

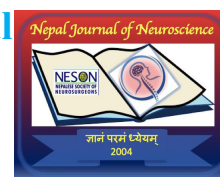
Surgical Outcome and Extent of Resection in Endoscopic Endonasal Transphenoidal Excision of Pituitary Tumours

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Abstract

Introduction : Pituitary adenomas are common benign tumors located intracranially that arise from the pituitary gland. Depending on their size and endocrine function of the tumor, they can be either asymptomatic or present with symptoms due to hormonal dysfunction or compression of nearby structures. Among the various surgical approaches that exist for the management of pituitary adenomas, the endoscopic endonasal transsphenoidal approach is a widely used technique. The study evaluates the surgical outcomes and extent of tumor resection using this approach.

Materials and Methods: The study was conducted at Bir Hospital, Kathmandu, Nepal, which included 38 study participants with pituitary macroadenomas. A non-probability sampling method was used.

Results: The most common presenting symptom was visual defects (57.8%), followed by headaches (31.5%) and galactorrhea (26.3%). Preoperative Knosp grading revealed 26.3% of cases as grade 0, 39.5% as grade 1, 21.1% as grade 2, and 13.2% as grade 3. Postoperatively, 78.9% of patients had complete tumor excision. Significant improvement in visual acuity was observed, with 21.1% achieving 6/9 vision in the right eye and 23.7% in the left eye. However, two patients showed no perception of light both pre- and post-operatively. The hormonal level decreased significantly post operatively.

Conclusion: Pituitary adenomas often present late, leading to visual and endocrine impairment. The visual and endocrine improvement of the patient was significant following the endoscopic endonasal transsphenoidal surgery, with most patients achieving complete tumor excision. Surgical outcomes at our center are comparable to existing data.

Keywords: Pituitary Adenoma, Visual Outcome, Knosp Grading, Endoscopic Endonasal Tumor Resection

Introduction

Intracranial lesions originating in the pituitary region are common, with pituitary adenomas (PAs) constituting the most commonly observed benign neoplasms of the sellar area. These tumors arise from adenohypophyseal cells and may demonstrate considerable suprasellar extension, complicating therapy.¹⁻² The incidental detection of PAs in MRI and autopsy studies

varies between 14.4% and 22.5%, indicating their considerable incidence.³ Pituitary adenomas may impact surrounding organs such as the sella turcica, dura mater, blood vessels, cranial nerves, and brain, leading to varied clinical symptoms. Extensive macroadenomas with suprasellar extension frequently led to visual field impairments, notably bitemporal hemianopia, as a consequence of optic chiasm compression and associated crossing fibers. The clinical management of these tumors is determined by their biochemical activity and anatomical features, with treatment objectives focused on preservation and restoration of pituitary function, decompression of neurological structures and prevention of tumor recurrence.⁶⁻⁷

In the last century, the treatment of pituitary adenomas has progressed markedly, with improvements in pharmaceutical therapy, hormone replacement methods, surgical procedures, and targeted radiotherapy. The development of innovative drugs for biochemical management, enhanced hormone replacement therapy, and advancements in surgical and radiotherapeutic methods have improved patient outcomes.⁸⁻¹²

Pituitary surgery has been transformed by the emergence of endoscopic endonasal transsphenoidal methods, which offer a minimally invasive approach with enhanced vision and surgical precision.¹³ This procedure has largely supplanted previous microscopic and open surgical approaches

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notably for enormous pituitary macroadenomas (>4 cm) requiring optic nerve decompression. The extended endoscopic transsphenoidal method provides a direct channel for more aggressive tumor excision while reducing harm to surrounding structures.¹⁴

Despite breakthroughs in pituitary surgery, attaining total tumor removal while conserving critical structures remains a challenge, particularly in cases of cavernous sinus invasion. The Knosp grading system serves as a vital tool in determining the possibility of cavernous sinus invasion and forecasting the degree of surgical resection. Understanding the association between Knosp grades and postoperative outcomes is critical for optimizing surgical planning and patient prognosis. Additionally, visual impairment is a major presenting symptom in individuals with pituitary macroadenomas, however, postoperative visual recovery remains inconsistent. Evaluating postoperative visual outcomes in relation to tumor removal and Knosp grading can provide useful insights into predicting visual improvement following surgery.

This study intends to assess the extent of tumor excision using Knosp grading following endoscopic transsphenoidal resection of pituitary macroadenomas and postoperative visual results in relation to tumor invasion and surgical resection

MATERIALS AND METHODS

Study Design

This was a cross sectional study conducted at Bir Hospital in Kathmandu, Nepal conducted during a period of April 2021 to August 2022.

Sampling Size and Method

A non-probability sampling method was used. The sample size calculation was made using the equation $n = Z^2 \times p \times (1 - p) / e^2$ where n, Z, p, and e represented number of samples, required the z-score, sample proportion and the margin of error respectively. The estimated minimum sample size requirement calculated considering overall improvement rate of 72% following surgery in a study done in Pakistan is 34. The sample size of our study is 38.

Inclusion criteria:

-All patients admitted to the hospital with diagnosis of pituitary macroadenomas.
who underwent endoscopic transsphenoidal resection during study period

Exclusion criterias:

- Cases with prior pituitary surgeries or radiotherapy.
- Patient with active nasal infection

Knosp Grading System

Knosp et al. offered a grading system for showing invasion of cavernous sinus by pituitary macroadenoma. It was summarized that the more the laterally adenoma grows and surrounds the ICA, the higher grade it is. The grading is determined by the relation of carotid lines with the limits of invasion. Thereby en masse dissection is possible only when tumor lies with minimal or no suprasellar extension and also lies between the carotid. Patient motor activity was analyzed using knosp grading pre- and post-operatively simultaneously. Tumor invasion into the cavernous sinus was classified using the Knosp grading system

based on coronal MRI. Preoperative and postoperative MRI scans be analyzed to assess the extent of tumor resection .

Grading Criteria:

- **Grade 0:** Tumor medial to the medial tangent.
- **Grade 1:** Tumor between the medial tangent and intercarotid line.
- **Grade 2:** Tumor between the intercarotid line and lateral tangent.
- **Grade 3A:** Tumor lateral to the lateral tangent (above intracavernous ICA).
- **Grade 3B:** Tumor lateral to the lateral tangent (below intracavernous ICA).
- **Grade 4:** Complete encasement of the intracavernous ICA. 16

Study Procedure

Data collection was started after receiving ethical approval letter from ethics committee of NAMS, Kathmandu, Nepal. At first, all the patient went through detailed assessment with history, clinical examinations and all relevant investigations were performed which a magnetic resonance imaging (MRI) brain with pituitary protocol. Also, a navigation CT scan of the patient was also done to facilitate intra-operative neuronavigation during the surgery. The operative time, findings of procedure and intra operative complications was noted. Postoperative MRI scans was used to determine and note the extent of tumor resection. Gross total resection (GTR) was defined as no visible residual tumor, while subtotal resection (STR) was defined as any remaining tumor postoperatively. Visual Outcome Assessment: Preoperative and postoperative visual function was assessed using visual acuity and perimetry (visual field) tests. The correlation between pre operative and postoperative visual outcomes was evaluated using paired t-tests.

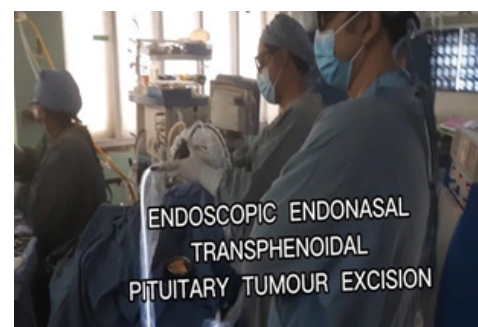


Figure 1: Intra-operative Set-up

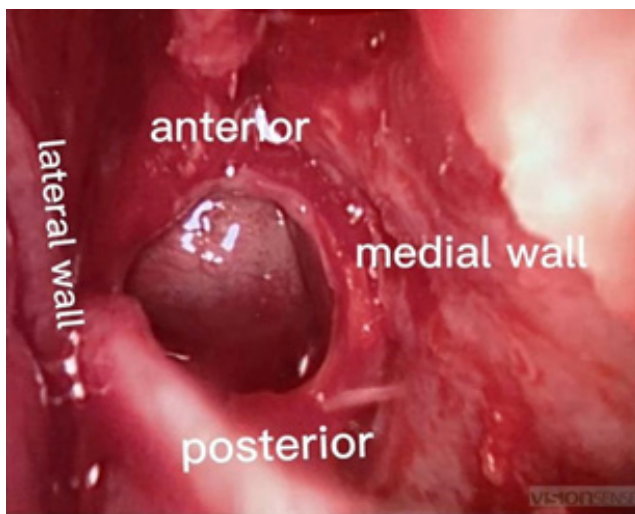


Figure 2: Endoscopic visualization of nasal stage

Data analysis

The results were expressed as the mean \pm S. D / median (range) for the quantitative data. The categorical data were compared using the Fisher's exact test. Analysis was performed in statistical package for social sciences software version 22. P value <0.05 was taken as statistically significant.

RESULTS

As in table 1, among the total 38 patients who underwent the surgery, there were 52.60% (20) female and 47.4% (18) male with a mean age of around 40 years.

The mean tumor size was 6994.9 ± 4.3 mm³. The intraoperative blood loss was 129.50 ml with standard deviation 65.28. The mean operating time was 145.30 ± 47.93 min and the mean duration of stay in the hospital postoperatively was 10.03 ± 3.31 days. Hormone serum level was evaluated pre- and post-operatively. There was clinically and statistically significant reduction in mean serum prolactin level, growth hormone level, cortisol level post-operatively. The common complications of the surgery included Diabetes insipidus in 12 patients and CSF leak in 5 patients .

Table 1: Gender distribution of the study population

Gender	Number of individuals	Percentage
Male	18	47.40%
Female	20	52.60%
Total	38	100%

Table 2: Distribution of types of pituitary adenomas

Diagnosis	Number of individuals	Percentage
Prolactinoma	11	28.90%
Acromegaly	9	23.70%
Non-secretory	18	47.40%
Total	38	100%

As in table 2, the total number of non-functioning or non-secretory adenomas was 18 (47.40%) while rest were functioning (Prolactinoma and Acromegaly).

Table 3: Symptomatology

Clinical presentation	Number of individuals	Percentage
Headache	12	31.5%
Galactorrhoea	10	26.31%
Apoplexy	2	5.21%
Visual defects	22	57.8%
Acromegalic picture	8	21.05%
Seizure	2	5.26%
Amenorrhoea	5	13.15%
Loss of libido	1	2.6%

The common presenting symptoms of the patients were visual defects, headache, galactorrhoea, etc. (Table 3)

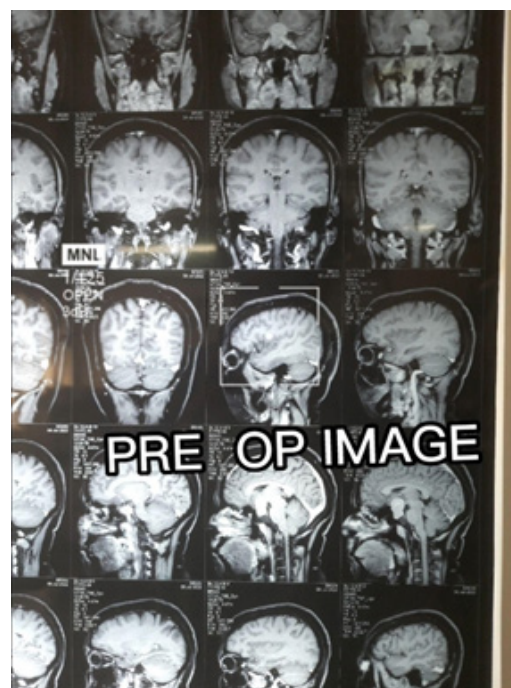


Figure 3: Pre operative MRI Brain

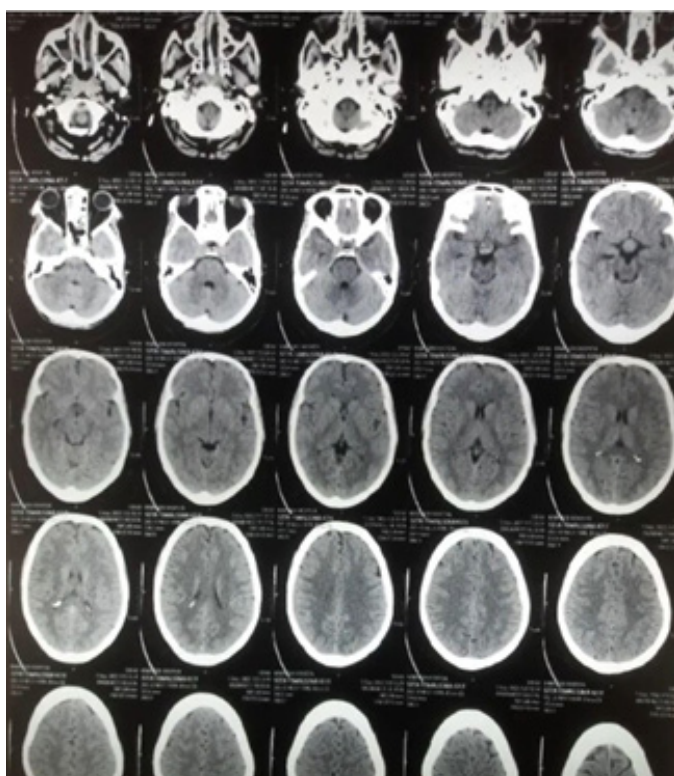


Figure 4: Post Operative CT Brain

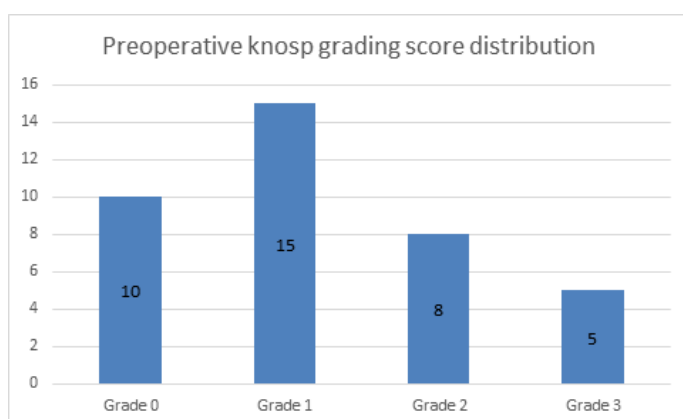


Figure 5: Bar chart representation of distribution of Knosp grading score

In pre-operative evaluation, 26.3% (n=10) of the cases were categorized as grade 0. Similarly, 39.5% (n=15) patients had grade 1 knosp grading score, 8 patients had grade 2 which accounted for 21.1% of the total cases and 13.2% (n=5) had grade 3 (figure 5)

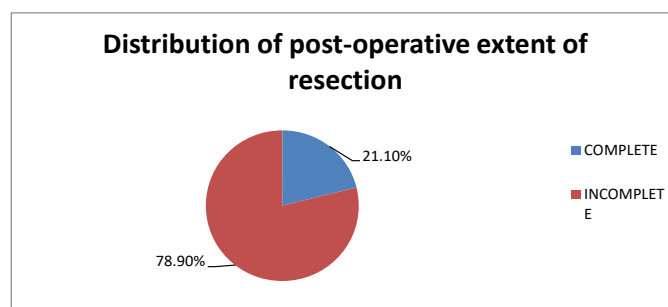


Figure 6: Distribution of post-operative extent of resection

The post-operative evaluation for knosp grading showed 78.9% (n=30) had complete while 8 patients (21.1%) had incomplete excision (figure 6).

Table 4: Frequency distribution of visual defects

S.no	Visual defects	Frequen- cy	Percentage (%)
1.	Bitemporal hemianopia	12	31.5%
2.	Bilateral superotemporal quadrantanopia	5	13.16%
3.	Hemianopia on one eye and superolateral quadrantanopia in another eye	1	2.63%

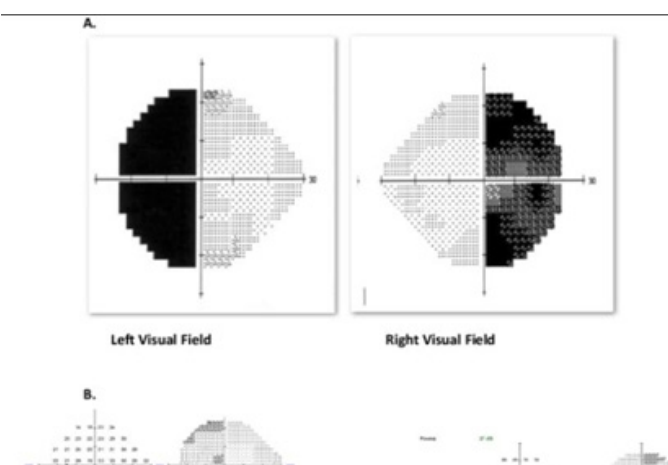


Figure 7: Bitemporal Hemianopia on visual perimetry

Visual acuity among 22 patients was disturbed, out of which 18 patients had visual defect. Visual defects among 18 patients were distributed as mentioned accordingly.¹² patients (31.5%) had bitemporal hemianopia, 13.16% (n=5) had bilateral superotemporal quadrantanopia and 1 patient (2.63%) had hemianopia on one eye and superolateral quadrantanopia in another eye (Table 3).

Table 5: Frequency distribution of Visual acuity of right eye

Visual acuity	Pre-op right eye		Post op right eye		p - v a l u e (u s i n g Fischer exact test)
	F r e - quency (n)	P e r - centage (%)	Frequen- cy (n)	Percent- age (%)	
6/6	--	-	2	5.3%	0.01
6/9	1	2.6%	8	21.1%	
6/12	3	7.9%	2	5.3%	
6/18	3	7.9%	1	2.6%	
6/24	2	5.3%	5	13.2%	
6/36	4	10.5%	-	-	
6/60	5	13.2%	1	2.6%	
Finger count	1	2.6%	-	-	
NPL	2	5.3%	2	5.3%	
PL	-	--	-	-	

On preoperative examination of right eye, 1 (2.6%) patient had visual acuity 6/9, 3 (7.9%) patients had 6/12 visual acuity and other 3 (7.9%) had visual acuity 6/18. Similarly, 2 patients had visual acuity 6/24, 4 had visual acuity 6/36 and 5 had 6/60 which accounted for 13.2%. On postoperative evaluation of right eye, 2 (5.3%) patients had normal visual acuity i.e., 6/6. Visual acuity was improved in 21.1% (n=8) cases to 6/9. 2 (5.3%) patients had visual acuity 6/12, 1 (2.6%) had 6/18, 5 (13.2%) had 6/24 while 1 (2.6%) patient had no improvement in visual acuity from 6/60. 2 patients showed persistent no perception to light both pre- and post-operatively (Table: 4

Table 6: Frequency distribution of visual acuity of left eye

Visual acuity	Pre-op right eye		Post op right eye		p - v a l u e (u s i n g Fischer exact test)
	F r e - quency (n)	P e r - centage (%)	Frequen- cy (n)	Percent- age (%)	
6/6	1	2.6%	3	7.9%	0.05
6/9	2	5.3%	9	23.7%	
6/12	3	7.9%	3	7.9%	
6/18	4	10.5%	-	-	
6/24	1	2.6%	3	7.9%	
6/36	2	5.3%	1	2.6%	
6/60	7	18.4%	-	-	
NPL	-	-	2	5.3%	
PL	-	-	1	2.6%	

On examination of left eye pre-operatively, 1 (2.6%) patient had normal visual acuity of 6/6, 2 (5.3%) cases had 6/9 visual acuity, 3 (7.9%) patients had visual acuity of 6/12, 4 (10.5%) cases had 6/18, 1 (2.6%) patient had 6/24, 2 (5.3%) patients had 6/36 and 7 (18.4%) patients had 6/60 visual acuity respectively. On postoperative evaluation, visual acuity was normal in 3 (7.9%) patients. There were increased patients with visual acuity up to 6/9 in among 23.7% (n=9) in left eye. 7.9% (n=3) had visual acuity 6/12, other 3 patients had visual acuity 6/24 while 1 patient had visual acuity of 6/36. 2 patients (5.3%)

were observed to have no perception to light (Table: 5). Though clinical improvement on visual acuity was significant in many patients but it is statistically insignificant.

DISCUSSION

In our study, 57.8% of the presenting cases had visual disturbance. 12 patients (31.5%) reported with complaint of headache, 2 (5.2%) patients had apoplexy and seizure was complained by 2 (5.2%) patients. Similar to our findings however, at higher end, Li Zhu et al. in their study reported 628 (83.5%) preoperative headache patients, 513 (68.9%) visual acuity and visual field impaired patients, 218 (66.4%) endocrine symptom patients and 26 (53.1%) SIADH (Syndrome of Inappropriate secretion of Antidiuretic Hormone).¹³⁶ Another study reported, common complaint of vision loss and only 50% had hormonal symptoms. 6/6-6/24 visual acuity was present in 73.3% patients and 13.3% had optic atrophy, 43.3% patients had bi-temporal hemianopia.¹⁷

Azab MA et al, in his study reported most common presentation was visual disturbance followed by headache and endocrinopathy.¹⁸ Though the incidence of the presentation may vary but the clinical presentations are almost similar to those described in the literature. Cawich et al reported visual defects as the predominant symptom followed by headache which is in accordance to our findings.¹⁹

In a retrospective review by Seuk et al, out of the 29 patients, 26 patients presented with decreased visual acuity and 23 patients revealed the defective visual field respectively which is comparable to ours. Postoperatively, improvement in the visual acuity was seen in 15 patients (83.3%) who underwent surgery within the first 48 hours of presentation, as compared to those in whom surgery was delayed beyond 48 hours (n=5; 62.5%) (p=0.014).²⁰ A study by Juraschka et al observed 73% of patients experienced improvement in visual acuity, while 24% were unchanged. Visual fields were improved in 61.8% and unchanged in 5.5%.²¹

Complete resection was done in all cases where there was clear plane of dissection with no or minimal suprasellar extension and en masse resection was also possible only when tumor lies within the carotid. Complete excision was achieved in 78.9% (n=30) of cases which is close to study done by Yan et al that reports total excision of 85% of the cases via mononostil approach.²² Meanwhile, 8 cases were incompletely excised in our study which is also similar to results reported by Yan et al. They observed incomplete excision of 12 cases reported in the literature.²² The incomplete excision may be due to the extensive nature of the tumors and their higher knosp grading. Another study from literature favoring our result reported total resection in 18 (60.0%) patients, subtotal in 8 (30.7%) and partial in 4 (7.7%) patients.²³ A study by Li Zhu reported gross total resection in 1627 patients (80.1%) and incomplete resection in 405 patients (19.9%).²⁴ Omar et al in their study noted gross removal of tumour is seen in 92.4% and subtotal resection in 7.8%. by endonasal endoscopic trans sphenoidal surgery.²⁵

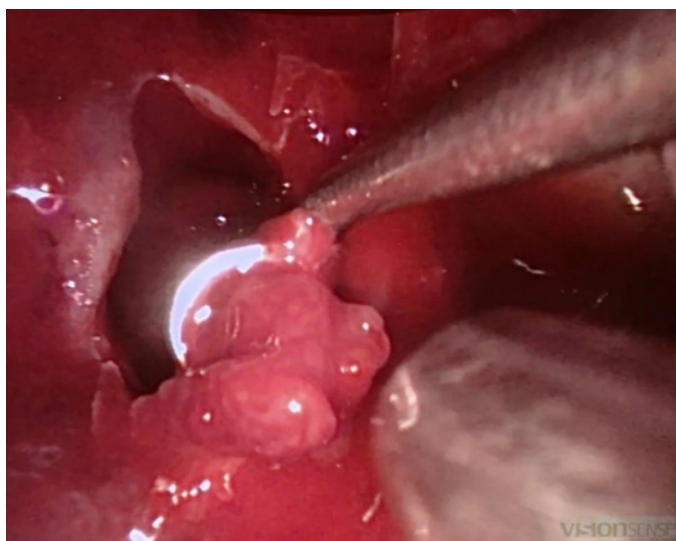


Figure 8: Enucleation of pituitary macroadenoma

Table 7: Comparison of extent of resection

Extent of resection	Yan J et al 22	Dixit et al 23	Li Zhu et al 24	Omar et al	Our study
Complete	76%	60%	80.1%	92.4%	78.9%
Incomplete	24%	Sub-total-30.7%	80.1%	92.4%	78.9%

In pre-operative evaluation, 26.3% (n=10) of the cases were categorized as grade 0. Similarly, 39.5% (n=15) patients had grade 1 knosp grading score, 8 patients had grade 2 which accounted for 21.1% of the total cases and 13.2% (n=5) had grade 3 (Fig: 4.5). The post-operative evaluation showed 78.9% (n=30) had complete while 8 patients (21.1%) had incomplete (Table: 4.8). Hlaváč et al in his study described 60.3% of pituitary adenomas classified as Knosp grades 0–2 which is similar to our findings.²⁶

This was a single center prospective cross-sectional study with small sample size. The result outcome analyzed was done in early post-operative period and result can have varied outcome which also differs according to different level of operating surgeons. However relevant the results might be, it needs similar kind of larger studies to confirm the findings of our study. Moreover, experimental randomized control trial would have been better answer to justify the results more accurately.

CONCLUSION

Pituitary adenomas present significant treatment challenges, particularly in terms of preserving function and neurovascular structures. Presentation of the patient at our centre are usually in late stage with larger size of tumour leading to compromised visual and endocrinal status. There was clinically significant visual improvement post operatively. Complete excision was achieved as shown by postoperative knops grading in most of the patients. Outcomes of endoscopic endonasal transphenoidal surgery for pituitary macroadenoma at our centre is comparable to other available data.

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