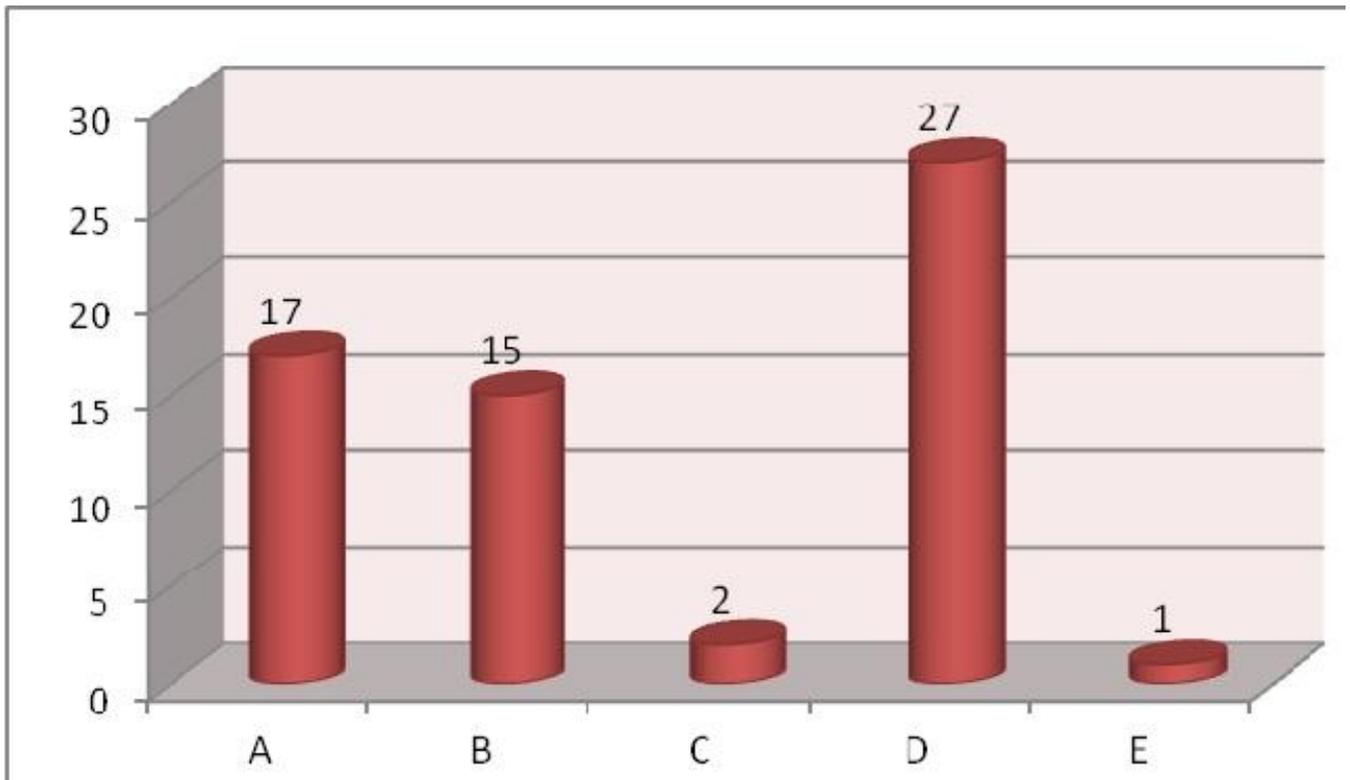


Figure 7: The various approaches to sellar and parasellar lesions
KEY

- A- pterional trans-sylvian approach
- B- subfrontal approach with frontal lobe retraction
- C- midline trans-callosal craniotomy
- D- Sublabial trans-sphenoidal approach
- E- Endoscopic trans-nasal biopsy

Table 1: The hormonal profile of patients with pituitary tumors managed at the neurosurgical unit

Hormone	Levels	
Prolactin (n=47)	High	22 (46.8%)
	Normal	21 (44.7%)
	Low	4 (8.5%)
Thyroid profile TSH,T3,T4 (n=49)	Hyperthyroid	5 (10.2%)
	Euthyroid	39 (79.6%)
	Hypothyroid	5 (10.2%)
Cortisol levels AM and PM (n=41)	High	8 (19.5%)
	Normal	18 (43.9%)
	Low	15 (36.6%)

Hormone	Levels	
Growth hormone levels (n=15)	High	10 (66.7%)
	Normal	4 (26.7%)
	Low	1
FSH (n=7)	Normal	5
	Low	2
Testosterone (n=2)	Normal	2
	Low	0
Estradiol (n=5)	High	2
	Normal	2
	Low	1

Table 2: Patients with pituitary tumors who were not operated. RVD=Retroviral disease, HAART= Highly Active Antiretroviral Therapy, CT= Computed Tomography

1.	A 54 year old RVD patient on HAART who developed bilateral blindness over a period of 4 months, he declined surgery and was lost to follow up.
2.	A 72 year old man who had progressive visual deterioration over 5 year who had a large suprasellar mass on CT, and a normal 4-vessel angiogram who developed dementia and cognitive impairment.
3.	An 88 year old patient with bilateral blindness for 4 years who also had metastatic bronchogenic carcinoma

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