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Frequency of Cerebrospinal Fluid (CSF) Rhinorrhea Following Endoscopic Transsphenoidal Pituitary Macroadenoma Excision at Tertiary Care Hospital

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ABSTRACT

Background: Cerebrospinal fluid (CSF) rhinorrhea remains a significant postoperative complication after endoscopic transsphenoidal surgery for pituitary macroadenomas. Early identification and prevention are essential to reduce morbidity. **Objective:** To determine the frequency of CSF Rhinorrhea following endoscopic transsphenoidal pituitary macroadenoma excision at public tertiary care hospital. **Material and Methods:** The current cross-sectional descriptive study was conducted during 20 January, 2025 to 15 May, 2025 at the Department of Neurosurgery, Liaquat National Hospital & Medical College, Karachi. Total 143 participants of both genders having age of 18 to 60 years patients diagnosed with pituitary macroadenoma and underwent endoscopic endonasal transsphenoidal surgery were enrolled. Patients having recurrent tumors or whose have severe co-morbidities were excluded from this study. The collected data was entered, compiled and analyzed by using SPSS-27and taking p-value < 0.05 as statically significant. **Results:** The mean age was 41.99 ± 11.39 years (range: 18–60), with 97 (67.8%) males and 46 (32.2%) females. Obesity (BMI > 30 kg/m^2) was noted as 45(31.45%) of patients. Hypertension was present in 24(16.8%), diabetes mellitus 33(23.1%) were noted. Headache 140(97.9%) and vision loss 136(95.1%) were the most common presenting symptoms, followed by fatigue 35(24.5%), dizziness 17(11.9%), and decreased libido 10(7.0%). Maximum patients 12(22.2%) observed for CSF rhinorrhea with tumor size as 26-40(mm) compared with 56-70 (mm) group as 8(30.8%) with statistically significant p-value as 0004. **Conclusion:** Larger pituitary tumors were significantly associated with a higher risk of postoperative CSF rhinorrhea. Careful surgical planning and reconstruction are essential in such cases to reduce this complication.

INTRODUCTION

Pituitary adenomas (PAs), also called pituitary neuroendocrine tumors, are among the most common brain tumors in adults, nearly 15% of all central nervous system tumors. [1,2] The preferred and recommended treatment for mostly cases is transsphenoidal resection, performed either through endoscopic or microscopic techniques. [3,4] Once the tumor is removed, preventing postoperative cerebrospinal fluid (CSF) leakage becomes crucial, as it can lead to serious complications such as meningitis, brain abscess, subdural hematoma, or pneumocephalus. [5] In recent years, endoscopic endonasal transsphenoidal surgery (EETS) has become the standard approach for treating pituitary macroadenomas. When experienced surgeons performed, it is generally safe and associated with low complication rates. [6] Still, CSF leakage remains the most concerning postoperative complication of EETS, as it not only increases the risk of infections like meningitis or pneumocephalus but also contributes to longer hospital stays and recovery times. [7]

Cerebrospinal fluid (CSF) leakage is most commonly identified in the early postoperative period, often when patients report a salty taste in the throat or observe clear fluid draining from the nasal passages. [8] The incidence 5% to 13%. of this complication after endoscopic endonasal transsphenoidal surgery (EETS) has been reported. [7] In some instances, however, CSF leakage may present later weeks or even months following surgery typically as a result of a slowly expanding defect within the arachnoid layer. [9–11] Romero et al. [12] documented a postoperative CSF rhinorrhea rate of 8.2% in their series of transsphenoidal cases. The risk of developing postoperative CSF rhinorrhea is closely associated with both the surgeon's technical proficiency and tumor-related factors. [13] Likewise, Ali et al. (2022) [14]

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reported intraoperative CSF leakage in 32% of patients, while postoperative leakage was observed in 3.6%, the majority of whom had already demonstrated intraoperative leakage. [14].

Zhang et al. [15] studied 100 patients with tumors who experienced intra-operative CSF leaks. among them, 17 (17%) patients developed postoperative leaks, usually appearing within a 2 days after surgery (range: 0–34 days). Notably, patients with clival tumors had a significantly higher risk of postoperative leakage compared to tumors in other sites ($p < 0.05$). However, factors such as body mass index (BMI), tumor size, reconstruction method, or medical comorbidities showed no significant association. The grade III intraoperative leaks were nearly twice as common in patients who later developed postoperative leaks with statistically i significance p = 0.12.

In another large study, Patel et al. [16] analyzed 806 patients undergoing endoscopic transsphenoidal surgery. Overall, 205(25.4%) patient's experienced CSF leakage, including 188(23.3%) during surgery and 38(4.7%) cases after surgery. Of these, 21(2.6%) patients developed postoperative leaks despite repair of an intraoperative leak, and more than half (55%) of those with postoperative leakage had previously undergone intraoperative leak repair. Multivariate analysis found that body mass index (BMI), hydrocephalus, suprasellar extension, and craniopharyngioma to be significant predictors of intraoperative leaks. BMI and hydrocephalus were the only significant predictors in the case of postoperative leaks. Surprisingly, patients, whose leaks had been repaired using septal flap method, were more likely to experience postoperative leakage than those repaired using other repair methods (odds ratio 6.37; p = 0.013).The occurrence of postoperative cerebrospinal fluid (CSF) leakage appears to be more common in patients with elevated body mass index (BMI) or increased intracranial pressure. Despite this association, the precise risk factors remain poorly defined, and reported prevalence rates vary widely, ranging from 0% to 40%.[17] Compared with transcranial neurosurgical procedures, CSF leak rates following transsphenoidal surgery (TSS) are generally higher, largely due to factors such as gravitational effects and the absence of protective anatomical barriers, including watertight dural closure and layered subcutaneous or cutaneous closure.

Kim et al. [18] conducted a meta-analysis of 56 studies, including 11,826 patients, and reported that 753 patients developed cerebrospinal fluid (CSF) leakage following skull base surgery. The pooled incidence of postoperative CSF leakage was 7.2% \[95% CI: 5.9–8.7%, $I^2 = 82.3\%$]. Sensitivity analysis showed that the leakage rate remained consistent over time, regardless of the year of publication.

Similarly, Ozawa et al. [19] analyzed 230 cases of endoscopic endonasal skull base surgery (EESBS), in which 11(4.8%) experienced postoperative CSF leakage. When stratified by pathology, leakage rates were 3.5% in pituitary adenomas, 0% in Rathke's cleft cysts, 3.6% in chordomas, and 8.0% in meningiomas. Multivariate analysis revealed that repeat surgery (p = 0.008) and intraoperative CSF leakage (p = 0.044) were independent predictors of postoperative leakage. The authors emphasized that both tumor resection strategy and skull base reconstruction should be tailored according to tumor type and patient-specific factors, as repeated procedures increase the risk of CSF leakage.

Despite these reports, data on postoperative CSF leakage specifically in endoscopic endonasal transsphenoidal surgery for pituitary macroadenomas remain limited. The present study was therefore designed to evaluate the frequency of CSF rhinorrhea in the Pakistani population, with the aim of identifying its burden and guiding preventive as well as management strategies to reduce patient morbidity.

Objective

To determine the frequency of CSF rhinorrhea following endoscopic transsphenoidal pituitary macroadenoma excision at tertiary care hospital.

Operational Definition

Pituitary Macroadenoma: Pituitary macroadenomas are benign tumors larger than 10 mm, usually formed on pituitary gland.

Cerebrospinal Fluid (CSF) Rhinorrhea: Post-operatively 24 hours and on follow-up up to 1 month, any discharge of cerebrospinal fluid (CSF) from the nose and confirmed by Provocative test.

If Provocative test is positive, then CT Brain including bone window (with fine coronal cuts to see bony defect) and MRI (T2 sequence thin coronal cuts to see CSF signal) both tests done and deemed as positive on each patient.

Provocative Test: It can be provoked by placing the patient's face in a downward position and observing for leakage for several minutes.

MATERIAL AND METHODS

The current Cross-sectional study was conducted from month of 20 January, 2025 to 15 May, 2025 in Department of Neuro-Surgery, Liaquat National Hospital & Medical College, Karachi, after the acquiring approval Hospital Ethics Committee and CPSP CPSP/REU/NSG-2023-192-948. Sample size calculation was based on the study conducted by Romero et al [12] has reported frequency of CSF rhinorrhea as 8.2% after transsphenoidal surgery. A total of 143 patients with pituitary adenoma included to estimate expected frequency of CSF rhinorrhea within 4.5% margin of error and 95% confidence interval. The study purpose and benefits of the study were explained to study participants or to their attendants to obtain their consent to enroll them into the study. Informed consent was obtained before surgery from all the patients. The participants of both genders having age between 18 years to 60 years of both gender, ASA-I and II and patients were diagnosed with pituitary macroadenoma and who underwent endoscopic endonasal transsphenoidal surgery, were enrolled, while those who did not want to participate or had recurrent tumors. And patients who had severe co-morbidities like uncontrolled diabetes mellitus (fasting blood sugar more than 126 mg/dl) and uncontrolled hypertension blood pressure more than 140/90 mm Hg were excluded from the current research study.

The surgical procedure was done under general anesthesia. Preoperatively, all patients were reviewed by

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the team to reach a consensus with regard to the surgical approach, post-operative care, and fitness to undergo surgery. All patient data was collected in a predesigned proforma. Demographic and surgical characteristics, including patient age, sex, weight by weighing machine in kg, height by mounted scale in cm, and body mass index calculated by the formula (Weight/ Height^2[kg/m^2]), Comorbid like hypertension by history of patients, diabetic mellitus also by history of patients about drug history taking from 6 or more months, symptoms (headache, Vision loss & loss of libido evident on history) prompting surgical presentation, tumor size, postoperative CSF rhinorrhea at 24 hours and after 1 months as discussed above, surgery duration, and estimated blood loss, outcome taken at 1 month.

All statistical analyses were conducted using SPSS version 27.0. Categorical variables including demographic information, comorbidities such as hypertension and diabetes mellitus, reported symptoms, family history of pituitary adenomas, history of congestive heart failure, family history of stroke, and instances of CSF rhinorrhea at 24 hours and one month post-operation, along with other complications were summarized using frequencies and percentages. To account for potential confounding variables, a stratification analysis was carried out. This analysis controlled for the influence of factors such as age, body mass index (BMI), gender, duration of surgery, comorbid conditions, associated symptoms, and relevant family medical histories in order to better evaluate the occurrence of CSF rhinorrhea. Chi-square test or Fisher's exact test was used to see the effect of these modifiers with $p<0.05$ as a significant.

RESULTS

Table 1

Age, Gender, BMI and Comorbidities among Research Participants

Age		
Total Patients		143
Mean± Std. Deviation		41.99±11.39
Median		43.00
Range		18--60
Gender		
Male		97(67.8%)
Female		46(32.2%)
BMI (Kg/m^2)		
>30 kg/m2		45(31.45%)
< 30 kg/m2		98(68.55%)
Comorbidity n(%)		
Hypertension	Yes	24(16.8%)
	No	119(83.2%)
Diabetic Mellitus	Yes	33(23.1%)
	No	110(76.9%)
Both DM and HTN	Yes	13(9.1%)
	No	130(90.9%)
DM ,HTN, and Hypothyroidism	Yes	1(0.7%)
	No	142(99.3%)
HTN and Acromegaly	Yes	3(2.1%)
	No	140(97.9%)

A total of 143 patients enrolled, among these 97(67.8%) were male and 46(32.2%) were female. The Median and Mean age of these patients was 43.00 and 41.99±11.39 Sd (range 18 to 60 years). Regarding **c**omorbidities i.e, hypertension 24(16.8%), diabetic mellitus 33(23.1%), both DM and HTN 13(9.1%), DM, HTN and Hypothyroidism 1(0.7%) and HTN and Acromegaly 3(2.1%). **(Table 1)**

Table 2

Associated Symptoms Assessed By Clinical or History of Patients

Associated Symptoms n(%)		
Headache	Yes	140(97.9%)
	No	2(1.4%)
Vision Loss	Yes	136(95.1%)
	No	7(4.9%)
Decreased libido	Yes	10(7.0%)
	No	1330(93.0%)
Fatigue	Yes	35(24.5%)
	No	108(75.5%)
Dizziness	Yes	17(11.9%)
	No	126(88.1%)
Family History of Pituitary Adenomas:	Yes	7(4.9%)
	No	136(95.1%)
History of Chronic Heart Failure	Yes	0(0/0%)
	No	143(100.0%)
History of Stroke	Yes	0(0/0%)
	No	143(100.0%)
Duration of Surgery (Hours)	3.09±0.41	

Associated symptoms assessed by clinical or history of patients showed that the Headache 140(97.9%), vision loss 136(95.1%), decreased libido 10(7.0%), fatigue 35(24.5%), dizziness 17(11.9%) , family history of pituitary adenomas 7(4.9%), history of CHF 0(0/0%), history of stroke 0(0/0%) and duration of surgery (hours) 3.09±0.41.

Table 3

Postoperative Surgical Outcomes

CSF Rhinorrhea n(%)		
24 hours Postoperative	Yes	17(11.9%)
	No	126(88.1%)
After 1Month	Yes	2(1.4%)
	No	141(98.6%)
Length of Stay (Days)	2.98±0.50	

Postoperative surgical outcomes showed that CSF rhinorrhea observed within 24 hours postoperative 17(11.9%) while compare with after 1 month 2(1.4%). The length of stay (days) showed that the 2.98±0.50.

Table 4

Post-stratification Results of CSF Rhinorrhea within 24 hours and after 1 Month among Male and Female Patients.

Research Variables		**CSF Leak (within 24 Hours)**		**Total**	**P-value**
		Yes	**No**		
Gender	Male	9(9.3%)	88(90.7%)	97(67.8%)	0.175
	Female	8(17.4%)	38(82.6%)	46(32.2%)	
		CSF Leak (within 1 Month)			
Gender	Male	1(1.0%)	96(99.0%)	97(67.8%)	0.541
	Female	1(2.2%)	45(97.8%)	46(32.2%)	

The findings of Table 4 showed that CSF Rhinorrhea within 24 hours and after 1 Month among Male and Female Patients observed 9(9.3%) and 8(17.4%) with a statistically insignificant p-value 0.175. while comparing with after 1 month only one patients of both genders was observed with a statistically insignificant p-value 0.541.

Table 5

Comparison of CSF Rhinorrhea with Tumor size GroupWise

Research Variables	
Tumor Size (mm)	26.92±12.45 (Mean±SD)
Yes	26(18.2%)

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CSF Rhinorrhea	No	117(81.8%)		
Tumor Size (mm) Group wise		**CSF Rhinorrhea**		**p-value**
		Yes	No	
11-25 mm		4(6.5%)	58(93.5%)	
26-40 mm		12(22.2%)	42(77.8%)	
41-55 mm		2(50.0%)	2(50.0%)	0.004
56-70 mm		8(30.8%)	15(65.2%)	

The tumor size (mm) was observed as 26.92±12.45 , CSF leak rate was 28(18.2%), while comparison has been made for tumor size and CSF leak, it was found that 12(22.2%) maximum patients observed for CSF rhinorrhea with tumor size as 26-40(mm) compared with 56-70 (mm) group as 8(30.8%) with statistically significant p-value as 0004.

DISCUSSION

The present study assessed the frequency and short-term outcomes of cerebrospinal fluid (CSF) rhinorrhea following endoscopic transsphenoidal excision of pituitary macroadenomas, highlighting demographic characteristics, comorbidities, symptom patterns, and postoperative complications in a tertiary care setting.

In this study, 143 patients who had endoscopic transsphenoidal excision of pituitary macroadenomas participated. The median age of the study participants was 43 years and the mean age of the participants was 41.99± 11.39 years and the age ranged between 18 and 60. The cohort was mainly males 97 patients (67.8%), and females included 46 cases (32.2%). In terms of body mass index (BMI) 45 patients (31.45%) were already obese (BMI > 30 kg/m 2), and 98(68.55%) patients.

Li et. al, [20] enrolled eight hundred forty-three patients, the mean age: 45.0 ± 13.4 years with pituitary adenomas (PA) were included in this study. [20] The high prevalence of preoperative headache 140(97.9%) and vision loss 136(95.1%) in our cohort points toward delayed presentation, which is common in low-resource settings due to limited access to specialist care. This late presentation often correlates with larger tumors and greater surgical complexity, indirectly influencing CSF leak rates. Moreover, comorbidities such as hypertension and diabetes found in 24(16.8%) and 33(23.1%) of patients, respectively are important considerations for perioperative management, although our data did not demonstrate a direct association with CSF rhinorrhea. Patel et. al [21] a total of 806 patients undergoing endoscopic transsphenoidal surgery were included in this study, they found that hypertensive patients were observed as 80 (42.6%), which was almost doubled as compared with study findings. [21]

In the present study, the most frequently reported presenting symptoms among patients with pituitary adenomas were headache (97.9%) and vision loss (95.1%), while other complaints such as fatigue (24.5%), dizziness (11.9%), and decreased libido (7.0%) were observed less commonly. A positive family history was noted in 4.9% of cases, whereas comorbidities such as congestive heart failure and stroke were absent. The mean duration of surgery was 3.09 ± 0.41 hours.

These findings are consistent with previously published data, where headache and visual disturbances remain the predominant symptoms due to the tumor's mass effect on surrounding structures. Scaf et. al, [22] who discovered that 62 percent of the 104 patients had headache within the past 3 months. Migraine and tension-type headache were the most common phenotypes. Only prolactinoma patients had trigeminal autonomic cephalalgia (TACs). Headache was offered equally by both sexes (64% in females and 58% in males) but patients with headache were younger (41.5 ± 13.8 vs. 56.8 ± 13.6 years). Headache was not dependent on the characteristics of tumor. GH levels in patients with acromegaly that presented with headache were greater. Prolactinomas had more headache (83) compared to NFPA (52). Headache resolution was seen in 83, 50 and 33% of NFPA, somatotropinomas and prolactinomas after disease remission or control, respectively [22]

In this study, it observed a statistically significant association between tumor size and postoperative CSF rhinorrhea following endoscopic transsphenoidal excision of pituitary macroadenomas. Patients with tumors measuring 26–40 mm exhibited a CSF leak rate of 22.2%, while those in the 56–70 mm group demonstrated the highest rate at 30.8% (p=0.004). These findings support prior evidence that larger tumors increase surgical complexity by extending beyond the dural barriers, thereby raising the risk of postoperative leaks. Previous studies have reported that tumor size greater than 30 mm is an independent predictor of CSF leakage, as increased resection difficulty and greater dural exposure predispose to intraoperative breach. Our results are consistent with those of Ivan et al. and Slot et al., who emphasized the impact of tumor dimensions and suprasellar extension on postoperative leak rates.[23,24]

The overall incidence of CSF rhinorrhea in our cohort was 18.2%, with 11.9% occurring within the first 24 hours and only 1.4% persisting after one month. This progressive decline highlights the effectiveness of early detection and repair techniques, as well as close postoperative surveillance. In comparison, previously published series have reported leak rates ranging from 2% to 15%, varying with surgical expertise, reconstruction technique, and intraoperative preventive strategies. Our slightly higher rate in the early postoperative phase may reflect the larger average tumor size in our cohort (26.92 ± 12.45 mm), yet the substantial reduction over time underscores the success of repair methods and the importance of early intervention. The finding that most leaks resolved or were effectively managed within the first few days supports current literature advocating for proactive measures to prevent secondary complications such as meningitis, pneumocephalus, or prolonged hospitalization.

From a clinical standpoint, these results emphasize the need for individualized surgical planning, particularly in patients with larger tumors. Advanced reconstruction techniques, such as the vascularized nasoseptal flap, multilayered closure, and the use of autologous grafts, have been shown to significantly reduce persistent CSF leak rates in high-risk cases. Our mean hospital stay of three days suggests that early identification and prompt repair strategies allowed for efficient postoperative recovery, reducing unnecessary inpatient days and associated costs. This has important implications for both

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patient safety and healthcare resource utilization. Future research should aim to refine risk stratification models incorporating tumor size and intra-operative findings to identify patients at greatest risk of CSF leak and to standardize repair protocols accordingly.CSF leak risk in our study is consistent with earlier reports by Ivan et al. [22] indicating that surgical technique and anatomical factors play a more decisive role than gender alone.

According to the authors PRISMA guidelines, authors searched for articles reporting CSF leak after TSS in the adult population by using the PubMed, Embase, and Cochrane Library databases. They pooled data from 70 studies published since 2015, which included results from nearly 25,000 surgeries. Their analysis revealed that overall, about 3.4% of patients experienced this complication. The risk was higher more than double for people who had the surgery for a reason other than a standard pituitary tumor. They also found that patients whose tumors had grown into a surrounding area (cavernous sinus invasion) or who had a leak noticed during the surgery itself were at a significantly greater risk. However, whether someone had previous surgery or if the surgeon used a microscope didn't make a noticeable difference in the leak risk.[23].

Limitations

While this research provides valuable insights, its scope presents some important constraints. The findings are drawn from a single medical center, which may affect how broadly applicable the results are to other healthcare settings. Additionally, though the number of cases included was sufficient for analysis, a larger and more diverse sample could better account for variations in surgical skill and institutional practices that influence patient outcomes. Third, the study did not stratify results based on reconstruction techniques or surgeon experience, both of which are known to influence CSF leak rates. Finally, long-term follow-up beyond one month was not performed, which may have overlooked delayed or recurrent CSF leaks.

Recommendations

Future studies should be multi-centric with larger cohorts to validate these findings and provide greater external applicability. Longer follow-up periods are essential to assess the risk of delayed or recurrent leaks. Incorporating stratification by surgical technique, reconstruction method, and surgeon experience would provide more nuanced insights into risk factors and preventive strategies. Clinically, we recommend that patients with larger tumors, particularly those exceeding 40 mm, be considered high risk for postoperative CSF rhinorrhea and managed with advanced multilayer closure techniques and intensive early postoperative surveillance. Standardized repair protocols tailored to tumor size and intra-operative findings could further reduce CSF leak rates and improve patient outcomes.

CONCLUSION

This study demonstrated a significant association between tumor size and the incidence of postoperative CSF rhinorrhea following endoscopic transsphenoidal pituitary macroadenoma excision. Larger tumors, particularly those measuring above 40 mm, were associated with higher leak rates, underscoring the impact of tumor size on surgical complexity and outcome. Although the initial incidence of CSF rhinorrhea was relatively high within the first 24 hours (11.9%), it markedly declined to 1.4% after one month, reflecting the effectiveness of timely repair strategies and vigilant postoperative monitoring. The overall short hospital stay further supports the role of efficient management protocols in minimizing morbidity and optimizing recovery.

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