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# ROLE OF CONTRAST ENHANCED FLAIR MRI AS A NEW TOOL IN DIAGNOSING TUBERCULOUS MENINGITIS

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## ABSTRACT

***Objective:*** To determine the diagnostic accuracy of contrast-enhanced FLAIR images as an imaging tool in diagnosing tuberculous meningitis considering CSF analysis as gold standard.

***Study Design:*** Comparative Cross sectional Study.

***Place and Duration of Study:*** This study was conducted in Radiology Department of Pakistan Institute of Medical Sciences, Islamabad, from May to Oct 2016 in collaboration with Neurology Department.

***Methodology:*** Total 255 patients having clinical suspicion of Tuberculous meningitis were included. Patients having intracranial hemorrhage, claustrophobia and metallic implants in body were excluded. MRI scan of brain from the vertex till the base of skull was performed at 1.5 Tesla MRI machine. Contrast enhanced T2 FLAIR images were acquired and evaluated by radiologists for tuberculous meningitis. CSF analysis was done after lumbar puncture of the patient. Diagnostic accuracy of the procedure was determined by taking CSF analysis as the gold standard. Data was analyzed by using SPSS 21.

***Results:*** One hundred and fifty four (61%) patients were found to have abnormal enhancement on contrast enhanced FLAIR images. One hundred and forty six (58.4%) were True Positive and 8 (3.2%) were False Positive. Among, 101 contrast enhanced FLAIR images negative patients, 6 (2.4%) were False Negative where as 95 (38%) were True Negative. Overall sensitivity was 96.05%, specificity 92.23%, positive predictive value 94.81%, negative predictive value 94.06% and diagnostic accuracy 94.51%.

***Conclusion:*** This study concluded that contrast-enhanced FLAIR magnetic resonance images have high sensitivity and specificity in diagnosing tuberculous meningitis.

**Keywords:** Meningitis, Magnetic resonance imaging, Tuberculous.



## INTRODUCTION

Meningitis is an acute inflammatory condition of the protective membranes called meninges, covering the brain and spinal cord[1]. The inflammation may be caused by infection with different microorganisms, and rarely by some medication[2]. Although there has been much advancement in the complete management of infectious diseases, meningitis is still considered as a big cause of mortality and morbidity, especially in the children[3]. There are many causative bacteria for meningitis according to the patients' age group. In premature babies and infants, common causes are group B streptococcus and bacteria that normally inhabit the gastrointestinal tract such as *Escherichia coli.* Listeria monocytogenes (sero type IVb) affects the newborns and may occur in epidemics[4].

Sixty nine lac fifty thousand seven hundred and fifty 69,507,50 total cases were reported worldwide in WHO 2019 annual report. The global incidence was 132 per 100,000 and in Pakistan was 265 per 100,000. Meningitis is an important disease affecting the world and can lead to serious emergency if not appropriately diagnosed and further treated accordingly. Meningitis is one of the biggest causes of neurological and medical emergency and causes considerable morbidity and mortality affecting all age groups[5]. Infective diseases like meningitis including tuberculous and bacterial meningitis has been a common cause of stroke in younger population of Pakistan[6].

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According to the latest World Health Organization (WHO report), there were an estimated 11 million prevalent cases of tuberculosis. Out of estimated 9 million people who got TB in 2013, (56%) were in the South-East Asia. It is estimated that 1.5 million people died of TB in 2013. Among 6.1 million cases, 0.83 million patients had extra-pulmonary TB. Tuberculous Meningitis (TBM) accounted for 25.4% of all adult meningitis[7]. TBM is a complex disease further leading to neurological deficit as well as other complications, demanding early diagnosis and treatment. Its diagnosis needs very high index of clinical suspicion. TBM must always be considered if a patient presents with signs of meningeal irritation, particularly in extremes of age, immunocompromised people and patients with history of TB contact[8].

Incidence of extrapulmonary Tuberculosis varies greatly among different countries of the world and is affected by overall incidence of Tuberculosis. Population based estimation of TBM is not commonly reported. TBM causes death and disabilities with other complications in children. Intracerebral as well as spinal disease is mediated by inflammation leading to meningitis, tuberculous abscess formation, vasculitis, hydrocephalus and infarction[9].

Diagnosis of TBM is often not microbiologically confirmed. Delay in diagnosis may lead to delayed initial treatment, advanced disease and complications as being predictors of poor outcome. Clinical and lab findings are imperfect. CT scan and MRI have been widely used to diagnose TBM. CT scan and routine MRI may be normal in 15%[10-13].

CT scan may reveal abscess formation, tuberculoma and hydrocephalus (early communicating and late non communicating hydrocephalus) however, the earliest signs of TBM may not be manifested on CT scan. Findings may be overlooked due to conspicuous vascular enhancement further masking the meningeal enhancement. Lumbar puncture (LP) may be contraindicated in cases of increased intracranial pressure. Patients may not OPT the LP as it is an invasive procedure. Contrast enhanced T1 weighted images have been used in MRI brain for diagnosing meningitis as well as various other pathologies but Contrast enhanced FLAIR (fluid attenuated inversion recovery) sequence is a new tool. These are T2 weighted images with dark CSF and showing more accurate meningeal enhancement and conspicuity[14].

LP has been the previous method of choice for confirmation of Tuberculous meningitis. CT scan as well as common MRI images are not very helpful so CE FLAIR MRI remains a non-invasive method of investigation. We had planned this study to assess the diagnostic accuracy of CE FLAIR images as a diagnostic tool, so as to make highest possible effective use of this method in the non-invasive diagnosis of tuberculous meningitis in our local population.

## METHODOLOGY

This comparative cross sectional study was conducted in Radiology Department of Pakistan Institute of Medical Sciences, Islamabad from May to October 2016 with collaboration of Department of Neurology.

Sample size was calculated by taking sensitivity 96%[16], specificity 85.71%[16], expected prevalence 25.4%[7], precision 4% & confidence level 95% and sample size came out to be 255 by using WHO calculator.

After taking approval from Ethical Committee, male and female patients in the age range of 13-70 yrs diagnosed on clinic presentation of fever (>38°F), headache ,vomiting and neck stiffness were included in the study through non probability consecutive sampling. Informed consent was taken from all patients. Patients having intracranial hemorrhage, brain tumour and those with MRI contraindications (severe claustrophobia or with cardiac pacemakers) were excluded.

MRI brain was performed with standard head coil and routine protocol from base of the skull to vertex. After that IV contrast Gadolinium was injected with dose adjusted according to the weight of the patient as 0.1mmol/kg body weight, using automatic injector at speed of 0.2 ml/second. MRI images were reported by senior radiologists having experience >3 years in neuro-radiology. CE FLAIR images were labeled as "positive" when there was thick meningeal enhancement in extra axial CSF spaces, along the superficial brain surfaces or within the sulci and along the nerves and cisterns. It was compared and confirmed on CSF examination by pleocytosis of ≥50 cells/µL predominantly lymphocytes (≥50%), CSF protein ≥40 mg/dl, CSF sugar ≤40.0% of blood sugar. Lumbar puncture was done by neurologist and report was sent to hospital lab verified by pathologist. Findings were noted on questionnaire as positive on MRI, Positive on CSF analysis, Negative on MRI and Negative on CSF analysis. The data was analyzed on SPSS version 21. A 2 x 2 table was used to determine sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy. Mean and standard deviation were calculated for quantitative variables like age. Frequency and percentage were calculated for qualitative variables like gender and positives contrast-enhanced FLAIR images (table-I).

**Table-I: Tuberculous meningitis on contrast enhanced FLAIR.**

| Tuberculous meningitis on contrast enhanced FLAIR | | Tuberculous meningitis on CSF | |
|---|---|---|---|
| | | **Yes** | **No** |
| | Yes | True Positive (a) | False Positive (b) |
| | No | False Negative (c) | True negative (d) |

*Sensitivity: a / a+c x 100, Specificity: d / b+d x 100, Positive predictive value: a / a+b x 100, Negative predictive value: d / c+d x 100, Diagnostic accuracy: a+d / a+b+c+d x 100*

**Table-I: Contrast-enhanced FLAIR images and CSF findings.**

| | Positive on CE FLAIR | Negative on CE FLAIR | *p*-value |
|---|---|---|---|
| Positive on CSF | 146 (TP)* | 6 (FN)*** | 0.857 |
| Negative on CSF | 8 (FP)** | 95 (TN)**** | |

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

## RESULTS

Age range in our study was 13-70 years with Mean ± SD = 41.37 ± 15.94 years. Majority of the patients 98 (38.43%) were between 31 to 50 years of age. Out of 255 patients, 153 (60%) were males and 102 (40%) were females with male to female ratio of 1.5:1 as shown in fig-1.

In each patient, MRI scan of brain from the vertex till the base of skull was performed and contrast enhanced FLAIR images were acquired. Contrast enhanced FLAIR images supported the diagnosis of tuberculous meningitis in 154 (61%) patients. CSF analysis confirmed tuberculous meningitis in 152 (59.61%) cases where as 103 (40.39%) patients revealed no TBM. In 154 CE FLAIR images positive patients, 146 (58.4%) True Positive cases had tuberculous meningitis and 8 (3.2%) False Positive cases had no tuberculous meningitis on CSF analysis. Among, 101 contrast enhanced FLAIR images negative patients, 6 (2.4%) False Negative cases had tuberculous meningitis on CSF analysis where as 95 (38%) true Negative cases had no tuberculous meningitis on CSF analysisas shown in table-II.

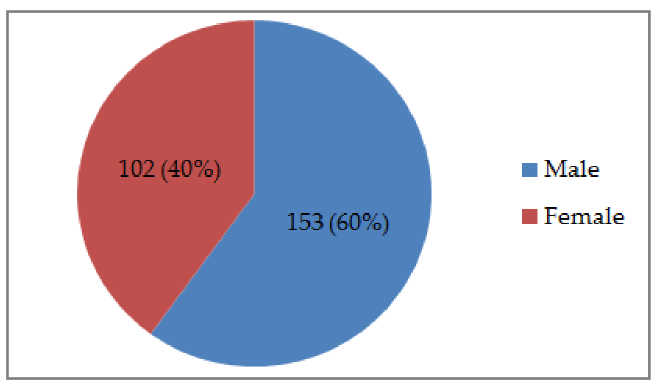


**Figure-1: Distribution of patients according to gender.**

Overall sensitivity was found to be 96.05%, specificity 92.23%, positive predictive value 94.81%, negative predictive value 94.06% and diagnostic accuracy 94.51% (fig-2).

## DISCUSSION

The diagnosis of meningitis is established by history, physical examination, and laboratory evaluation but the ability to detect and differentiate intracranial infections has markedly improved with the introduction of MRI. The lack of bone artifacts and the multiplanar capability of MRI have led to this preeminence[15,16].

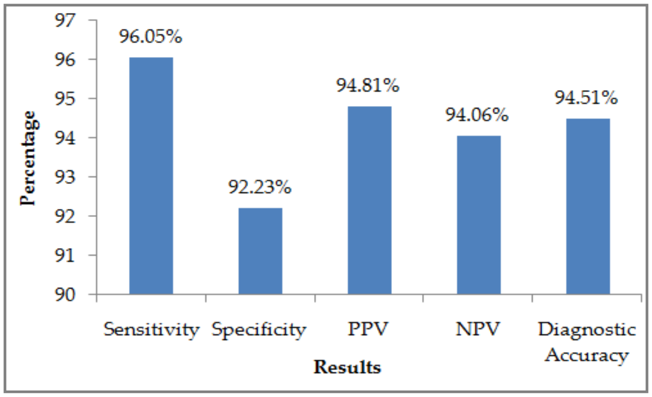


**Figure-2: Diagnostic accuracy of contrast-enhanced FLAIR images as an imaging tool in diagnosing tuberculous meningitis.**

Vaswani *et al* in 2014 performed a prospective study in Karachi, Pakistan similar to our study. The number of patients was 57. Patients presented with signs of meningeal irritation in the form of headache, photophobia, neck rigidity, fever and vomiting. The study signifies the clinical parameters and symptoms showing that 90% patients presented with history of vomiting. They also calculated diagnostic accuracy of T1 weighted post contrast images. The sensitivity of FLAIR post contrast MRI was 96% and specificity was 85.71%[16].

In a prospective study by Splendiani, Twenty seven patients were evaluated with plain routine and contrast enhanced T1WI and FLAIR sequences. On T1WI only six patients were diagnosed and on FLAIR imaging twelve patients were positive. After MRI, all patients underwent spinal tap and it was found that twelve patient had CSF positive findings. Thus, sensitivity of Contrast enhanced FLAIR remained 100%[17].

In a retrospective study at Karachi, Pakistan, fifty patients were included through their medical records. This study was different from our study as it was done retrospectively and it included the Plain unenhanced FLAIR sequence rather than contrast enhanced images. There were 36 true positive cases and 10 were true negative. One of the two false positive patients was due to motion blurr the other proved out to be meningeal carcinomatosis. They revealed 94.7% sensitivity and 83.3% specificity[18].

Galassia *et al*[19] retrospectively studied 24 patients. This research was more complex as it consisted of total 35 studies of 24 patients, consisting of two groups. First group comprised of 21 out of 33 studies with T1 weighted Fat suppression images performed before CE FLAIR images. Second group consisted of 12 out of 33 studies included CE FLAIR imaging before CE T1 weighted Fat Suppression images. Time interval between both types of groups was 2-5 minutes. The results showed that CE FLAIR images are less sensitive than CE T1 weighted Fat Suppres-sion imaging. The conclusion of the study was totally opposite to ours as they found out con-trast-enhanced T1-weighted images were rated better than CE-FLAIR in 25 of 33 studies. Limi-tations of this study were small sample size and complex study design.

Another study by Ahmad A20 has quantified the differences in MR signal intensities using T1WI FS and FLAIR images, thus providing better results favoring FLAIR images in meningitis patients. It also shows that suppressing the vascular enhancement on FLAIR images signifies better visualization and discrimination of meningeal enhancement. The overall accuracy was 90.3% for CE_FLAIR sequence compared to 54.8% for conventional post contrast T1WI.

## CONCLUSION

It is concluded that MRI could have an important role in the early screening for infectious tuberculous meningitis, provided a CE FLAIR sequence is used.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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