

# Contrast-Enhanced Fluid-Attenuated Inversion Recovery versus Contrast-Enhanced T1-Spin Echo Magnetic Resonance Imaging in the Evaluation of Infectious Meningitis

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## ABSTRACT

### Background

Infectious meningitis is an infection of the subarachnoid space causing inflammation of the leptomeninges. Early diagnosis is crucial to initiate appropriate therapy, avoid complications, and improve prognosis. Cerebrospinal fluid analysis is important in the diagnosis and is done by performing lumbar puncture with some limitations and complications. MRI plays a role in the diagnosis by depicting abnormal leptomeningeal enhancement.

### Aim of the study

To evaluate the efficiency of contrast-enhanced fluid-attenuated inversion recovery compared with contrast-enhanced T1 spin echo in the diagnosis of infectious meningitis.

### Patients and Methods

A prospective analytical study of diagnostic tests was conducted. Brain MRI was done using a 3-Tesla system. Gadolinium was used as contrast material. The final diagnosis of meningitis was made based on cerebrospinal fluid analysis. Validity parameters, predictive values, and diagnostic accuracy for both sequences were calculated and compared to each other. Quantitative and qualitative analysis was performed.

### Results

Fifty-six patients were involved (31 males and 25 females) in this study, and they ranged from 15 to 68 years in age. Cerebrospinal fluid analysis was positive in 41 patients and negative in 15. Contrast enhanced–fluid attenuated inversion recovery has higher sensitivity, specificity, positive predictive value, negative predictive value, and accuracy compared with contrast enhanced–T1 spin echo. The mean net meningeal enhancement is significantly higher in contrast enhanced–fluid attenuated inversion recovery. Substantial interobserver agreement between the two sequences was observed.

### Conclusion

Contrast- enhanced fluid attenuated inversion recovery is superior to contrast enhanced–T1 spin echo in the diagnosis of infectious meningitis.

**Keywords:** Meningitis, Enhanced-FLAIR, Enhanced -T1.

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## INTRODUCTION

### Anatomy

The brain is surrounded by three layers of membranes (cranial meninges), from outermost to innermost: dura mater (pachymeninges), arachnoid mater, and pia mater, the latter two are together called Leptomeninges.<sup>1</sup> Subarachnoid space (SAS) is the space between the arachnoid and Pia mater and is fluid-filled space associated with the meninges. The SAS surrounds the brain and contains cerebrospinal fluid (CSF) and blood vessels.<sup>2</sup>

### Infectious meningitis

Infectious meningitis (IM) is an infectious disease primarily of the SAS causing inflammation of the leptomeninges, characterized by serious illness.<sup>3</sup> IM can be caused by bacteria, mycobacteria, viruses, or, in rare cases, fungi.<sup>4</sup> It is associated with high morbidity and mortality as it causes significant problems of diagnosis and management.<sup>5</sup> Early diagnosis is key to initiate appropriate therapy, avoid complications, and improve prognosis.<sup>6</sup>

### Clinical features

Headache, drowsiness, fever, and neck stiffness are the usual presenting features. In severe bacterial meningitis, the patient may be presented with an altered mental status or even be comatose.<sup>7</sup> On examination, nuchal rigidity is observed in up to 90% of patients and may persist for several weeks despite clinical improvement. A positive Kernig's and Brudzinski's sign may be elicited in patient with meningitis. Increased

intracranial pressure may lead to severe hypertension, bradycardia, photophobia, papilledema, and cranial nerve palsies.<sup>7,8</sup>

### Diagnosis

CSF analysis which is done by lumbar puncture (LP) include: (cytological and biochemical), Gram-stain, and culture constitute an important diagnostic method in IM.<sup>9</sup> The cornerstone for the diagnosis of meningitis remains a positive CSF Gram stain, and culture, and additional support for the diagnosis can be based on positive blood cultures (50% cases), a positive throat swab (in cases of *N. meningitidis*), CSF biochemical analysis, and the PCR of blood or CSF.<sup>5</sup>

### Neuroimaging

Neuroimaging is performed in patients who present with evidence of head trauma, sinus or mastoid infection, skull fracture, and congenital anomalies to look for conditions that may predispose them to bacterial meningitis. Also, neuroimaging studies are useful to identify and monitor complications of meningitis.<sup>10</sup> Routine contrast-enhanced brain MRI including contrast enhanced-T1 spin-echo sequence (CE-T1SE) is a sensitive modality for the identification of IM as it helps detect the presence and extent of inflammatory changes in the meninges, as well as complications. Diffuse enhancement of the SAS is characteristic of IM but not specific.<sup>11-12</sup> An immediate imaging after the intravenous injection of contrast material can help depict abnormal meningeal enhancement (ME) and facilitate the

diagnosis of early meningitis. ME is nonspecific for IM; it may be caused by hemorrhage, neoplasm, sarcoidosis, and other non-infectious inflammatory disorders.<sup>13</sup>

### MRI Physics

Fluid attenuation inversion recovery (FLAIR) is an inversion recovery pulse sequence with a very long time of repetition (TR) and time of echo (TE), with an inversion time (TI) values of 2000-2500 ms. Gadolinium (Gd) is a contrast medium frequently used during MRI examinations; it mainly affects T1 relaxation time (makes it shorter) and T2 relaxation time (also makes it shorter but to a lesser extent than T1) of the tissues in which it has concentrated.<sup>(14)</sup> Leptomeningeal enhancement occurs by contrast leakage from vessels into the CSF in the sulci and basal cisterns.<sup>(15)</sup> The T2 shortening effect of Gd inversely proportional to Gd concentration resulting in increased contrast to noise ratio of the obtained image.<sup>(16)</sup>

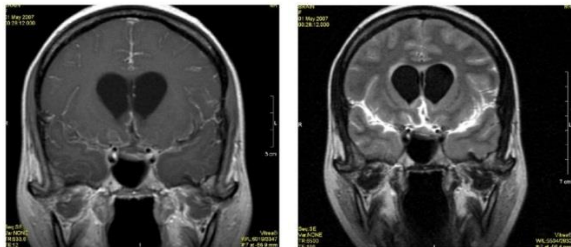
Contrast enhanced (CE)-FLAIR images, unlike CE-T1 Weighted images (WI), do not show contrast enhancement in normal vascular structures and normal meninges.<sup>(17)</sup>

Consequently, CE-FLAIR images are very efficient in the revelation of meningeal or sulcal infective processes, inflammatory reactions, and metastases that border on the CSF. However, FLAIR sequence should be performed with both pre- and post-contrast scans because the hyper intense lesion observed, in CE-FLAIR imaging alone, may be due to either T1 shortening or T2 lengthening, so restrict the utility of FLAIR sequence.<sup>(18)</sup>

FLAIR sequence has long TI, this causes shortening of T1 and results in enhancement on the heavily T2 weighted images; thus, lesions that show enhancement on CE-T1WI also show enhancement on CE-FLAIR images. On T2-FLAIR images, the post-gadolinium enhancement occurs because of the T2- prolongation effect of various lesions and T1-shortening effect of gadolinium acting in synergism.<sup>(19)</sup>

### Aim of the study

To evaluate the efficiency of the CE-FLAIR sequence compared with CE-T1 SE sequence in the diagnosis of infectious meningitis.



**Figure 1:** MRI of a 35-year-old male patient presented with high-grade fever and vomiting. Left: Post contrast T1 WI shows only dilated ventricles with no evidence of meningeal enhancement. Right: Post contrast FLAIR image shows the enhancement of meninges at tentorium and in the parietal region with evidence of dilated ventricles.<sup>20</sup>

### Patients and Methods

This is a prospective analytical study of diagnostic tests. Informed oral consent was taken from all patients after explaining to them the study's purpose and procedure. Sixty-seven patients, clinically suspected to have bacterial meningitis, were referred to the department of radiology / MRI units (of AL-Imamain AL-Kadhimain Medical City), from November 2018 till December 2019 for brain MRI examination.

### Inclusion criteria

Patients who were clinically assessed by a specialist neurologist or by internal physician and suspected to have infectious meningitis.

### Exclusion criteria

1. Pediatric age group that needs general anesthesia
2. Contraindications to MRI examination
3. Contraindications to contrast media
4. History of recent attack of treated meningitis
5. MRI findings of other conditions such as subarachnoid hemorrhage

Those patients presented with symptoms and signs suggestive of infectious meningitis, were sent for brain MRI examination. The history of each patient was reviewed, and they were asked about the following: any possible contact with a patient having infectious meningitis or active pulmonary tuberculosis, impaired renal function, claustrophobia, or a history of contrast allergy, and the presence of metallic implants in their bodies. Eleven patients were excluded (three with metallic implants, two with claustrophobia, three with high renal indices, one with a history of contrast allergy, one with a history of recent attack of meningitis, and one with MRI findings of subarachnoid hemorrhage). There, CE-MRI examination was done for the remaining 56 patients who represent the sample of the study. The final diagnosis of meningitis was based on CSF analysis (biochemistry, cytology, gram stain, culture and sensitivity), which was done after performing MRI examination.

MRI examination was performed on a 3Tesla system (**PHILIPS** – MR Systems Achieva – Nederland, using a SENSE Head coil). The examination protocol includes the following MRI sequences: T2W-TSE axial, T2W-FLAIR coronal, DWI axial, T1W-SE axial, post-contrast T1W axial and post-contrast T2W-FLAIR axial and coronal. The post-contrast sequences were done immediately after administering the contrast, and post-contrast T1W axial was done before post-contrast T2W-FLAIR axial and coronal.

**Table 1:** Parameters of T1-SE and T2-FLAIR sequences.

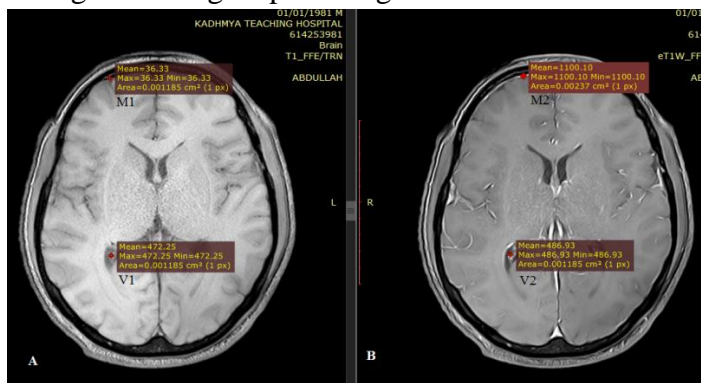
Parameter	T1-SE	T2-FLAIR
Plane: pre-contrast	axial	coronal
Plane: post-contrast	axial	coronal and axial
TR (ms)	259	11000
TE (ms)	4.6	120
FOV(mm)	230x214x143	230x184x177
section thickness (mm)	5	4
Slice gap (mm)	1	3
Slices number	24	22
Acquisition matrix	400x298	270x139
Voxel size (mm)	5x0.72x0.57	4x1.48x.96
Scan percentage (%)	80.1	71.9
Acquisition time (min.)	01:18:1	01:39:0

Gadolinium was used as contrast material, given intravenously by direct injection in a dose of 0.1 ml/kg body weight.

For each patient, images from all MRI sequences were assessed both qualitatively and quantitatively on a monitor in separation. Then, the pre-contrast and post-contrast images for T1W-SE and T2-FLAIR sequences were displayed and assessed simultaneously by using the cross-linking maneuver accessible in MRI software applications.

The quantitative estimation was done by taking the single pixel signal intensities

(SPSI) in the regions of meningeal or vascular enhancements. The SPSI were obtained in the exact region of interest (ROI) by placing a cursor at the same table positions using customized co-registration software in both the pre- and-post contrast T1WI and FLAIR sequences. This was done in the meninges at either basal cisterns or cortical sulci between the pre- and post-contrast sequences to calculate the basal and leptomeningeal enhancements. An average of two measurements was taken. The average vascular enhancement was similarly calculated at the intraventricular vascular choroid plexus. The above two values were subtracted to obtain the net leptomeningeal enhancement. The statistical comparison of the meningeal and vascular enhancement between the CE-T1W and CE-FLAIR sequences was then made. The net meningeal enhancement (NME) is the difference between the meningeal enhancement (ME) and vascular enhancement (VE).<sup>21</sup>

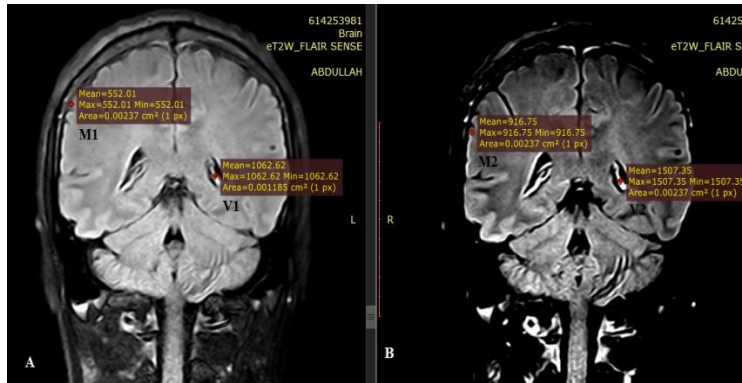


**Figure 2:** An example from the current study cases showing the site of measuring meningeal and vascular signal intensities

(SI) in T1 WI. A: pre-contrast T1 WI (axial). M1: pre-contrast meningeal SI, V1: pre-contrast vascular SI. B: post-contrast T1 WI

(axial) M2: post-contrast meningeal SI, V2: post-contrast vascular SI. M1 and M2 are measured at frontal cortical sulci, while V1

and V2 are measured at the choroid plexus in the occipital horns of lateral ventricles.



**Figure 3:** An example from the current study cases depicting the site of measuring meningeal and vascular signal intensities (SI) in FLAIR images. A: pre-contrast FLAIR (coronal). M1: pre-contrast meningeal SI, V1: pre-contrast vascular SI. B: post-contrast FLAIR (coronal). M2: post-contrast meningeal SI, V2: post-contrast vascular SI. M1 and M2 are measured at frontal cortical sulci, while V1 and V2 are measured at the choroid plexus in the occipital horns of lateral ventricles.

### Qualitative evaluation:

Two expert radiologists evaluated the images in all sequence independently, those experts were masked to all patients' information including: clinical features, radiological information and CFS analysis results. All interpretations done by on-site investigators and the evaluated images should be technically adequate. The images of pre and post contrast FLAIR and T1-SE sequences were separately, evaluated by visual inspection by the two expert

radiologists and attention was concentrated on the following features: existence or nonappearance, the position and the extent of abnormal leptomeningeal enhancement. Positive or negative results were documented on a previously prepared form. By the same method, T1WI (before and after Gd contrast) were evaluated. Later, after administration of Gd, images from T1 SE and FLAIR sequences were compared together by the same experts depending on the same imaging criteria, the findings were documented on a separate proforma as: (F: CE-FLAIR is superior, E: sequences equal, T: CE-T1W is superior).

### Statistical analysis

Each patient assigned a serial identification number. The data were possessed, arranged and stated into presentation software using Statistical Package for Social Sciences (SPSS) version 20 for evaluation. Categorical variables were

presented in frequency and percentages. Continuous variables were presented by mean and standard deviation. Chi squared test and its subtypes were used to study the association between categorical variables. Continuous variables were examined for normality of their distribution. If normality criteria were violated, nonparametric tests were used to investigate and test hypotheses. The level of significance of P- value was set to be 0.05. Lower values were considered significant. To measure the magnitude of agreement of two radiologists reading sets, Kappa agreement coefficient was used. Cohen (American statistician) suggested the Kappa result be interpreted as in the following table: <sup>(21)</sup>

Table 2: Interpretation of Kappa value for interobserver agreement

Kappa value	Interpretation
≤ 0	No agreement
0.01– 0.20	Slight agreement
0.21–0.40	Fair agreement
0.41– 0.60	Moderate agreement
0.61–0.80	Substantial agreement
0.81–1.00	Almost perfect agreement

## RESULTS

This study had a sample of 56 patients, including 31 (55.35%) males and 25

(44.65%) females. They were aged between 15 and 68 years with mean ± SD = 39.40 ± 13.68 in years.

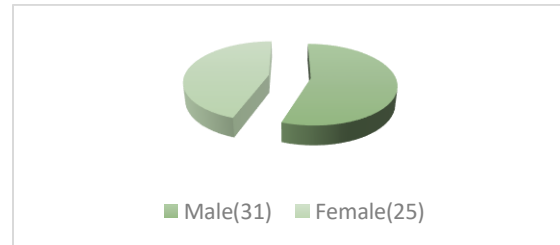


Figure 4: Pie chart showing the gender composition of the sample

The final diagnosis of infectious meningitis was made based on CSF analysis that showed that 41(73.21%) patients were affected (CSF positive), and the remaining 15 (26.79%) patients were not affected (CSF negative), as illustrated in the following figure.

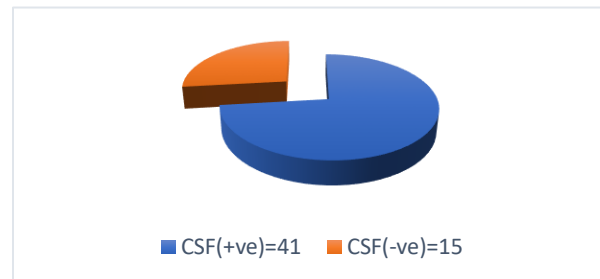


Figure 5: Pie chart showing the results of CSF analysis of the sample

Table 3: Basic characteristics

	Male (N = 31)	Female (N = 25)	P value
Age (mean ± SD) in years	36.42 ± 14.53	42.36 ± 12.83	0.115*
Positive CSF	23 (74.2%)	18 (72.0%)	0.854**
Positive CE-FLAIR	22 (71.0%)	18 (72%)	0.932**
Positive CE-T1 SE	17 (54.8%)	14 (56.0%)	0.931**

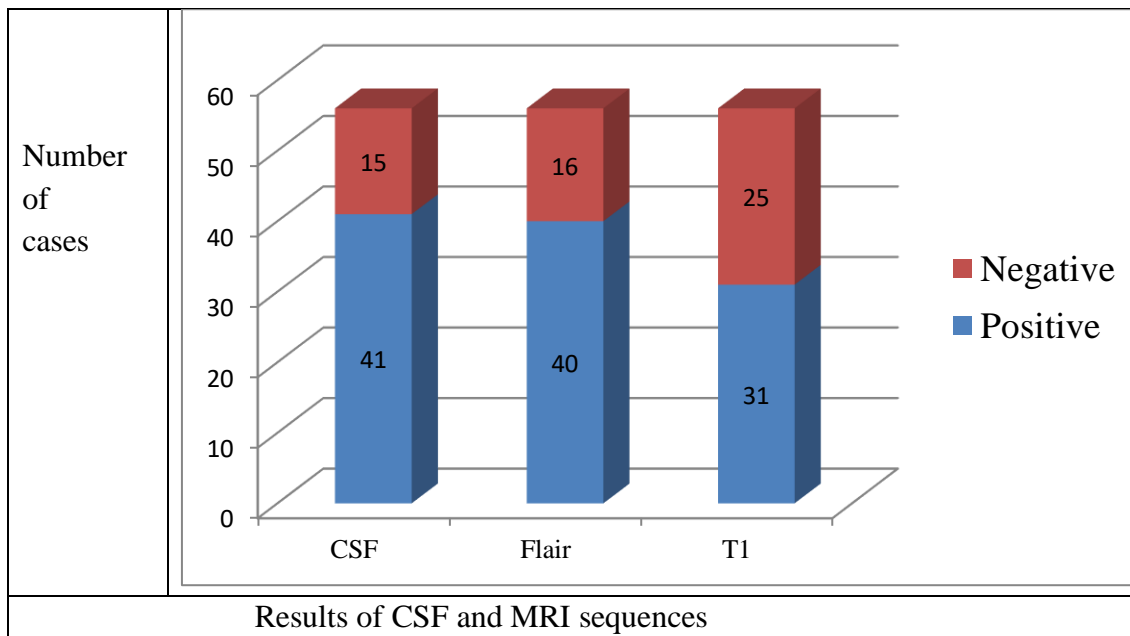
\*Student's t-test

\*\*Chi-squared test

This table suggests the following:

- 1- The mean age does not show a significant statistical difference between male and female patients (P value >0.05).
- 2- The distribution of the results regarding CSF, CE-FLAIR and CE-

T1 SE does not show a significant statistical difference between male and female patients (P value >0.05). This means that the results of CSF analysis and MRI examination are not related to gender of patients.



**Figure 6:** Bar chart showing the results concerning CSF, CE-FLAIR, and CE-T1-WI

**1) Diagnostic validity**

**Table 4:** Distribution of the results of CE-FLAIR in comparison with CSF

		CSF		Total
		Positive	Negative	
CE-FLAIR	Positive	35	5	40
	Negative	6	10	16
	Total	41	15	56

This table shows that out of the 41 'CSF-positive' patients, 35 were positive by CE-FLAIR, whereas the remaining 6 showed negative results; meanwhile, only 5 out of the 15 'CSF-negative' patients were positive by CE-FLAIR, whereas the other 10 showed negative results. Validity parameters,

predictive values, and the overall accuracy of CE-FLAIR were calculated: high sensitivity (85.36%), 66.66% specificity, high PPV (87.5%), 62.5% NPV, and overall accuracy of 69.23%.

**Table 5:** Distribution of the results of CE-T1 SE in comparison with CSF

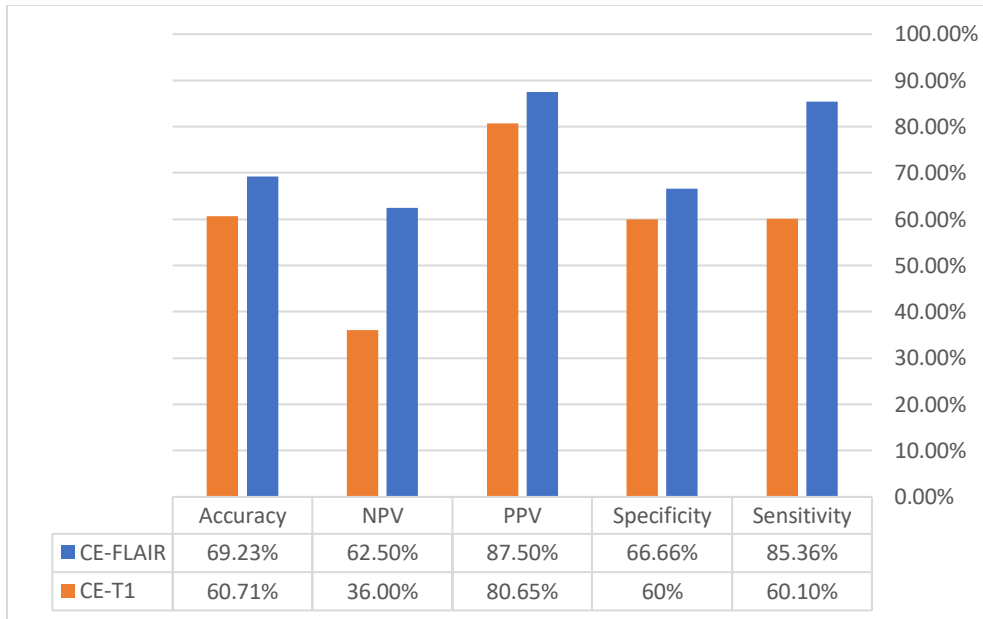
		CSF		Total
		Positive	Negative	
CE-T1 SE	Positive	25	6	31
	Negative	16	9	25
	Total	41	15	56

This table shows that out of the 41 CSF-positive patients, 25 were positive by CE-T1, while the remaining 16 showed negative



results; meanwhile, only 6 out of the remaining 15 CSF-negative patients were positive by CE-T1, whereas the other 9 presented negative results. Validity parameters, predictive values, and the

overall accuracy of CE-T1 were calculated; 60.1% sensitivity, 60% specificity, 80.65% PPV, 36% NPV, and overall accuracy of 60.71%.



**Figure 7:** Bar chart showing the comparison of validity parameters, predictive values, and the overall accuracy of both CE-FLAIR and CE-T1 sequences.

This figure suggests that CE-FLAIR is better than CE-T1 in all mentioned parameters; it

is more sensitive, more specific, and more accurate as well as having higher positive and negative predictive values. The extent to which it is better varies from parameter to another, with CE-FLAIR being best in NPV and the least in specificity.

## 2) Quantitative comparison

**Table 6:** Correlation of ME, VE, and NME between CE-FLAIR and CE-T1 SE.

	N	Mean	SD(+/-)	P value*	
CE-FLAIR ME	35	553.94	179.89	0.190	Not significant
CE-T1 ME	25	506.44	208.69		
CE-FLAIR VE	35	316.34	145.09	0.284	Not significant
CE-T1 VE	25	391.16	211.08		
CE-FLAIR NME	35	237.34	157.56	0.0001	Significant
CE-T1 NME	25	116.52	57.55		
CE-FLAIR ME	35	553.94	179.89	0.001	Significant
CE-FLAIR VE	35	316.34	145.09		
CE-T1 ME	25	506.44	208.69	0.001	Significant
CE-T1 VE	25	391.16	211.08		

\*Mann-Whitney test, ME = meningeal enhancement, VE = vascular enhancement, NME = net meningeal enhancement

This table indicates that the means and SD of ME, VE, and NME for CE-FLAIR (N = 35 patients who showed positive results) as well as the means and SD of ME, VE, and NME for CE-T1 (N = 25 patients who showed positive results) were calculated. A comparison was made by calculating the P-value of each similar two parameters. There is no significant difference in ME and VE

enhancement between CE-FLAIR and CE-T1 (P-value > 0.05). However, there is significant difference in the means of NME between CE-FLAIR and CE-T1 (P-value <0.05) with higher mean is present in FLAIR group. Also, the difference between ME and VE is significant in both CE-FLAIR and CE-T1 sequences with P-value <0.05 in both.

## 4) Qualitative comparison (Kappa analysis)

**Table 7:** Interobserver agreement between the two radiologists

		Radiologist 1			Total	Kappa	P value
		F	T	E			
Radiologist 2	F	15	0	1	16	0.778	0.0001
	T	0	5	0	5		
	E	0	2	2	4		
Total		15	7	3	25		

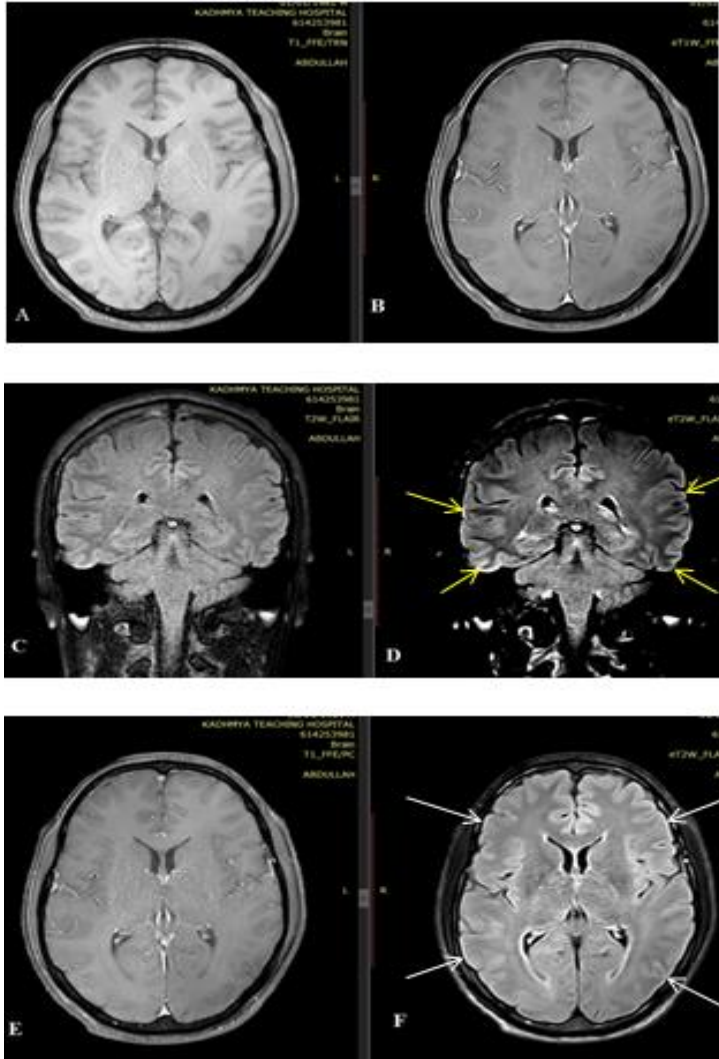
F (CE-FLAIR is superior to CE-T1)

E (Both FLAIR and T1 are equal)

T (CE-T1 is superior to CE-FLAIR)

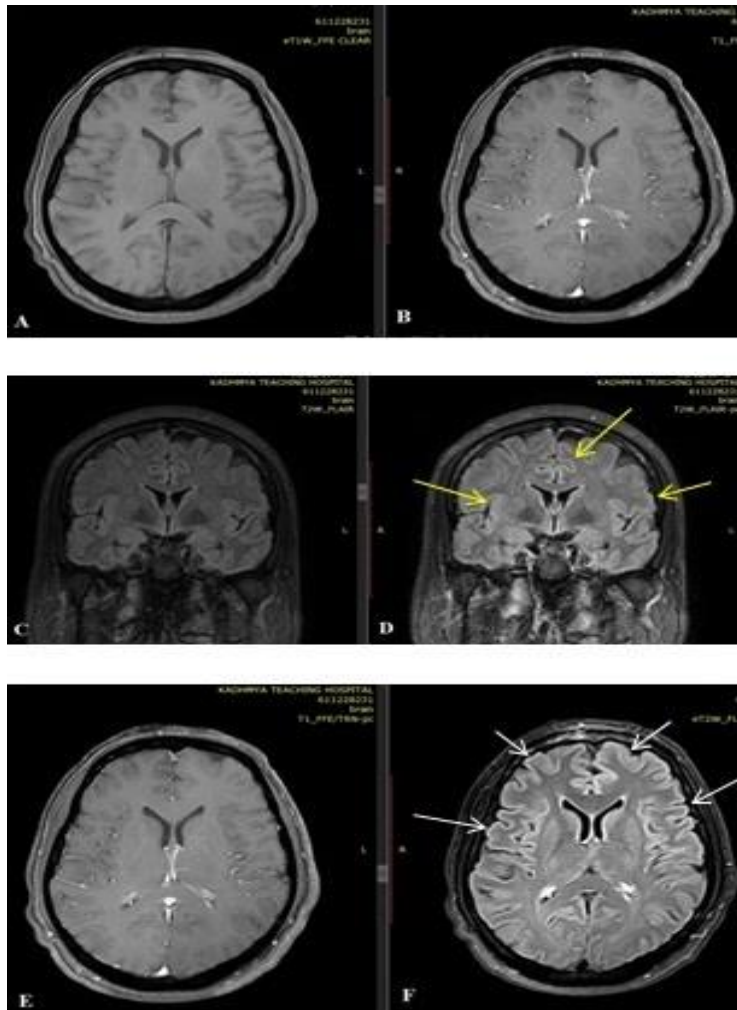
The two observers agreed on 15 F, 5 T, and 2 E readings for 22 out of 25 readings. The kappa agreement coefficient indicates substantial agreement (Kappa = 0.778) that proved significant (P value <0.05). So, there is substantial interobserver (between the two radiologists) agreement regarding the comparison of the findings between the two sequences (CE-FLAIR and CE-T1 SE) of MRI.

Cases from the current study:



**Figure 8:** MRI of a 39-year-old male patient presented with a five-day history of headache, fever, and photophobia with signs of meningism. A: precontrast axial T1WI, B: post contrast axial T1WI, C: precontrast coronal FLAIR, D: post contrast coronal FLAIR, E: post contrast axial T1WI. F: post contrast axial FLAIR. No leptomeningeal enhancement seen on post contrast T1 image (B) compared with precontrast T1 image (A). Evidence of leptomeningeal

enhancement in post contrast FLAIR image (D), as pointed by the yellow arrows, compared with precontrast FLAIR image (C). Leptomeningeal enhancement is prominent in both frontal, left occipital and right temporal surfaces in post contrast FLAIR image (F) as pointed by the white arrows, while no leptomeningeal enhancement seen in post contrast T1 image (E). CSF analysis result was positive.



**Figure 9:** MRI of a 49-year-old male patient presented with a ten-day history of headache, fever, and photophobia and vomiting in the last two days, with evidence of meningism on examination and a history of sinusitis. A: precontrast axial T1WI, B: post contrast axial T1WI, C: precontrast coronal FLAIR, D: post contrast coronal FLAIR, E: post contrast axial T1WI. F: post contrast axial FLAIR. No leptomenigeal enhancement seen on post contrast T1 image (B) as compared with precontrast T1 image (A). Evidence of leptomenigeal enhancement in post contrast FLAIR image (D), as pointed by the yellow arrows, compared with precontrast

FLAIR image (C). Prominent bilateral fronto-parietal leptomenigeal enhancement in post contrast FLAIR image (F) as pointed by the white arrows, while no leptomenigeal enhancement seen in post contrast T1 image (E). CSF analysis result was positive.

## DISCUSSION

Infectious meningitis is a serious infection of the meninges with poor prognosis if untreated properly, early and proper diagnosis is vital for a better clinical outcome. CSF analysis still represents the gold standard for the definite diagnosis,

done by LP which is an invasive procedure with many possible complications. <sup>(22)</sup>

Neuroimaging plays a vital role in identification of IM especially in cases where the viruses and mycobacteria tuberculosis are the causative agents, as CSF analysis can be either non-conclusive or

need a longer period to show the results of culture. <sup>(22)</sup> However, non-enhanced MRI may be unremarkable in patients with uncomplicated acute IM. <sup>(23)</sup> Conventional MRI sequences, including CE-T1WI, are routinely performed for diagnosis of IM. <sup>(20)</sup>

Table 8: The demographic characters of this study sample compared with Rajiv A. et al study <sup>(24)</sup> and Aneel K.V. et al <sup>(20)</sup> study.

Character	This study	Study by Rajiv et al.	Study by Aneel et al.
Total patients	67	65	65
Excluded	11	5	8
Sample size	56	60	57
Age (range)	15 to 68 y.	2 to 91 y.	1 m.to 75 y.
Age(mean ± SD	39.40 ± 13.68	27.3 ± 19	30.65 ± 21.25
Male	31(55.35%)	28(46.67%)	30 (52.6%)
Female	25(44.65%)	32(53.33%)	27 (47.4%)
CSF (-VE)	15	10	7
CSF(+VE)	41 (73.21%)	50 (83.33%)	50 (87.72%)

The minor differences in age range, age mean and gender composition between the three studies may be due to different life styles, races, ethnicities, and different countries where the studies were carried out and this may explain the difference in the numbers of excluded patients related to the cause. In this study, the number of patients showing positive results of CSF analysis is lower than in Rajiv A. et al <sup>(24)</sup> and Aneel K.V. <sup>(20)</sup> studies; the explanation for this could be due to by technical variations and availability of facilities.

Table 3: displays no significant correlation between sex distribution and positive results of CSF, CE-T1, CE-FLAIR examination, which could be explained by the fact that contracting IM does not depend on sex and

the pathophysiology of the disease is not different between the two genders.

Table 9: comparison of (sensitivity, specificity, PPV, NPV and accuracy) between the current study and Aneel K. et al study. <sup>(20)</sup>

Study Parameter	Study			
	Current Study		Study by Aneel et al.	
	CE-FLAIR	CE-T1	CE-FLAIR	CE-T1
Sensitivity	85.36%	60.1%	96%	68%
Specificity	66.66%	60%	85.71%	85.71%
PPV	87.5%	80.65%	97.9%5	97%.14
NPV	62.5%	36%	75%	27.27%
Accuracy	69.23%	60.71%	94.73%	70.17%

Results of this study are comparable to what Aneel K. et al <sup>(20)</sup> found regarding sensitivity, NPV and diagnostic accuracy (higher in CE-FLAIR compared with CE-T1 but with a different extent between them),

this could be explained as FLAIR sequence lets on a better discrimination between the meninges and the cortical veins, as cortical veins show less enhancement FLAIR images. In this study, there is slight difference in specificity and PPV between the two sequences (higher in CE-FLAIR) while Aneel K. et al <sup>(20)</sup> showed similar specificity and PPV of the two sequences possibly because of no difference in

meningeal enhancement in CSF negative patients and so, the affection of FLAIR on cortical veins will be minor making no obvious leptomeningeal enhancement to be detected in both sequences. Also, Allesandra et al <sup>(23)</sup> study (carried out at 2005) showed higher sensitivity of CE-FLAIR compared with CE-T1WI as our study results but similar specificity of the two sequences.

Table 10: comparison of quantative parameters (ME, VE and NME) between our study and Armmen A. et al study <sup>(22)</sup>

	This study		Study by Armmen et al.		Comparison
	Mean	P-value	Mean	P-value	
ME FLAIR	553.94	Not significant	106.48	Significant	Not comparable
ME T1	506.44		155.91		
VE FLAIR	316.34	Not significant	17.33	Significant	Not comparable
VE T1	391.16		192.57		
NME FLAIR	237.34	Significant	89.14	Significant	Comparable
NME T1	116.52		-36.19		
ME FLAIR	553.94	Significant	106.48	Significant	Comparable
VE FLAIR	316.34		17.33		
ME T1	506.44	Significant	155.91	Not significant	Not comparable
VE T1	391.16		192.57		

Quantative comparison between CE-FLAIR and CE-T1 sequences showed that:

In the present study, ME in CE-FLAIR was non-significantly higher than in CE-T1 and this is incomparable with Armmen A. et al study. <sup>(22)</sup> The VE in CE-FLAIR compared with CE-T1 was not significant while this was significant in Armmen A. et al study <sup>(22)</sup> with higher mean value of the latter, this could be explained by the different parameters used and possibility of technical differences while the higher mean value of CE-T1 is due to the fact that small blood

vessels are not enhanced on FLAIR sequence.

In the present study, NME in CE-FLAIR was significantly higher than in CE-T1 and this is comparable with the results of Armmen A. et al study <sup>(22)</sup>, and this is explained by the small vessels are not enhanced by FLAIR sequence making the visibility of enhanced Leptomeninges better in CE-FLAIR. Also, Rajiv A. et al <sup>(24)</sup> showed same results in their study.

In the present study, ME-FLAIR is significantly higher than VE-FLAIR and this

is comparable with Armmen A. et al study.  
(22)

However, ME-T1 is significantly higher than VE-T1 but this is incomparable with what Armmen A. et al (22) found in their study, possible explanation for that are technical differences.

Regarding the qualitative evaluation, table (3-5) showed that; there is substantial interobserver agreement about comparison of the findings between the two sequences (CE-FLAIR and CE-T1 SE) of MRI. The two readers agreed on 23 out of 25 readings. They agreed on that; in 15 cases visibility leptomenigeal enhancement is better on CE-FLAIR than on CE-T1 sequences, the reverse preference in five cases and equivocal in two only. This means that qualitatively, the leptomenigeal enhancement is better seen on CE-FLAIR than CE-T1 which reconfirms the results obtained by quantative evaluation, but no previous study found to be compared with it.

## LIMITATIONS

1. SPSI analysis is not automated and has intra- and inter-observer variability in the accurate placement of the ROI, this can be minimized by increasing experience in working with software.

2. The use of qualitative assessment is subject to some intra-observer and inter-observer biases and may lead to variable interpretations. The experience of the radiologists limits biases.

## CONCLUSIONS

1. The CE-FLAIR sequence has higher sensitivity, specificity, and diagnostic accuracy compared with the T1-SE sequence in the diagnosis of infectious meningitis.
2. The CE-FLAIR sequence is able to unequivocally differentiate meningeal enhancement from vascular enhancement.
3. Overall, CE-FLAIR is better than CE-T1SE in the early detection of infectious meningitis.

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