

**ORIGINAL ARTICLE****Visual Outcome of Patients with Pituitary Adenomas Following Surgery and Its Contributory Factors at a Tertiary Hospital in Ghana****Naa Naamuah Tagoe<sup>1\*</sup>, Vera Adobeia Essuman<sup>2</sup>, Patrick Bankah<sup>3</sup>, Thomas Dakurah<sup>4</sup>, Vincent Kwaku Hewlett<sup>5</sup>, Josephine Akpalu<sup>6</sup>, Thomas Akuetteh Ndanu<sup>7</sup>****OPEN ACCESS**

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**ABSTRACT**

**BACKGROUND:** *Craniotomy and transphenoidal microsurgery are surgical options for treatment of pituitary adenoma at Korle Bu Teaching Hospital(KBTH). Despite major advances and reported success rates of transphenoidal resection globally, paucity of local data regarding visual outcome of either procedure exists. We evaluated the visual outcome of patient with pituitary adenoma following surgery in a tertiary hospital in Ghana.*

**METHODS:** *This is a prospective study of 18 of 45 consecutive new patients with pituitary adenoma seen from November 2010 to July 2013 at Korle-Bu Teaching Hospital(KBTH), Accra, Ghana. Sixteen (88.9%) of the 18 had surgery by transphenoidal route and 2(11.1%) by craniotomy. All patients had macroadenoma (tumour size >1cm) and histological confirmation of diagnosis. Pre-operative and post-operative visual acuity and its relationship to tumour size and duration of symptoms before diagnosis were evaluated.*

**RESULTS:** *Data on 18 patients aged 33-60 years, mean (SD) 45.9±8.5, was analysed. Eleven (61.1%) were females. Visual blur, 15(83.3%), and headache, 13(72.2%), were predominant presenting complaints. Common neuro-ophthalmic signs included unilateral or bilateral optic atrophy, 17(94.4%), Relative Afferent Pupillary Defect (RAPD) in 8(44.4%) and impaired colour vision in 32 of 36(88.9%) eyes. Preoperatively, 8(22.2%) and 13(36.1%) of 36 eyes were visually impaired or blind respectively. Postoperatively, 6(16.7%) eyes were visually impaired and 17(47.2%) eyes blind. Blindness was associated with late presentation ( $p<0.005$ ) and larger tumour width ( $p<0.036$ ).*

**CONCLUSIONS:** *More than a third of eyes of patients with pituitary adenoma were blind before and after surgery. Blindness was associated with late presentation and larger tumours. Transphenoidal surgery may be beneficial following early diagnosis to avoid irreversible blindness/visual impairment.*

## INTRODUCTION

Pituitary adenomas account for 10 to 17% of all intracranial tumours (1–4), and remain in many cases undiagnosed since they may be asymptomatic (4). However, some patients may present with well-defined clinical syndromes due to hormonal hypersecretion, including hyperprolactinemia, acromegaly, Cushing's disease and hyperthyroidism or with impaired pituitary function due to compression of the gland (4).

Larger tumours with severe supra- and/or parasella extension may cause severe headache, visual compromise and oculomotor nerve palsy (4,5). Surgery remains the treatment of choice for majority of these tumours and the gold standard for hormonally inactive adenomas (4). In most of these tumours, surgery is required for the relief of visual symptoms and prevention of further visual deterioration (5).

The most widely used surgical approach for pituitary adenomas since the 1960s has been the transphenoidal route, using the operating microscope. It is the preferred approach for most cases of pituitary adenomas, due to its low risk of complications coupled with good outcome (4–8).

Microsurgical transphenoidal surgery has been the main surgical method employed at Korle Bu Teaching Hospital (KBTH) for pituitary adenomas since 2002. Craniotomy is performed for giant tumours which are inaccessible by the transphenoidal approach. There are, however, no published data in Ghana on the visual outcome of these patients following transphenoidal resection or craniotomy. This study sought to determine the visual outcome of patients presenting at KBTH with pituitary adenoma after surgery and to identify the factors which may influence this outcome.

## MATERIALS AND METHODS

This was a prospective case series involving 18 consecutive patients diagnosed with pituitary adenoma and treated surgically from November 2010 to July 2013. Patients who received either medical or no treatment, as well as those who did not consent to participation were excluded from the study.

Ethical approval was obtained from the Ethical and Protocol Review Committee of the University of Ghana Medical School. Pre-operatively, all the 18 patients had clinical (neurological, endocrine and ophthalmic) diagnosis of pituitary adenoma with confirmation by either computerised tomography (CT) or magnetic resonance imaging (MRI).

Patients had surgery either by transphenoidal route or by craniotomy. All patients had histological confirmation of their diagnosis. Demographic (age, sex, history of symptoms), clinical (ophthalmic, endocrine, neurologic) and histopathological data were recorded using a predesigned questionnaire.

Ophthalmic evaluation included visual acuity (VA) tested using Snellen's chart. For patients who were unable to see the letters at the closest test distance, the following test sequence was used: count fingers (CF) at 1 m, hand movement (HM) at 1 m, light perception (LP) and no light perception (NLP). Best corrected Visual Acuity with spectacles (BCVA) was recorded using WHO categories of visual impairment adapted from the International Classification of Diseases (9th revision, 1975), visual status was graded as:  
(a) 'Blind' when visual acuity (VA) was  $<3/60$   
(b) 'Impaired' when VA was  $<6/18-3/60$   
(c) 'Normal' when VA was  $6/6-6/18$ .

Colour vision was tested using Ishihara Colour Vision Charts (38 Plate Edition 1994). Anterior segment assessment included slit lamp examination (using Topcon ATE-600 2004, Japan), pupil reaction to light and Relative Afferent Pupillary Defect (RAPD).

Fundus examination was done using biomicroscopy with a +90D lens, indirect ophthalmoscope with +20D/ +28D lenses and direct ophthalmoscope through dilated pupils (using tropicamide 1%, and or cyclopentolate 1% combined with phenylephrine 2.5% eye drops). Visual field (C30-2) was assessed using a Humphrey visual field analyser (SITA, Carl Zeiss Meditec; Dublin CA, USA, 2005).

Assessment of the size of the tumour was done radiologically using Computerised Tomography scan (CT scan) Hitachi Eclos -2009 or Magnetic resonance imaging (MRI) Hitachi Airis elite (OPEN).

**Endocrine evaluation:** This included clinical examination of patients by the endocrinologist and assessment of anterior pituitary hormones namely leutinizing hormone(LH), follicle stimulating hormone(FSH), 9am serum cortisol, prolactin (PRL), triiodothyronine(free T3), thyroxin(free T4), and thyroid stimulating hormone (TSH).

**Neurosurgical evaluation:** Neurosurgical evaluation by the neurosurgeons included history and examination of the nervous system: Mental state, cranial nerves, coordination, motor and sensory examinations.

**Outcome measures:** Primary outcome measures studied included

- visual acuity at presentation
- visual acuity after surgery

Secondary outcome measures were

- size of tumour at presentation.
- duration of symptoms before presentation.

**Statistical data analysis:** Data was captured using Microsoft Access and analysed using Statistical Package for Social Scientists(SPSS) Version 16.0. Continuous numeric data were summarized as Mean and Standard deviation (SD) and categorical data as percentages (%). Results were presented as frequencies, tables and charts. To prove significant outcomes, t-test was used to compare mean levels of visual acuity between right and left eyes. Mann-Whitney Test was used for establishing significant association between, duration before presentation and, visual acuity, and tumour size. Chi-squared was used to compare proportions, at 0.05 significant levels. Logistic regression analysis was used to establish significant association between visual acuity and tumour type and size.

The association between categorical variables was determined using Chi-square test while comparison of mean values was performed using the one-way analysis of variance (ANOVA) test for more than two means.

## RESULTS

Forty-five consecutive patients were diagnosed with pituitary adenoma during the study period, but data on 18 patients who had surgical treatment was analysed. The ages of the 18 ranged from 33-60 years with mean(SD) = 45.9±8.5. Eleven (61.1%) were females and 7(38.9%) males. Neuroimaging

diagnosis was confirmed by CT scan in 15(83.3%) of the cases and MRI in 3(16.7%) of them.

All 18 patients had pituitary macroadenoma (tumour size>1cm), confirmed by neuroimaging. Out of the 18 patients who had surgery, 16(88.9%) were by transphenoidal route and 2(11.1%) by craniotomy.

**Duration of symptoms before presentation:** The duration of symptoms before presentation ranged from one day to 96 months with mean (SD) of 29.9±30.8 months and median of 24 months. Table 1 shows duration before presentation.

Table 1: Duration of symptoms before presentation in 18 patients with pituitary adenoma

Duration of symptoms (months )	Number (%)
0-6	7(38.9)
7-12	1(5.6)
13-24	2(11.1)
>24	8(44.4)

**Presenting symptoms and signs:** Visual blur (15, 83.3%) and headache (13,72.2%) were the commonest presenting complaints. The commonest neuro-ophthalmic signs encountered were RAPD in 8(44.4%) and unilateral or bilateral optic atrophy in 17(94.4%) of which 10(55.6%) were bilateral. Impaired colour vision occurred in 32(88.9%) of the 36 eyes (Table 2).

### Pre- and post-operative Best Corrected Visual Acuity (BCVA):

Pre-operatively, 21(58.3%) of the 36 eyes were visually impaired or blind . Of these, 5(13.8% eyes had visual acuity of No Perception of Light (NPL). Post-operatively, 23(63.9%) of the 36 eyes were visually impaired or blind (Table 3). Post-operatively, out of 36 eyes, visual acuity improved in 9(25%), worsened in 10(27.8%) and remained the same in 17(47.2%).

Considering visual acuity in 32 eyes of the 16 patients who had transphenoidal resection, vision improved in 21(21.9%), worsened in 10(31.2%) and remained the same in 15(46.9%) eyes. Eight (25%) eyes had pre-operative visual acuities of Counting Fingers (CF) to Perception of Light (PL), and 4 eyes had visual acuity of NPL (Table 3). Two

of 8 eyes with pre-operative visual acuity ranging from CF to PL had improved visual acuity after surgery. This included one patient with pre-operative visual acuity of CF in one eye improving by 3 Snellen lines to 6/24 and the other with visual acuity of Hand Motion (HM) improving by a line to Counting fingers(CF). None of the patients with visual acuity of NPL had improvement in visual acuity after transphenoidal surgery (Table 3).

Table 2: Presenting symptoms and signs in 18 patients with pituitary adenoma

<i>Symptoms / signs</i>	<i>Number (%)</i>
<i>Ocular Symptoms</i>	
Visual blur	15(83.3%)
Ocular pain	4(22.2)
Diplopia	3(16.7)
<i>Ocular signs</i>	
Colour vision impairment (Out of 36 eyes)	32(88.9)
Optic atrophy	17(94.4)
RAPD	8(44.4)
Strabismus	2(11.1)
Optic disc swelling	1 (5.6)
Red eye	1 (5.6)
<i>Non ocular symptoms</i>	
Headache	13(72.2)
Irregular menses	7(38.9)
Ammenorrhoea	4(22.2)
<i>Non Ocular signs</i>	
Galactorrhoea	3(16.7)
Cranial nerve palsies	0 (0.0)

Table 3: Preoperative and postoperative monocular visual status of 18 patients with pituitary adenoma.

<i>Visual status</i>	<i>Preoperative visual status</i>			<i>Postoperative visual status</i>		
	<i>n (%)</i>			<i>n (%)</i>		
	<i>Right eye</i>	<i>Left eye</i>	<i>Total</i>	<i>Right eye</i>	<i>Left eye</i>	<i>Total eyes</i>
	<i>(n=18)</i>	<i>(n=18)</i>	<i>(n=36)</i>	<i>(n=18)</i>	<i>(n=18)</i>	<i>(n=36)</i>
<i>Normal</i>	9(50.0)	6(33.3)	15(41.7)	6(33.3)	7(38.9)	13(36.1)
<i>Visually impaired</i>	2(11.1)	6(33.3)	8(22.2)	2(11.1)	4(22.2)	6(16.7)
<i>Blind</i>	7(38.9)	6(33.3)	13(36.1)	10(55.6)	7(38.9)	17(47.2)
<i>Total</i>	18(100)	18(100)	36(100)	18(100)	18(100)	36(100)

n = number, %= percent

One of the patients who had craniotomy had improved vision whilst the other had a drop in visual acuity by a Snellen line in one eye (Table 4). Time between onset of symptoms and presentation at the hospital was longer in the blind patients. This was found to be statistically significant ( $p < 0.005$ ). Considering the eyes, there was a significant association between duration of symptoms and blindness in the right eye ( $p < 0.020$ ) but not in left eyes ( $p < 0.518$ ). There was a significant association between duration of presentation for the blind eyes and the normal ( $p < 0.004$ ) or visually impaired eyes. ( $p < 0.002$ ).

**Visual field status:** The commonest pre-operative visual field defects encountered in this series were unilateral or bitemporal hemianopia 10(55.6%). Other visual field defects were superior quadrantanopia 2(11.1%), total field loss 2(11.1%) and Junctional scotoma 1(5.6%). Visual field test was not performed in 3(16.6%) patients because the best corrected visual acuity in their better eyes ranged from CF to NPL. Post-operatively, visual field test results could only be obtained in a few patients; hence, the pre-operative and post-operative results could not be compared. The majority of the patients could not do the test due to poor vision and financial difficulties. There was no

significant association found between age of patient and visual status at presentation ( $p < 0.465$ ). Tumour size, the widest dimension of tumours, was assessed. This ranged from 28.0mm to 79.4mm, mean (SD) =  $39.7 \pm 1.3$ .

Larger tumour width was associated with visual impairment in right eyes ( $p < 0.036$ ). These

eyes were more likely to remain visually impaired after surgery ( $p < 0.002$ ). In the left eye, however, there was no significant association found between tumour width and visual impairment before ( $p < 0.565$ ) or after ( $p < 0.537$ ) surgery.

Table 4. Pre and post-operative best corrected visual acuities in 18 patients with pituitary adenoma

<i>Serial number of patient</i>	<i>Preoperative visual acuity Right eye</i>	<i>Post-operative visual acuity Right eye</i>	<i>Preoperative visual acuity Left eye</i>	<i>Postoperative visual acuity Left eye</i>
1	6/5	6/5	6/36	6/36
2	6/12	6/12	6/36	6/36
4	CF	NPL	6/36	CF
7	6/9	6/9	HM	CF
10*	6/36	6/60	NPL	NPL
18	6/18	NPL	NPL	NPL
30	6/36	NPL	6/5	NPL
37	NPL	NPL	6/9	6/12
40	6/5	6/5	6/36	6/18
41	NPL	NPL	CF	6/24
42	6/9	6/6	6/24	6/60
49	CF	HM	6/9	6/6
56	CF	CF	PL	PL
62	6/5	NPL	6/5	6/12
65	6/12	6/6	6/36	6/9
66*	6/12	6/24	6/12	6/9
67	HM	HM	6/18	6/18
68	CF	CF	NPL	NPL

\*Patients who had craniotomy CF= Counting fingers, HM= Hand motion, NPL= No perception of light, PL= Perception of light

## DISCUSSION

Surgery is the treatment of choice for the majority of pituitary adenomas and the "gold standard" for hormonally inactive adenomas (1,4). The presence of visual deficit is the major indication for surgery by either the transcranial or transphenoidal route (7).

Transphenoidal surgery however is the most common and successful approach due to its low risk of complications and applicable to majority of the cases (1,4,5,8). In most of these tumours, it is required for the relief of visual symptoms and prevention of further visual deterioration (4,5).

In this series, visual deterioration was the commonest mode of presentation in 83.3% of the patients. Visual deterioration was confirmed on ocular examination. The majority (58.3%) of eyes were found to be either blind or visually impaired at presentation.

This finding is higher than that reported in a series by Turner HE et al which showed 39.3% presenting with primary symptom of impaired visual acuity (9) but corroborates the findings from a study in Kenya (10) which reported visual impairment of 87.7%.

The visual outcome after a trans-sphenoidal procedure is usually excellent (4,5,8,10–12). Severe visual defects secondary to optic nerve or chiasm compression can regress or resolve completely (11). Most of the improvement occurs during the first few days or weeks following surgery (11). Pre-operatively, 58.3% of 36 eyes in this study were visually impaired or blind. This increased to 63.9% after surgery. This high proportion of eyes blind or visually impaired, is not surprising considering the fact that a greater percentage (94.4%) of patients presented with unilateral or bilateral optic atrophy as opposed to 29% in other studies (10) with better surgical outcome.

Close to half of the patients maintained their visual acuity, about 20% improved by 1 to 3 Snellen lines whereas about a third worsened. This study showed lower improvement than in other studies, i.e. 78% (8), 71% (11), 71.5% (10) and 76.9% (13). Only one patient with pre-operative visual acuity of CF improved to 6/24. None of the patients with visual acuity of NPL had improvement in visual acuity after transphenoidal surgery. This differs from the findings in Elgamal et al's (11) and Ayub et al (5) in which visual acuities of patients with NPL and CF improved after surgery. This disparity may be due to the late presentation, with over a third of the patients in this study presenting after 24 months as opposed to Ayub's (5) study in which the patients whose visual acuities improved from NPL had been blind for only 2 to 10 days. This strengthens the need for early diagnosis and surgery in patients with pituitary adenoma.

Visual field defects are recognized presentations of pituitary adenoma (11,14). The typical visual field defect pre-operatively is bitemporal hemianopia (15). Other visual field defects encountered in other studies include superior quadrantanopia, homonymous hemianopia, junctional scotoma, total field loss, central scotoma, arcuate scotoma and monocular visual constriction (16-18).

The type of visual field defect depends on the relation between the optic chiasm and the tumor itself (16). Bitemporal hemianopia is due to the anatomical compression of the optic chiasm, where the crossing nasal fibers of each optic nerve occurs (15). In an anatomical post-fixed chiasm (tumor is placed more anterior to the chiasm) visual field defects such as central scotoma, arcuate scotoma and monocular visual constriction can occur. On the contrary, if the tumor compresses the optic tracts or there exists a pre-fixed chiasm, a homonymous hemianopia may occur (16,17). This study demonstrated some of these defects pre-operatively, with unilateral or bitemporal hemianopia being the commonest. Other factors that influence the type of visual defects include the size of pituitary adenoma (6, 19,20) and tumor volume (21).

Some studies have demonstrated recovery of visual function including visual field defects post-operatively, with a shorter duration of symptoms, younger age and a better preoperative Best Corrected Visual Acuity found to be associated with better postoperative recovery (7,22). However, others have shown little or no recovery of the visual fields (23,24), especially in patients with severe optic atrophy, suggesting a direct relation between the degree of optic atrophy and visual recovery (1,23,25). Given that optic atrophy was a major presentation, coupled with

prolonged duration of symptoms before presentation in our patients, post-operative visual field testing (if done) could have demonstrated little or no recovery in those who had pre-operative visual field defects. Unfortunately, post-operative visual field test results were obtained in only a few patients. Therefore, the pre-operative and post-operative results could not be compared to corroborate these findings.

The choice of transphenoidal approach as opposed to craniotomy is determined by a number of factors including degree of suprasella extension, tumour consistency, brain invasion, cerebral edema and encasement of the optic apparatus (10). This study included only two cases of pituitary adenoma who had craniotomy compared with 16 cases who had transphenoidal resection. It was, therefore, not possible to statistically compare the two surgical options. Kiboi et al (10) in their series, where 45% of the patients had transphenoidal and 55% transcranial surgeries, found no significant difference, statistically, between these two approaches. A larger number of cases of craniotomy will be needed in this study population to draw any meaningful conclusion.

Visual presentation of pituitary adenoma varies depending on the size of the tumour and its proximity to optic pathway (11). Large tumour size and closer proximity to the optic chiasma in this series may also be responsible for poorer postoperative visual outcome. Macro adenomas are characterised by a higher frequency of neuro-ophthalmological symptoms and poorer response to surgical therapy (3). Whereas micro adenomas may have negligible effect, macro adenomas can cause severe impairment of visual acuity, colour vision and visual field defects by their compressive effect on the optic nerves and chiasma (26).

Optic atrophy was present in 94% of cases in this study as opposed to 13% in Ayub's (5). It is a sign of long standing chiasmal compression from pituitary macro adenomas and is responsible for poorer prognosis following surgery (5). It results from secondary retrograde axonal degeneration as the tumour grows upwards (5,11). Tumour growth upwards towards the optic chiasma is the most frequent extrasella extension of pituitary adenoma(3). Macro adenomas with significant suprasella extension have been correlated with significantly worse postoperative outcomes(3,5,10).

Tumour consistency, extent of suprasella extension and brain invasion are some factors that influence the choice of transphenoidal resection as opposed to craniotomy. Firmer consistency of tumour has been documented to pose a challenge to adequate resection of suprasella component of large pituitary

tumours (5,10). This, however, could not be confirmed in our study because the tumour consistency was not assessed.

Duration of symptoms before presentation ranged from one day to 96 months with a median of 24 months. This corroborates findings by Marcus et al (12), but differs from Elgamal's (11). The extensive time interval between onset of visual symptoms and diagnosis has been noted in many studies (10,11,13). Patients who presented blind in this study were more likely to present to the hospital later than the visually impaired or normal patients ( $p < 0.005$ ). This was similar to findings in Kiboi's series (10). Late presentation, as seen in this study, is associated with poorer visual outcome following surgery (5,10). Indeed, studies have demonstrated that the longer the duration of the symptoms of the patients, the poorer the visual outcome after surgery (27).

The degree of visual improvement after surgery for pituitary tumours correlates with the size of the tumour (28). Largest tumour diameter in this study was 79.4mm which is larger than that seen in other studies (4,13). Wider tumour diameter at presentation in this study was associated with preoperative visual impairment in the right eye ( $p < 0.036$ ), but not the left eye ( $p < 0.565$ ). This significant association between tumour size and pre-operative visual acuity corroborates findings from Turkey (13). Thotakura et al, demonstrated from their series that better visual outcome would be achieved in patients with adenomas with mean diameter size  $< 3.65$  cm (27) while Ho et al showed worse visual impairment at presentation and after trans-phenoidal adenectomy with tumour size  $> 2$  cm (29). Other studies, however, have found improvement in vision post-operatively in larger tumors ( $> 3$  cm in diameter and volume  $> 10$  cm<sup>3</sup>) suggesting that tumor size does not seem to greatly influence both post-operative visual acuity and visual field deficits (30,31). The reason for these varying outcomes is not clear, but it may also suggest that visual status pre- and post-operatively for pituitary adenoma may be influenced by an interplay of multiple factors. The significant disparity between tumour size and right and left eyes however is not surprising since pituitary tumour growth is usually asymmetrical, resulting in asymmetric visual field and vision loss (11).

Invasiveness of tumour is directly associated with tumour diameter and extrasella extension (3). Garibi et al's study on giant pituitary adenomas found a significant association between tumour diameter greater than 40mm and extra-sella invasiveness (3). Our study did not assess tumour invasiveness.

In conclusion, more than a third of eyes of patients with Pituitary adenoma were blind before and

after surgery. Blindness was associated with prolonged duration of symptoms and larger tumour size. The commonest clinical presentations were visual blur and optic atrophy. Transphenoidal surgery may be beneficial following early diagnosis to avoid irreversible blindness or visual impairment.

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