ORIGINAL ARTICLE

Diagnostic Accuracy of Contrast Enhanced Flair Magnetic Resonance Imaging in Diagnosis of Meningitis Taking Lumbar Puncture as Gold Standard

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ABSTRACT

Objective: The objective of this article is to determine and compare the diagnostic accuracies of contrast enhanced FLAIR and T1W sequences of MRI brain in the detection of meningitis keeping lumbar puncture as gold standard.

Study Design: Cross-sectional validation study.

Place and Duration of Study: The study was carried out at Department of Diagnostic Radiology of POF Hospital, Wah Cantt from 23rd June 2019 to 22nd March 2020.

Materials and Methods: A total of 173 patients were included in the study by non-probability purposive sampling. Patients of age between 2-70 years, of either gender with suspected meningitis based on clinical presentation are included in our study. Patients in whom contrast enhanced MRI and lumbar puncture was contraindicated, diagnosed patient of meningitis and non-consenting patients were excluded from this study. All patients received intravenous contrast medium gadolinium at rate of 0.2 ml/second. Post gadolinium T1W and post gadolinium FLAIR images were acquired and evaluated by a consultant radiologist**.** Findings were recorded on a prescribed performa. Patients were followed and results of lumbar puncture were collected from laboratory.

Result: The mean age was 26.4±23.5 year ranging from 2 to 70 years. Out of 173 patients, 98 patients (56.6%) were male and 75 patients (43.4%) were female. Clinical presentations were as follows: poor feeding, irritability and lethargy 86 (49.7%), headache 137 (79.2%), nausea/vomiting 125 (72.3%), neck stiffness 89 (51.4%), altered level of consciousness 132 (76.3%), seizures 78 (45.1%) and local neurological deficit 45 (26%). Diagnostic accuracy of contrast enhanced MRI FLAIR in diagnosing meningitis taking lumbar puncture gold standard showed sensitivity 91%, specificity 85%, PPV 87.6%, NPV 89.4% and diagnostic accuracy 88.4%. Diagnostic accuracy of contrast enhanced MRI T1W in the diagnosis of meningitis taking lumbar puncture gold standard revealed sensitivity 60.2%, specificity 77.5%, PPV 75.6%, NPV 62.6% and diagnostic accuracy 68.2%.

Conclusion: The sensitivity and specificity of post contrast FLAIR sequence is greater as compared to post contrast T1W sequence to detect meningeal enhancement. Therefore, for all patients with suspicion of meningitis, post contrast FLAIR sequence should be added to MRI brain protocol as a routine sequence.

Keywords*: Contrast Enhanced Flair Magnetic Resonance Imaging, Diagnostic Accuracy, Lumbar Puncture, Meningitis.*

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Introduction

Meningitis is inflammation of the meninges. Disease process is usually not only confined to the meninges only, but also involves brain (encephalitis), ventricles (ventriculitis) and spinal cord (myelitis). It mostly affects children under 5 years and adults above 60 years of age.[1] In Pakistan prevalence of bacterial meningitis is 1.57% and it is leading cause of childhood morbidity.[2]

It can be bacterial including tuberculous (70%), viral (24%) and fungal (6%).[2] Neisseria meningitidis and streptococcal pneumoniae are the most common causes of acute bacterial meningitis (ABM) in developed countries.[3]

Acute bacterial meningitis is associated with significant mortality and neurological morbidity. If left untreated, death results in 100 % of cases and delay in treatment in first few hours of presentation increases the risk of death by 8.4-fold. Its incidence is 5-7 per 100,000 population with mortality rate of 5-10%. 20% of survivors worldwide suffer from permanent neurological deficit.[2,3]

As acute bacterial meningitis is a life-threatening emergency, so early diagnosis and prompt treatment is mandatory. Clinical symptoms vary according to age of patient and duration of disease. Diagnosis is made by history and physical examination and confirmed on lumbar puncture.[3,4]

Most common neurological squeals are neurological impairment, hearing loss, cognitive impairment and epilepsy.[5]

Magnetic resonance imaging (MRI) has been used mostly to detect the complications of meningitis, but nowadays it has also been recommended for diagnostic purposes.[6] Although computed tomography (CT) scans and MRI both detect intracranial infections but MRI is superior due to its ability to show soft tissue details, lack of bone artifacts and its multiplanar capability. Gadolinium enhanced MRI is more sensitive and specific to detect meningeal enhancement as compared to contrast enhanced CT scans.[2]

Post contrast T1W MRI sequences are being traditionally used to diagnose several intracranial pathologies including CNS infections. But in the last decade, post contrast FLAIR sequences have been proved to be superior to post contrast T1W sequences to detect meningeal enhancement due to dark CSF signal, faint vascular enhancement and early meningeal enhancement at low dose of gadolinium.[7] The sensitivity and specificity of post contrast FLAIR sequences is 95.3% and 83.3% respectively as compared to post contrast T1W sequences which shows the sensitivity and specificity 76.6% and 75% respectively taking findings of lumbar puncture as gold standard.[8] Prevalence of meningitis is reported 78% in this study.[8]

Despite the fact that meningitis is very common in Pakistan, very limited local literature is available on the importance of post contrast FLAIR MRI in early detection of meningitis. The aim of our study is to investigate whether post contrast FLAIR sequence of MRI is better than post contrast T1W sequence and comparable alternative to lumbar puncture to diagnose meningitis.

Materials and Methods

It is cross-sectional validation study conducted in Department of Diagnostic Radiology, POF Hospital, Wah Cantt over a period of nine months from 23rd June 2019 to 22nd March 2020. Sample size of 173 cases was calculated from WHO calculator with confidence level 95%, taking prevalence of meningitis as 78% [8] and sensitivity and specificity of post contrast FLAIR MRI as 95.3% and 83.3% respectively.[8] Lumbar puncture was taken as gold standard. Sampling technique was non probability purposive sampling. Patients of age between 2-70 years, of either gender with suspected meningitis based on clinical presentation were included in our study. Patients in whom contrast enhanced MRI and lumbar puncture is contraindicated, diagnosed patients of meningitis and non-consenting patients were excluded from study.

Data Collection Procedure

The study was carried out after institutional ethical committee approval. Patients fulfilling the inclusion criteria were included in study after obtaining their consent. A questionnaire regarding history of selected patients was completed as shown in participant flow chart (figure 1). MRI scan of brain from the vertex to base of the skull of all the participants was performed by using Tesla 1.5 MR unit Syngo.via Siemens medical system, Germany. Imaging parameters for post contrast T1W imaging were: TR: 500, TE: 7.8, FOV: 230mm, image matrix: 224x 256, slice thickness: 5mm, slice interval: 1.5mm, phase encoding direction, and R to L and acquisition time: 3 min 48 seconds. Imaging parameters for post contrast FLAIR imaging were: TR: 9000, TE: 109, TI: 2500, FOV: 230m, image matrix: 224x256, slice thickness: 5mm, slice interval: 1.5mm, phase encoding direction, and R to L and acquisition time: 2 min 08 seconds. All patients received intravenous contrast medium gadolinium (dose was adjusted according to patient body weight) at rate of 0.2 ml/second (by computer-controlled injector). Post contrast T1W and post contrast FLAIR images were acquired and evaluated by consultant radiologist. Findings were recorded on Performa. Patients were followed and results of lumbar puncture were collected from laboratory.

Data Analysis Procedure

Data were entered and analyzed using SPSS version 23. Descriptive statistics were calculated for qualitative variables. For qualitative variables frequency and percentage was calculated. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of CE FLAIR and CE T1W Sequence of MRI was calculated by 2x2 table (Table A1) taking LP as gold standard. Receiver operator curve (figure 2) was formed. All results were presented as tables.

TABLE A1: 2x2 Table

	Meningitis on LP	**Meningitis not proven on LP**
Meningitis on CE MRI FLAIR Test positive	True positive	False positive
No meningitis on CE MRI FLAIR Test negative	False negative	True negative
Meningitis on CE MRI T1WI Test positive	True positive	False positive
No meningitis on CE T1WI FLAIR Test negative	False negative	True negative

For CE MRI FLAIR:
Sensitivity: TP/ (TP + FN) *100
Specificity: TN/ (TN+ FP) *100
PPV: TP/ (TP + FP) *100
NPV: TN/ (TN + FN) *100
For CE MRI T1W:
Sensitivity: TP/ (TP + FN) *100
Specificity: TN/ (TN+ FP) *100
PPV: TP/ (TP + FP) *100
NPV: TN/ (TN + FN) *100

Results

Diagnostic accuracy of contrast enhanced MRI FLAIR in diagnosis meningitis taking lumbar puncture gold standard showed sensitivity 91%, specificity 85%, PPV 87.6%, NPV 89.4% and diagnostic accuracy 88.4% (Table B1). Diagnostic accuracy of contrast enhanced MRI T1W in the diagnosis of meningitis taking lumbar puncture gold standard revealed sensitivity 60.2%, specificity 77.5%, PPV 75.6%, NPV 62.6% and diagnostic accuracy 68.2% (Table B2). The mean age was 26.4±23.5 years ranging from 2 to 70 years (table C1). Out of 173 patients, 98 patients (56.6%) were male and 75 patients (43.4%) were female (Table C2). Clinical presentations were as follows: poor feeding, irritability & lethargy 86 (49.7%), headache 137 (79.2%), nausea/vomiting 125 (72.3%), neck stiffness 89 (51.4%), altered level of consciousness 132 (76.3%), seizures 78 (45.1%) and local neurological deficit 45 (26%) (Table C3).

Table B1: Diagnostic accuracy of contrast enhanced MRI FLAIR in diagnosis of meningitis taking lumbar puncture gold standard

Contrast enhanced MRI FLAIR	Lumbar Puncture (Gold Standard)		Total
	Positive	Negative	
Positive	85 (TP) a	12 (FP) b	97
Negative	8 (FN) c	68 (TN)d	76
Total	93	80	173

Sensitivity: a/a+c x 100 91.0%
Specificity: d/d+b x 100 85.0%
Positive Predictive Value: a/a+b x 100 87.6%
Negative Predictive Value: d/c+d x 100 89.4%
Diagnostic accuracy: a+d/a+d+b+c x 100 88.4%

Key:

TP = True positive
FP = False positive
FN = False negative
TN = True negative

Table B2: Diagnostic accuracy of contrast enhanced MRI T1W in diagnosis of meningitis taking lumbar puncture gold standard

Contrast enhanced MRI T1W	Lumbar Puncture (Gold Standard)		Total
	Positive	Negative	
Positive/	56 (TP) a	18 (FP) b	74
Negative	37 (FN) c	62 (TN) d	99
Total	93	80	173

Specificity: d/d+b x 100 77.5%
Positive Predictive Value: a/a+b x 100 75.6%
Negative Predictive Value: d/c+d x 100 62.6%
Diagnostic accuracy: a+d/a+d+b+c x 100 68.2%

Key:

TP = True positive
FP = False positive
FN = False negative
TN = True negative

Table C1: Distribution of patients by age

Age (Year)	**Number**	**Percentage**
≤ 17	90	52.0
18-50	42	24.3
51-70	41	23.7
Total	173	100.00
Mean±SD	26.4±23.5	

Table C2: Distribution of patients by gender

Gender	Number	Percentage
Male	98	56.6
Female	75	43.4
Total	173	100.00

Table C3: Distribution of patients by clinical presentation

Clinical presentation	Number	Percentage
Poor feeding, irritability & lethargy	86	49.7
Headache	137	79.2
Nausea/vomiting	125	72.3
Neck stiffness	89	51.4
Altered level of consciousness	132	76.3
Seizures	78	45.1
Local neurological deficit	45	26.0

Note: Total is not 100% because of multiple responses

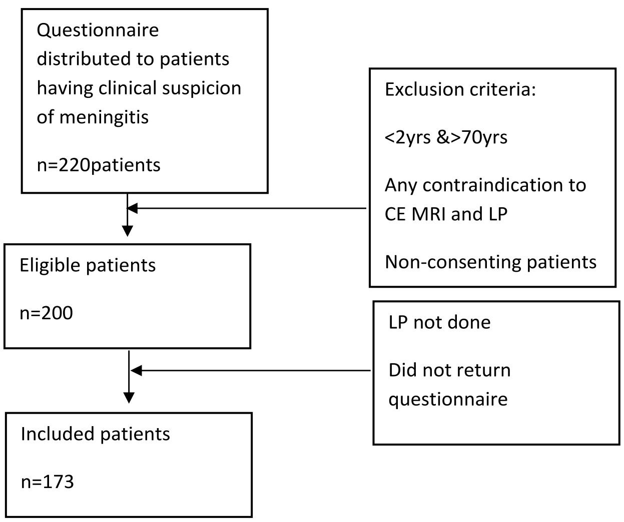

Fig 1: Participant flow diagram

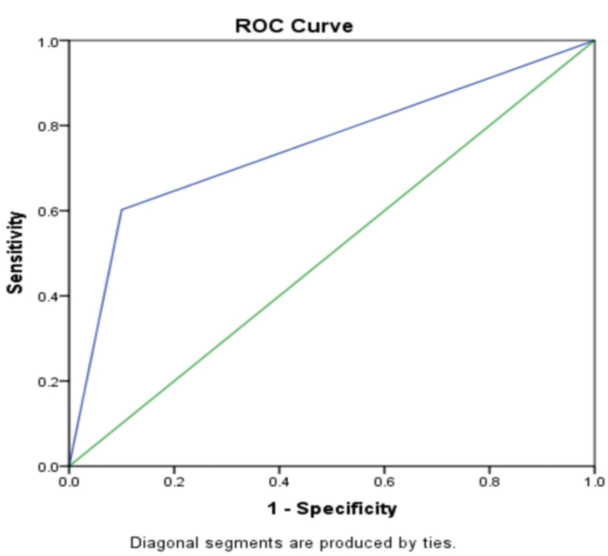

Fig 2: Receptor operative curve

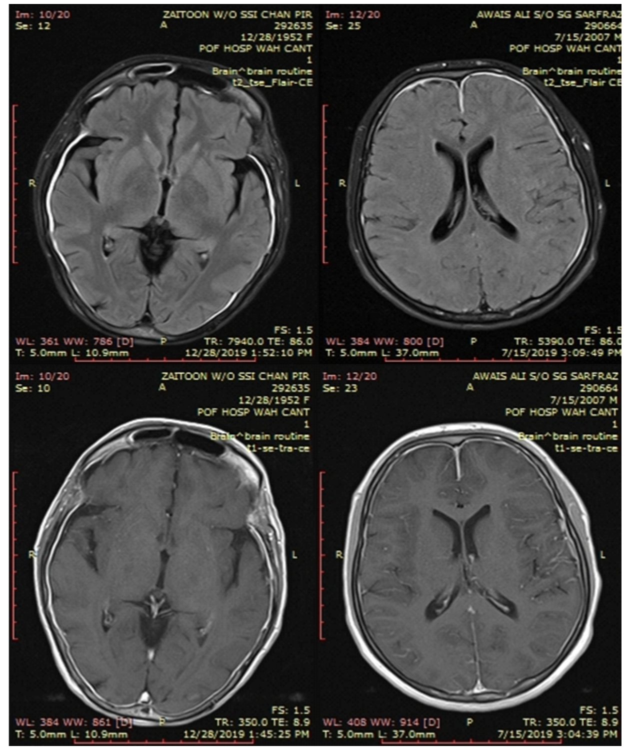

Fig 3: Pachymeningeal enhancement is noted along the bilateral cerebral hemispheres on post contrast FLAIR (above) and T1WI (below) images

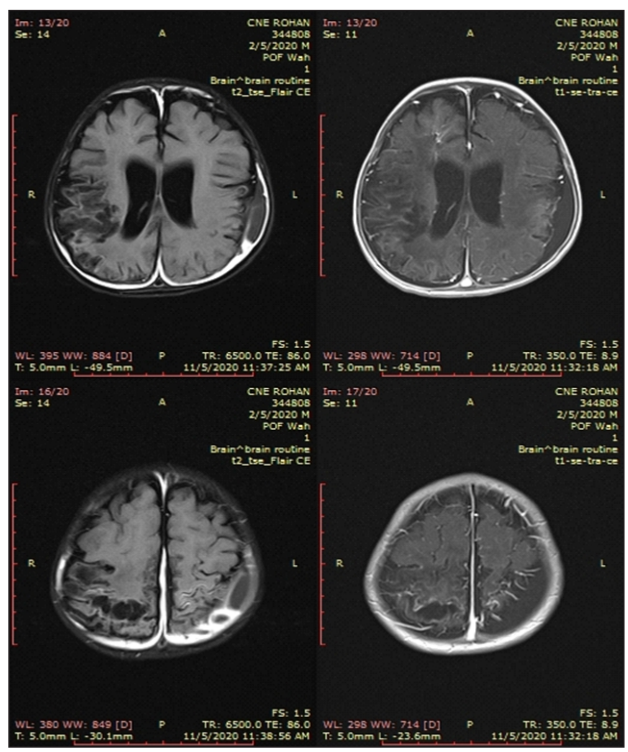

Fig 4: Left sided subdural collection and pachymeningeal Enhancement concerning for meningitis more marked on post contrast FLAIR (right) than on post contrast T1WI (left)

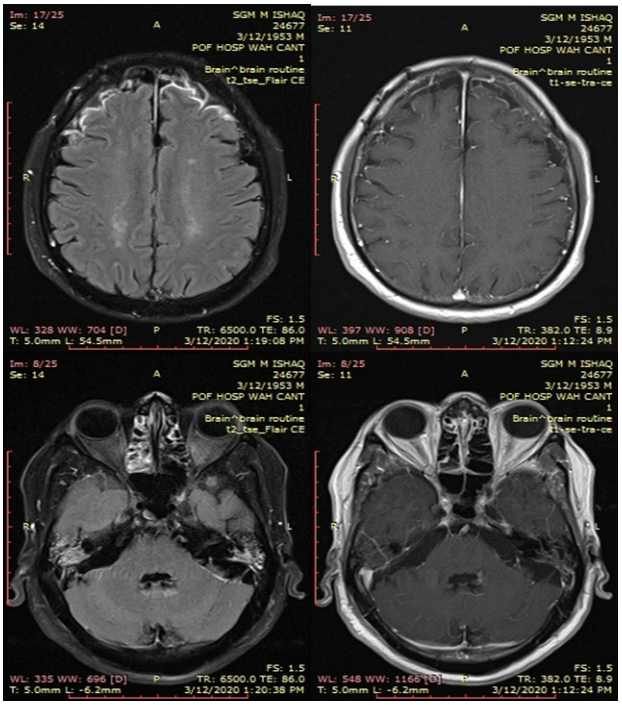

Fig 5: Vivid meningeal enhancement on post contrast FLAIR (right) sequence is seen as compared to T1WI (left) in subarachnoid space in bilateral frontal region and anterior to left cerebellar hemisphere

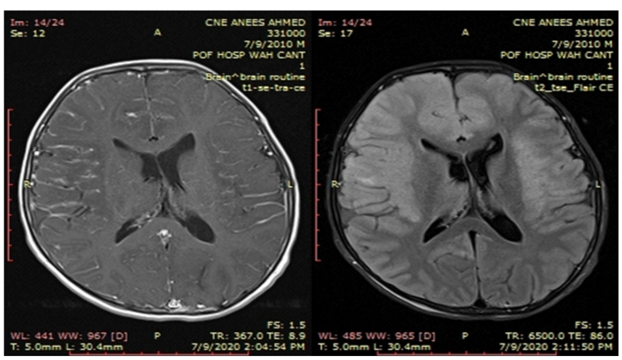

Fig 6: Swollen gyri of bilateral frontal and parietal lobe appear Isointense on T1WI (right) and hyperintense on FLAIR (left) with leptomeningeal enhancement (arrow) on post contrast T1WI images only

Discussion

In our study the sensitivity and specificity of contrast enhanced FLAIR was found to be 91% and 85%, respectively when compared with contrast enhanced T1W which revealed sensitivity 60% and specificity 90% taking lumbar puncture as gold standard. Our findings are consistent with a study carried out by Ahmed.[8] They demonstrated the sensitivity and specificity of contrast enhanced FLAIR sequences are 95.3% and 83.3% respectively after comparison with contrast enhanced T1W sequences, they showed the sensitivity and specificity 76.6% and 75% respectively taking results of lumbar as gold standard.[8] In our study, although most of the patient showed meningeal enhancement on both contrast enhanced FLAIR and T1WI sequences (figure 3), but avid enhancement was seen on contrast enhanced FLAIR (figure 4). Some patients showed meningeal enhancement on contrast enhanced FLAIR only (figure 5) and only a few patients show meningeal enhancement on contrast enhanced T1WI only (figure 6).

There were 12 patients included in our study as suspected meningitis but found to have other intracranial pathologies. Avid meningeal enhancement was seen on contrast enhanced FLAIR but negative lumbar puncture (Table B1). A study by Mustafa and colleagues also demonstrated that meningeal enhancement by tumors, multiple sclerosis and infections are more efficiently detected on contrast enhanced FLAIR sequences than on contrast enhanced T1WI.[9]

Another study by WH Kamr et al shows sensitivity and specificity of contrast enhanced FLAIR sequences 91.1%and 100% respectively after comparison with contrast enhanced T1W sequences they showed the sensitivity and specificity 73% and 100% respectively taking results of lumbar as gold standard.[10]

MRI is now modality of choice to diagnose intracranial and meningeal pathologies. Meningeal enhancement is a characteristic feature of intracranial infections and neoplastic lesions. Although meningeal enhancement can be visualized on contrast enhanced CT brain scans, but post contrast T1WI and FLAIR sequences accurately detect meningeal enhancement.[10] The CE FLAIR was first used to detect meningeal enhancement in 1996, but its use is debatable due to artefactual hyper-intensity in posterior fossa.[11]

Meningeal enhancement is avidly detected on contrast-enhanced FLAIR images than on contrast-enhanced T1-weighted images because FLAIR sequence clearly demarcates enhancing meninges from less enhancing cortical veins, where as in contrast enhanced T1WI sequence meninges and cortical veins are equally enhancing. Thus very subtle meningeal enhancement can be detected confidently on post contrast FLAIR sequence.[10,11,12]

Two decades ago there were studies that showed that non contrast enhanced FLAIR sequence is better than contrast enhanced T1WI to detect intracranial infections. A study, carried out by Singer and his colleagues.[13] stated that non-contrast enhanced FLAIR sequence is superior to post contrast T1W1. The reason behind is that during meningitis, protein concentration increases in CSF which returns hyper intense signals as compared to brain parenchyma, thus CSF become hyper intense on FLAIR. But it is only possible when protein content of CSF crosses a certain threshold level.[14,15]

A study by Hyun and colleauges[16] shows contrast enhanced FLAIR imaging is superior than contrast enhanced T1-WI imaging in the evaluation extra-axial cerebral pathologies in children.

In 2006, Parmar and his colleagues[17] conducted a study in which they showed that contrast enhanced FLAIR is superior than contrast enhanced T1WI and non-contrast enhanced FLAIR to detect meningeal enhancement in meningitis. They included patients with and age range between 3-78 years, which is similar as that of our study.

Meningeal enhancement is not a feature of meningitis only but it is also a sign of neoplastic and metastatic lesions. One study by Ercan N and his group concluded that contrast enhanced FLAIR more accurately detect intra and extra axial metastatic disease in brain than contrast enhanced T1WI and non-contrast enhanced FLAIR due to its ability to clearly demarcate meningeal enhancement.[18]

Now post-contrast FLAIR sequence is included as protocol to assess various leptomeningeal diseases whether infectious or neoplastic.[19]

Thus, our study supports all of aforementioned studies.

There are certain limitations in our study. Contrast enhanced MRI is much more expensive than lumbar puncture. Moreover, MRI takes much longer time as compared to lumbar puncture which is a bedside procedure. Most of patients with clinical suspicion of meningitis are drowsy and irritable anesthesia department has to be involved to sedate these patients and as well as the pediatric age group. Due to aforementioned facts, clinicians are reluctant to suggest contrast enhanced MRI as first line investigation. But its noninvasiveness and ability to detect complications of disease make it more useful than routine CSF analysis.

Conclusion

In conclusion, the sensitivity and specificity of post contrast FLAIR sequence is greater as compared to post contrast T1W sequence to detect meningeal enhancement. Therefore, for all patients with suspicion of meningitis, post contrast FLAIR sequence should be added to MRI brain protocol as a routine sequence.

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