



Original Article

## Comparison of Cerebrospinal Fluid Leakage in Endoscopic Endonasal Transsphenoidal Surgery for Pituitary Adenoma with and without Sellar Floor Reconstruction

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### ABSTRACT

**Objectives:** This study aimed to compare CSF leak in endoscopic endonasal TSS of pituitary adenoma with and without reconstruction of the sellar floor with no intraoperative CSF leakage.

**Materials and Methods:** It was a randomized controlled trial of 116 patients of both genders diagnosed case of pituitary adenoma who underwent endoscopic endonasal TSS over 1 year. The cases were randomized into 2 groups. In Group A endoscopic endonasal TSS and the sellar floor, reconstruction was done while in Group B only endoscopic endonasal transsphenoidal surgery was done without reconstruction.

**Results:** The patient's mean age in group A was  $40.7 \pm 9.56$  years, and in group, B was  $41.9 \pm 10.5$  years. The gender distribution, for group A, males and females were 29 each (50%) and in group B, the males were 36 (62%) and females were 22 (38%). There were 52 (89.7%) cases of macroadenoma and 6 (10.3%) cases of microadenoma in each group. On the 1st postoperative day, CSF leakage was noted in 2 (3.4%) patients of group A, and CSF leakage was observed in 2 (3.4%) patients of group B. Results revealed no difference in CSF leakage between both groups. There were minor nasal complications in both groups.

**Conclusion:** There is an equal chance of success with endoscopic endonasal transsphenoidal surgery (TSS) of pituitary adenoma with and without reconstruction of the sellar floor, concerning post-operative CSF leak, in patients who have no intraoperative CSF leak which enlarges the pool of options for treatment.

**Keywords:** Endoscopic endonasal transsphenoidal surgery, Pituitary adenoma, Cerebrospinal Fluid (CSF) leakage, Reconstruction of Sellar floor.

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## INTRODUCTION

The third most frequent type of primary brain tumor is pituitary adenomas. They make up about 10% to 15% of all intracranial tumors and are benign.<sup>1,2</sup> Recent research of residents of a town in a developed country found the frequency to be greater than reported before, at 77.6 per 100,000 people. However, few big studies have pinpointed the precise prevalence.<sup>3</sup> According to secretion, they can be classified as functioning or non-functioning, and their size can be classified as microadenomas (less than one cm) or macroadenomas (more than one cm).<sup>1,2</sup> Prolactin, adrenocorticotrophic hormone, growth hormone, thyroid stimulating hormone production, or non-secretory tumors is used to classify these tumors.<sup>4</sup> Additionally, since the pituitary gland is located at the base of the skull within the sella, neurosurgeons have been removing pituitary adenomas through the sphenoid sinus.<sup>5</sup> The majority of patients prefer surgery, however, prolactinomas are typically treated medically, frequently with dopamine agonists.<sup>4,6</sup> Neurosurgery is the preferred treatment for patients with pituitary adenomas, to completely remove the tumor while protecting the pituitary gland. From a craniotomy technique, pituitary surgery transitioned to less invasive methods, including microscopic and endoscopic methods.<sup>6</sup> The transsphenoidal route is the most popular method for operations affecting this region because it provides a direct, less invasive extracerebral entry to the sellar region.<sup>6,7</sup> The traditional access used in pituitary surgery has been the transsphenoidal method. The conventional transsphenoidal approaches by operating microscope include the sublabial transseptal, nasal transseptal, and endonasal one-nostril approaches. In rhinology, nasal endoscopy has been used clinically for many years.<sup>7,8</sup> Postoperative CSF leaks can be reduced by universal sellar reconstruction.<sup>7-10</sup> Therefore, by incorporating sellar floor reconstruction, it may be possible to maintain the vascularity of the

sphenoid mucosal flaps, thereby minimizing postoperative problems like CSF leakage, recurrent sinusitis, meningitis, encephalitis, and pneumocephalus. The rationale of our study was that there was a paucity of data regarding randomized controlled trials on the risk of postoperative CSF leakage in endoscopic endonasal transsphenoidal surgery of Pituitary adenoma with and without sellar floor reconstruction. The current study was designed to compare the outcome of the two approaches in terms of postoperative CSF leakage. Sellar reconstruction during the endoscopic endonasal transsphenoidal approach to pituitary tumor resection may not be required for patients without evidence of intraoperative CSF leakage. The preferred approach can be endoscopic endonasal Transsphenoidal surgery without sellar floor reconstruction in patients with no intraoperative CSF leakage to accomplish less invasive, cost-effective, short hospital stay and with lesser complications. This study will help to optimize the surgical procedure and prevent overtreatment.

## MATERIALS AND METHODS

### Study Design

This study was a randomized controlled trial following CONSORT guidelines.

### Study Setting & Patients

This research involved 116 patients<sup>9</sup> with pituitary adenoma (mean age, in group A was  $40.7 \pm 9.56$  years and in the group B was  $41.9 \pm 10.5$  years) of both genders who had endoscopic endonasal transsphenoidal surgery at the Punjab Institute of Neurosciences Unit III over 12 months between December 2020 and January 2022.

## Sampling Technique and Randomization

Non-probability purposive sampling and randomization by the balloting method were followed. Participants were randomly allocated into two groups using a random number table with a 1: 1 allocation ratio for both groups with no restrictions. Implementation for intervention was done by the operating consultant/supervisor enrolled participants and assigned them for intervention. Losses and exclusion after randomization could be due to the participants who did not receive the intended intervention and deviation from the study protocol.

## Sample Size

A total of 116 (58 cases in each group) was estimated. The sample size was calculated as follows.

$$n = \frac{\left\{ z_{1-\alpha} \sqrt{2\bar{P}(1-\bar{P})} + z_{1-\beta} \sqrt{P_1(1-P_1) + P_2(1-P_2)} \right\}^2}{(P_1 - P_2)^2}$$

n = 58 in each group

P1 = 0 % CSF leak in Sellar Floor Reconstruction<sup>9</sup>

P2 = 10% CSF leak in without Sellar floor reconstruction<sup>9</sup>

Z<sub>1- $\alpha$ /2</sub> = 95% = 1.9

Z<sub>1- $\beta$</sub>  = 80% = 0.84

## Inclusion Criteria

Patient with a pituitary adenoma between the ages of 18 to 60 years who underwent endoscopic endonasal transsphenoidal surgery at Punjab Institute of Neurosciences Unit III.

## Exclusion Criteria

Patients with substantial suprasellar/3rd ventricular/parasellar extension, an infected nasal cavity, a small or shallow sphenoid sinus, and postoperative CSF leaking who have undergone previous transsphenoidal surgery for pituitary adenoma.

## Data Collection Procedure

A total of 116 cases having Pituitary Adenoma who had Endoscopic Endonasal Transsphenoidal Surgery at the Punjab Institute of Neurosciences Unit III over 1 year from December 2020 to January 2022 meeting inclusion criteria after approval taken from the ethical committee from the department of neurosurgery PINS were included in our study. After obtaining informed consent, a thorough demographic (name, age, gender) and contact information were obtained. The cases were divided randomly into two groups. Endoscopic transsphenoidal surgery for pituitary adenoma in Group A was performed along with sellar floor reconstruction, whereas in Group B, just endoscopic transsphenoidal surgery for pituitary adenoma was performed. SPSS version 24 was used to enter and evaluate the gathered data. For quantitative information like age and tumor size, mean  $\pm$  S.D. was used. For categorical information like gender and post-operative CSF, frequency (%) was used. The CSF leakage in the two groups was compared using the chi-square test. P-value  $\leq$  0.05 was considered significant.

## SURGICAL PROCEDURE

The patients were shifted to Operation Theatre. General anesthesia was given and the patient was placed supine. Under aseptic measures, with help of an endoscope, middle turbinate identification and septotomy were done. Vomer and Sphenoid Ostia on both sides were identified. The Sphenoid sinus outer wall and mucosa were removed and the seller floor was identified. The Seller floor was removed with the help of a high-speed drill, mini chisel, and Kerrison rongeur. Dura was opened in an X-shaped manner. Tumor identification and excision were performed until the suprachiasmatic cistern falls on the sellar floor. Gross total excision was achieved and hemostasis was secured. If postoperative CSF leakage was noted then IV Antibiotics were started and the

patients were observed if CSF leakage does not stop then the Lumbar drain and sellar reconstruction were adapted accordingly.

### Sellar Floor Reconstruction

The defect in the sellar floor was reconstructed with fat, bone, Nasal septum flaps (Hadad-Bassagasteguy Flap), and Fibrin Glue, followed by Bismuth Iodine Paraffin paste (BIPP) nasal packing.

**Without Sellar Floor Reconstruction:** After tumor excision, surgical was used for hemostasis. The nasal septum was brought into a preoperative position and dressed.

## RESULTS

### Age and Gender Distribution

The mean age of patients in group A had 40.7 + 9.56 years, whereas those in group B had a mean age of 41.9 + 10.5 years. The difference in the mean ages of the two groups was unremarkable, according to the independent sample t-test ( $p = 0.686$ ) (Table 1). The gender distribution in both groups was contrasted using the chi-square test. The findings showed that neither group's gender distribution differed significantly from the others (Table 2).

**Table 2:** Gender distribution of both groups.

Gender	Group-A	Group-B	p-value
Male	29 (50.0%)	36 (62.1%)	0.190
Female	29 (50.0%)	22 (37.95%)	(insignificant result)
Total	58 (100%)	58 (100%)	

### SIZE OF TUMOR

The Chi-square test was utilized to compare the tumor sizes in the two groups. There was no discernible change in tumor size between the two

**Table 1:** Mean age comparison of both groups.

Group	Mean ± SD	Minimum	Maximum	p-value
Group-A	40.7 ± 9.56	20	60	0.686
Group-B	41.5 ± 9.23	20	60	(Insignificant result)

groups in the results. (Table 3)

**Table 3:** Size of tumors between both groups.

Pituitary Adenoma	Group-A	Group-B	p-value
Macro Adenoma	52 (89.7%)	52 (89.7%)	>0.999
Micro Adenoma	6 (10.3%)	6 (10.3%)	(insignificant result)
Total	58 (100%)	58 (100%)	

### CEREBROSPINAL FLUID (CSF) LEAK

On the 1st postoperative day, CSF leakage was noted in 2 (3.4%) patients of group A. Similarly, CSF leakage was noted in 2 (3.4%) patients of group B. All patients of both groups with CSF leak had macroadenoma. The chi-square test was utilized to compare the CSF leakage in two groups. The results revealed that there was no difference in CSF leakage between both groups (Table 4). Patients were observed for CSF leakage on discharge (usually 3rd day) and after two weeks as well, however, no CSF leakage was observed in both groups.

**Table 4:** Comparison of CSF leakage on the 1st postoperative day between both groups.

CSF Leak	Group-A	Group-B	p-value
Yes	2 (3.4%)	2 (3.4%)	>0.999
No	56 (96.6%)	56 (96.6%)	(insignificant result)
Total	58 (100%)	58 (100%)	

## OTHER COMPLICATIONS

In group A, postoperative nasal problems in patients included sphenoid sinusitis in 4 (6.9%), septal perforation in 3 (5.2%), nasal adhesion in 2 (3.43%), and atrophic rhinitis in 1 patient (1.7%), while there were no cases of nasal issues were recorded in group B. The complications in the two groups were compared using the chi-square test. A minimal difference in complications in the two groups was noted (Table 5).

## DISCUSSION

Pituitary adenomas make up the common brain tumors. The prevalence rate for it is 16 percent. In the presence of many other microsurgical techniques, transsphenoidal surgery is the safest and most effective. Most pituitary adenomas can be treated with it; it has been modified to this end.<sup>13</sup> Additionally, one of the suggested methods for treating pituitary adenomas is endoscopic transsphenoidal surgery. The most serious risk, nevertheless, continues to be post-cerebrospinal fluid leakage, which can result in cerebral dysfunction, pneumocephalus, or intracranial infection.<sup>14</sup> Therefore, it's crucial to use sellar repair and reconstruction to hide the sella turcica following transsphenoidal surgery<sup>15</sup>. Intrasellar packing and reconstruction of the sellar floor are both necessary steps in the operation known as sellar reconstruction. To reduce dead space and stop the fall of the chiasm into the sellar cavity, a barrier is required.<sup>16</sup>

In this study, pituitary adenoma patients with no intraoperative CSF leaks had endoscopic endonasal TSS with and without reconstruction of the sellar floor to compare the outcomes of postoperative CSF leaking. For this purpose, a total of 116 participants were taken with pituitary adenoma with a size less than 4cm and extension Knosp grade < 2.<sup>18</sup> The participants were divided

**Table 5:** Comparison of other complications in both groups.

Other Complications	Group-A	Group-B	p-value
Sphenoid sinusitis	4 (6.9%)	0 (0.0%)	0.199 (insignificant result)
Septal perforations	3 (5.2%)	0 (0.0%)	0.244 (insignificant result)
Nasal adhesions	2 (3.4%)	0 (0.0%)	0.496 (insignificant result)
Atrophic rhinitis	1 (1.7%)	0 (0.0%)	> 0.999 (insignificant result)

into two categories that are group A and group B. For group A, endoscopic endonasal TSS was done with sellar reconstruction while for group B endoscopic endonasal TSS was done without sellar reconstruction. The surgery was done at the neurosurgery department unit III of PINS. The independent sample t-test analysis revealed that the mean age group for groups A and B was  $40.7 \pm 9.56$  years and  $41.9 \pm 10.5$  years, respectively (Table 1). The result of the chi-square revealed no significant difference in gender among both the groups, that is, for group A, males and females were 29 each (50%). However, in group B, the males were 36 (62%) and females were 22 (38%) (Table 2). The chi-square test was utilized to compare the tumor sizes in the two groups. There was no discernible change in tumor size between the two groups. There were 52 (89.7%) cases of macro adenoma and 6 (10.3%) cases of microadenoma in each group. (Table 3) On the 1st postoperative day, it was seen that there was a cerebrospinal fluid leakage in two patients in group A (with sellar floor reconstruction). Whereas similar leakage was seen in group B (without sellar reconstruction) in two patients. The chi-square tests revealed no significant difference in the outcome for both groups. Insignificant P-values in the results supported our null hypothesis. (Table 4) In group A, postoperative nasal problems included sphenoid sinusitis in 4 (6.9%), septal perforation in 3 (5.2%), nasal adhesion in 2 (3.43%), and atrophic rhinitis in 1 patient (1.7%), while there were no cases of nasal issues recorded in group B. The complications in both groups were compared using the chi-square

test. Results demonstrated no significant difference in problems in both groups (Table 5). Our results were congruent with the results of Strickland et al, where patients with pituitary adenomas were treated using sellar construction based on the requirement. Twenty-six patients (2.6% of the total group) experienced postoperative CSF leaks, including thirteen patients (1.3% of the total group), and no leak was found during the operation. Thirteen of 26 patients who experienced postoperative CSF leak were found to have had an intraoperative leakage and undergone sella repair and the other thirteen patients did not. Those patients that did not have intraoperative leakage did not require reconstruction and revealed the same outcomes as that of patients treated with sellar reconstruction.<sup>7</sup> They are also in correspondence with the findings of Ismail and his colleagues who did sellar reconstruction with and without intrasellar packing. They discovered no discernible difference between the three groups, which are respectively devoid of intrasellar packing, hemostatic materials packing, and belly fat packing. It was concluded that the results of no intrasellar packing reconstruction were not inferior to any other approach used for sellar construction and have more radiological advantages. Which makes it a preferred choice of treatment.<sup>17</sup> Like those of Sonnenburg et al, Twenty-eight cases were found in a study of 45 patients who had endonasal transsphenoidal surgery without sellar floor repair. Only one case of post-operative CSF leak was documented. The complication rate was low and favorably compared to those reported in the literature. Who concluded that sellar reconstruction with no signs of a CSF leak during operation may risk the patients of complications at the donor site, higher costs, and challenges with postoperative measurement of tumor volume without reducing the possibility of postoperative CSF leak and other complications, our findings are similar.<sup>11</sup>

## **STRENGTHS**

In Pakistan, less literature is present on the outcomes of postoperative CSF leakage using endoscopic endonasal transsphenoidal surgery for pituitary adenoma with and without sellar floor reconstruction in patients with no intraoperative CSF leak. This could act as an initiative for further research in this area. Moreover, our results suggest that there is an equal chance of success in endoscopic endonasal transsphenoidal surgery for pituitary adenoma with and without sellar floor reconstruction in patients with no intraoperative CSF leak which enlarges the pool of options. Patients with pituitary adenomas can be treated without sellar floor reconstruction and could be saved from overtreatment and pain.

## **LIMITATIONS**

The sample size was small due to which the results can't be generalized. It was a cross-sectional research design due to which no causative decisions could be made with certainty. Though without sellar reconstruction, the patients do not undergo overtreatment, however, contemporary techniques are costly, require more hospitalization time, and puts the patients at risk of contracting infections.

## **FUTURE RECOMMENDATION**

This study has laid the basis for future studies. It is recommended that in future studies, a longitudinal research study is used to see the long-term effects and differences in the outcome of postoperative CSF leakage using endoscopic endonasal transsphenoidal surgery for pituitary adenoma with and without sellar floor reconstruction in patients with no intraoperative CSF leak. Moreover, different methods for sellar reconstruction could be used to see if that makes any difference in the outcomes.

## CONCLUSION

The results of CSF leakage following endoscopic endonasal TSS for pituitary adenoma with and without reconstruction of the sellar floor did not significantly differ in cases when there is no intraoperative CSF leak, this highlights the significance of endoscopic endonasal surgery without sellar reconstruction and protecting the patients from overtreatment.

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### Additional Information

**Disclosures:** Authors report no conflict of interest.

**Ethical Review Board Approval:** The study was conformed to the ethical review board requirements.

**Human Subjects:** Consent was obtained by all patients/participants in this study.

**Conflicts of Interest:**

In compliance with the ICMJE uniform disclosure form, all authors declare the following:

**Financial Relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

**Other Relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

### AUTHORS CONTRIBUTIONS

Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:
1.	Muhammad Naveed Majeed	1. Study design and methodology.
2.	Zubair Mustafa Khan	2. Paper writing.
3.	Mubashir Malik	3. Data collection and calculations.
4.	Sumira Kiran	4. Analysis of data and interpretation of results.
5.	Tariq Imran Khokhar	5. Literature review and referencing.
6.	Asif Bashir	6. Editing and quality insurer.