



## Diagnostic Accuracy of Contrast-enhanced Flair Magnetic Resonance Imaging in Detecting Meningeal Abnormalities in Suspected Cases of Infectious Meningitis

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### ARTICLE INFO

#### Article history:

Received 06 October 2024

Received in revised form 13 November 2024

Accepted 25 November 2024

Available online 28 November 2024

#### Keywords:

Cerebrospinal Fluid  
Magnetic Resonance Imaging  
Meningitis

### ABSTRACT

**Background and aim:** To determine the diagnostic accuracy of contrast-enhanced fluid-attenuated inversion recovery in the diagnosis of meningitis and compare it with contrast-enhanced T1 sequence, taking cerebrospinal fluid (CSF) analysis as the gold standard.

**Material and methods:** Forty patients referred to the Department of Radiodiagnosis of Assam Medical College and Hospital (AMCH) with clinical symptoms of meningitis were subjected to Magnetic Resonance Imaging (MRI) examination of the brain with pre- and post-contrast sequences, including T1 and fluid-attenuated inversion recovery sequences. Cerebrospinal fluid (CSF) analysis reports were the gold standard and correlated with the MRI findings. Also, an attempt was made to identify patterns of leptomeningeal enhancement in various aetiologies of meningitis.

**Results:** The post-contrast fluid-attenuated inversion recovery (PC FLAIR) showed a significantly higher sensitivity of 97.06% (95% CI: 84.67% to 99.93%) than the PC T1FS, which had a sensitivity of 76.47% (95% CI: 58.83% to 89.25%). The specificity for PC FLAIR was found to be 83.33% (95% CI: 35.88% to 99.58%), while for PC T1FS, it is 66.67% (95% CI: 22.28% to 95.67%) without significant difference in specificity between the two sequences. The diagnostic accuracy of the PC FLAIR sequence was 95.00%, compared to 75.00% for the post-contrast T1 fat suppression (PC T1FS) sequence in diagnosing meningitis.

**Conclusions:** The PC FLAIR sequence outperforms the PC T1FS sequence regarding sensitivity, area under the curve, and diagnostic accuracy. Adding this sequence to the conventional sequence can optimize the early detection of abnormal meningeal enhancement.

### 1. Introduction

Meningitis is defined as inflammation of the meninges surrounding the brain and spinal cord and is characterized by headache, neck stiffness, and cerebrospinal fluid (CSF) pleocytosis.<sup>[1]</sup> The key to the disease prognosis is promptly identifying the condition and its underlying cause. This enables us to initiate appropriate and effective treatment plans immediately. While we strive to develop newer, faster diagnostic methods for detecting and treating meningitis sooner, we must not overlook the already available tools. Analysis of cerebrospinal fluid (CSF) remains pivotal for diagnosis. MRI (Magnetic Resonance Imaging) is a potentially potent tool in our fight against meningitis. For initial neuroimaging, an immediate CT scan should be conducted even prior to performing a lumbar puncture. This helps identify any hidden raised intracranial pressure and prevents brain herniation resulting from cerebrospinal fluid (CSF) removal. While there are limitations with CT imaging due to bone-related artifacts that obscure extra-cerebral fluid

collection, this issue can be overcome with MRI.<sup>[2]</sup> Studies have demonstrated that gadolinium-enhanced FLAIR images outperform conventional gadolinium-enhanced T1 weighted images in detecting abnormal leptomeningeal enhancement in meningeal pathologies. This superiority is attributed to FLAIR's ability to provide a distinct differentiation between enhancing cortical veins and enhancing meninges.<sup>[3]</sup> Distinguishing leptomeningeal enhancement from contrast enhancement in blood vessels can pose a challenge. However, a post-contrast FLAIR sequence may enhance the diagnoses of abnormal leptomeningeal enhancement. This sequence appears less sensitive to vascular enhancement, thereby improving diagnostic accuracy.<sup>[4]</sup> This study aims to examine different imaging findings seen on MRI in infectious meningitis caused by various etiological agents and correlate these findings with patients' cerebrospinal fluid (CSF) analyses. We aim to assess the sensitivity, specificity, and diagnostic accuracy and compare the contrast-enhanced MR sequences, particularly the contrast-enhanced

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<https://doi.org/10.30485/IJSRDMS.2025.493096.1625>



FLAIR sequence, in early diagnosis of meningitis (infectious) in our hospital settings.

## 2. Material and methods

The research was conducted at the Department of Radiodiagnosis at Assam Medical College & Hospital in Dibrugarh. The study lasted over one year, specifically from March 2023 to February 2024. The study is described as a hospital-based cross-sectional study. The participants in this study were patients aged between 13 and 70 years. These patients were referred to the Radiodiagnosis department because they showed clinical symptoms of meningitis. The researchers decided to include 40 patients in their study. They aimed for a 95% confidence interval; the margin of error was 10%, indicating how much the results could vary from the actual population values. The researchers considered the sensitivity of Contrast-Enhanced Fluid-Attenuated Inversion Recovery (CE FLAIR) MRI in diagnosing meningitis to be 91%. The study also noted that the prevalence of meningitis in the population was estimated to be 8.68%.

### Ethical approval

The study proposal was approved by the Ethics Committee of Assam Medical College & Hospital, Dibrugarh was held in the College Council Room on 21/2/2023 Informed written consent was obtained from all the participants before sample collection.

### Inclusion criteria

- Patients between the age group of 13-70 years who were hemodynamically stable and presented with signs and symptoms of meningitis, such as fever, severe headache, photophobia, neck stiffness, vomiting, nausea, and altered consciousness.
- Patients with meningitis for whom CSF analysis results were available.
- Patients giving written informed consent for participation in the study.

### Exclusion criteria

- Patients with contraindication to MRI or a history of allergy to contrast (gadolinium) were contraindicated.
- Patients in whom lumbar puncture was contraindicated.
- Patients did not provide consent for the study.

All patients fulfilling the inclusion criteria undergoing magnetic resonance imaging in the radiodiagnosis department, AMCH, and Dibrugarh during the study period were taken up for study. Informed written consent was obtained from patients or their attendants who were included in the study. The scheme started with the patient's unique identification code, age, and sex. Detailed clinical history and brief clinical examination were performed. All patients were screened for cardiac pacemakers, ferromagnetic objects, and aneurysm clips before admission into the MRI room. After positioning the patient properly, they were examined in the MRI machine, and their heads were immobilized. The scan was performed using the head coil. A topography of the brain was obtained, following which sequences were taken according to the MRI brain protocol (plain and with contrast). The MRI scans were performed using Siemens MagnetomAvantofitA Tim+ Dot 1.5 Tesla Whole body MRI (Magnetic Resonance Imaging) system. Scans were acquired in 5 mm thickness slices and 0.5 mm interslice gaps in the axial, coronal, and sagittal planes. The following plain sequences were taken:

a. T1

b. T2

c. Fluid-attenuated inversion recovery

d. Diffusion Weighted Image

e. Apparent Diffusion Coefficient

f. Susceptibility Weighted Images

After that, those patients with a standard range of serum creatinine received intravenous gadolinium. Gadobutrol 1.0 mmol/ml was used as an MRI contrast agent. A dose of 0.1 mg/kg body weight (customized for each patient according to their body weight) was injected manually. Emergency drugs and other emergency requirements were kept readily available.

### Post-contrast sequences were obtained with the following imaging parameters

a. Post-contrast T1-weighted sequence: TR-500 ms, TE-7.8 ms, slice thickness-5mm, interslice gap-1.5 mm, FOV-230 mm, and matrix-224 x 256. Total imaging time was 3 min and 48 sec.

b. Post-contrast T2 FLAIR sequence: TR-9000 ms, TE-109 ms, slice thickness-5mm, interslice gap-1.5 mm, FOV-230 mm, and matrix-224 x 256. Total imaging time was 2 min and 08 sec.

Scorer 1 and Scorer 2 viewed the scans separately and evaluated leptomeningeal enhancement as seen on the two post-contrast sequences (PC T1WI and PC FLAIR), using the pre-contrast T1 FS and FLAIR sequences as reference. Before examining the images, the scorers were unaware of the clinical history and CSF analysis results. The abnormal leptomeningeal enhancement was compared and characterized, following which the intensity of enhancement was scored using a 4-point scoring system that was determined prior to the study. The scoring system is mentioned below:

3: Distinct abnormal LE (leptomeningeal enhancement) that can be clearly distinguished from meningeal vasculature.

2: Likely abnormal LE that appears to be distinct from meningeal vasculature.

1: Potential abnormal LE that is indistinguishable from meningeal vasculature.

0: Without any abnormal LE.

Patients were followed and results of lumbar puncture were obtained from the laboratory. An attempt to study the association of the location of the LE (leptomeningeal enhancement) and the morphological pattern with etiological agents of infectious meningitis was made, CE FLAIR images were reviewed, and the findings were recorded in the master chart as follows:

A. Site of leptomeningeal enhancement:

Cisternal

Sulcal space

Pachymeningeal

B. Pattern of LE (leptomeningeal enhancement):

Thick

Thin

Nodular

Smooth

Combination of the above

### CSF analysis

The patient was put in lateral recumbent with the back vertical along the edge of the bed or in a sitting position. After disinfecting with povidone-

iodine, a sterile lumbar puncture needle (20-22 gauge) was passed between L3 and L4 or L4 and L5 vertebrae to obtain the CSF.

**3-5 ml of CSF was collected and divided into four clot activator vials for the analyses**

Chemical (glucose and protein) and serology – 1 ml: TUBE 1.

Microbiology (Gram's staining, bacterial culture, and sensitivity) – 2 ml: TUBE 2.

Total cell counts and Differential count – 1 ml: TUBE 3.

Cytology, special studies if required – 1 ml: TUBE 4.

**Physical, Chemical and cytological assessment**

CSF appeared turbid in the following cases:

- Bacterial and fungal infections
- Raised proteins
- Clot formation (cobweb coagulum) was seen in tubercular meningitis.
- If significant leucocytosis is present, then the leucocyte count in CSF is corrected.
- The differential count is performed on a stained smear made from CSF.
- Reported in the percentage of each type of cell present.
- Predominant neutrophils are present in meningitis (bacterial, early viral, early tubercular, and fungal).
- Predominant lymphocytes are present in meningitis (viral, tubercular, and fungal), incompletely treated bacterial meningitis, syphilitic meningoencephalitis, toxoplasmosis, and cysticercosis.
- A mixed cell pattern is present in tubercular, fungal, and chronic bacterial meningitis.

j) Protein content was estimated in the CSF quantitatively using the pyrogallol red method with spectrophotometric analysis.

k) Glucose estimation in CSF was done using the God-Pod method with spectrophotometric analysis.

**Microbiological assessment of CSF**

- The sample was centrifuged at 2000 rpm for 20-30 minutes.
- A sterile pipette supernatant was separated and sent for serological investigations (e.g., a cryptococcal antigen test).
- Sediment was first cultured in Nutrient agar, blood agar, Mc Conkey agar (overnight aerobic incubation at 37 degrees Celsius), and chocolate agar (In a candle jar for fastidious agents) using a sterile loop.
- Plates were checked after 48 hours. Colony characteristics were assessed, and the automated MALDI TOF mass spectrometry system was used for identification and biochemical testing.
- According to clinical and laboratory standard institutes, antibiotic susceptibility testing was performed.
- Gram staining was done on the sediment using the sandwich method, and it was examined under oil immersion at 100x magnification.

**3. Results**

The current study group is comprised of 40 patients between the ages of 13 and 70, 28 of whom are male and 12 female. Most of the patients were between the ages of 31 and 40. Variation is noted in the age groups according to different causative agents.

Table 1. Association between leptomeningeal enhancement score on PC FLAIR scorer one and CSF analysis.

Leptomeningeal Enhancement Score PC FLAIR	Negative(n=6)	Bacteria(n=6)	Fungal(n=2)	TB(n=26)	Total	P-value
0	5 (83.33%)	0 (0%)	0 (0%)	1 (3.85%)	6 (15%)	
1	0 (0%)	0 (0%)	1 (50%)	1 (3.85%)	2 (5%)	
2	1 (16.67%)	0 (0%)	1 (50%)	6 (23.08%)	8 (20%)	<.0001*
3	0 (0%)	6 (100%)	0 (0%)	18 (69.23%)	24 (60%)	
Total	6 (100%)	6 (100%)	2 (100%)	26 (100%)	40(100)	

This table examines the relationship between the results of leptomeningeal enhancement scores on post-contrast FLAIR MRI (scored by Scorer 1) and CSF analysis. Among 26 cases of tubercular meningitis, 69.23% had a score of 3, while 23.08% had a score of 2, demonstrating that tubercular meningitis often presents with strong leptomeningeal enhancement. All six bacterial meningitis cases scored 3, indicating strong leptomeningeal enhancement in bacterial infections. Two fungal meningitis cases were evenly

split between scores of 1 and 2, suggesting mild-to-moderate enhancement patterns. Among six patients with negative CSF results, five (83.33%) scored 0, while one scored 2. It suggests that patients without meningitis on CSF analysis generally showed no or minimal enhancement on PC FLAIR. The statistical analysis ( $P < 0.0001$ ) shows a significant association between enhancement scores and CSF-confirmed meningitis.

Table 2. Association of leptomeningeal enhancement score on PC T1FS scorer 1 with CSF analysis.

Leptomeningeal Enhancement Score PC T1FS	Negative(n=6)	Bacteria(n=6)	Fungal(n=2)	TB(n=26)	Total	P-value
0	4 (66.67%)	0 (0%)	2 (100%)	6 (23.08%)	12 (30%)	
1	2 (33.33%)	0 (0%)	0 (0%)	2 (7.69%)	4 (10%)	
2	0 (0%)	3 (50%)	0 (0%)	12 (46.15%)	15 (37.50%)	0.009*
3	0 (0%)	3 (50%)	0 (0%)	6 (23.08%)	9 (22.50%)	
Total	6 (100%)	6 (100%)	2 (100%)	26 (100%)	40 (100%)	

This table evaluates the diagnostic ability of PC T1FS compared to CSF analysis. Among 26 tubercular meningitis cases, 46.15% had a score of 2, while 23.08% had a score of 3, showing that tubercular meningitis exhibited moderate-to-strong enhancement. Half of bacterial meningitis cases (3/6) had a score of 3, while the rest had a score of 2, indicating moderate-to-high

enhancement. Both fungal meningitis cases scored 0, suggesting poor detectability of fungal infections using PC T1FS. Four (66.67%) scored zero among six CSF-negative cases, while two scored 1. The statistical analysis (P = 0.009) indicates a significant correlation between enhancement scores and CSF findings, but the association is weaker than that observed for PC FLAIR.

Table 3. Specificity, sensitivity, PPV (positive predictive value), and NPV (negative predictive value) of PC FLAIR scorer 1, scorer 2, PC T1FS scorer 1, and scorer 2 to predict meningitis after taking CSF analyses as gold standard.

Variables	Leptomeningeal Enhancement score PC FLAIR Scorer 1	Leptomeningeal Enhancement score PC FLAIR Scorer 2	Leptomeningeal Enhancement Score PC T1FS Scorer 1	Leptomeningeal Enhancement Score PC T1FS Scorer 2
Sensitivity (95% CI)	97.06%(84.67% to 99.93)	97.06%(84.67% to 99.9%)	76.47%(58.83% to 89.25%)	76.47%(58.83% to 89.25%)
Specificity (95% CI)	83.33%(35.88% to 99.58)	83.33%(35.88% to 99.58%)	66.67%(22.28% to 95.67%)	66.67%(22.28% to 95.67%)
AUC (95% CI)	0.9(0.77 to 0.97)	0.9(0.77 to 0.97)	0.72(0.55 to 0.85)	0.72(0.55 to 0.85)
Positive Predictive Value (95% CI)	97.06%(84.67% to 99.93)	97.06%(84.67% to 99.93%)	92.86%(76.50% to 99.12%)	92.86%(76.50% to 99.12%)
Negative Predictive Value (95% CI)	83.33%(35.88% to 99.58)	83.33%(35.88% to 99.58%)	33.33%(9.92% to 65.11)	33.33%(9.92% to 65.11)
Diagnostic accuracy	95%	95%	75.00%	75.00%

This table compares the diagnostic performance of PC FLAIR and PC T1FS sequences using sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). PC FLAIR had the highest sensitivity (97.06%) and specificity (83.33%) among both scorers, making it the superior sequence for detecting meningitis. PC T1FS had lower sensitivity (76.47%) and specificity (66.67%), suggesting it is less reliable in detecting leptomeningeal enhancement than PC FLAIR. The area under the curve

(AUC) was higher for PC FLAIR (0.9) than PC T1FS (0.72), indicating better diagnostic accuracy for PC FLAIR. The PPV was higher for PC FLAIR (97.06%) than PC T1FS (92.86%), reinforcing its reliability in detecting actual positive cases. The NPV was significantly higher for PC FLAIR (83.33%) than PC T1FS (33.33%), suggesting PC FLAIR is less likely to miss actual cases of meningitis.

Table 4. Comparison of sensitivity, specificity, and diagnostic accuracy of PC FLAIR and PC T1FS for predicting meningitis.

CSF Analysis	Leptomeningeal Enhancement Score PC FLAIR	Leptomeningeal Enhancement Score PC T1FS	P-value
Sensitivity (95% CI)	97.06%(84.67% to 99.93%)	76.47%(58.83% to 89.25%)	0.016 <sup>†</sup>
Specificity (95% CI)	83.33%(35.88% to 99.58%)	66.67%(22.28% to 95.67%)	1 <sup>†</sup>
AUC (95% CI)	0.9(0.77 to 0.97)	0.72(0.55 to 0.85)	0.039 <sup>‡</sup>
Diagnostic accuracy	95.00%	75.00%	0.028 <sup>§</sup>

<sup>†</sup> McNemar test, <sup>§</sup> Chi-square test, <sup>‡</sup> DeLong et al test.

This table statistically compares the sensitivity, specificity, and diagnostic accuracy of PC FLAIR and PC T1FS for diagnosing meningitis. The sensitivity of PC FLAIR (97.06%) is significantly higher than that of PC T1FS (76.47%) ( $P = 0.016$ ), indicating that PC FLAIR is better at detecting meningitis cases. The specificity of PC FLAIR (83.33%) is slightly higher than PC T1FS (66.67%), but the difference is not statistically significant ( $P = 1$ ). The AUC for PC FLAIR (0.9) is significantly higher than PC T1FS (0.72) ( $P = 0.039$ ), supporting the superior diagnostic performance of PC FLAIR. The diagnostic accuracy of PC FLAIR (95.00%) is significantly better than PC T1FS (75.00%) ( $P = 0.028$ ), reinforcing that PC FLAIR should be preferred for diagnosing meningitis.

#### 4. Discussion

Out of 40 patients, most of them (26/40) were positive for TB, followed by bacterial meningitis (6/40), the least common being fungal meningitis (2/40), and 6/40 cases were negative in the CSF study. Tubercular meningitis was the most common etiological agent in the study conducted on 50 patients of infectious meningitis by Azad R et al.<sup>[7]</sup> Bacterial meningitis (non-tubercular) was found to be the most common etiology in a study conducted by Kohil et al., highlighting regional variations in meningitis etiology.<sup>[8]</sup> The variations in the etiology of infectious meningitis were most probably due to differences in demographics, as emphasized by Akaishi T et al.<sup>[9]</sup> Out of culture-positive meningitis, 2/6 cases were positive for *Acinetobacter baumannii*, and 1/6 cases each were positive for *Citrobacter koseri*, *Stenotrophomonas maltophilia*, *Escherichia coli*, and *Klebsiella pneumoniae*. The low incidence of fungal meningitis (2/40) aligns with Reddy GK et al., who noted diagnostic challenges and improved antifungal therapies in resource-limited settings.<sup>[10]</sup> In the present study, PC FLAIR shows a significantly higher sensitivity of 97.06% (95% CI: 84.67% to 99.93%) compared to the PC T1FS, which has a sensitivity of 76.47% (95% CI: 58.83% to 89.25%). A statistically significant ( $P$ -value of 0.016) difference was observed between the sensitivity of the two sequences. The specificity for PC FLAIR is 83.33% (95% CI: 35.88% to 99.58%), while for PC T1FS, it is 66.67% (95% CI: 22.28% to 95.67%). No statistically significant ( $P$ -value of 1) difference in specificity between the two imaging modalities was noted. The diagnostic accuracy of PC FLAIR is 95.00%, compared to 75.00% for

the PC T1FS. A statistically significant ( $P$ -value of 0.028) difference in diagnostic accuracy was observed between the two sequences. These findings are supported by Mustafa W et al., who validated the superiority of CE-FLAIR in detecting leptomeningeal lesions, and Gad M et al., who emphasized its utility in infectious meningitis due to enhanced contrast-to-noise ratios.<sup>[11, 12]</sup> Marwan M et al., further demonstrated CE-FLAIR's diagnostic advantages in qualitative and quantitative analyses of intracranial pathologies, aligning with the high accuracy (95%) observed in our study.<sup>[13]</sup> The role of advanced MRI techniques, such as radiomics for TB meningitis detection Ma Q et al., reinforces the clinical value of FLAIR sequences.<sup>[14]</sup> While Akaishi et al., reported conflicting results favoring CE T1W with fat saturation, their small sample size ( $n=24$ ) limits generalizability, unlike our larger cohort.<sup>[9]</sup> Wu D et al., provided mechanistic insights into blood-brain barrier disruption, potentially explaining PC FLAIR's superior sensitivity to meningeal enhancement patterns.<sup>[15]</sup>

#### 5. Conclusion

We concluded that MRI is an excellent non-invasive modality in diagnosing abnormal meningeal enhancement attributed to FLAIR's insensitivity in detecting enhancement from vasculature, allowing better delineation of meningeal enhancement. CE FLAIR sequence, in addition to the conventional sequence of CE T1 FS sequence, can help provide better visualization of attenuated lesions, that may otherwise be missed if only one sequence is used. Also, observing the patterns and characteristics of enhancement can help us direct toward the etiological agent.

#### Conflict of Interest

The authors declared that there is no conflict of interest.

#### Acknowledgments

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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**How to Cite this Article:** Bhagawati A, Dhanowar LN, Dhanowar RK, Choudhury G, Borah P, Dharavath V. Diagnostic Accuracy of Contrast-enhanced Flair Magnetic Resonance Imaging in Detecting Meningeal Abnormalities in Suspected Cases of Infectious Meningitis. *International Journal of Scientific Research in Dental and Medical Sciences*. 2024;6(4):157-162. <https://doi.org/10.30485/IJSRDMS.2025.493096.1625>.