ORIGINAL ARTICLE

Frequency of CSF Rhinorrhoea in Patients Undergoing Endoscopic Transsphenoidal Surgery (ETSS) for Pituitary Macroadenoma

SOHAIB ALI1, TAUSEEF ULLAH2, MUHAMMAD IBRAHIM AFRIDI3, TABRAIZ WALI SHAH4, SHAFIQ UR REHMAN5, HANIF UR RAHMAN⁶, IDRIS KHAN⁷, MUHAMMAD TAIMUR KHAN⁸, EHSAN SAYYED⁹

^{1,2,3}Department of Neurosurgery, Hayatabad Medical Complex, Peshawar. PGR Neurosurgery

- ⁴Department of Neurosurgery, Hayatabad Medical Complex, PGR Neurosurgery ⁵Department of Neurosurgery, Hayatabad Medical Complex, PGR Neurosurgery
- ⁶Assistant Professor Neurosurgery Department of Neurosurgery, Prime Teaching Hospital, Peshawar.

⁷Department of Neurosurgery, Khyber Teaching Hospital, Peshawar. Professor Neurosurgery, HOD Neurosurgery

⁸Department of General surgery, Hayatabad Medical Complex, Peshawar. PGR General Surgery

⁹Department of Anatomy, Nowshera Medical College, Nowshera. Lecturer Corresponding author: Muhammad Ibrahim Afridi, Email: miafridi8@gmail.com

ABSTRACT

Introduction: Pituitary adenoma resection via the transsphenoidal approach (TSS)is a safe and common neurosurgical procedure that can be done both through microscopic and endoscopic methods.

Objectives: The main objective of the study is to find the frequency of CSF rhinorrhoea in patients undergoing endoscopic transsphenoidal surgery (ETSS) for pituitary macroadenoma.

Material and methods: The study data was collected from 1st Oct to 1st Nov 2022, in the departments of Neurosurgery of Hayatabad Medical complex, Khyber Teaching Hospital, Lady Reading Hospital, Peshawar. The data was collected through non-probability consecutive sampling technique. There were 315 patients which were included in the study. The surgical procedure is done under general anesthesia. All patient data was collected and a standardized form was filled by the attending surgeon caring for the patient. Importantly, the primary end points to be recorded were: (1) techniques of intraoperative cranium base reconstruction used, and (2) postoperative CSF rhinorrhoea biochemically confirmed and/or requiring intervention (CSF diversion and/or operative restoration).

Results: Of the 315 consecutive patients diagnosed with pituitary adenomas, a total of 250 patients met the inclusion criteria and were included. The pathology included 187 (74.8%) non-functioning adenomas, 40 (16.0%) GH-secreting pituitary adenomas, 3 (1.2%) PRL-secreting pituitary adenomas, and 20 (8.0%) ACTH-secreting pituitary adenomas. There were 30 (12.0%) cases of microadenomas, 205 (82.0%) cases of macroadenomas, and 15 (6.0%) cases of giant adenomas. Intraoperative CSF leakages were determined throughout surgical procedure in eighty patients (32.0%). Postoperative CSF leaks occurred in 9 patients (3.6%), including seven patients with intraoperative CSF leaks.

Practical implication: Practical implications of this study is: (1) easily find the CSF leakage (2) frequency of CSF rhinorrhoea in patients undergoing endoscopic transsphenoidal surgery

Conclusion: It is concluded that macroadenoma ETSS surgery should be strictly monitored for post-operative CSF leakage and lumber drain is an effective prophylactic strategy.

Keywords: Postoperative CSF Leakage, Pituitary Adenomas, ETSS, Surgery, Lumber

INTRODUCTION

Pituitary adenoma resection via the transsphenoidal technique (TSS) is a safe and not unusual neurosurgical procedure that can be finished both through microscopic and endoscopic techniques. it is usually an extraarachnoid technique however it isn't infrequent to go into the subarachnoid area within the surgery¹ for this reason, intra-operative, and subsequently, post-operative cerebrospinal fluid (CSF) leak, happens in¹ 5-12.7% of the cases, remains the most typical issue with this resection technique. During the last few years, lumbar drainage has been taken into consideration to be of specific significance in securing CSF Leak, and reconstruction of sellar base and optimizing tumor elimination, in addition to providing CSF drainage to lessen the threat of perioperative CSF leakage². Pituitary adenomas account for 15% of all intracranial tumors. Endoscopic endonasal transsphenoidal surgery (EETS) has ended up as the usual surgical remedy for pituitary adenomas. it is a fairly safe procedure with low morbidity, particularly when undertaken by skilled surgeons³. however, the risk of postoperative cerebrospinal fluid (CSF) leakage is a worrisome chief morbidity following EETS, which may additionally lead to meningitis or pneumocephalus, and is also related to prolonged hospitalization. The occurrence of CSF Leak ranges from 5 to 15% following EETS4.

Pituitary adenomas (PAs) are benign neoplasms that represent the most commonplace type of pituitary disease. a number of medical case studies have reported a prevalence for PA among community-dwelling adults starting from 1 in 865 to 1 in 2,6885. The desired end result of PA surgery consists of the complete elimination of the adenomas, the correction of hormonal hypersecretion, the retention of pituitary stalk, and the reduced risk of tumor recurrence. In comparison with transcranial surgical

treatment, transsphenoidal surgery (TSS) is advantageous, as it does not require brain retraction, resulting in reduced iatrogenic damage thus improved recovery post op, shorter medical institution stays, and improved patient satisfaction with surgery. With the evolution of imaging and surgical techniques, TSS has grown to be a powerful and preferred surgical approach for most PA's and is associated with a really low morbidity and mortality statistic6.

Arguably, the maximum critical determinant for the improvement of CSF rhinorrhea is the skull base restoration method used intraoperatively. Other threatening factors for postoperative CSF rhinorrhea encompass preceding cranial radiotherapy or surgical procedure; tumor length and infiltration; excessive intraoperative CSF leak; dural incision length and technique; Obesity is also a risk factor (BMI, calculated as weight in kilograms divided through the square of top in meters); and the skill of the operating surgeon7. There are a great array of alternatives and combinations available for repairing the cranium base, consisting of direct closure of the dura, the use of sutures; dural reconstruction using autologous fascia or artificial substances; vascularized flaps (e.g. nasoseptal and turbinate flaps, Hadaad Flap); avascular grafts (e.g. fat grafts); artificial grafts; and tissue glues (Duraseal - Integra Brazil)8.9

MATERIAL AND METHODS

The study data was collected from 1st Oct to 1st Nov 2022, in the departments of Neurosurgery of Hayatabad Medical complex, Khyber Teaching Hospital, Lady Reading Hospital, Peshawar. Inclusion criteria

• All patients who underwent endoscopic transsphenoidal surgery (ETSS) for pituitary macroadenoma were included in the study.

Exclusion criteria

- Those who do not want to participate.
- patients who have severe co-morbidities and Infections

Sampling technique: The data was collected through nonprobability consecutive sampling technique.

Data Collection: There were 315 patients which were included in the study. An informed consent was taken preceding surgery from all the chosen patients. The surgical procedure is done under general anesthesia. All patient data was collected and a standardized form was filled by the attending surgeon caring for the patient. Importantly, the primary end points to be recorded were: (1) techniques of intraoperative cranium base reconstruction used, and (2) postoperative CSF rhinorrhoea biochemically confirmed and/or requiring intervention (CSF diversion and/or operative restoration). Secondary endpoints were: (1) Intraoperative CSF leak; (2) working time; (3) costs of different postoperative morbidity; and (four) period of medical institution stay.

Statistical analysis: The data was collected and analyzed using SPSS version 21.0. All the data is represented in mean and standard deviation.

RESULTS

Of the 315 consecutive patients diagnosed with pituitary adenomas, a total of 250 patients met the inclusion criteria and were included. The average age of the patients became 44.1 ± 12.3 years. The mean hospitalization time was 8.4 days. The pathologies identified were 187 (70.4%) non-functioning adenomas, 40 (16%) GH-secreting pituitary adenomas, 03 (1.2%) PRL-secreting pituitary adenomas, and 20 (08%) ACTH-secreting pituitary adenomas. There have been 30 (12%) cases of microadenomas, 205 (82%) cases of macroadenomas, and 15 (6%) cases of massive adenomas. Intraoperative CSF leakages were determined throughout surgical procedure in eighty patients (32.0%), of the 80 instances with intraoperative leaks, 61 had been minor CSF leaks. Postoperative CSF leaks occurred in 9 patients (3.6%), including seven patients with intraoperative CSF leaks and patients with none identified intraoperative CSF leakage were 02. Of the 9 patients with postoperative CSF rhinorrhea, six patients underwent passive lumbar drainage for 5-7 days, and measures such as mattress rest, prophylactic antibiotics, and urinary catheterization, antitussives, and antiemetic's. Out of 09, 03 patients required surgical restoration of the cranial base through a trans-sphenoidal method utilizing Duraseal (Integra) as a primary adjunct. The CSF leakage in all nine patients became resolved. 04 patients with postoperative CSF leaks developed meningitis 2 to 7 days after EETS. They were treated with antibiotics (meropenem + vancomycin) for 14 days and discharged with normalization of all clinical parameters.

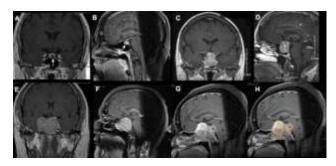
Table 1: Clinical Characte		
N/ 111	NI 1 1 1 1	

No intra-op leak	Intraop leak	P value
82 (48.2%)	48 (60.0%)	.219
88 (51.8%)	32 (40.0%)	
44.15 ± 14.52	44.13 ± 15.85	.992
24 (14.1%)	20 (25.0%)	.013
88 (51.8%)	50 (62.5%)	
44 (25.9%)	6 (7.5%)	
14 (8.2%)	4 (5.0%)	
144 (84.7%)	60 (75.0%)	.191
26 (15.3%)	20 (25.0%)	
154 (90.6%)	72 (90.0%)	1.000
16 (9.4%)	8 (10.0%)	
•	•	
	82 (48.2%) 88 (51.8%) 44.15 ± 14.52 24 (14.1%) 88 (51.8%) 44 (25.9%) 14 (8.2%) 144 (84.7%) 26 (15.3%) 154 (90.6%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$

No	162 (95.3%)	72 (95.0%)	1.000	
Yes	8 (4.7%)	4 (5.0%)		
Coronary heart diseas				
No	154 (90.6%)	76 (95.0%)	.621	
Yes	16 (9.4%)	4 (5.0%)		
Knosp Grade				
0	28 (16.5%)	16 (20.0%)	.641	
1–2	106 (62.4%)	40 (50.0%)		
3–4	36 (21.2%)	24 (30.0%)		
Tumor size	16.84 ± 6.16	26.20 ± 7.83	<.001	
Consistency of the adenoma			.032	
Tenacious	50 (29.4%)	57 (71.3%)		
Soft	120 (70.6%)	23 (28.7%)		
Degree of tumor rese	ction			
GTR	152 (89%)	66 (83%)	.248	
STR	14 (8.2%)	12 (15%)		
PR	4 (2.8%)	2 (2%)		
Pathology				
NF	124 (72.9%)	63 (78.8%)	.972	
ACTH	16 (9.4%)	4 (5.0%)		
GH	28 (16.5%)	12 (15%)		
PRL	2 (1.2%)	1 (1.2%)		

Table 2: Impact of Clinical Characteristics Upon Postoperative CSF Leak

Variable	OR	95% CI for OR	P value
CRD	57.500	8.031-411.682	<.001
Intraoperative CSF leak	7.707	1.336-44.455	.022
VNSF+ abdominal fat	0.107	0.013-0.894	.039
graft			



Tumor Classification based on size. Microadenoma: Coronal and sagittal T1 weighted MRIs with contrast with arrow indicating the location of the tumor (A and B). Macroadenoma: Coronal and sagittal T1 weighted MRIs of a typical macroadenoma (C and D). Giant invasive macroadenoma: Coronal and sagittal T1 MRIs with contrast in a patient in whom the tumor compresses the right temporal lobe and invades the sphenoid sinus (E and F). In another patient, the sagittal MRI reveals a tumor that has not only invaded the sphenoid sinus but compresses the brainstem; the tumor is highlighted (G and H).

DISCUSSION

In most studies of pituitary adenomas and CSF leakages after transnasal surgery, researchers have found that postoperative CSF leakage occurred in most patients with intraoperative CSF leakage. For this reason, intraoperative CSF leakage seems to be a crucial factor for postoperative CSF leakage¹⁰. Our results reflect these findings. In our study, 09 patients had postoperative CSF leakages. The final multivariate regression analysis showed that intraoperative CSF leakage become an unbiased hazard element for postoperative CSF leakage¹¹.

Based on the findings of our study it is imperative to avoid intraoperative CSF leak to save you the hassle of post-operative CSF leak¹². moreover, the relevant know-how of the risk elements of intraoperative CSF leakage is beneficial in the management and prevention of postoperative CSF leakage¹³. it is apparent that any of the factors that can cause diaphragma sellae rupture can cause

CSF leakage. Therefore, the operating factors impacting the rupture of the diaphragma sellae can also result in intraoperative CSF leakage¹⁴. We located the sizeable distinction in the tumor length between those who had an intraoperative CSF rhinorrhea and those who did not. Zhou et al additionally reported a high prevalence of intraoperative CSF leakage following a large pituitary adenoma resection15. Their final multi-component regression evaluation proved it to be an impartial threat for intraoperative CSF rhinorrhea. Tumor length is a major determinant for CSF leakage throughout surgery and can be due to suprasellar extension in huge-sized tumors¹⁶. Therefore, mild manipulation is necessary for big pituitary adenomas to avoid rupture of a rather skinny diaphragm sellae at some stage in surgical operation. disposing of the tumor within the following order rear, two facets, and the front can also avoid losing the diaphragma sellae too early and too fast (which may result in its rupture and consequently CSF leakage)17,18.

CONCLUSION

It is concluded that during nasal transsphenoidal endoscopic resection of pituitary adenomas, patients with a large tumor should be strictly monitored for intraoperative CSF leakage. In the presence of intraoperative CSF leakage, the sellar base defects should be carefully repaired and reconstructed with triple layer technique to avoid postoperative CSF leakage.

REFERENCES

- Wang, Ming MD; Cai, Yang MD; Jiang, Yugang MD; Peng, Yong MD*. Risk factors impacting intra- and postoperative cerebrospinal fluid rhinorrhea on the endoscopic treatment of pituitary adenomas: A retrospective study of 250 patients. Medicine: December 10, 2021 -Volume 100 - Issue 49 - p e27781 doi: 10.1097/MD.00000000027781
- Shamim MS, Bari ME, Khursheed F, Jooma R, Enam SA. Pituitary adenomas: presentations and outcomes in a South Asian country. Can J Neurol Sci 2008;35:198-203.
- Khan I, Shamim MS. Comparison between endoscopic and microscopic approaches for surgery of pituitary tumours.J Pak Med Assoc. 2017;67:1777-9.
- Rabadan AT, Hernandez D, Ruggeri CS. Pituitary tumors: our experience in the prevention of postoperative cerebrospinal fluid2 leaks after transsphenoidal surgery. J Neurooncol. 2009;93:127-31.
- Caggiano C, Penn DL, Laws ER, Jr. The Role of the Lumbar Drain in Endoscopic Endonasal Skull Base Surgery: A Retrospective Analysis of 811 Cases. World Neuro surg. 2018; 117:e 575-e9.
- 6. Tien DA, Stokken JK, Recinos PF, Woodard TD, Sindwani R. Cerebrospinal Fluid Diversion in Endoscopic Skull Base

Reconstruction: An Evidence-Based Approach to the Use of Lumbar Drains . Otolaryngol Clin North Am. 2016;49:119-29.

- Sade B, Mohr G, Frenkiel S. Management of intra-operative cerebrospinal fluid leak in transnasal transphenoidal pituitary microsurgery: use of post-operative lumbar drain and sellar reconstruction without fat packing. Acta Neurochir (Wien). 2006;148:13-8; discussion 8-9.
- Mehta GU, Oldfield EH. Prevention of intraoperative cerebrospinal fluid leaks by lumbar cerebrospinal fluid drainage during surgery for pituitary macroadenomas. J Neurosurg. 2012;116:1299-303.
- Zhan R, Chen S, Xu S, Liu JK, Li X. Postoperative Low-Flow Cerebrospinal Fluid Leak of Endoscopic Endonasal Transsphenoidal
- 10. Surgery for Pituitary Adenoma--Wait and See, or Lumbar Drain? J Craniofac Surg. 2015;26:1261-4.
- Thawani JP, Ramayya AG, Pisapia JM, Abdullah KG, Lee JY, Grady MS. Operative strategies to minimize complications following resection of pituitary macroadenomas. J Neurosurg Part B: Skull Base. 2017;78:184-90.
- Ransom ER, Palmer JN, Kennedy DW, Chiu AG. Assessing risk/benefit of lumbar drain use for endoscopic skull-base surgery. Int Forum Allergy Rhinol 2011;1:173-7.
- Hussein K, Rabino G, Feder O, Eghbaryeh H, Zayyad H, Sviri G, et al. Risk factors for meningitis in neurosurgical patients with cerebrospinal fluid drains: prospective observational cohort study. Acta Neurochir (Wien). 2019;161:517-24.
- Zhou, Z., Zuo, F., Chen, X. et al. Risk factors for postoperative cerebrospinal fluid leakage after transsphenoidal surgery for pituitary adenoma: a meta-analysis and systematic review. BMC Neurol 21, 417 (2021). https://doi.org/10.1186/s12883-021-02440-0
- Xue H, Wang X, Yang Z, Bi Z, Liu P. Risk factors and outcomes of cerebrospinal fluid leak related to endoscopic pituitary adenoma surgery. Br J Neurosurg. 2020;34(4):447– 52. https://doi.org/10.1080/02688697.2020.1754336.
- Liu B, Wang Y, Zheng T, Liu S, Lv W, Lu D, et al. Effect of intraoperative lumbar drainage on gross total resection and cerebrospinal fluid leak rates in endoscopic transsphenoidal surgery of pituitary macroadenomas. World Neurosurg. 2019;135:629– 39. https://doi.org/10.1016/j.wneu.2019.12.100.
- Riesgo P, Marino P, Platero A, Tarazona FJ, Fajardo C, Llacer JL, et al. Postoperative CSF leakages after transsphenoidal surgery for pituitary adenomas: analysis of a series of 302 surgical procedures. Neurocirugia. 2019;30(5):215– 21. https://doi.org/10.1016/j.neucir.2019.03.003.
- Fujimoto K, Yano S, Shinojima N, Hide T, Kuratsu JI. Endoscopic endonasal transsphenoidal surgery for patients aged over 80 years with pituitary adenomas: Surgical and follow-up results. Surg Neurol Int. 2017;8(1):213. https://doi.org/10.4103/sni.sni_189_17.
 Wang XD, Tang YY, Liu HQ, Neurosurgery DO. Comparison of
- Wang XD, Tang YY, Liu HQ, Neurosurgery DO. Comparison of neuroendoscopic and transnasal-sphenoidal microscopic resection of pituitary adenoma[In Chinese]. J Clin Neurosurg. 2018;4(15):292– 5. https://doi.org/10.3969/j.issn.1672-7770.2018.04.011.