Updates in Diagnosis and Management of CSF Rhinorrhea: A Systematic Review

Maali Subhi T Alshammari ¹, Ghadah Khalid H. Alanazi ¹, Taif Khalaf K. Alanazi ¹, Reef Ayed R. Alshammari ², Wasan Ghathwan A Alanazi ², Madhawi Abdulaziz Alanazi ², Dhaidan Mohsen Alshammari ³, Ikechukwu Odeh Odeh ⁴

- ¹ General Practitioner, Northern borders health cluster, Arar, Saudi Arabia
- ² Faculty of Medicine, Northern border university, Arar, Saudi Arabia
- ³ Otolaryngology Consultant Rhinology-Skull Base And Facial Plastic Surgery Fellow, North Medical Tower Hospital, Arar, Saudi Arabia
- ⁴ Consultant Otorhinolaryngologist, Rafha Central Hospital, Rafha, Saudi Arabia

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ABSTRACT

Objectives: To synthesize current evidence on the diagnosis and management of cerebrospinal fluid rhinorrhea (CSFR).

Methods: A thorough search of pertinent databases following the PRISMA guidelines was done in order to find studies that satisfied the requirements for inclusion. A thorough search of PubMed, Web of Science, SCOPUS, and Science Direct was conducted to find pertinent literature.

Results: Eleven studies, including a total of 382 CSFR patients and 170 (44.5%) of them were males, were included in our data. The success rate of the trans-nasal endoscopic approach ranged from 66.6% to 100%, while Endoscopic endonasal eustachian tube obliteration (EEETO) reported a success rate of 65.1%. Meningitis, pneumocephalus, frontal Sinusitis, failure of closure (immediate), and failure of closure (delayed) were the reported adverse effects following trans-nasal endoscopy in CSFR. No adverse effects were reported among patients who underwent EEEO. 0.06% ipratropium bromide nasal spray reaction was useful in excluding CSFR, and computed tomography cisternography (CTC) and magnetic resonance hydrography (MRH) had excellent sensitivity for CSFR diagnosis.

Conclusion: The preferred and most reported technique for repairing CSF fistulae in the majority of clinical situations is now endoscopic surgery with success rates ranged from 66.6% to 100%. CSFR is a general diagnostic that encompasses several locales and etiologies.

INTRODUCTION

CSFR is a condition characterized by the leakage of CSF through the nose. It can be a serious medical concern as it can lead to complications such as meningitis, brain abscess, and intracranial hypotension. CSFR can be caused by a variety of factors, including head trauma, intracranial surgery, and congenital defects in the skull base [1].

In recent years, there have been significant advancements in the diagnosis and management of CSF rhinorrhea. These advancements have helped improve outcomes for patients with this condition and have led to a better understanding of its underlying causes [2].

One of the key updates in the diagnosis of CSFR is the use of imaging techniques such as MRI and CT scans. These imaging modalities can help identify the exact location of the CSF leak and determine the underlying cause of the leakage. In addition, newer imaging techniques such as high-resolution CT cisternography and

MR cisternography have improved the detection of small CSF leaks that may have been missed with traditional imaging methods [3]. Another important update in the diagnosis of CSFR is the use of beta-2 transferrin testing. Beta-2 transferrin is a specific marker for CSF, and testing for its presence in the nasal fluid can help confirm the diagnosis of CSF rhinorrhea. This test is highly sensitive and specific, making it a valuable tool for diagnosing this condition [4].

In terms of management, there have been several updates that have improved the treatment of CSF rhinorrhea. One of the key advancements is the use of endoscopic surgical techniques for repairing CSF leaks. Endoscopic surgery is less invasive than traditional open surgery and can often be performed on an outpatient basis. This approach has a lower risk of complications and can lead to faster recovery times for patients [5].

In addition to endoscopic surgery, other minimally invasive techniques such as the use of tissue sealants and fibrin glue have been developed for repairing CSF leaks. These techniques can effectively seal the leak and prevent further leakage of CSF. In

cases where surgical repair is not possible, conservative management techniques such as bed rest and avoiding activities that increase intracranial pressure can also be effective in managing CSFR [6].

Overall, the updates in the diagnosis and management of CSFR have significantly improved outcomes for patients with this condition. Advances in imaging techniques, diagnostic testing, and surgical approaches have made it easier to diagnose CSF leaks and effectively treat them, leading to better outcomes and quality of life for affected individuals. It is important for healthcare providers to stay current on these updates in order to provide the best possible care for patients with CSFR [3, 5].

The study is significant due to the implications of accurate diagnosis and effective management of CSFR. This condition can lead to serious complications if left untreated, such as meningitis or brain abscess. Therefore, updates in the diagnosis and management approaches are crucial for improving patient outcomes and minimizing associated risks. CSFR poses a diagnostic challenge due to its non-specific symptoms and overlapping features with other nasal conditions. Additionally, the optimal management strategies for CSF leaks remain a topic of debate, with various surgical and non-surgical options available. Therefore, there is a need to systematically review the current literature to consolidate evidence on the diagnosis and management of CSFR. The aim of this study is to conduct a systematic review to summarize the current evidence on the diagnosis and management of CSFR. By synthesizing the available literature, we aim to provide insights into the optimal approaches for diagnosing and managing this condition, ultimately improving patient care and outcomes.

Methods

We followed the recommendations in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [7] for this systematic review. An electronic search was performed on databases like PubMed, Web of Science, SCOPUS, and Science Direct in order to find English-language research that looked at the diagnosis and management of CSFR. The search strategy will encompass keywords pertinent to CSFR. Independently, two reviewers went through the search results, chose pertinent papers, collected data, and used the right assessment methods to determine how good the included research was.

Eligibility Criteria

Inclusion Criteria:

- English-language studies published in peer-reviewed journals.
- Studies focusing on the diagnosis and management of CSFR.
- Studies reporting on the effectiveness and safety of various treatment approaches for CSFR.
 Studies evaluating diagnostic modalities for identifying
- Studies evaluating diagnostic modalities for identifying CSFR.
- Randomized controlled trials, observational studies, case-control studies, cohort studies, and systematic reviews/meta-analyses.
- 6. Studies conducted between 2022-2024.

Exclusion Criteria:

- . Non-English language studies.
- 2. Studies not related to CSFR diagnosis and management.
- 3. Animal studies, reviews, commentaries, editorials, letters, and conference abstracts.
- 4. Studies with insufficient data on outcomes related to CSFR.
- 5. Studies focusing on pediatric populations exclusively.
- 6. Duplicate publications or studies with overlapping data.
- 7. Studies with a high risk of bias or methodological limitations.

Data Extraction

Rayyan (QCRI) was used to validate the search results in order to guarantee accuracy [8]. The inclusion and exclusion criteria were used to determine the relevancy of the titles and abstracts that the search produced. Papers that satisfied the inclusion requirements were carefully examined by the study team. Consensus was used to settle disagreements. Using a predetermined data extraction form, key study data, such as titles, authors, publication year, study location, gender distribution, participant demographics, management plan/diagnostic modality, hospital stay, adverse effects, success rate, and primary outcomes, will be documented. To evaluate the possibility of bias, an impartial assessment instrument was created.

Data Synthesis Strategy

Summaries of the research findings and elements were created utilizing information taken from pertinent studies in order to offer a qualitative assessment. The best method for making use of the data from the studies that were included was decided upon after the data collection for the systematic review was finished.

Risk of Bias Assessment

The Joanna Briggs Institute (JBI) [9] critical assessment criteria for studies reporting prevalence data were utilized to assess the study's quality. This tool had nine questions. A score of one was given for a positive response, while a score of zero was given for a negative, ambiguous, or irrelevant response. The following scores will be categorized as low, moderate, and high quality, respectively: below 4, between 5 and 7, and above 8. The quality of the studies was evaluated by researchers independently, and differences were settled through discussion.

Results

Systematic search outcomes

After 699 duplicates were removed, a total of 1312 study papers were found through a systematic search. After 613 studies had their titles and abstracts evaluated, 558 papers were discarded. Merely four articles were not located out of the 55 reports that were required to be retrieved. 51 articles passed the screening process for full-text evaluation; 22 were rejected due to incorrect study results, 14 due to incorrect population type, 2 articles were editor's letters, and 2 were abstracts. Eleven research publications in this systematic review satisfied the requirements for eligibility. An overview of the procedure used to choose the research is illustrated in Figure 1.

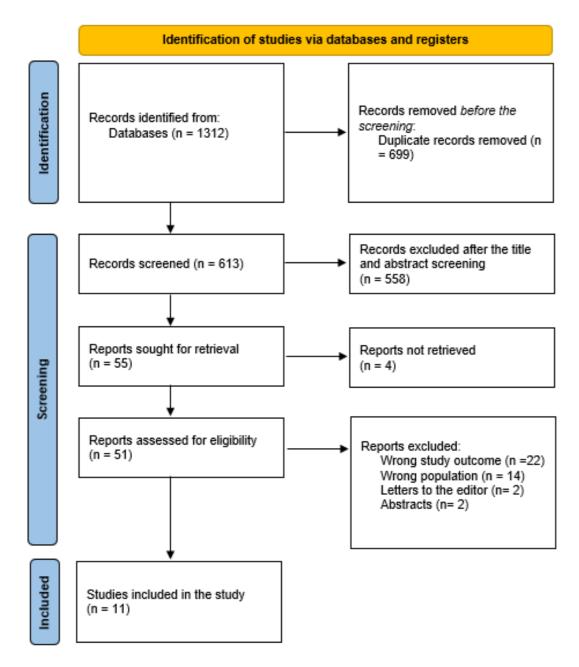


Figure (1): Study decision is summed up in a PRISMA diagram.

Sociodemographic features of the comprised studies

The research publications' sociodemographic information is displayed in Table 1. Eleven studies, including a total of 382 CSFR patients and 170 (44.5%) of them were males, were included in our data. Seven studies were retrospective cohorts [10, 12, 14-17, 20], two were retrospective cohorts [13, 18], and two were case series [11, 19]. Three studies were conducted in the USA [11, 16, 18], two in India [12, 17], two in Egypt [13, 19], two in China [10, 20], one in Saudi Arabia [14], and one in Pakistan [15].

Clinical outcomes

Management

The clinical features are displayed in Table (2). Eight studies discussed the management approaches of CSFR; seven used the trans-nasal endoscopic approach [10, 12, 15, 17] and one used Endoscopic endonasal eustachian tube obliteration (EEETO) [16]. The success rate of the trans-nasal endoscopic approach ranged from 66.6% [12] to 100% [11, 13], while EEETO reported a success rate of 65.1% [16]. Meningitis, Pneumocephalus, Frontal Sinusitis, Failure of closure (immediate), and Failure of closure (delayed) were the reported adverse effects following trans-nasal

endoscopy in CSFR [12, 14, 15, 17]. No adverse effects were reported among patients who underwent EEEO [16].

Diagnosis

Three studies discussed the diagnostic modalities of CSFR; ipratropium bromide nasal spray [18], computed tomography cisternography (CTC) [19], and CTC and magnetic resonance hydrography (MRH) [20]. 0.06% ipratropium bromide nasal spray reaction was useful in excluding CSFR [18], and CTC and MRH had excellent sensitivity for CSFR diagnosis [19, 20].

Table (1): The sociodemographic attributes of the participating populations.

Study	Study design	Country	Participants	Mean age	Males (%)	
Tan et al. 2024 [10]	Retrospective cohort	China	65	47.6 ± 16.5	36 (55.4%)	
Shaftel et al. 2023 [11]	Case-series	USA	4	59.5	1 (25%)	
Chadaram et al. 2023 [12]	Retrospective cohort	Retrospective cohort India 18		20-61	11 (61.1%)	
Maltan et al. 2023 [13]	Prospective cohort	Egypt	37	40.1 ± 11.2	6 (16.2%)	
Noori et al. 2023 [14]	Retrospective cohort	Saudi Arabia	20	42.6 ± 13.9	4 (20%)	
Arshad et al. 2024 [15]	Retrospective cohort	Pakistan 44		32.8 ± 9.7	26 (59%)	
Rimmer et al. 2022 [16]	Retrospective cohort	USA	7	55.3 ± 14.4	4 (57.1%)	
Chadaram et al. 2022 [17]	Retrospective cohort	India	81	NM	32 (39.51%)	
Nulty et al. 2024 [18]	Prospective cohort	USA	20	NM	12 (60%)	
Hablas et al. 2022 [19] Case-series		Egypt	48	19-67	20 (41.7%)	
Lu et al. 2022 [20] Retrospective cohort		China	38	53	18 (47.4%)	

Table (2): Clinical features and results of the included research.

Study ID	Hospital stay (days)	Management/ diagnostic modality	Adverse effects	Success rate	Main outcomes	JBI
Tan et al. 2024 [10]	8.5-24	Trans-nasal endoscopic approach	NM	93.8%	In controlling CSF rhinorrhea, the transnasal endoscopic reconstruction of the skull base defect utilizing the Hadad-Bassagasteguy flap, fascia lata, and free middle turbinate mucosa showed excellent repair outcomes.	Moderate
Shaftel et al. 2023 [11]	NM	Trans-nasal endoscopic approach	NM	100%%	After an anterior clinoidectomy for aneurysm clipping, the endoscopic endonasal transsphenoidal technique proved to be a safe and efficacious method for repairing the skull base in four patients suffering from CSF rhinorrhea.	Moderate
Chadaram et al. 2023 [12]	7 - 10	Trans-nasal endoscopic approach	Meningitis, Pneumocephalus, Frontal Sinusitis, Failure of closure (immediate), and Failure of closure (delayed)	66.6%	Endoscopic correction of CSF leaks is standard practice because it is minimally invasive. To prevent major issues, the strategy must be considered on a case-by-case basis.	Moderate
Maltan et al. 2023 [13]	NM	Trans-nasal endoscopic approach	NM	100%	Although direct endoscopic inspection and repair of abnormalities in the skull base have a high success rate, failure is nevertheless possible, particularly in cases where leaks occur spontaneously.	Moderate

Noori et al. 2023 [14]	9	Trans-nasal endoscopic approach	There were just two patients who experienced a recurrence. There were no significant difficulties mentioned.	90%	CSF leak repair with endoscopic endonasal surgery is a safe, dependable method with a high success rate and minimal risk of complications.	Moderate
Arshad et al. 2024 [15]	NM	Trans-nasal endoscopic approach	Meningitis was the most often reported complication, occurring in 2 (4.5%) of the patients and also treated conservatively.	89%	Successful endoscopic correction of CSFR appears to depend on the precise location of the leakage site.	Moderate
Rimmer et al. 2022 [16]	NM	EEETO	NM	65.2%	Following lateral skull base surgery, EEETO can be used to treat CSFR. Surgery for revision is frequent and unpredictable.	Moderate
Chadaram et al. 2022 [17]	4	Trans-nasal endoscopic approach	Meningitis was acquired by 2 patients (2.46%) out of the 3 recurrence instances after surgery.	96.3%	CSF repair using the transnasal endoscopic method has an excellent success rate and several benefits, including improved visualization and leak site identification, fewer problems, quick recovery following surgery, low recurrence rate, and high patient satisfaction.	High
Nulty et al. 2024 [18]	NM	Ipratropium bromide nasal spray	NA**	NA	The 0.06% Ipratropium bromide nasal spray reaction is a useful screening test for ruling out CSFR in individuals with unilateral clear thin rhinorrhea and should be taken into account in the diagnostic workup of CSFR.	Moderate
Hablas et al. 2022 [19]	NM	стс	NA	NA	A CSF leak can be confirmed and the precise defect site can be detected with excellent sensitivity using CT cisternography, which already uses non-contrast pre-cisternography pictures.	Moderate
Lu et al. 2022 [20]	NM	CTC and MRH	NA	NA	The precision of identifying and diagnosing CSFR can be enhanced by CTC and MRH.	High

*NM=Not-mentioned **NA=Not-applicable

DISCUSSION

This systematic review discusses the recently published investigations on the management approaches of CSFR. Seven used the trans-nasal endoscopic approach [10, 12, 15, 17] and one used EEETO [16]. The success rate of the trans-nasal endoscopic approach ranged from 66.6% [12] to 100% [11, 13], while EEETO reported a success rate of 65.1% [16]. LaCour et al. reported that in the majority of clinical situations, endoscopic repair of CSF fistulae has emerged as the preferred technique. On the first try, success percentages are roughly 90%, and on the second attempt, they are 96%. The failure rate is higher in patients with elevated ICP or lateral recess leaks associated with a well-pneumatized sphenoid sinus [21]. Makary et al. also reported that when children present with CSF rhinorrhea, endoscopic repair procedures have a very high closure rate.

We also found that meningitis, Pneumocephalus, Frontal Sinusitis, Failure of closure (immediate), and Failure of closure (delayed) were the reported adverse effects following trans-nasal endoscopy in CSFR [12, 14, 15, 17]. No adverse effects were reported among patients who underwent EEEO [16]. In their review, LaCour et al. found that with a prevalence of 2.5% overall, endoscopic repair has minimal rates of complications. Meningitis (1.1%) is the most frequent consequence; all other problems are less than 1%. The largest risk of complications (3.1%) after endoscopic encephalocele surgery are seizures (2.3%) and meningitis (2.3%) [21].

Three studies in this review discussed the diagnostic modalities of CSFR. 0.06% ipratropium bromide nasal spray reaction was useful in excluding CSFR [18], and CTC and MRH had excellent sensitivity for CSFR diagnosis [19, 20]. In order to enable direct visualization, CTC uses intrathecal contrast injection, which travels via the fistula [23, 24]. On the other hand, leaks must be active during imaging; overpressure techniques can be applied in the event that leaks are not active [25]. Kim et al. reported that CSFR can be precisely localized with high-resolution CT due to its high-detail imaging of bone abnormalities. However, its usefulness in assessing active leakage is limited, and localization becomes challenging when concurrent lesions are present [26].

Limitations

The systematic review encompasses research that exhibits notable variations in patient demographics, diagnostic criteria, and treatment modalities. Because of this variety, it may be difficult to draw firm conclusions and restrict how broadly the

findings may be applied. The examined research contains varying degrees of quality evidence; for example, some studies have small sample numbers, retrospective designs, or possible biases. The trustworthiness of the results derived from the review may be impacted by this variance in the quality of the evidence.

It can be challenging to directly compare results due to discrepancies in reported outcomes caused by the lack of prospective protocols and RCTs for the identification and treatment of CSF rhinorrhea among studies.

Future directions and clinical implications

Subsequent investigations ought to endeavor to institute uniform diagnostic standards for CSF rhinorrhea, encompassing particular imaging methods and biomarkers, in order to enhance the coherence and dependability of diagnosis in diverse clinical contexts. Larger and more varied patient groups in prospective trials will improve the quality of the evidence and yield more reliable data on the efficacy of different diagnostic and treatment modalities.

Subsequent research endeavors ought to concentrate on assessing the efficacy of novel diagnostic technologies, like sophisticated imaging modalities and molecular biomarkers, in the timely and precise identification of CSF rhinorrhea. Long-term follow-up studies are necessary to evaluate the long-term efficacy of various treatment modalities, especially surgical treatments, and to keep an eye out for any complications or recurrences. In order to develop a more thorough understanding of CSF rhinorrhea and its management and to develop more potent and broadly applicable treatment techniques, it can be helpful to promote international collaboration and data sharing among researchers and institutions.

CONCLUSION

The preferred and most reported technique for repairing CSF fistulae in the majority of clinical situations is now endoscopic surgery with success rates ranging from 66.6% to 100%. CSFR is a general diagnostic that encompasses several locales and etiologies.

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