From Leak to Repair: Journey of CSF Rhinorrhea Patients

Khurram Khan[1], Tabish Maqbool[2], Sarbjit Singh Chhiber[3], Mohsin Fayaz Bhat[4], Abrar Ahad Wani[5], Nayil Khursheed Malik[6], Sajad Hussain Arif[7], Mudassir Amin[8], Ihsan Ali[9]

1. *Khurram Khan: Department of Neurosurgery, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India.*
2. *Tabish Maqbool: Department of Otolaryngology, Government Medical College, Srinagar, Jammu and Kashmir, India.*
3. *Sarbjit Singh Chhiber: Department of Neurosurgery, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India.*
4. *Mohsin Fayaz Bhat: Department of Neurosurgery, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India.*
5. *Abrar Ahad Wani: Department of Neurosurgery, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India.*
6. *Nayil Khursheed Malik: Department of Neurosurgery, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India.*
7. *Sajad Hussain Arif: Department of Neurosurgery, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India.*
8. *Mudassir Amin: Department of Neurosurgery, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India.*
9. *Ihsan Ali: Department of Otolaryngology, Government Medical College, Srinagar, Jammu and Kashmir, India.*

Corresponding Author:
*Tabish Maqbool taby.maqbool16@gmail.com
Department of Otolaryngology, Government Medical College, Srinagar, Jammu and Kashmir, India.

Author details:
Dr. Khurram Khan - DrNB Neurosurgery - Direct 6 year Course (Manipal Hospital, Bangalore)
Email - drkhurramkhan7@gmail.com

Dr. Tabish Maqbool - MS ENT (Government Medical College, Srinagar) Email - taby.maqbool16@gmail.com

KEYWORDS

Cerebrospinal fluid rhinorrhoea, spontaneous Cerebrospinal fluid rhinnorhea, traumatic cerebrospinal fluid rhinnorhea, skull base defect, transnasal endoscopic repair

ABSTRACT

BACKGROUND: Cerebrospinal Fluid (CSF) rhinorrhea is a potentially life threatening condition characterized by the leakage of CSF through the nasal cavity, resulting from a breach in the dural membranes surrounding the brain and a bony defect. These osteodural defects cause a direct communication between the CSF-containing subarachnoid space and the paranasal sinuses. This condition poses significant threat to transmit bacteria intracranially leading to life threatening meningitis or intracranial infections. It as well poses a diagnostic and therapeutic challenge, necessitating prompt recognition and management to prevent devastating complications.

MATERIAL AND METHOD: Our sample size consisted of 50 patients. Our study is a retrospective cohort study which was conducted for a period of 5 years between January 2018 and December 2022. Descriptive statistics were used to summarize patient demographics and clinical characteristics. Chi-squared tests and Fisher's exact tests were used to compare categorical variables. Continuous variables were compared using t-tests or Mann-Whitney U tests.

RESULTS: The mean age was 48.5 years. CSF rhinorrhea was the presenting symptom in all patients. Majority (58%) of cases seen were traumatic with cribriform plate being the most common location (44%). Endoscopic repair was done in 34 patients, open surgery in 10 patients, and 1 patient underwent VP shunt placement. Spontaneous recovery was seen in 6 patients.

CONCLUSION: Our results support individualized treatment approaches, considering spontaneous recovery, endoscopic repair, and open surgery or shunt placement for complex cases. Our study demonstrates high success rates for endoscopic repair of CSF rhinorrhea, with significant factors influencing outcome.
.

LIST OF ABBREVIATIONS:

CSF: cerebrospinal fluid
HRCT: high resolution computed tomography MRI: magnetic resonance imaging
MRI CISS: constructive interference in steady state

Background

Cerebrospinal Fluid (CSF) rhinorrhea is a potentially life threatening condition characterized by the leakage of CSF through the nasal cavity, resulting from a breach in the dural membranes surrounding the brain and a bony defect. These osteodural defects cause a direct communication between the CSF-containing subarachnoid space and the paranasal sinuses [1]. This condition poses significant threat to transmit bacteria intracranially leading to life threatening meningitis or intracranial infections [2]. It as well poses a diagnostic and therapeutic challenge, necessitating prompt recognition and management to prevent devastating complications.

Epidemiology

The incidence of CSF rhinorrhea is estimated to be approximately 1-5 per 100,000 individuals annually, with traumatic head injuries accounting for the majority of cases [3]. Structural compromise is the most common cause of CSF leak followed by craniofacial trauma, making up 80% of CSF leaks. Iatrogenic causes comprise 16% of CSF leaks, with the last 4% due to varied etiologies. CSF leak is typically classified into spontaneous/idiopathic, traumatic, and iatrogenic [3] [4]. However, spontaneous CSF leaks are increasingly recognized as a significant subset, often associated with underlying conditions such as hypertension, obesity, tumors, or congenital defects [5][6] . Spontaneous CSF rhinorrhea predominantly occurs in middle-aged women, with a typical age of presentation around 45-65 years [19].

Classification

CSF rhinorrhea is generally classified based on etiology, anatomical location, or extent of bony defect. Generally most classification systems first separate patients into traumatic or non-traumatic etiologies.

Broadly CSF Rhinorrhea can be classified into three primary types:

1. Traumatic CSF Rhinorrhea: Resulting from head trauma, skull fractures, or facial injuries [7].
2. Spontaneous CSF Rhinorrhea: Occurring without identifiable trauma, often associated with conditions like hypertension, tumors, or congenital defects [7].
3. Iatrogenic CSF Rhinorrhea: Caused by medical procedures, such as endoscopic sinus surgery or cranial surgery [7].

Fig. 1 Classification of cerebrospinal fluid leaks. (Adapted from Ziu et al. [7]).

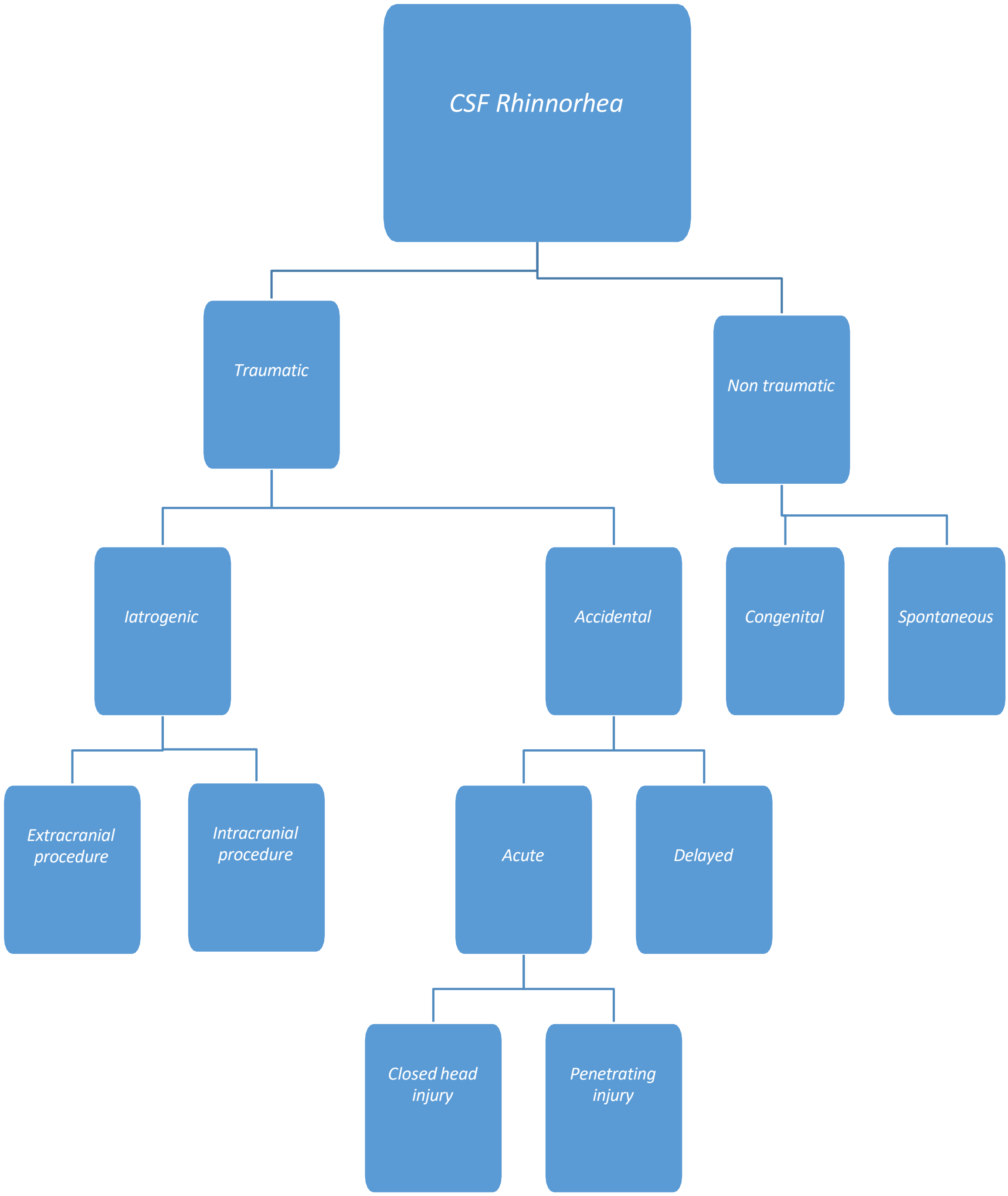


Fig.1 Classification of cerebrospinal fluid leaks (Adapted from Ziu et al. [7]).

Head trauma	**Inflammat ory**	**Congenital**	**Neoplasm**	**Surgical**	**Other**
Closed head injury	Osteomyeli tis of skull	Meningoc ele	Skull base meningiomas	Endoscopic sinus injury	Elevated BMI
Open head injury	Erosive lesions: Cystic fibrosis	Meningoe nc-ephalocel	Pituitary adenomas	Skull base surgery	Idiopathic intracranial hypertension
Penetrating injury	Mucoceles	Cribriform plate defect		Transtempor al approaches	
Post traumatic hydrocephalu s	Polypoid disease				
	Fungal sinusitis				

Table 1. Common causes of CSF rhinnorhea.

Pathophysiology

Cerebrospinal fluid is a capillary ultrafiltrate formed by the choroid plexuses during various metabolic processes at a rate of 0.35 ml/minute (350–500 ml/ day). At any given time the total volume of CSF is approximately 150 ml. This repetitive cycle of production and absorption results in the total volume of CSF being turned over 3-5 times/day. CSF gets absorbed in the arachnoid villi and into the venous system. Normal pulsations are noted in CSF pressure which are related to fluctuations in cerebral blood flow and proximity to the major branches of the circle of Willis [8]. A pressure gradient of 1.5-7 cm of water is required to drive CSF through these structures [9]. For CSF rhinnorhea to occur both a communication between the intracranial space and the nasal cavity and a breach in the dura mater should be present. CSF leaks due to trauma begins mostly within 48 hours of injury, and within 3 months 95% of traumatic CSF leaks are manifested [9]. Traumatic CSF Rhinorrhea might cease with conservative management. CSF leaks that close without surgical repair are mostly covered by a layer of fibrous tissue or regenerated nasal mucosa [9]. In some instances, the presence of an encephalocele or a meningocele through the bony defect may disrupt the healing process. Furthermore, the size of the defect is an important factor in predicting the possibility of spontaneous cessation of the leak [10] [11] .The treatment approaches must be tailored and individualized, especially when considering patients with closed-head injuries and small fractures versus those with large and comminuted fractures or those with penetrating injury to the skull base [9] [10] .

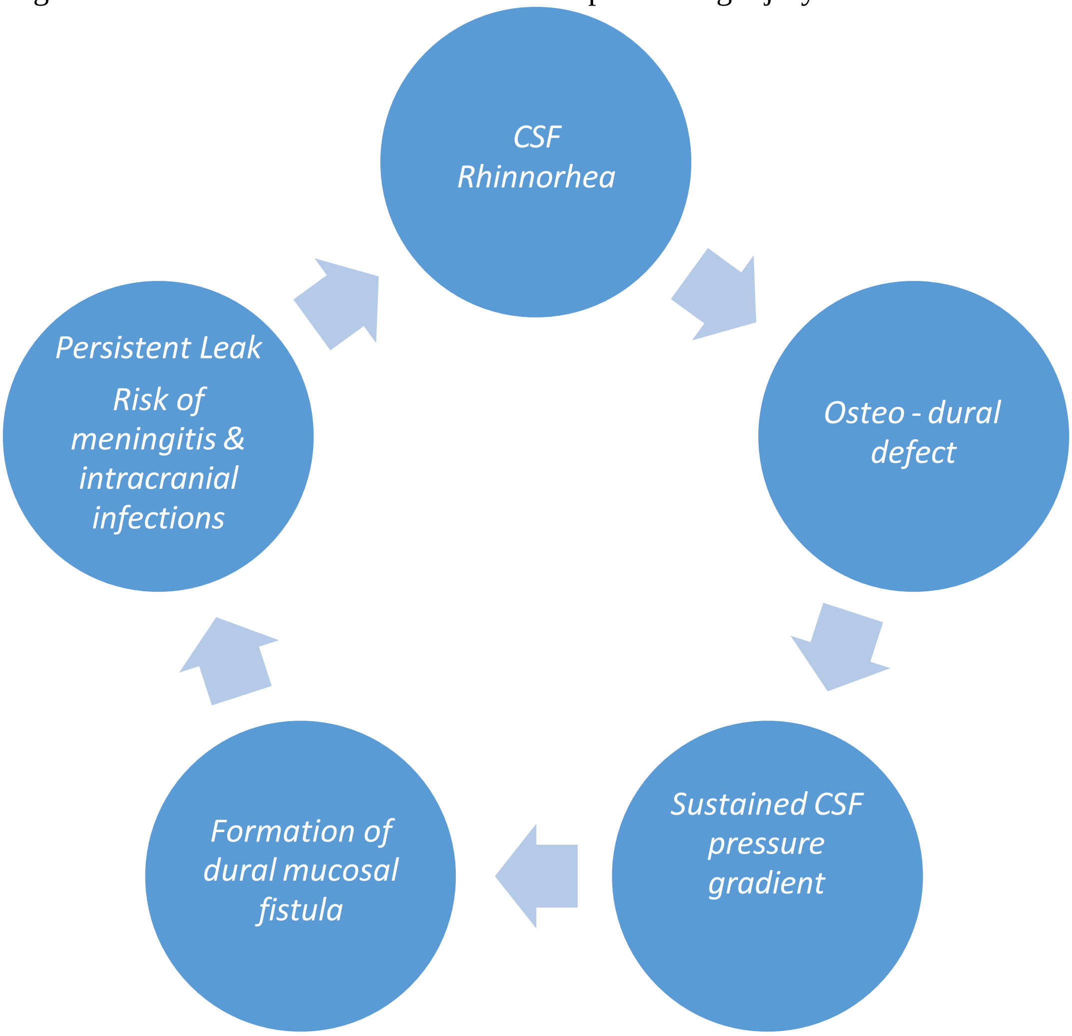


Fig.2. Pathophysiological cycle of CSF rhinnorhea.

Clinical Presentation

The most common clinical presentation of CSF Rhinorrhea is a watery, unilateral, non-sticky clear fluid discharge from the nose which is intermittent in periodicity and is position dependent(Reservoir sign), characterized by intermittent CSF leak on a transient increase in intracranial pressure like standing up, straining, coughing. The CSF cannot be sniffed back readily and patients usually complaint of a low pressure headache. Patients may as well experience a salty sensation down the throat on swallowing.

CSF Rhinorrhea in the acute phase after trauma has been reported in as many as 39% of the patients with skull base fractures **[12]**. In acute traumatic event, patients may present with epistaxis, nasal discharge, periorbital ecchymosis, chemosis, oculomotor impairment, anosmia, motor deficit, loss of vision, cranial nerve deficits, meningismus (neck stiffness, fever, photophobia) and pneumocephalus **[12] [13]** . Any diagnostic delay can increase the risk of meningitis or brain abscess **[12]**

Diagnosis

The diagnosis of CSF Rhinorrhea is first experienced by the patient itself as a unilateral, clear, free flow watery discharge from the nose which is intermittent in periodicity. The discharge is usually clear and non-sticky, as CSF has no mucoprotein hence has no viscosity, but in some cases especially trauma it can be mixed with mucous giving it an altered appearance.

Bed side analysis

Reservoir sign – Free flow of CSF from the nose as the patient bends down his head.

Halo sign – The bloody nasal drainage is allowed to drip onto filter paper or guaze. The CSF will diffuse faster than blood and result in a clear halo around the blood. This is reportedly as a very unreliable sign since blood tinged watery nasal secretions may produce the same pseudochromatographic pattern **[14]**.

Both these tests are non-specific and difficult to reproduce.

Chemical analysis of CSF

β2 Transferrin: The gold standard for detecting the presence of CSF is by testing for beta-2 transferrin **[15] [16]**. Beta-2 transferrin protein is involved in ferrous ion transport .it is produced by neuraminidase. It is exclusively found in CSF, perilymph of the cochlea, and the vitreous humor of the eye, and has a sensitivity of 100% and a specificity of 95% **[15]**. The reason for infrequent use of this laboratory test is that it is expensive and laborious with “send out” test for most institutions with a week’s turnaround time **[17]**.

β Trace protein: Is another marker for detecting the presence of CSF. Beta-trace protein is identical to prostaglandin-D synthase. It is primarily synthesized in the arachnoid cells, oligodendrocytes, and choroid plexus and is thought to be important for maturation and maintenance of the CNS **[17] [18]**.

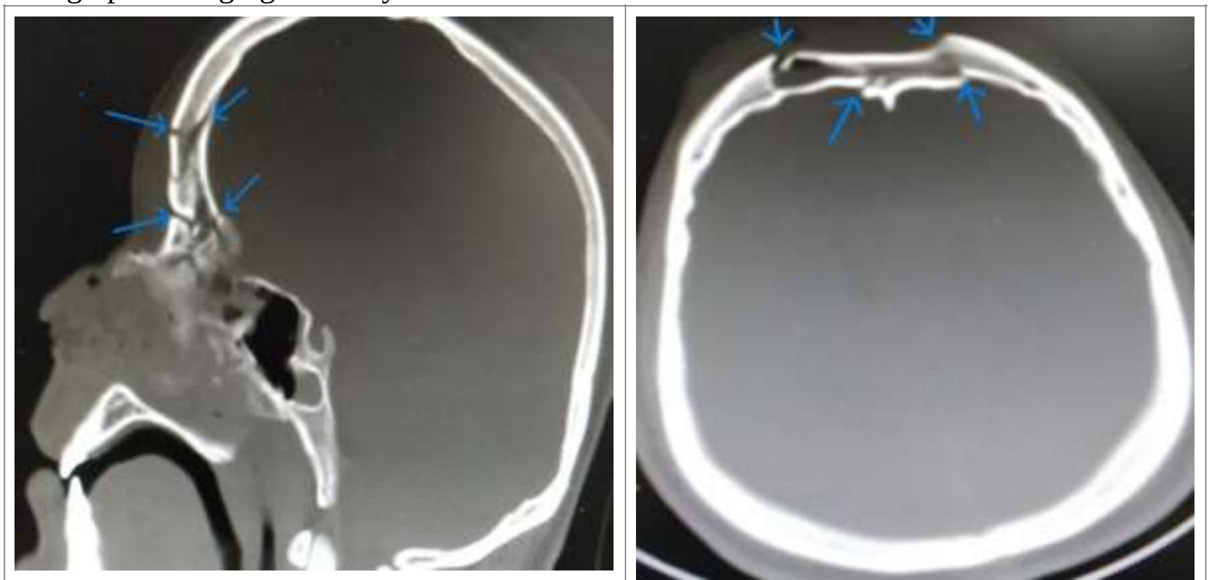
The advantages of using beta-2 trace protein rather than beta-2 transferrin as a marker for CSF

rhinorrhea have been described by Meco and colleagues [17] as less time consuming, less labor intensive (< 15 minutes),and less expensive.
However this technique is still designated for research purposes only. Additionally, it is unreliable in the setting of renal disease and meningitis [17].

Glucose oxidase: The concentration of glucose in CSF exceeds 50% of the serum concentration except during meningitis, subarachnoid haemorrhage, or some other unusual circumstance [14]. The glucose concentration in nasal secretions is 10 mg/dl or less. However the false positive rates for this test are high and does not hold much significance in the given date.

Radiographic evaluation

High resolution computed tomography scan (HRCT): The gold standard for anatomic localization of anterior skull base defects is a high resolution, thin cut (1-1.5 mm) CT scanning with coronal and sagittal reconstructions (Fig.3). It has a sensitivity of approximately 87% for identification of CSF fistulas [20].The Coronal images are used for identification of sphenoethmoid defects and are more important in identifying the site of CSF leakage, while axial and sagittal images are more accurate for identification of posterior table, frontal sinus defects [13]. HRCT is a fast, inexpensive, easily available and reliable radiographic imaging modality for identification of CSF leak.



A. B.

Fig.3 A.B. Sagittal and axial HRCT in a patient of CSF rhinnorhea showing fracture of the outer and inner table of frontal sinus (blue arrows) and ACF base fracture.

CT cisternography: CT cisternography needs placement of a lumbar drain after which an intrathecal injection of radiopaque contrast material is injected followed by thin cut CT imaging. An active CSF leak is a pre requisite for localization. Sensitivity of CT cisternography is reported to be 80 to 95% [17] [22].

The maximum benefit of CT cisternography is in frontal or sphenoid sinus leaks because these sinuses act as reservoirs of the contrast material [9]. Cribriform and ethmoid leaks are more challenging to identify with cisternography because the contrast material can drain more readily into the nasopharynx [9].

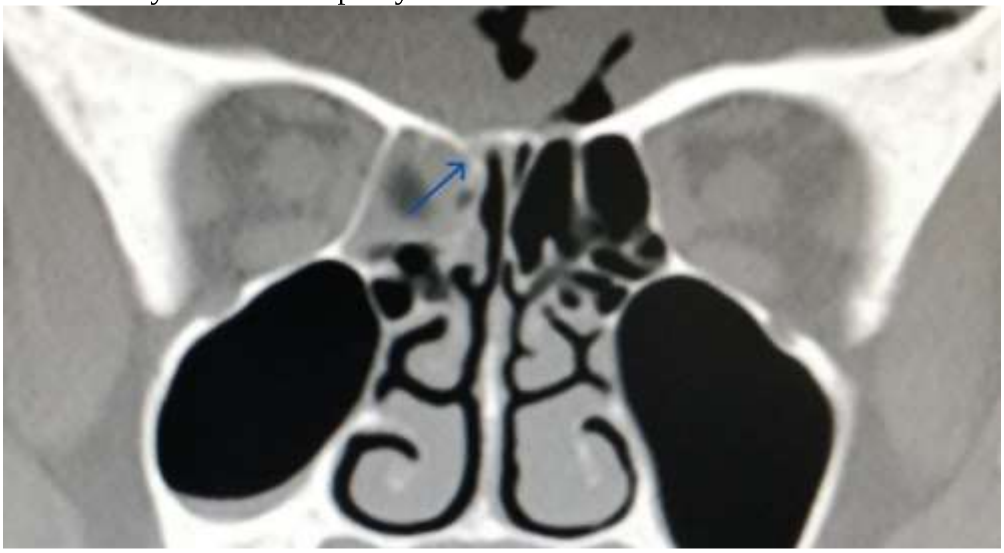


Fig.4. CT cisternogram, coronal view of a CSF rhinnorhea patient showing extravasation of the radiopaque dye from the right cribriform (blue arrow).

Magnetic Resonance Imaging (MRI):

MRI is another effective imaging modality for localizing CSF fistulas. CSF is hyperintense on T2-weighted imaging and can be readily identified within the nasal cavity [21]. MRI also provides higher soft tissue resolution for identification of brain or dural herniations. Current imaging modalities can achieve a sensitivity of 85 to 92% and specificity of nearly 100% [9]. As compared to HRCT, MRI is more costly and time consuming, however MRI can readily detect other anatomic abnormalities such as an encephalocele or meningocele.

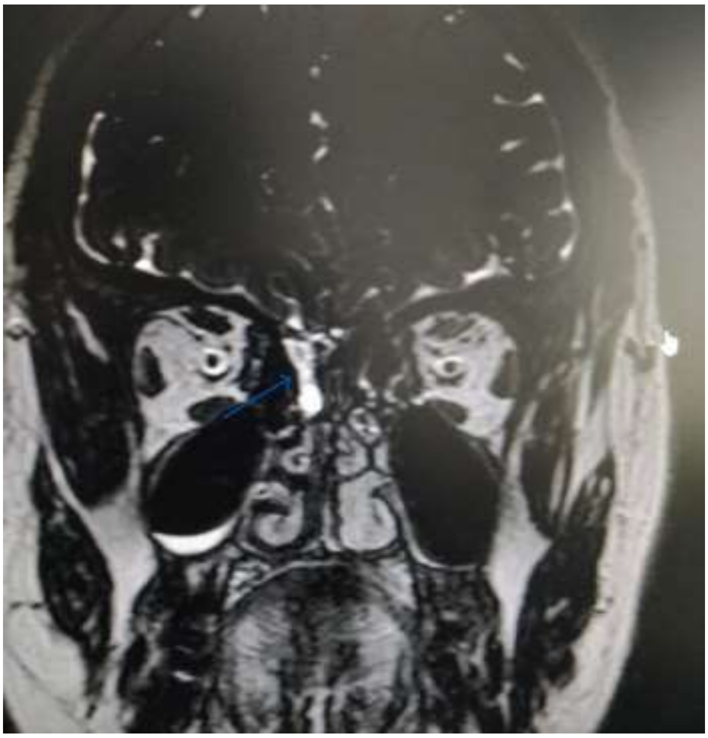


Fig.5 MRI, coronal view showing showing right sided defect and herniation (blue arrow).

MR Cisternography: MR cisternography is performed with an intrathecal injection of gadolinium contrast material via lumbar puncture. This enhances the detection of CSF within the nasal cavity. The risk of neurological changes or seizure activity with the use of gadolinium is extremely low [17]. The sensitivity of this image modality for detection of CSF leak is approximately 85 to 92% and specificity of 100% [9]. Post lumbar puncture headaches, nausea, vomiting are commom side effects of both MR cisternography and CT cisternography which however get resolved within 24 hours of conservative bed rest [22]. MRI and magnetic resonance cisternography are generally reserved for patients who have a diagnostic dilemma have already undergone high-resolution CT and the CT cisternogram.

MRI CISS 3D: In many series the sensitivity of HRCT has been 88.25% and that of MRI CISS 3D has been 88.88% and when combined the sensitivity further rises to 89.74% and thus invasive techniques like CT cisternography and MR cisternography can be avoided [31].

Endoscopic Evaluation
After clinical or chemical diagnosis of CSF leak a nasal endoscopy can be performed. It is a rapid and cheap method to localize the side or general location of the leak.
Otoscopic Examination
Middle ear effusion should be excluded as a defect in the middle or posterior cranial fossa can be the origin of the CSF rhinorrhoea.
Intrathecal Fluorescein Test
To confirm CSF leakage and identify potential sites of leakage in the intraoperative setting. The dye is injected intrathecally by a lumbar drain and anatomic localization of the CSF leak stained by the dye is detected endoscopically.
Radioisotope Cisternography
To evaluate CSF dynamics and detect potential sites of leakage. The sensitivity of the test is only 62 to 76% [23] and is of historic significance.

Test		**Inference**
Chemical	βtransferrin	Gold standard; highly sensitive and specific
	βtrace protein	Highly sensitive and specific Not suitable in patient bacterial meningitis or low glomerular filtration rate
	Glucose oxidase	Non reliable
Radiological	HRCT	Gold standard; rapid, highly sensitive Fracture not always co related with site of leak
	CT cisternography	Highly sensitive Co-relates with active site of leak Most useful in frontal and sphenoid leaks as these reservoirs collect fluid

	MRI	T2 sequences yield anatomical detection of CSF and encephaloceles High sensitivity and specificity but more time consuming and expensive than CT
	MR cisternography	High sensitivity and specificity Co-relates with site of leak Better contrast penetration in smaller fractures and tears More costly and time consuming
	MRI CISS 3D	High sensitivity Inavsice techniques of CT cisternography and MR cisternography can be avoided
Nasal Endoscopy		Rapid and cheap diagnostic measure Difficult to perform in acute trauma setting
Intrathecal Fluorescein		The dye has to be given intrathecally via a lumbar drain and the dye stained CSF leak has to be diagnosed intraoperatively
Topical Intranasal Fluorescein		Is a non-invasive method and avoids complications of a lumbar puncture

Table.2 Diagnostic modalities of CSF Rhinorrhea.

Differential Diagnosis

CSF Rhinorrhea should be differentiated from:

1. Nasal discharge due to other causes (e.g., sinusitis, allergies, vasomotor rhinitis).
2. Sinonasal saline irrigations
3. Traumatic nasal injury
4. CSF otorrhea presenting as CSF rhinorrhea
5. Congenital nasal anomalies

Management

Prompt diagnosis and effective management are crucial to prevent complications and optimize patient outcomes.

Conservative Management

The conservative management essentially consists of the following three Steps:

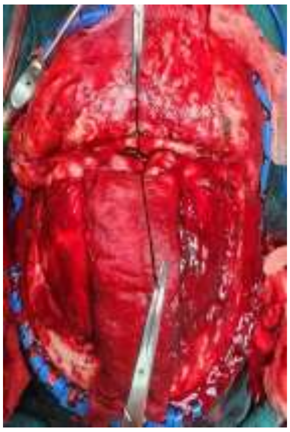
1. **Bed rest:** To reduce intracranial pressure and promote healing of the defect. Bell et al reviewed 34 cases of traumatic skull base CSF fistulas treated conservatively had resolution of CSF leak in 85% of the patients **[24]**. Mincy found that 68% of the posttraumatic CSF fistulas closed spontaneously within 48 hours and 85% closed within 7 days of initial injury **[25]**. Persistent CSF rhinorrhea after conservative management can be successfully treated with CSF diversion for 7 to 10 days **[13] [24]**.
2. **Lumbar drainage:** To divert CSF and reduce intracranial pressure and promote healing of the defect. A lumbar catheter is used to drain the lumbar fluid. It drains the fluid 5-10 ml per hour for 48 hours without resulting in CSF hypovolemia **[26]**. The drain is clamped after 48 houurs for a period of 6 hours. At this point, the opening pressure is measured. Opening pressure > 20 mm Hg, is an indication of adjunctive therapy like mannitol or acetazolamide to reduce ICP. During this treatment, the patient is advised to avoid coughing, sneezing, nose blowing, straining and is put on stool softners and strict bed rest.
3. **Antibiotic prophylaxis:** To prevent meningitis and other intracranial infections. It is of routine practise to use prophylactic antibiotics in patients with CSF rhinnorhea. However most recent Cochrane database review from 2011 does not support prophylactic antibiotics to prevent the risk of meningitis **[27]**.

Surgical Management

CSF leaks that do not heal spontaneously by conservative management or with CSF diversion need to undergo surgery **[13]**. Surgery is considered for post traumatic patients after failure of medical management for 3 to 7 days **[10] [13] [28]**. Early surgical intervention has been recommended in cases in which the intracranial pathology requires acute intervention or the extent of the skull fracture suggests that spontaneous closure would be impossible, such as in a large depressed skull base fracture, a fracture accompanied by complications, or tension pneumocephalus **[12][29]**.

Transcranial approach

Dandy was the first to describe a transcranial approach for repair of CSF Rhinorrhea in 1926 **[30]**. Usually a bifrontal craniotomy is performed with exteriorization of the bifrontal air sinuses. A bifrontal craniotomy and dynamic brain retraction give access to the sphenoid sinus and the ACF base. The frontal air sinuses are stripped off the mucosa, plugged with muscle or betadine soaked gelfoam and sealed with bone wax and exteroirised. Various flaps such as galea aponeurosis, temporalis muscle fascia and vascularised pericranial flap can be used to seal the . Tissue glue, sutures, or a combination of both can be used to keep the graft in place. This technique gives us a direct access to plug / seal the osteo-dural defects however complications like anosmia due to injury of olfactory nerves, brain contusions, intraparenchymal haemorrhages due to constant brain traction and seizures are commonly encountered **[32]**. In severe traumatic cases it becomes inevitable to do a transcranial approach as one has to align and anchor the fractured bony fragments and if need be evacuate a haematoma if any. Fig.6 shows step wise technique of bifrontal craniotomy and sealing of the ACF base defect with a vascularised pericranial graft in a case of road traffic accident (trauma).

 *A.*	 *B.*	 *c.*
 *D.*	 *E.*	 *F.*

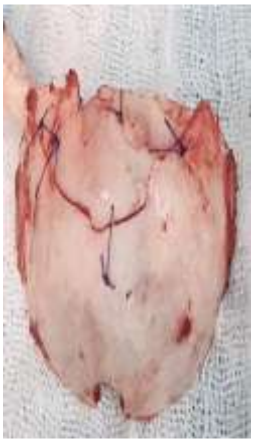
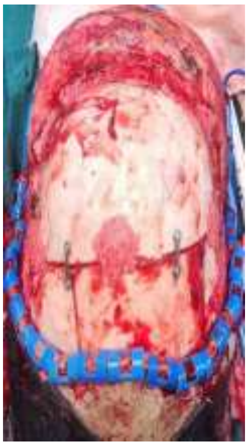
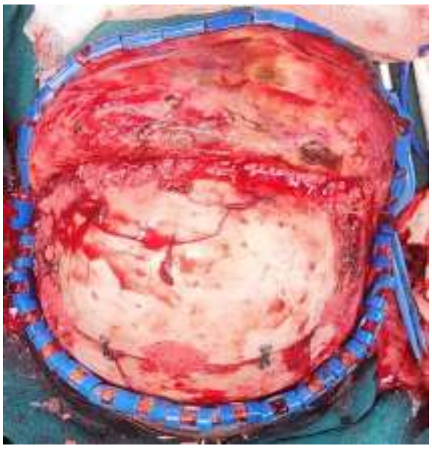
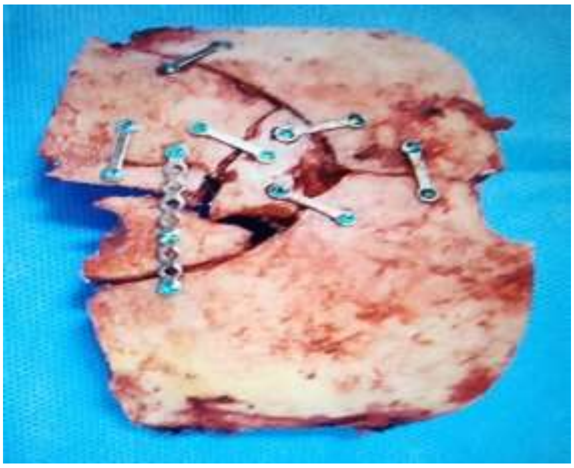
 *G.*	 *H.*	 *I.*

Fig.6 Showing step wise bifrontal craniotomy and intracranial repair of CSF leak in one of our trauma patients. A.Bicoronal flap marking (Souttar flap) B. Harvesting a vascularised pericranial graft C. Bifrontal craniotomy done (bifrontal fractures appreciated) D. Dynamic retraction of the frontal lobe E. Ligation of the superior sagittal sinus and cutting on anterior falx F. Placement of the vascularised pericranial graft on the ACF base after dynamic retraction of the bifrontal brain lobes and suturing of the dura with the pericranial graft G. Anchoring the fractured bone fragments with sutures H.I. Bone flap replacement and anchoring with mini plates with bone dust placement in the burr holes.

 *A.*	 *B.*

C.

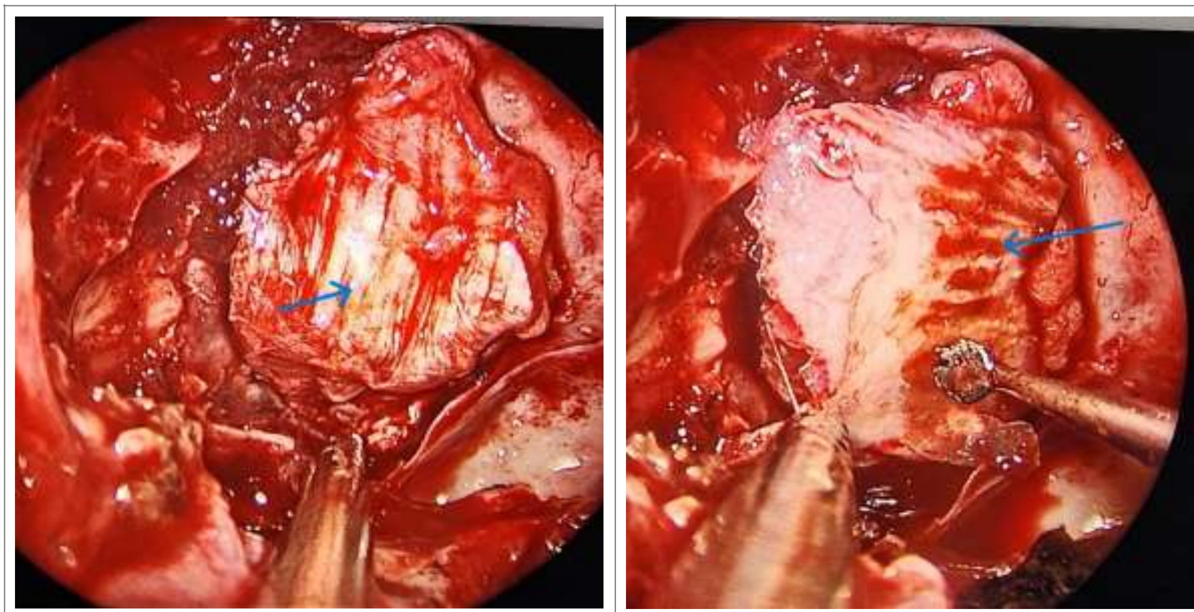
D.

Fig.7 Showing another of our trauma patient in whom bifrontal craniotomy, ACF base repair with vascularised pericranial graft and extensive frontal bone fracture repair was done. A.Bifrontal craniotomy and dural stitching with the pericranial graft which has been layered over the ACF base. B.Bone fragment anchoring with screws and plates. C. Replacement of the one flap and anchoring with mini plates and screws. E. Final suturing of the skin flap over two subgaleal drains.

Endoscopic endonasal approach

It was Wigand in 1981 who first described an endoscopic transnasal approach for repair of an anterior skull base defect **[33]**. In 1989 Papay et al expanded on this approach, describing the first endoscopic endonasal repair of a CSF fistula **[34]**. Since then, there have been several case series and reports that describe various endoscopic methods and materials for repair, with success rates varying between 60 and 100%, averaging around 90% **[43]**. Intranasal endoscopy become the first choice of treating CSF rhinnorhea of ethmoid and sphenoid sinuses. Endoscopic endonasal repair has replaced other traditional approaches due to its safety, high efficacy, minimal invasiveness and limited injury and is the preffered method of CSF rhinnorhea repair **[12] [35] [36]**.

Endoscopic approach shows excellent visualization of the entire anterior skull base from the sphenoid sinus to the frontal sinus. Visualization of the lateral sphenoid sinus can be achieved with the use of angled endoscopes or a direct dissection through the pterygomaxillary space **[37] [38]**. Access to the frontal sinus itself can be achieved via a modified Lothrop procedure, however, far lateral defects can still be challenging to access endoscopically **[37] [38]**. Different types of autologous and nonautologous grafts have been successfully used such as such as a mucoperiosteal flap from the middle turbinate or septum or mucoperichondrial, osseous, cartilaginous, fat, muscular fascia, middle turbinate, or septum pedunculated graft, or any combination of these grafts **[2] [14] [29]** .



A. B.

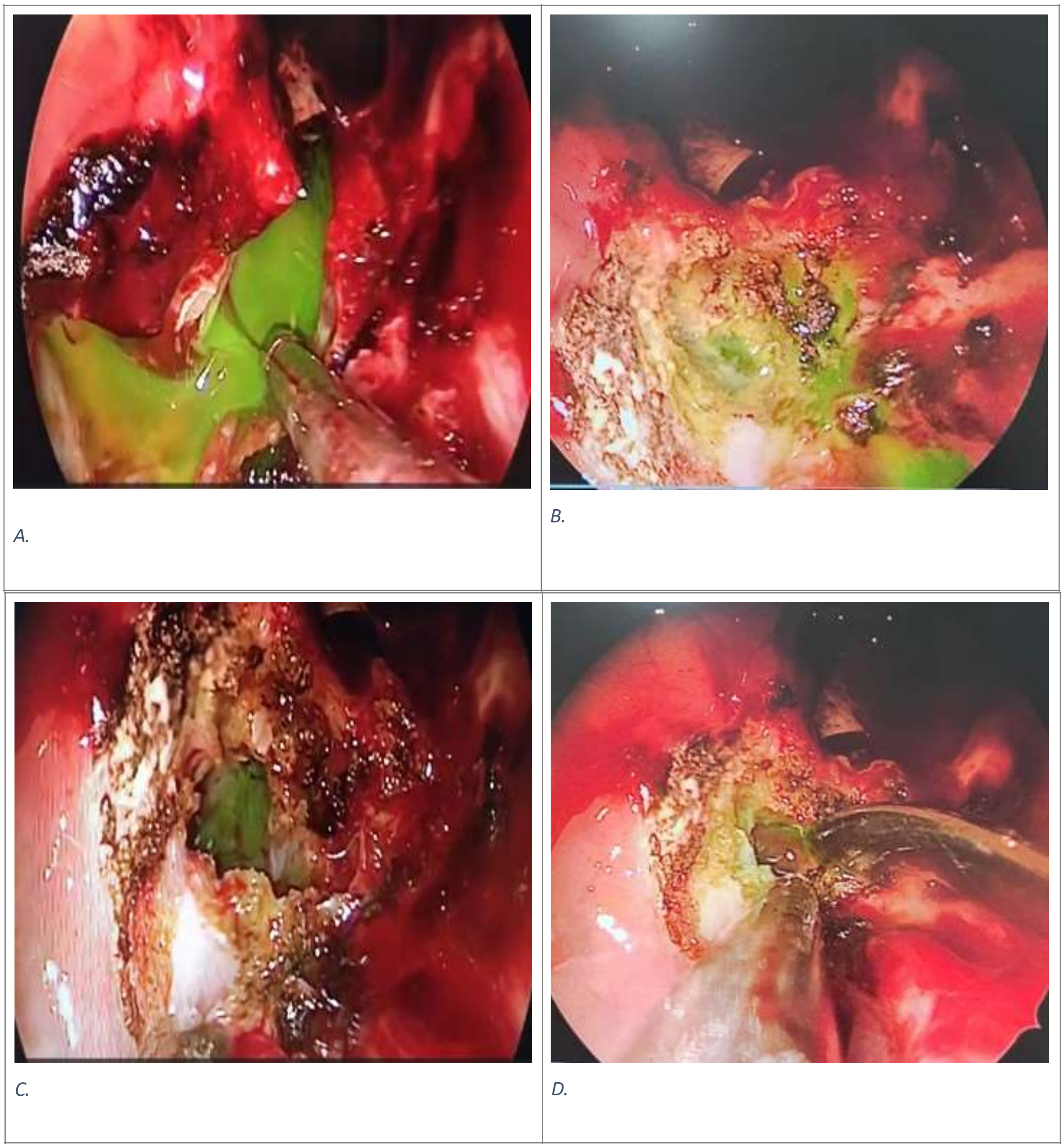
Fig.8 A.B. Endoscopic endonasal view of harvesting the pedicled naso septal mucocutaneous flap (Hadad flap). A. Mucosal surface of Hadad flap (blue arrow). B. Periosteal surface of Hadad flap (blue arrow).

Intrathecal Fluorescein

The use of intrathecal fluorescein was first described by Messer Klinger in 1972 and it is still commonly used for intraoperative identification of difficult skull base defects. Lumbar puncture is done to administer fluorescein allowing 30 to 60 minutes for diffusion throughout the CSF. Intraoperatively, it is seen as a bright green/yellow coloured material draining from the skull base defect. seizures, coma, and death are some of the complications of intrathecal fluorecein that occur at high concentrations[39].

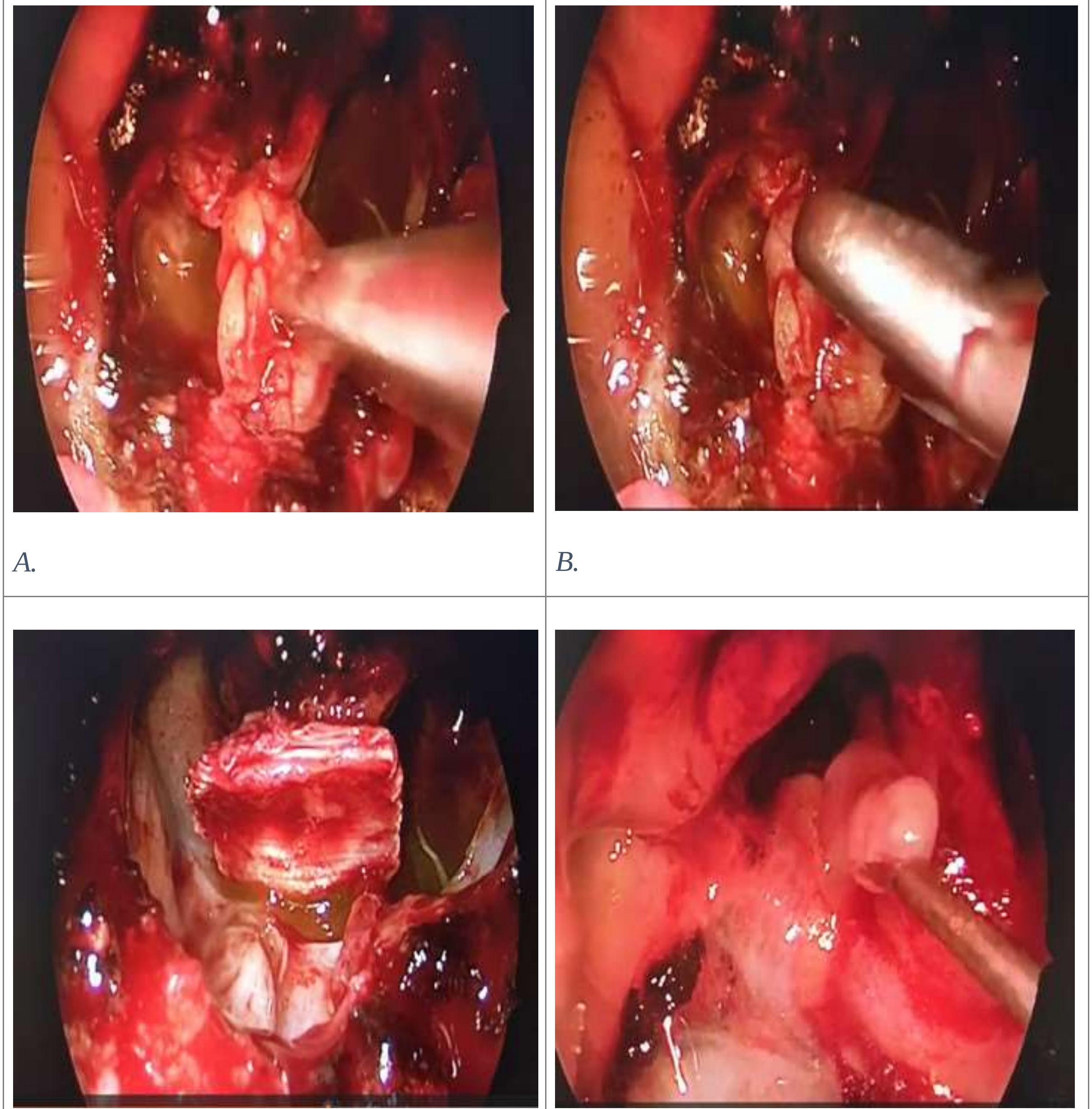
Topical intranasal fluorescein

In this recently developed technique CSF is stained with fluorescein dye endonasaly. This technique has an advantage of high accuracy of localization of the CSF fistula and avoids complications from lumbar puncture as well as the potential complications of intrathecal fluorescein [40] [41]. Jones [42] first localized the intraoperative CSF fistula by using topical nasal fluorescein in 3 patients and achieved 100% accuracy rate, and the method demonstrated no side effect as well.



A. B. C. D.

Fig. 9 A. Intrathecally placed fluorescein dye noted to leak intraoperatively. B.C.D. Osteal defect identified and the surrounding mucosa removed and bone denuded.



A. B. C. D.

Fig.10. A. B. Osteal defect being sealed with an autologous fat plug. C. Harvested fascia lata being placed over the fat plug. D. Glue being used as the final sealant.

Complications

Untreated CSF Rhinorrhea can lead to severe complications, including:

1. Meningitis
2. Cerebral abscesses
2. Pneumocephalus
4. Seizures

Materials and Methods

Study Design

Our study is a retrospective cohort study which was conducted at two tertiary care hospitals; Sher-i-Kashmir Institute of Medical Sciences (SKIMS) and Government Medical College (GMC), Srinagar for a period of 5 years between January 2018 and December 2022.

Inclusion Criteria

Patients were included if they:

1. Had a confirmed diagnosis of cerebrospinal fluid (CSF) Rhinorrhea
2. Underwent surgical or conservative management
3. Had complete medical records available

Exclusion Criteria

Patients were excluded if they:

1. Had incomplete medical records
2. Were diagnosed with other conditions mimicking CSF Rhinorrhea
3. Did not undergo treatment at our institutions

Data Collection

We collected data on:

1. Demographics (age, sex, comorbidities)
2. Clinical presentation (symptoms, duration)
3. Diagnostic tests (CSF analysis, CT scan, MRI scan,)
4. Treatment modalities (conservative, surgical)
5. Outcomes (success of treatment, complications)

Statistical Analysis

Descriptive statistics were used to summarize patient demographics and clinical characteristics. Chi-squared tests and Fisher's exact tests were used to compare categorical variables. Continuous variables were compared using t- tests or Mann-Whitney U tests.

Software

Statistical analysis was performed using SPSS version 23.

Sample Size

Our sample size consisted of 50 patients.

Results

Demographics

A total of 50 patients were included in this study. The mean age was 48.5 years (range: 35-65 years), with a peak incidence in the 40-55 year age group. The male-to-female ratio was 1.5:1, with 60% (30/50) males and 40% (20/50) fe males.

Table 3: Demographic Characteristics**Characteristic**		**Mean/Number**	**Percentage/Range**
Age (years)		48.5	35-65
Sex	Male	30	60%
	Female	20	40%
Comorbidities	Hypertension	15	30%
	Diabetes Mellitus	9	18%
	Obesity	11	22%

Table 4: Clinical Presentation

Symptom	**Number**	**Percentage**
CSF rhinorrhea	50	100%
Headache	40	80%
Dizziness	22	44%
Meningismus	6	12%
Visual disturbances	4	8%

Table 5: Etiology and Location of Leak

Etiology	**Number**	**Percentage**
Traumatic	29	58%
Spontaneous	17	34%
Iatrogenic	4	8%
Location		
Cribriform plate	22	44%
Sphenoid sinus	12	24%
Ethmoid sinus	7	14%
Frontal sinus	7	14%

Other	2	4%

Table 6: Duration of Symptoms

Duration	**Number**	**Percentage**
Acute (<1 week)	10	20%
Subacute (1-4 weeks)	25	50%
Chronic (>4 weeks)	15	30%

Treatment Outcomes

Out of the 50 patients 6(12%) had spontaneous recovery after 2 weeks, 10(20%) underwent open surgery, 1 (2%) underwent VP shunt placement (post open surgery) and 34 (68%) were managed with endoscopic repair.

Table 7: Treatment Outcomes

Treatment	**Number**	**Percentage**
Spontaneous recovery	6	12%
Open surgery	10	20%
VP shunt placement	1 (post open surgery)	2%
Endoscopic repair	34	68%

Discussion

This retrospective study of 50 patients with CSF rhinorrhea highlights the clinical presentation, etiology, location, and treatment outcomes of this complex condition. The majority of our patients (58%) had traumatic etiology, followed by spontaneous (34%) and iatrogenic (8%) causes. Our results are consistent with existing literature. Notably, 12% of our patients experienced spontaneous recovery after 2 weeks, emphasizing the importance of conservative management in select cases.

The term spontaneous CSF rhinorrhoea is restricted to CSF leaks that occur in the absence of trauma, tumor, surgery, or previous radiation therapy [44]. Although spontaneous leaks are idiopathic in nature, CSF rhinnorhea in reality is secondary to an increased intracranial pressure. Obesity is one of the causes as it invariably increases intra-abdominal and intra-thoracic pressure and may effect blood circulation in cranial venous collectors and lead to development of permanent benign intracranial hypertension [5]. Spontaneous CSF leak might also occur secondary to focal atrophy of the olfactory nerve in the region of the cribriform plate, any developmental anomaly which may cause thinning and remodelling of the bone overtime and could allow the arachnoid and brain tissue to protrude through the skull base into the nasal cavity [45] as the arachnoid sacs filled with CSF pulsate and gradually erode bone causing spontaneous CSF leak [48]. Expansive pneumatisation of the sphenoid sinus can also lead to dehiscence of skull base and CSF rhinnorhea [47].

Kljajic´ et al. [46] reported that male patients outnumbered female ones in the group of traumatic CSF leaks, while most of the patients with spontaneous CSF leaks were female ones. Our study confirms that spontaneous leak patients are more commonly middle-aged females (mostly obese) and most of the traumatic CSF leak patients are males. This may be due to the fact that traffic
injuries are more common among males, as well as occupational injuries of male workers whose job includes hard physical labour.

In cases of CSF rhinnorhea the clinical evaluation of the leak endoscopically is of primary importance along with the laboratory evaluation of β-transferrin with a high specificity of 98-100 % [50] as well β-trace proteins. But the radiological imaging modalities play a major role in the identification of the exact site of leak especially HRCT. In our study only those patients underwent MRI in whom there was a suspicion of brain herniation through the defect following endoscopic examination and HRCT.

An endoscopic approach is less morbid and has a success rate of 90 to 100%. [49]. Endoscopic repair was performed in 34 patients (68%) using a standardized protocol. Nasal endoscopy was done to identify the CSF leak site. Debridement of the affected area was done, surrounding mucosa was removed and the adjacent bone was denuded. Fascia lata (Fig.10) was harvested as a graft/flap in graft in 20 patients and in 15 patients a Hadad flap (Fig.8.) was used for repair. Superimposition of the graft was done with the application of topical fibrin glue (Tisseel) and/or tissue sealants. Gel foam was placed over the glue to reinforce the repair. Nasal packing with antibiotic-impregnated Meroseal nasal packs for 24-48 hours. Kljajic´ et al. [46] reported a high success rate of 97% after endoscopic CSF leak repair which co-relates with our endoscopic success rate of 91.17% (31/34 patients).

Open surgery was performed in 10 patients (20%) with complex skull base defects or failed endoscopic repair. A bicoronal (Sautar's flap) incision was marked and the musculocutaneous flap was carefully elevated .Vascularised pericranial graft was harvested and preserved. Fig.6. A bifrontal craniotomy was done and bilateral frontal air sinuses were stripped off the mucosa and plugged with betadine soaked gelfoam and sealed with bone wax. Dura was incised in a linear fashion, anterior superior sagittal sinus was ligated and the anterior falx cut. Repair of the CSF leak site was done by layering the vascularised pericranial graft over the ACF base and superimposing with application of fibrin glue and/or tissue sealants. Dura was sutured to the vascularised pericranial patch as well to the both edges of the incised dura.Fig.7. Reconstruction of the fractured bony fragments was done with titanium plates and screws. Musculocutaneous flap was closed in layers over a drain. Reported failure rates for intracranial repair of rhinorrhea rangefrom 6% to 27% [13]. In our study the overall success rate of an open repair was 80.0%
(8/10 patients).

Shunt placement was performed in 1 patient (2%) with refractory hydrocephalus on whom an open surgery was done previously at our institution. A medium pressure non programmable ventriculo-peritoneal shunt was placed and the CSF leak subsequently stopped.

Table 8: Success rate of various surgical procedures

Surgical approach	No. of patients	Success rate
Endoscopic repair with fascia lata graft	20 (18/20)	90.0%
Endoscopic repair with Hadad flap	15 (14/15)	93.3%
Open surgery	8 (8/10)	80.0%
VP Shunt placement (post open repair)	1	100%

The most common complications were a transient nasal congestion seen in 10 patients, epistaxis in 2 patient's and meningitis was noted in 1 patient. All complications were managed conservatively with nasal decongestants and saline irrigation for nasal congestion. Pressure dressing and topical hemostatic agents for epistaxis and antibiotic therapy and close monitoring was done for meningitis. No patients with these complications required reoperation or invasive interventions.

Complication	No. of patients	Percentage
Transient nasal congestion	10 (10/44)	22.7 %
Epistaxis	2 (2/44)	4.5%
Meningitis	1 (1/44)	2.2%
Recurrent CSF Leak	3 (3/44)	6.8%

Table 9: Failure Rate and Complications

Traumatic CSF leak repair had a higher success rate compared to spontaneous or iatrogenic leaks and it was observed that surgeons with more experience (>50 cases) had a higher success rate compared to less experienced surgeons (<50 cases).

Limitations

Our study's limitations include its retrospective design and relatively small sample size.

Conclusion

CSF Rhinorrhea is a complex condition requiring prompt recognition and management to prevent devastating complications. A multidisciplinary approach, involving otolaryngologists, neurosurgeons, and intensivists, is essential for optimal patient outcomes. Prompt diagnosis and effective management are crucial to prevent complications and optimize patient outcomes. This study contributes to the understanding of CSF rhinorrhea's clinical presentation, etiology, and treatment outcomes. Our results support individualized treatment approaches, considering spontaneous recovery, endoscopic repair, and open surgery or shunt placement for complex cases. Our study demonstrates high success rates for endoscopic repair of CSF rhinorrhea, with significant factors influencing outcome. Understanding these factors can help surgeons optimize treatment strategies and improve patient outcomes.

Funding: Nil

References:

1. Non-traumatic cerebrospinal fluid rhinorrhoea. Ommaya AK, Di Chiro G, Baldwin M, Pennybacker JB. J Neurol Neurosurg Psychiatry. 1968; 31:214–225. doi: 10.1136/jnnp.31.3.214.
2. Bernal-Sprekelsen M, Alobid I, Mullol J, et al. Closure of cerebrospinal fluid leaks prevents ascending bacterial meningitis. Rhinology. 2005; 43:277–281.
3. Le C, Strong EB, Luu Q. Management of Anterior Skull Base Cerebrospinal Fluid Leaks. J Neurol Surg B Skull Base. 2016 Oct; 77(5):404-11. [PMC free article] [PubMed]
4. Tang R, Mao S, Li D, Ye H, Zhang W. Treatment and Outcomes of Iatrogenic Cerebrospinal Fluid Leak Caused by Different Surgical Procedures. World Neurosurg. 2020 Nov; 143: e667-e675.
5. Badia L, Loughran S, Lund V: Primary spontaneous cerebrospinal fluid rhinorrheaand obesity. Am J Rhinol. 2001, 15:117-119. 10.2500/105065801781543736
6. Kerr JT, Chu FW, Bayles SW. Cerebrospinal fluid rhinorrhea: diagnosis and management. Otolaryngol Clin North Am 2005; 38(4):597–611
7. Ziu M, Savage JG, Jimenez DF. Diagnosis and treatment of cerebrospinal fluid rhinorrhea following accidental traumatic anterior skull base fractures. Neurosurg Focus 2012; 32(6):E3
8. Han CY, Backous DD. Basic principles of cerebrospinal fluid metabolism and intracranial pressure homeostasis. Otolaryngol Clin North Am 2005; 38(4):569– 576
9. Schlosser RJ, Bolger WE: Nasal cerebrospinal fluid leaks: critical review and surgical considerations. Laryngoscope 114:255–265, 2004
10. Rocchi G, Caroli E, Belli E, Salvati M, Cimatti M, Delfini R: Severe craniofacial fractures with frontobasal involvement and cerebrospinal fluid fistula: indications for surgical repair. Surg Neurol 63:559–564, 2005
11. Sakas DE, Beale DJ, Ameen AA, Whitwell HL, Whittaker KW, Krebs AJ, et al: Compound anterior cranial base fractures: classification using computerized tomography scanning as a basis for selection of patients for dural repair. J Neurosurg 88:471–477, 1998
12. Scholsem M, Scholtes F, Collignon F, et al. Surgical management ofanterior cranial base fractures with cerebrospinal fluid fistulae: a single-institution experience. Neurosurgery 2008; 62(2):463–469, discussion 469–471
13. Yilmazlar S, Arslan E, Kocaeli H, Dogan S, Aksoy K, Korfali E, et al: Cerebrospinal fluid leakage complicating skull base fractures: analysis of 81 cases. Neurosurg Rev 29:64–

71, 2006

14. Cukurova I, Cetinkaya EA, Aslan IB, Ozkul D: Endonasal endoscopic repair of ethmoid roof cerebrospinal fluid fistula by suturing the dura. Acta Neurochir (Wien) 150:897–900, 2008

15. Chan DTM, Poon WS, IP CP, Chiu PWY, Goh KYC: How useful is glucose detection in diagnosing cerebrospinal fluid leak? The rational use of CT and Beta-2 transferrin assay in detection of cerebrospinal fluid fistula. Asian J Surg. 2004, 27:39-42. 10.1016/s1015-9584(09)60242-6

16. Reiber H, Walther K, Althaus H: Beta-trace protein as sensitive marker for CSF rhinorhea andCSF otorhea. Acta Neurol Scand. 2003, 108:359-362. 10.1034/j.1600-0404.2003.00173.

17. Meco C, Oberascher G, Arrer E, Moser G, Albegger K. Beta-trace protein test: new guidelines for the reliable diagnosis of cerebrospinal fluid fistula. Otolaryngol Head Neck Surg 2003; 129 (5):508–517

18. Melegos DN, Diamandis EP, Oda H, Urade Y, Hayaishi O: Immunofluorometric assay of prostaglandin D synthase in human tissue extracts and fluids. Clin Chem 42:1984–1991, 1996

19. LeVay, A.J.; Kveton, J.F. Relationship between obesity, obstructive sleep apnea, and spontaneous cerebrospinal fluid otorrhea. Laryngoscope 2008, 118, 275–278

20. Zapalac JS, Marple BF, Schwade ND. Skull base cerebrospinal fluid fistulas: a comprehensive diagnostic algorithm. Otolaryngol Head Neck Surg 2002; 126 (6):669–676

21. Eljamel MS, Pidgeon CN, Toland J, Phillips JB, O'Dwyer AA. MRI cisternography, and the localization of CSF fistulae. Br J Neurosurg1994; 8(4):433–437

22. Tali ET, Ercan N, Krumina G, Rudwan M, Mironov A, Zeng QY, et al: Intrathecal gadolinium (gadopentetate dimeglumine) enhanced magnetic resonance myelography and cisternography: results of a multicenter study. Invest Radiol 37: 152–159, 2002

23. Stone JA, Castillo M, Neelon B, Mukherji SK. Evaluation of CSF leaks: high-resolution CT compared with contrast-enhanced CT and radionuclide cisternography. AJNR Am J Neuroradiol 1999; 20(4):706–712

24. Bell RB, Dierks EJ, Homer L, Potter BE. Management of cerebrospinal fluid leak associated with craniomaxillofacial trauma. J Oral Maxillofac Surg 2004; 62(6):676–684

25. Mincy JE. Posttraumatic cerebrospinal fluid fistula of the frontal fossa. J Trauma 1966; 6(5):618–622

26. Prosser JD, Vender JR, Solares CA. Traumatic cerebrospinal fluid leaks. Otolaryngol Clin North Am 2011; 44(4):857–873, vii

27. Ratilal BO, Costa J, Sampaio C, Pappamikail L. Antibiotic prophylaxis for preventing meningitis in patients with basilar skull fractures. Cochrane Database Syst Rev 2011; (8):CD004884

28. Kirtane MV, Gautham K, Upadhyaya SR. Endoscopic CSF rhinorrhea closure: our experience in 267 cases. Otolaryngol Head Neck Surg 2005; 132(2):208– 212

29. Silva LR, Santos RP, Zymberg ST: Endoscopic endonasal approach for cerebrospinal fluid fistulae. Minim Invasive Neurosurg 49:88–92, 2006

30. Dandy WE: Pneumocephalus (intracranial pneumatocele or aerocele). Arch Surg 12:949–982, 1926

31. B.E. Mostafa, A. Khafagi, Combined HRCT and MRI in the detection of CSF rhinorrhea, Skull Base 14 (3) (2004) 157–162, https://doi.org/10.1055/s-2004-832259

32. Ray BS, Bergland RM. Cerebrospinal fluid fistula: clinical aspects, techniques of

localization, and methods of closure. J Neurosurg 1969; 30 (4):399–405

33. Wigand ME. Transnasal ethmoidectomy under endoscopical control. Rhinology 1981; 19 (1):7–15

34. Papay FA, Maggiano H, Dominquez S, Hassenbusch SJ, Levine HL, Lavertu P. Rigid endoscopic repair of paranasal sinus cerebrospinal fluid fistulas. Laryngoscope 1989; 99 (11):1195–1201

35. Mattox DE, Kennedy DW. Endoscopic management of cerebrospinal fluid leaks and cephaloceles. Laryngoscope 1990; 100 (8):857–862

36. McMains KC, Gross CW, Kountakis SE. Endoscopic management of cerebrospinal fluid rhinorrhea. Laryngoscope 2004; 114 (10): 1833–1837

37. Locatelli D, Rampa F, Acchiardi I, Bignami M, De Bernardi F, Castelnuovo P. Endoscopic endonasal approaches for repair of cerebrospinal fluid leaks: nine- year experience. Neurosurgery 2006; 58 (4, Suppl 2): ONS-246–ONS-256, ONS-256–ONS-257

38. Martin TJ, Loehrl TA. Endoscopic CSF leak repair. Curr Opin Otolaryngol Head Neck Surg 2007; 15 (1):35–39

39. Hegazy HM, Carrau RL, Snyderman CH, Kassam A, Zweig J. Transnasal endoscopic repair of cerebrospinal fluid rhinorrhea: a metaanalysis. Laryngoscope 2000; 110 (7):1166–1172

40. Keerl R, Weber RK, Draf W, et al. Use of sodium fluorescein solution for detection of cerebrospinal fluid fistulas: an analysis of 420 administrations and reported complications in Europe and the United States. Laryngoscope 2004; 114:266-72

41. WolfG, Greisdorfer K, Stammberger H. Endoscopic detection of cerebrospi nal fl uid fistulas with a fluore sce nce te chnique . Laryngorhinootologie 1997; 76:595-607

42. Jones ME, Reino T, Gnoy A, et al. Identification of intranasal cerebrospinal fluid leaks by topical application with fluorescein dye. Am J Rhinol 2000; 14:93-6

43. Psaltis AJ, Schlosser RJ, Banks CA, Yawn J, Soler ZM (2012) A systematic review of the endoscopic repair of cerebrospinal fluid leaks. Otolaryngol Head Neck Surg 147(2):196–203

44. Chen GY, Ma L, Xu ML, et al. Spontaneous cerebrospinal fluid rhinorrhea. Med (United States). 2018; 97(5). doi:10.1097/MD.0000000000009758

45. Casiano RR, Jassir D (1999) Endoscopic cerebrospinal fluidrhinorrhea repair: is lumbar drain necessary? Otolaryngol Head Neck Surg 121:745–750

46. Kljajic´ V, Vulekovic´ P, Vlasˇki L, Savovic´ S, Dragicˇevic´ D, Papic´ V (2017) Endoscopic repair of cerebrospinal fluid rhinorrhea. Braz J Otorhinolaryngol 83(4):388–393

47. R.J. Schlosser, B.A. Woodworth, E.M. Wilensky, M.S. Grady, W.E. Bolger, Spontaneous cerebrospinal fluid leaks: A variant of benign intracranial hypertension, Ann. Otol. Rhinol. Laryngol. 115 (7) (2006) 495–500, https://doi. org/10.1177/000348940611500703

48. J.E.A. O'connell, The cerebrospinal fluid pressure as an ætiological factor in the development of lesions affecting the central nervous system, Brain 76 (2) (1953) 279–298, https://doi.org/10.1093/brain/76.2.279

49. Banks CA, Palmer JN, Chiu AG, O'Malley BW Jr, Woodworth BA, Kennedy DW. Endoscopic closure of CSFrhinorrhea: 193 cases over 21 years. Otolaryngol Head Neck Surg. 2009; 140 (6):826-833.doi:10.1016/j.otohns.2008.12.060

50. Schnabel C, Di Martino E, Gilsbach JM, Riediger D, Gressner AM, Kunz D (2004) Comparison of beta2-trasferrin and betatrace protein for detection of cerebrospinal fluid in nasal and ear fluid. Clin Chem 50:661–663

DECLARATION:

Ethical approval: IEC GMC Srinagar (CDSCO registered) Regd no. ECR/1422/ Inst/JK/2020
Consent for publication: Consent for publication was taken.
Availability of data and material: All data generated or analysed during this study are included in this published article [and its supplementary information files].
Competing interests: The authors declare that they have no competing interests.
Funding: Nil
Author’s contribution:
KK: Assistant surgeon, analysation of data & statistics
TM: Assistant surgeon, analysation of data & statistics
SSC: Main surgeon, analysation of data & statistics
MFB: Analysation of data & statistics
AAW: Analysation of data & statistics
NKM: Analysation of data & statistics
SHA: Analysation of data & statistics
MA: Analysation of data & statistics
IA: Analysation of data & statistics
All authors read and approved the final manuscript.
Acknowledgements: Not applicable