Original Article **Nepal Journal of Neuroscience 2025;22(2): 40-46**

Ocular manifestations of pituitary adenoma in patients presenting at a tertiary eye hospital in Nepal.

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Date of Submission:18th May 2025 Date of Acceptance: 14th July 2025 Date of Publication: 15th August 2025

Abstract

Introduction: Visual outcomes following surgical resection of pituitary adenomas (PA) are generally favorable with early diagnosis and intervention. However, delayed decompression can result in irreversible visual loss, underscoring the need for prompt surgery. There is limited data from Tilganga Institute of Ophthalmology (TIO) on the demographic characteristics and visual outcomes of patients with PA. This study aims to describe the demographic profile and ocular manifestations of PA with a focus on visual symptoms, field defects, and postoperative outcomes.

Materials and Methods: A retrospective longitudinal study conducted at TIO involving 24 patients (48 eyes) who underwent microscopic endonasal transsphenoidal approach of surgical resection for MRI-confirmed pituitary macroadenomas between April 2015 and March 2018. Visual presentation patterns and outcomes before and after surgery were assessed. Demographic data, clinical presentation, and visual outcomes were analyzed using IBM SPSS ver. 20 software.

Results: The study included 24 patients (mean age 40.9 ± 13.3 years; range 18–79), with a male predominance (13/24, 54.2%). Most (11/24, 45.8%) presented within 1–6 months of symptom onset, with younger patients presenting earlier ($p < 0.002$). Blurred vision was the most common symptom (23/24, 95.8%), while bitemporal hemianopia (13/24, 54.2%) and optic atrophy (36/48,75%) were the most frequent signs. 29/48 eyes had abnormal color vision, while 16/24 patients had a relative afferent pupillary defect (RAPD). Postoperatively, visual acuity improved in 25/42 eyes (62.5%), and visual fields improved in 15 patients (62.5%).

Conclusions: Timely diagnosis and surgery can significantly improve visual outcomes in pituitary adenoma patients. This study highlighted that early surgical intervention of Magnetic Resonance Imaging (MRI)-confirmed macro adenomas improved both visual acuity and visual fields in nearly 63% of eyes and patients, respectively.

Keywords: Bitemporal hemianopia, optic atrophy, optic chiasm; pituitary adenoma, visual field defects, visual outcomes.

Introduction

Pituitary adenomas, accounting for 10–15% of intracranial tumours,[1–4] are a frequent cause of ocular manifestations due to their anatomical proximity to the optic apparatus.[2,5] These tumors may be asymptomatic or symptomatic in clinical presentation.[3,6] Tumors may be classified as secretory or non-secretory, with non-secretory adenomas often presenting initially with visual complaints resulting from the mass effect on the anterior visual pathway.[2] They are further categorized based on size into microadenomas (<10 mm) and macroadenomas (>10 mm).[2]

Visual impairments associated with pituitary adenomas include: vision loss, visual field defects, abnormal color vision, diplopia and optic atrophy – which is primarily caused by compression of the optic chiasm or optic nerves, and is typically proportional to tumor size and the extent of compression[2,5,7] Pituitary adenomas through mass effect may invade the cavernous sinuses which contain the oculomotor, trochlear, first and second divisions of the trigeminal nerve in the lateral wall. The sixth cranial nerve, or abducens nerve, is also within the sinus. Any of these nerves may be compressed by expansion laterally, resulting in ophthalmoplegia, misalignment of the

Access this article online

Website: https://www.nepjol.info/index.php/NJN

DOI: https://doi.org/10.3126/njn.v22i2.78943

HOW TO CITE
Keepa V, Tagoe NN, Essuman Y, Poudel M. Ocular manifestations of pituitary adenoma in patients presenting at a tertiary eye hospital in Nepal. NJNS. 2025;22(2):40-46

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ISSN: 1813-1948 (Print), 1813-1956 (Online)

visual axis and diplopia.[8,9] Visual field defects are present in the majority of patients with macroadenomas, with bitemporal hemianopia being the most common finding.[10] The presence of visual symptoms is one of the primary considerations for tumor resection and chiasmal decompression.[3]

Despite these advancements, the variability in outcomes remains dependent on factors such as preoperative visual status and the duration of optic nerve compression.[1,5] Preoperative factors associated with better visual outcomes following decompression of the anterior visual pathway in patients with pituitary adenoma include: younger age,[7,11] shorter duration of symptoms,[1,5,7,11] visual acuity > 6/3,[7,12] absence of optic disc pallor,[7] and the size of the lesion.[12] Early intervention with surgical resection has demonstrated substantial improvement in visual outcomes, with over 80% of patients showing recovery in some studies.[11]

This study examined ocular manifestations of pituitary adenomas at a single institution, focusing on demographics, symptoms, and visual outcomes before and after tumor excision via microscopic, endonasal, transsphenoidal resection. It also analyzed visual field changes and their correlation with patient demographics and presentation duration, to find factors (demographics, pre-operative visual status, presentation duration, and tumor size) that predict a good visual recovery post-surgery.

Methods and Materials

This retrospective study involved 24 patients (48 affected eyes) who presented at the Neuro-ophthalmology Unit of Tilganga Institute of Ophthalmology between April 2015 and March 2018. Ethical approval was given by the Tilganga Institute of Ophthalmology-Institutional Review Committee (Ref number: 13/2018).

Case notes of patients with a clinical diagnosis of pituitary adenoma, confirmed by MRI, and who had surgical resection of a pituitary tumor over the study period were identified, reviewed, and included in the study. The exclusion criteria employed in this study were: patients without a radiological confirmation of a pituitary tumor, patients with other causes of brain compression, such as abscesses, hemorrhages, inflammatory or vascular intracranial lesions, demyelinating diseases, or infections, and patients with co-existing pituitary adenomas and ocular conditions affecting visual fields, including glaucoma, choroiditis, retinitis pigmentosa, optic neuropathies caused by other brain tumors besides pituitary adenoma, or other significant ocular pathologies.

Demographic parameters, including age, sex, history of symptoms, and clinical information (symptoms and signs), were captured using a predesigned, structured questionnaire. Pre- and post-operative Best Corrected Visual Acuity (BCVA) measurements were recorded using a Snellen's chart. Visual acuity was categorized as normal (6/5-6/9) or as impaired according to the World Health Organization's International Classification of Diseases 10 severity criteria,[13] as follows (Table 1):

Table 1: Classification of visual acuity.

Category	Worse than	Equal to or better than
0 Mild or no visual impairment	6/12	6/18
1 Moderate visual impairment	6/18	6/60
2 Severe visual impairment	6/60	3/60
3 Blindness	3/60	1/60*
4 Blindness	1/60*	PL
5 Blindness	NPL	
9 Undetermined/unspecified	--	

**Counting fingers (CF) at 1 meter included; Abbreviations: NPL=No Perception of light; PL=Light perception.*

The presence of a relative afferent pupillary defect (RAPD), diplopia, or cranial nerve palsy was recorded. Optic disc findings (normal, temporal pallor, swelling, or optic atrophy) were also noted. Color vision tests using Ishihara's Color Vision Chart (14-plate concise edition, 1980), Visual field abnormalities documented qualitatively using a Humphrey Visual Field Analyzer (SITA standard protocol) were also recorded and analyzed.

Data was entered into Microsoft Excel software (version 2016, Microsoft Corporation, Redmond, Washington) and verified. The cleaned dataset was then transferred into the Statistical Package for Social Sciences (SPSS) software (version 20.0; IBM Corp., Armonk, NY, USA) for statistical analyses. Descriptive statistics were used to summarize demographic and clinical data, and results were presented in tables and graphs. For categorical variables, Chi-square tests were applied, and Fisher's Exact test was used if the expected count was less than five. For median comparison of non-normally distributed data of three categories, the Kruskal-Wallis test was used. Pre- and post-operative comparisons of categorical data having two categories were analyzed using McNemar's test. A p-value < 0.05 was considered statistically significant.

Results

Demographic characteristics and duration of symptoms

Records of 48 eyes from 24 patients with pituitary adenoma who underwent microscopic, endonasal, transsphenoidal resection were analyzed. Among the 24 patients, 18 (75.0%) had bilateral eye involvement, whereas 6 (25%) had unilateral eye involvement. The ages of the participants ranged from 18 to 79 years, with a mean age ± SD of 40.9 ± 13.3 years. There was a male predominance, with 13/24 patients (54.2%) being male. Most patients (11/24, 45.8%) presented within 1 to 6 months of symptom onset (Table 2).

Table 2: Sociodemographic characteristics and duration of symptoms of participants (N=24).

Characteristics	Frequency	%
Total	24	100.0
Age, mean ± SD	40.9 ± 13.3 (18-79)	
Age, years		
18-30	6	25.0
31-50	15	62.5
> 50	3	12.5
Sex		
Male	13	54.2
Female	11	45.8
Duration of symptoms		
1 to 6 months	11	45.8
> 6 months to 1 year	9	37.5
> 1 year to 2 years	4	16.7
> 2 years	0	0.0

Abbreviations: SD=Standard Deviation, %=Percentage.

The median duration of symptoms was 1.5 (range: 0.5 to 2.5) months in younger adults, 12 months (range: 2 to 48) in middle-aged adults, and 15 months (12 to 60) in older patients. Younger patients presented earlier than older patients (p=0.002, Table 3).

Table 3: Duration of presentation by age groups (N=24).

Characteristic	n	Median symptom duration, months	Range (min, max)	p-Value
Age groups, years				0.002
Young adults, 18-30	6	1.54	0.5, 2.5	
Middle-aged adults, 31-50	15	16.9	2, 48	
Older adults, > 50	3	29.0	12, 60	

Abbreviations: Max=Maximum, Min=Minimum, N=Frequency.

Clinical presentations of the study population

The most common complaint among the patients was a gradual progressive decrease in vision (23/24, 95.8%). One patient reported a headache and drooping of the left eyelid, while diplopia (double vision) was noted in another patient (each 1/24, 4.2%).

Ocular signs

Before surgery, 16/24 patients (66.7%) had a relative afferent pupillary defect. This decreased to 7/24 patients (56.3%) after surgery. This difference of RAPD before and after surgery was found to be statistically significant ($p < 0.021$). Before surgery, 29 /48 eyes (60.4%) had abnormal color vision. This decreased to 21/48 eyes (43.8%) after surgery, which was statistically significant ($p = 0.039$). Thirty-six of 48 eyes (75%) had optic atrophy, whereas 12/48 eyes (25%) were normal, which was the same after surgery.

Among 36 abnormal optic discs observed, 26/36 eyes (72%) had partial optic atrophy, while 10/36 eyes (27.84%) had total optic atrophy, which was slightly different after the surgery, where 25/36 eyes (69.4%) had partial optic atrophy and 11/36 eyes (30.64%) had total optic atrophy. There was no statistically significant association between optic disc atrophy before and after surgery ($p = 1.00$). Optic disc oedema/papilledema was not seen in any patient.

Table 4 highlights some visual field defects observed in study participants and improvements observed in these defects post-operatively.

Table 4: Visual field defects and improvement in defects post-operatively among participants (N=24).

Parameter	n	%
Total	24	100.0
Preoperative visual field defect		
Bitemporal hemianopia	13	54.2
Right hemifield defect	1	4.2
Left hemifield defect	2	8.3
Inferior quadrantanopia	3	12.5
Junctional scotoma	2	8.3
Unable to perform due to poor vision	3	12.5
Post-operative changes in visual fields		
Improved	15	62.5
Not improved	6	25.0
Worsened	3	12.5

There were postoperative improvements observed in visual field defects in patients, such as bitemporal defects (9/13, 69.2%), hemifield defects (3/3, 100%), and quadrant defects (2/3, 66.7%). Figures 1 and 2 illustrate a postoperative improvement in the bitemporal hemianopia in one of the study participants.

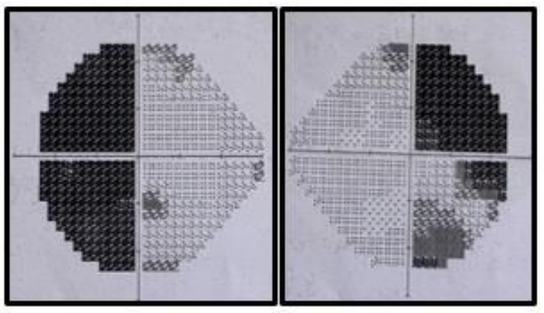

Figure 1: Visual field images of a patient showing bitemporal hemianopia (left, OS; right, OD) preoperatively

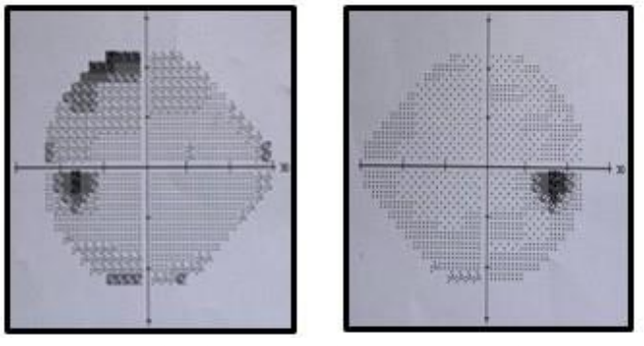

Figure 2: Visual field images showing postoperative improvement in visual field defects bilaterally (left, OS; right, OD).

The pre- and post-operative BCVA of participants are captured in Table 5. Thirteen of 48 eyes (27.1%) were moderately impaired at presentation, while 20 (41.7%) were normal. Postoperatively, eyes with normal vision increased to 32 (66.7%) (Table 5).

Table 5: Pre-operative and post-operative Best Corrected Visual Acuity of participants (N=48 eyes)

Pre-operative BCVA	Pre-operative BCVA		Post-operative BCVA	
	N	%	N	%
Total	48	100.0	48	100.0
Normal (6/6 to 6/12)	20	41.7	32	66.7
Mild visual impairment (>6/12 to 6/18)	1	2.1	2	4.2
Moderate visual im pairment (>6/18 to 6/60)	13	27.1	3	6.3
Severe visual impairment (>6/60 to 3/60)	2	4.2	0	0
Blindness (>3/60 to 1/60)	3	6.3	4	8.3
Blindness (>1/60 to PL)	6	12.5	4	8.3
Blindness (NPL)	3	6.3	3	6.3

Abbreviations: BCVA=Best Corrected Visual Acuity; N=Frequency, NPL=No Perception of Light; PL=Perception

A normal BCVA (6/6 to 6/12) was seen in 20/48 eyes (41.7%) pre-operatively, and subsequently increased to 32/48 eyes (66.7%) post-operatively. A statistically significant post-operative improvement in BCVA was also seen in moderately impaired, severely impaired, and blind eyes ($p < 0.001$).

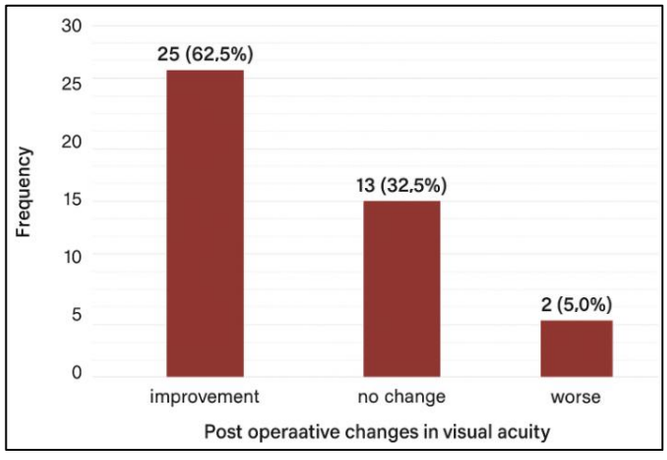

Figure 3: Post-operative changes in visual acuity of study participants (N=40 eyes).

A BCVA of 6/6 was recorded in 8 eyes preoperatively. Among the remaining 40 eyes, BCVA improved in 25 eyes (62 .5%), worsened in 2 eyes (5.0%), and remained constant in 13/40 eyes (32.5%). This postoperative improvement was found to be statistically significant ($p < 0.001$) (Figure 3).

No significant association was found between improvement of visual acuity and gender (p=0.374), age (p=0.635), laterality (p=0.354), and duration of symptoms (p=0.359). There was, however, a significant association between post-operative visual acuity and visual field (p=0.006), indicating patients who had improved vision after the surgery showed significant improvement in their visual fields as well.

Discussion

Pituitary tumors typically present with clinical manifestations that fall into two main categories. The first includes signs and symptoms arising from pituitary gland dysfunction, such as hormonal imbalances due to excessive or insufficient hormone production, and the second category consists of symptoms caused by the tumor's mechanical expansion beyond the sella turcica.[14] Pituitary adenomas with suprasellar extension may compress the visual pathway, especially the optic chiasm, as they grow superiorly, causing visual impairment and visual field defects.[3] This study focused on the visual disturbances associated with pituitary macroadenomas at Tilganga Institute of Ophthalmology, before and after microscopic, endonasal, transsphenoidal resection.

The highlights of this retrospective study are that the majority (95.8%) of patients presented with a gradual progressive decrease in vision. Bitemporal hemianopia (54.2%) and optic atrophy (76.2%) were the most common clinical signs. Postoperatively, there was an observable improvement in both visual acuity of eyes (25/40, 62.5%) and in the visual fields of patients (15/24, 62.5%).

A male preponderance of 54.2% was observed in our study. This was seen in many other similar studies globally.[1,15–18] In contrast, some studies found a female predominance among their participants.[3,19,20] These observations may be a result of differences in study designs and may not bear much significance. We found a mean age of 40.9 ± 13.3 years among our participants. Quite young, our population was similar to that in another similar Nepalese study.[18]

About 46% of patients with pituitary adenoma presented to the study site within 6 months of symptom onset, and 37.5% between 6 months and a year. This is slightly lower than in another study, where 51% of the patients were symptomatic for less than 6 months.[21,22] Although younger patients presented earlier than older patients ($p < 0.024$), our study did not find a statistically significant association between age at presentation and visual outcomes after surgery ($p = 0.635$).

Although studies suggest that a mean age of < 52 years and tumor size were associated with better visual outcomes.[16,21] Our study did not document or assess tumor size, making it impossible to evaluate its association with visual outcome.

In this study, only one patient presented with a headache. Headache patterns vary by tumor type and have been reported in 33–72% of patients with pituitary adenoma.[22] Ogra et al, however, documented headaches in 15% of patients and endocrine abnormalities in 21% of patients.[17] Headaches are generally thought to be more common in patients with prolactinomas and are associated with tumor size, dural stretch, and the hormonal activity of the tumour.[22] However, our study did not document tumor size or hormonal activity, which presents a potential area for future research.

Blurred vision was the most common presentation, occurring in nearly 96% of our participants. This is consistent with studies by Kiboi et al in Kenya[20] and Ogra et al in Australia[17] that similarly reported blurred vision as the most frequent symptom, in 88% and 39% of their participants, respectively. The higher percentage in our study may be attributed to the smaller sample size (24 patients compared to 65 and 103 in studies by Kiboi et al and Ogra et al respectively). A wide range of visual symptoms has been documented in the literature, varying from no impairment to complete blindness.[3] Visual deficits may include reduced visual acuity, impaired color vision, ocular movement abnormalities, and visual field defects—the most prevalent, with reported rates ranging from 37% to 96% across different studies.[3,6,15]

The primary cause of visual impairment is thought to be due to direct compression of the optic nerve by the tumor, causing reduced blood supply, leading to optic atrophy.[3] Possible mechanisms of axonal damage due to compression include: direct disruption of axonal conduction, impaired axoplasmic flow, demyelination resulting in compromised signal transmission, and ischemia caused by compression or stretching of the chiasm's blood supply.[3] In this study, 60.4% of 48 eyes had impaired color vision, 75% had optic atrophy, and nearly 67% had relative afferent pupillary defect (RAPD). Optic atrophy manifests clinically as pallor of the disc and is a manifestation of long-term compression on the optic nerve.[14] In this study, optic atrophy was partial (26/48, 54.2%) or complete (10/48, 20.8%). Cohen et al, however, reported lower values of 46% of mild disc pallor, 18% diffuse pallor, with only 6% being completely atrophic.[21] Still, lower percentages of optic atrophy of 29% have been reported in other studies.[11,20] This disparity is attributable to the variable definition of atrophy in these studies. Appearance of the optic disc may not be a true reflection of the function, especially when partially atrophic. It is believed that color vision, rather than optic atrophy, is a better indicator of chiasmal compression and recovery following surgery.[21] Optic disc oedema/papilledema was not found in any participants. Similar to another study by Kim et al, among a Korean population.[23] This varied from the study conducted in Nepal by Poudel et al., where papilledema was seen in 21% of participants.[18]

Both visual recovery and deterioration have been reported following surgical excision of pituitary adenomas.[4] An improvement in the visual function is believed to occur in three phases: an initial rapid recovery within minutes to a few days, a delayed recovery over weeks to months, and a late recovery that can extend over months to years.[3,14] In this study, visual acuity improved in 62.5% of 40 eyes in whom the preoperative visual acuity was worse than 6/6. This improvement was statistically significant ($p < 0.001$). This is corroborated by another study by Poudel et al, in a Nepalese population, which found an improvement in visual acuity of 60%.[18] This improvement was higher than a Chinese study, by Yu et al, in which about 54% of 366 eyes experienced an improvement in visual acuity postoperatively.[16] The difference may be due to a lower sample size in this current study.

The visual recovery observed in this current study is, however, lower than that of Cohen et al, who reported an improvement in visual acuity of 79% of eyes in their study.[21] Of note is the fact that our study evaluated 42 eyes as opposed to 100 eyes in Cohen's study, and the difference in the surgical technique employed in the two studies (microscopic, sublabial, transseptal, transsphenoidal decompression in Cohen's study versus a microscopic endonasal transsphenoidal resection used in this study). Further studies may be able to shed light

on the visual outcomes associated with both techniques and identify specific underlying factors for the observed difference in outcomes. Bitemporal hemianopia, the most common visual field defect described in patients with pituitary adenoma,[3,14] was present in 54.2% of patients. This is similar to findings in studies by Cohen et al in the USA (54%),[21] and Kiboi et al in Kenya (57%),[20] but higher than in a study by Ogra et al in an Australian population (41%).[17]

Owing to the suprasellar extension, pituitary macroadenomas can exert pressure on the optic chiasm, leading to visual impairment, primarily in the form of visual field deficits such as bitemporal hemianopia.[3] Initially, the compression affects the optic chiasm, resulting in visual field loss, and as the condition progresses, it may impact the macular fibers, leading to a decline in visual acuity.[3]

Visual field impairment is a major indication for surgical excision.[11] Visual field improvement was observed in 62.5% of the 24 patients in our study, which is higher than in the aforementioned studies by Poudel et al (Nepal, 57%),[18] and Fredes et al (Chile, 54.2%).[3] It was, however, significantly lower than reported in other studies.[11,16] This discrepancy may be attributed to differences in study focus. While our study described visual field defects, some of these studies provided a more detailed assessment of visual field changes over time. They also noted that preoperative visual field deficits were more pronounced in the temporal quadrants and that postoperative recovery was progressive across all quadrants, continuing for five years or more. Since our study did not track visual field changes in this manner, future prospective studies could benefit from incorporating a similar long-term follow-up approach. In this study, 25% of the patients did not notice any improvement in their visual fields, and in 12.5% of them, the visual field worsened postoperatively. Fredes et al similarly found no change in visual field in 22.8% of cases, while in 5.8% of cases, there was an unfavorable outcome in post-operative visual field.[3] Of note is the fact that patients with normal and improvement were classified together as favorable, and those with reduced field were classified as unfavourable.[3] The limitations of our study include the lack of documentation of tumor size and endocrine function, as well as the use of a microscopic surgical approach instead of an endoscopic approach, which would have provided better visualization and positively influenced visual outcomes. However, our study provides a foundational basis for understanding the visual outcomes of patients with pituitary adenoma who have undergone surgical resection of pituitary tumors in Nepal.

Conclusion

This study found that the majority of participants presented with blurred vision and optic atrophy, with bitemporal hemianopia being the most common clinical sign. Postoperatively, visual acuity and visual fields improved in the majority of eyes. These findings suggest the need for timely diagnosis and surgical intervention to significantly improve visual outcomes in patients with pituitary adenomas.

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