# Incidence and Risk Factors of Postoperative Meningitis Following Endoscopic Endonasal Transsphenoidal Surgery: A Study in Thailand

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## Abstract

**Objectives** Postoperative meningitis following endoscopic endonasal transsphenoidal surgery (TSS) is a critical outcome metric. Meningitis is one of the most severe complications in neurosurgery, particularly with transsphenoidal procedures, due to the potential for bacterial contamination from the nasal or sinus cavities. Identifying the risk factors associated with postoperative meningitis is crucial for preventing and minimizing this risk in future surgeries.

**Materials and Methods** The study reviewed admission forms, operative notes, and the occurrence of various complications in patients who underwent the TSS approach between 2010 and 2024, focusing on variations in health care access and surgical practices.

**Statistical Analysis** Descriptive statistics will summarize demographic, surgical, and clinical characteristics. Univariate analysis: risk factors for meningitis could be evaluated through chi-square tests for categorical variables (e.g., presence of a cerebrospinal fluid [CSF] leak) and *t*-tests or analysis of variance for continuous variables (e.g., age, surgery duration). Multivariate logistic regression: to identify independent predictors of meningitis, logistic regression could be used.

**Results** A total of 237 patients who underwent TSS between 2010 and 2024 were included in the final analysis. The overall incidence of postoperative meningitis was 23%. Intra- and postoperative CSF leakage, diabetes mellitus, obesity, and previous sinus or nasal infection were found to be a significant factor associated with postoperative meningitis.

**Conclusion** Understanding the risk factors for meningitis following TSS is crucial for improving patient outcomes. While preoperative nares cleaning with normal saline may reduce nasal congestion, our findings indicate that it does not significantly affect the rate of postoperative meningitis compared with Hibitane-only cleaning.

**Keywords**
- risk factors
- endoscopic endonasal surgery
- transsphenoidal surgery
- postoperative meningitis
- neurosurgery

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## Introduction

Postoperative meningitis following transsphenoidal surgery (TSS) is a significant concern, as it can lead to serious complications such as brain infections, prolonged recovery times, and increased health care costs. Understanding the risk factors for meningitis is essential to improving patient outcomes and minimizing complications.[1] Understanding the rate of occurrence of this complication in Thailand could provide valuable insight into the specific challenges of health care settings in the country.[2] Comparing these figures to global or regional data can highlight whether Thailand has a higher or lower incidence, shedding light on local factors that might be influencing outcomes (e.g., different surgical practices, infection control protocols, or patient populations).[3] Identifying the risk factors associated with postoperative meningitis is essential to help prevent and mitigate the risk in future surgeries. Some of these factors could include surgical factors, the complexity of the surgery, such as the location and size of the tumor, or the experience level of the surgeon, all of which could impact the likelihood of infection. Additionally, the use of endoscopic versus traditional methods could influence postoperative outcomes, as endoscopic techniques might offer advantages like reduced trauma but might come with their own set of risks, such as the inadvertent introduction of pathogens. Infection control practices, the use of antiseptics, prophylactic antibiotics, and the methods for nasal cavity irrigation (e.g., saline vs. more potent antiseptics like Hibitane) are crucial in infection prevention. The study could examine how Thailand's health care facilities manage these practices and whether there are gaps in infection control that contribute to the higher risk of meningitis. Patient factors, demographic elements such as age, comorbidities (e.g., diabetes, immunosuppressive conditions), and previous nasal or sinus infections could contribute to postoperative complications. Understanding how these factors play out in the Thai population could reveal unique insights into how personal health conditions influence surgical outcomes. Health care resources and the availability and quality of postoperative care could also be a factor. In some settings, limited access to specialized care, lower nurse–patient ratios, or insufficient follow-up could elevate the risk of infection. The study might look at how these issues vary across urban and rural hospitals in Thailand and how they correlate with the incidence of meningitis.[3–6]

Conducting the study in the Thai context also brings into play the regional health care infrastructure and socioeconomic factors. Differences in access to health care across urban and rural areas could affect how quickly patients receive postoperative care, which may influence infection outcomes. Economic factors might affect the availability of advanced surgical equipment, sterilization techniques, or high-quality antibiotics, all of which play a role in preventing infections like meningitis. Cultural factors or patient adherence to medical advice (e.g., follow-up appointments, medication adherence) could also contribute to the study's findings. The study could delve into whether antibiotic resistance is an issue in Thailand, which might complicate treatment for postoperative meningitis. If antibiotic-resistant bacteria are prevalent in Thai hospitals, it could contribute to the development of infections that are more difficult to treat and may lead to higher rates of meningitis postsurgery. Understanding the local microbial resistance patterns would be an important part of the study's findings. Based on the incidence and risk factors, the study might propose specific preventive strategies to reduce the risk of postoperative meningitis. Refining surgical protocols, such as better handling of the nasal cavity and better use of irrigation solutions or prophylactic antibiotics, and improving patient education and follow-up care to ensure proper healing, especially for those with risk factors, could be helpful. Tailored infection control practices could be implemented, possibly by focusing on high-risk patients (e.g., those with diabetes or compromised immune systems).[7–10]

TSS carries several potential complications, specifically the risk of meningitis following the procedure. The comparison of nasal cavity irrigation with saline solution versus Hibitane (chlorhexidine) is indeed a noteworthy approach, given that managing infection risks is a critical factor in surgical success, especially in neurosurgical procedures.[11–14] Effectiveness of irrigation solutions, while saline solution is typically considered neutral and nonirritating to the mucosa, Hibitane (chlorhexidine) has antimicrobial properties and is often used for infection prevention in surgical settings. However, it is important to examine the concentration and duration of Hibitane use. High concentrations or prolonged exposure might result in mucosal irritation, which could lead to complications or interfere with the healing process in the nasal cavity and surrounding structures. A balance between infection prevention and mucosal preservation should be considered.[15] Impact on the blood–brain barrier, meningitis risk following TSS is usually tied to the potential for infection in the sinuses or other pathways leading to the central nervous system (CNS). It would be important to understand how irrigation solutions interact with the blood–brain barrier, particularly in the case of Hibitane. Chlorhexidine might penetrate tissues in ways that could influence CNS safety. An investigation into whether Hibitane could have any neurotoxic effects or if it might alter the permeability of the blood–brain barrier could provide additional insights into the long-term safety of its use. This study aimed to evaluate the incidence and risk factors of postoperative meningitis.

## Materials and Methods

This study was approved by the Thai Clinical Trials Registry Committee and the Institutional Review Board of the Royal Thai Army Medical Department. A retrospective review was conducted on 237 patients with clinically and pathologically diagnosed sellar and suprasellar masses who underwent endoscopic endonasal TSS at the Phramongkutklao Hospital between October 2010 and November 2024. All 237 patients were included in the final analysis.

### Inclusion and Exclusion Criteria

Inclusion criteria included patients aged 18 years and older, with a clinical follow-up of at least 6 months and at least one

 

follow-up postoperative magnetic resonance imaging (MRI). Patients were excluded if they had less than 6 months of clinical follow-up or were lost to follow-up, did not have a postoperative MRI, had prior brain surgeries involving the dura mater, had preexisting acute or chronic meningitis, or were immunocompromised (e.g., patients with active human immunodeficiency virus/acquired immunodeficiency syndrome or on immunosuppressive drugs).

All data were obtained from the electronic medical records of Phramongkutklao Hospital. The requirement for informed patient consent was waived due to the retrospective design of the study. The primary indications for TSS included visual disturbances, pituitary hormone dysfunction, increasing tumor size, or patient preference for surgery despite absence of symptoms.

### Preoperative and Postoperative Assessments

All patients underwent comprehensive evaluations, including neurological, ophthalmological, and endocrine assessments. Visual field deficits were confirmed via automatic perimetry. Endocrine evaluation was performed through baseline serum hormonal testing, and nasal cavity assessment was completed by an otolaryngologist to screen for infections or structural abnormalities.

### Surgical Protocol and Infection Prevention

All patients received intravenous ceftriaxone as perioperative antibiotic prophylaxis. Surgeries were jointly performed by a neurosurgeon and otolaryngologist, following a standardized protocol. The nasoseptal flap was the preferred method for reconstruction, and the Valsalva maneuver was used intraoperatively to detect cerebrospinal fluid (CSF) leaks. Lumbar drainage was reserved for select cases with high-flow CSF leaks.

### Nasal Cavity Irrigation

A standardized preoperative nasal irrigation protocol was applied. Patients received either normal saline or Hibitane irrigation, based on surgeon preference rather than random assignment. This introduces the potential for selection bias, as surgeon-specific preferences may have been influenced by patient characteristics, surgical complexity, or other contextual factors. While every effort was made to ensure consistency, this nonrandomized design limits causal inference regarding the effect of irrigation type on postoperative infection risk. We acknowledge this as a key limitation and recommend that future studies implement a randomized controlled design to validate our findings.

Decongestion was achieved with ephedrine pledgets. Nasal irrigation and surgical technique were otherwise consistent across all cases.

### Postoperative Care

Patients were monitored for neurological status, serum electrolytes, and urine output in the postanesthesia care unit for 24 hours. Immediate postoperative computed tomography was used to detect complications such as pneumocephalus. A contrast-enhanced MRI was performed within 24 hours postsurgery to evaluate tumor resection and establish a baseline for follow-up.

Antibiotic prophylaxis was continued for 48 hours, and ceftriaxone was extended until nasal packing removal if packing was used (typically on days 3–5 postop).

### CSF Leak Monitoring

Patients were assessed daily for CSF rhinorrhea. If clear drainage was reported, head-tilting and nasal endoscopy were used to confirm leakage. Patients were advised to avoid activities increasing intracranial pressure and were prescribed stool softeners to minimize straining.

### Data Collection

Collected data included demographics (age, sex), comorbidities (e.g., diabetes, hypertension, obesity), smoking and alcohol history, preoperative infections, CSF leaks, surgical duration, tumor characteristics, intraoperative complications, and postoperative infections. Meningitis was defined based on clinical symptoms (fever, headache, neck stiffness, altered mental status) and confirmed via CSF analysis (e.g., elevated white blood cells, positive cultures, or polymerase chain reaction).

### Statistical Analysis

Descriptive statistics were used to summarize patient characteristics. Categorical variables were compared using chi-square or Fisher's exact tests; continuous variables were analyzed with *t*-tests or analysis of variance. Multivariate logistic regression identified independent predictors of postoperative meningitis, adjusting for confounders such as age, comorbidities, and surgical complexity. A $p$-value of $< 0.05$ was considered statistically significant. Statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, New York, United States).

### Ethics Approval and Consent to Participate

The study was approved by the Thai Clinical Trials Registry Committee under opinion number TCTR20240509003 on May 9, 2024, and by the Ethics Committee of the Institutional Review Board of the Royal Thai Army Medical Department on December 24, 2021 (Research No. S068h/64). The research adhered to the 2012 Council for International Organizations of Medical Sciences (CIOMS) Guidelines and the Good Clinical Practice (GCP) Guidelines of the International Conference on Harmonization (ICH) (Statement No. IRBRTA 1861/2564). As a retrospective study involving the review of medical records, inpatient department data, and other hospital clinical data that did not allow for patient identification, the study did not involve specific interventions. Written consent was obtained in accordance with the 2012 CIOMS Guidelines and GCP of the ICH, as required for retrospective studies that do not involve direct patient interaction.

## Results

A total of 237 patients who underwent TSS between 2010 and 2024 were included in the final analysis. The mean age

 

**Table 1** Baseline characteristics of patients undergoing TSS

| Characteristics | Overall ($N = 237$) |
|---|---|
| Male gender, *N* (%) | 111 (47%) |
| Age, mean, SD (y) | 49.36 (17.37) |
| Nares normal saline cleaning, *N* (%) | 123 (52%) |
| Intraoperative CSF leakage, *N* (%) | 75 (32%) |
| Intraoperative nasoseptal flap, *N* (%) | 66 (28%) |
| Postoperative CSF leakage, *N* (%) | 85 (36%) |
| Reoperation, *N* (%) | 28 (12%) |
| Tumor location | |
| Near sellar | 194 (82%) |
| Suprasellar | 23 (10%) |
| Sellar with suprasellar extension | 17 (8%) |
| Duration of surgery (h) | 5 (3.5) |
| Prophylaxis antibiotics | 225 (95%) |
| Comorbidity | |
| Hypertension | 97 (41%) |
| Diabetes mellitus | 113 (48%) |
| Obesity | 63 (27%) |
| Coronary artery disease | 35 (15%) |
| Kidney disease | 28 (12%) |
| Previous sinus or nasal infection | 52 (22%) |
| Postoperative meningitis with CSF leakage, *N* (%) | 30 (13%) |

Abbreviations: CSF, cerebrospinal fluid; SD, standard deviation; TSS, transsphenoidal surgery.
Note: Value presented as mean ± SD.

was 49.36 years (standard deviation = 17.37), with 47% ($n = 111$) being male. Fifty percent ($n = 118$) of the patients underwent nare cleaning with normal saline. Intraoperative CSF leakage occurred in 32% ($n = 75$), and the nasoseptal flap procedure was performed in 28% ($n = 66$). Postoperative CSF leakage was observed in 36% ($n = 85$), and reoperation for TSS was required in 12% ($n = 28$) (►**Table 1**). Overall, the incidence of postoperative meningitis was 23% ($n = 54$). In the nare cleaning with normal saline group, the incidence was 24% ($n = 28$), whereas in the non-nare group (patients who received only Hibitane), the incidence was 22% (►**Table 2**). Despite this, the nare cleaning with normal saline group had

**Table 2** Difference in the incidence of postoperative meningitis overall and between the nares normal saline cleaning groups and Hibitane groups

| | | |
|---|---|---|
| Prevalence (overall) | 54/237 | 23 % |
| Prevalence (nares normal saline cleaning) | 28/118 | 24 % |
| Prevalence (non-nares only Hibitane cleaning) | 26/119 | 22 % |

Note: Values are presented as mean.

**Table 3** Difference in secondary outcomes in postoperative meningitis between the nares normal saline cleaning groups and Hibitane groups

| | Outcome | | | | |
|---|---|---|---|---|---|
| Postoperative Meningitis | Nares normal saline | | Non-nares only with Hibitane | | *p*-Value |
| | $N = 118$ | % | $N = 119$ | % | |
| Yes | 28 | 24 | 26 | 22 | 0.417 |
| No | 90 | 76 | 93 | 78 | |

Note: Values are presented as frequencies (%). The *p*-value corresponds to Pearson's chi-squared test.

a slightly higher incidence of postoperative meningitis than the non-nare group, although this was not found to be a significant factor associated with postoperative meningitis (►**Table 3**). The period effect analysis findings are displayed in ►**Table 4**. The following factors were associated with postoperative meningitis: intraoperative CSF leakage, postoperative CSF leakage, tumor location near the sphenoid sinus, sphenoid sinus extension, diabetes mellitus, obesity, and previous sinus or nasal infections (*p*-values: 0.031, 0.001, 0.042, 0.028, 0.036, and 0.017, respectively). After further analysis using the independent *t*-test and Fisher's exact test, the factors identified as significantly affecting postoperative meningitis included intraoperative CSF leakage (odds ratio [OR] = 4.409, 95% confidence interval [CI]: 3.053–6.367, $p = 0.015$), postoperative CSF leakage (OR = 16.167, 95% CI: 7.448–35.092, $p = 0.024$), diabetes mellitus (OR = 3.517, 95% CI: 2.26–5.452, $p = 0.032$), obesity (OR = 2.576, 95% CI: 1.027–4.353, $p = 0.041$), and previous sinus or nasal infection (OR = 5.368, 95% CI: 4.18–7.15, $p = 0.017$) (►**Table 5**).

## Discussion

Postoperative meningitis is a serious complication following TSS, with reported incidence ranging from 1.8 to 31%, consistent with findings in the current study.[16–19] Despite being a minimally invasive approach, the anatomical proximity of the surgical site to the nasal and sinus cavities increases the risk of CNS infections due to potential exposure through CSF leaks or microbial contamination.[20] Identifying and mitigating risk factors associated with postoperative meningitis is critical to improving surgical outcomes.

Our study highlights several key clinical and intraoperative factors associated with increased risk of meningitis, including intraoperative and postoperative CSF leakage, comorbidities such as diabetes mellitus and obesity, and a history of chronic sinus or nasal infections. These findings underscore the importance of meticulous surgical technique, robust reconstruction of the sellar floor, and careful preoperative assessment of patients at elevated infection risk.

A particular focus of our study was the effect of preoperative nasal irrigation with either normal saline or Hibitane (chlorhexidine). Although Hibitane is known for its antiseptic properties, and saline is widely used for its safety and mucosal compatibility, our findings revealed no statistically

 

**Table 4** Factors associated secondary outcome in postoperative meningitis

| | Postoperative meningitis | | | | |
|---|---|---|---|---|---|
| | Yes | | No | | *p*-Value |
| | *N* = 54 | % | *N* = 183 | % | |
| Male gender | 31 | 57 | 80 | 43.7 | 0.081 |
| Reoperation | 11 | 20.3 | 17 | 9.3 | 0.514 |
| Intraoperative CSF leakage | 42 | 77.8 | 33 | 18 | 0.031* |
| Postoperative CSF leakage | 49 | 90.7 | 36 | 19.7 | 0.001* |
| Time of exposure to intraoperative CSF fistulas (h) | 6.4 | – | 4.2 | – | 0.76 |
| Tumor location | | | | | |
| Near sphenoid sinus and sphenoid sinus extension | 26 | 48.1 | 168 | 91.8 | 0.042* |
| Suprasellar | 11 | 20.3 | 12 | 6.6 | 0.63 |
| Sellar with suprasellar extension | 8 | 14.8 | 9 | 4.9 | 0.57 |
| Duration of surgery (> 6 h) | 47 | 87 | 174 | 95 | 0.82 |
| Prophylaxis antibiotics | 31 | 57.4 | 168 | 91.8 | 0.073 |
| Comorbidity | | | | | |
| Hypertension | 29 | 53.7 | 68 | 37.2 | 0.67 |
| Diabetes mellitus | 39 | 72.2 | 74 | 40.4 | 0.028* |
| Obesity | 27 | 50 | 36 | 19.7 | 0.036* |
| Coronary artery disease | 12 | 22.2 | 23 | 12.6 | 0.43 |
| Kidney disease | 10 | 18.5 | 18 | 9.83 | 0.24 |
| Previous sinus or nasal infection | 35 | 64.8 | 17 | 9.3 | 0.017* |

Abbreviation: CSF, cerebrospinal fluid.
Note: Values are presented as frequencies (%). The *p*-value corresponds to Pearson's chi-squared test. The asterisk "*" indicates variables that show statistically significant associations, defined as $p < 0.05$.

**Table 5** Multivariate for the logistic regression of factors associated with secondary outcomes in postoperative meningitis

| Multivariate analysis | *p*-Value | Odds ratio (95% CI) |
|---|---|---|
| Intraoperative CSF leakage | 0.015* | 4.409 (3.053–6.367) |
| Postoperative CSF leakage | 0.024* | 16.167 (7.448–35.092) |
| Tumor location | | |
| Near sphenoid sinus and sphenoid sinus extension | 0.061 | 5.38 (4.12–7.417) |
| Diabetes mellitus | 0.032* | 3.517 (2.26–5.452) |
| Obesity | 0.041* | 2.576 (1.027–4.353) |
| Previous sinus or nasal infection | 0.017* | 5.368 (4.18–7.15) |

Abbreviations: CI, confidence interval; CSF, cerebrospinal fluid.
Note: Values are presented as mean or *n* (%). *p*-Value corresponding to the independent *t*-test and Fisher's exact test. The asterisk "*" indicates variables that show statistically significant associations, defined as $p < 0.05$.

significant difference in postoperative meningitis rates between the two groups ($p = 0.417$). This suggests that while nasal cleaning may contribute to reduced nasal congestion, it does not significantly affect the risk of postoperative CNS infection when used in the context of standardized perioperative antibiotic protocols.

However, it is important to acknowledge a significant methodological limitation: the assignment of patients to the normal saline or Hibitane irrigation groups was based on surgeon preference rather than randomization. This introduces a potential for selection bias, as surgeon choice could be influenced by patient-specific characteristics, surgical complexity, or individual practices, which may not have been evenly distributed between groups. As such, differences in baseline risk, tumor type or location, and intraoperative factors may have confounded the observed outcomes. This nonrandomized, retrospective design limits our ability to draw causal inferences about the comparative efficacy of the irrigation agents.

Moreover, our study did not control for certain preoperative risk factors that might influence the development of CSF fistulas or meningitis, such as tumor size, location relative to

 

the sphenoid sinus, or previous nasal infections. Future research should incorporate these variables into the study design to better isolate the effect of irrigation type from other confounding influences.

The study's retrospective nature may also be subject to limitations such as incomplete records and unmeasured variables, and the sample size may not be sufficient to detect more subtle differences or rare complications. Additionally, results from a single tertiary center may not be generalizable to all practice settings.

Looking forward, prospective, randomized controlled trials with standardized protocols and balanced baseline characteristics are warranted to validate the impact of nasal irrigation strategies on postoperative infection risk. Furthermore, research exploring alternative irrigation agents, their effect on nasal flora and mucosal integrity, and long-term safety profiles could provide a more comprehensive understanding of infection prevention in TSS.

Our findings reinforce the multifactorial nature of postoperative meningitis risk and emphasize the importance of comprehensive perioperative care. While preoperative nasal cleaning remains a routine practice, its role in preventing postoperative infection appears limited in isolation. Ultimately, attention to surgical precision, appropriate antibiotic use, and identification of high-risk patients remain paramount in minimizing complications and optimizing outcomes in transsphenoidal procedures.

## Limitations

This study's retrospective design is subject to inherent limitations, including the potential for recall bias and incomplete records, which could affect data accuracy. Notably, the assignment of patients to the normal saline or Hibitane groups was based on surgeon preference, rather than randomization. This introduces a selection bias, where external factors, such as patient characteristics or surgical complexity, may have influenced group assignment and outcomes. As a result, the findings may not accurately represent the effect of the intervention and may be confounded by these variables. The sample size may also limit the ability to detect rare risk factors or generalize the results to a broader patient population, particularly if the study was conducted in high-volume academic centers.

Given these limitations, a prospective, randomized controlled trial is necessary to more rigorously assess the true impact of nasal irrigation methods on postoperative infection risk and to eliminate potential confounders introduced by surgeon preferences and nonrandomized group assignments. Future studies should aim to control for these biases and incorporate larger, more diverse patient populations.

## Conclusion

Understanding the risk factors for meningitis following TSS is crucial for improving patient outcomes. Key factors such as intraoperative and postoperative CSF leakage, diabetes mellitus, obesity, and previous sinus or nasal infections were significantly associated with an increased risk of postoperative meningitis. While preoperative nares cleaning with normal saline may reduce nasal congestion, our findings indicate that it does not significantly affect the rate of postoperative meningitis compared with Hibitane-only cleaning. Further prospective studies are recommended to better evaluate the role of nasal irrigation protocols in infection prevention and to identify additional modifiable risk factors.

### Authors' Contributions

P.B. was responsible for project administration and coordination, drafted the original manuscript, and actively participated in the review process. S.S. contributed to data curation and the review process. Both P.B. and P.F. were involved in data curation, manuscript drafting, and review. Additionally, P.B. and S.S. contributed to data curation, while P.B., P.F., and K.U. collaborated on data curation and formal analysis of the research. P.F. and K.U. were also involved in project administration and coordination, as well as the review process. All authors have reviewed and approved the final version of the manuscript.

### Ethical Approval

The study was approved by the Thai Clinical Trials Registry Committee under opinion number TCTR20240509003 on May 9, 2024, and by the Ethics Committee of the Institutional Review Board of the Royal Thai Army Medical Department on December 24, 2021 (Research No. S068h/64). The research adhered to the 2012 Council for International Organizations of Medical Sciences (CIOMS) Guidelines and the Good Clinical Practice (GCP) Guidelines of the International Conference on Harmonization (ICH) (Statement No. IRBRTA 1861/2564). As a retrospective study involving the review of medical records, inpatient department data, and other hospital clinical data that did not allow for patient identification, the study did not involve specific interventions. Written consent was obtained in accordance with the 2012 CIOMS Guidelines and GCP of the ICH, as required for retrospective studies that do not involve direct patient interaction.

### Conflict of Interest

None declared.

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