



RESEARCH ARTICLE

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Transforming Meningoencephalitis Diagnosis: A Study of Filmarray ME Panel in a North Indian Tertiary Care Centre

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ABSTRACT

Meningoencephalitis is a severe condition requiring rapid and accurate diagnosis for effective management. Traditional culture methods often fail to detect certain pathogens, leading to delayed treatment. This study was conceptualized with an aim to assess the BioFire FilmArray Meningitis/Encephalitis (ME) Panel as a first-line diagnostic tool. A total of 147 patients (91 males and 56 females) with suspected meningoencephalitis were included. Cerebrospinal fluid (CSF) samples were analyzed using the FilmArray ME Panel and results were compared with traditional culture methods. The BioFire FilmArray ME Panel detected pathogens in 14 out of 147 CSF samples, yielding a positivity rate of 9.52%. Detected pathogens included Cytomegalovirus (03), *Streptococcus pneumoniae* (03), HSV1 (02), *E. coli* K1 (01), Enterovirus (01), *Haemophilus influenzae* (01), HHV6 (01), Parechovirus (01), and Varicella Zoster Virus (01). In contrast, traditional culture methods detected pathogens in only 7 cases, highlighting the panel's superior sensitivity and underscoring the limitations of traditional methods. The ME Panel's ability to deliver accurate results from just 200 microliters of CSF and the rapid turnaround time of just 1 hour highlights its efficiency in providing critical diagnostic information from small sample volumes. The study also assessed the impact of CSF volume, with nearly one-third of samples being 0.5 mL, noting that the panel requires only 200 microliters to provide comprehensive results. The BioFire FilmArray ME Panel significantly outperformed traditional culture methods in detecting a wide range of pathogens in CSF samples, even with minimal sample volume. Its rapid and accurate diagnostics improve early diagnosis and patient management in meningoencephalitis, supporting its integration into routine clinical practice.

Keywords: Meningoencephalitis, BioFire FilmArray Meningitis/Encephalitis (ME) Panel, Cerebrospinal fluid (CSF)

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INTRODUCTION

Meningoencephalitis (ME) represents a significant global clinical challenge, characterized by high morbidity and mortality rates.¹⁻⁵ In India, the condition is particularly concerning due to the diverse epidemiology and high burden of infectious diseases. ME is a condition which involves inflammation of both the meninges and brain, with etiological agents including bacteria, viruses, fungi, and parasites.^{6,7} The Indian subcontinent experiences a substantial disease burden due to factors such as overcrowding, poor sanitation, and frequent outbreaks of infections.⁸

Epidemiological data on ME in India is limited, with many cases going unreported or undiagnosed, creating challenges in accurately assessing the disease's impact and developing effective public health interventions. Reliable information on the burden of this endemic disease is hindered by limited surveillance, insufficient laboratory resources, frequent misdiagnoses, and widespread antibiotic use, which is common in India.⁹ Reports indicate that certain regions, especially in northern and eastern India, experience seasonal outbreaks of ME, with viral infections like enterovirus contributing significantly to the burden.⁸ Additionally, bacterial pathogens like *Streptococcus pneumoniae* and *Neisseria meningitidis* are frequently involved, particularly affecting pediatric population.^{6,9}

In numerous cases of suspected central nervous system (CNS) infections, diagnostic testing requires large volumes of CSF and often involves lengthy turnaround times. The accuracy of these results can be influenced by factors such as prior antimicrobial therapy, timing of lumbar puncture, and the volume of CSF analyzed.¹⁰⁻¹³

In spite of extensive efforts to determine a cause, the diagnosis remains obscure in about 25-50% of patients with acute meningoencephalitis, leaving uncertainty regarding whether these cases stem from infectious agents or other origins.¹⁰⁻¹⁸

Multiplex molecular assays, which allow for the simultaneous detection of multiple microbial targets, have become essential tools and are now widely used for diagnosing various infections. The BioFire FilmArray ME panel can detect fourteen (14) meningoencephalitis-related pathogens - 06 bacteria, 07 viruses, and 01 yeast

- requiring only 200 µL of cerebrospinal fluid (CSF) and providing results in about an hour. By leveraging multiplex PCR technology, this panel enables rapid, simultaneous pathogen detection directly from CSF, supplying clinicians with crucial information to make timely therapeutic decisions (BioFire FilmArray ME panel Performance: 94.2% sensitivity and 99.8% specificity).^{19,20}

By detecting 14 different pathogens, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae*, and various viral agents, this multiplex FilmArray panel provides a valuable tool for managing central nervous system (CNS) infection. Its rapid turnaround time significantly reduces the time to diagnosis, enabling earlier and more appropriate therapeutic interventions, which can improve clinical outcomes in resource-constrained settings like India.^{5,21,22}

The present study aims to assess the clinical utility of the BioFire FilmArray ME Panel in a tertiary/quaternary care setting in North India, assessing its impact on diagnostic accuracy and patient management in cases of suspected meningoencephalitis.

MATERIAL AND METHODS

This retrospective study was conducted over 15 months at a tertiary/quaternary care hospital in North India. A total of 147 patients, both pediatric and adult, presenting with clinically suspected meningoencephalitis were included. CSF samples were analyzed using the BioFire FilmArray ME Panel, and pathogen detection

Table 1. Pathogens detected by FilmArray ME Panel

Pathogens Detected with FilmArray ME Panel	Number of pathogens detected
Cytomegalovirus	3 (21.5%)
<i>Streptococcus pneumoniae</i>	3 (21.5%)
HSV1	2 (14.4%)
<i>E. coli</i> K1	1 (7.1%)
Enterovirus	1 (7.1%)
<i>Haemophilus influenzae</i>	1 (7.1%)
HHV6	1 (7.1%)
Parechovirus	1 (7.1%)
Varicella Zoster Virus	1 (7.1%)
Total	14

was compared with results from traditional microbiological methods, including CSF culture.

Standard of care CSF testing

In addition to the FilmArray ME Panel, routine diagnostic tests were performed on all CSF samples, including: (i) Gram Stain: Used for bacterial identification and guiding initial antibiotic therapy. (ii) CSF Culture: For isolation and identification of bacterial, fungal,

and mycobacterial pathogens. (iii) Cytological Examination: including white blood cell (WBC) and red blood cell (RBC) counts and differential counts. (iv) Biochemical Analysis: assessing glucose and protein levels to differentiate between bacterial and viral infections. (v) India Ink Staining: used to detect *Cryptococcus* species, particularly in immunocompromised patients. (vi) PCR for Specific Pathogens: applied for the detection of organisms not included in the FilmArray panel.

POSITIVITY RATE OF FILMARRAY ME PANEL

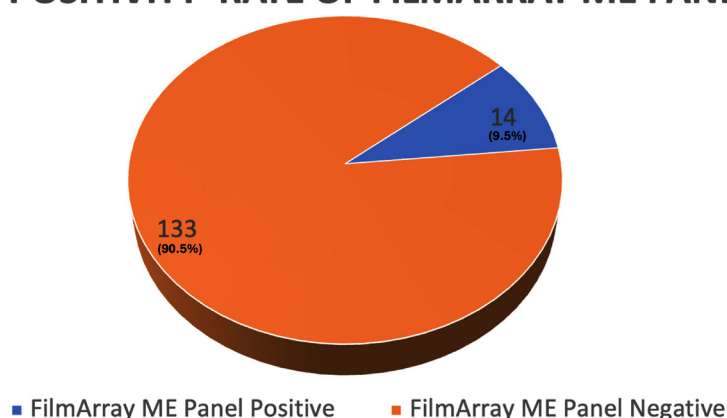


Figure 1. Positivity rate of BioFire FilmArray ME Panel Detection

PATHOGENS DETECTED BY BIOFIRE FILMARRAY ME PANEL

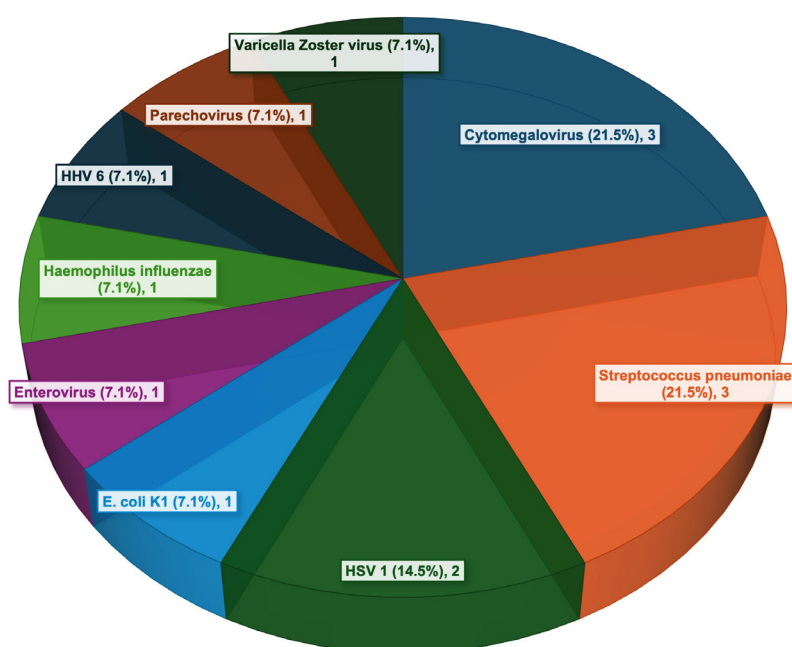


Figure 2. Pathogens detected by FilmArray ME Panel

These standard tests were performed alongside the FilmArray ME Panel to ensure comprehensive diagnostic coverage. FilmArray ME Panel Testing Procedure (Reference Instructions for Use (IFU) for BioFire ME Panel. BioFire Diagnostics, LLC. Available at: BioFire IFU).

RESULTS

The study population consisted of 147 patients, out of which 91 were males and 56 were females. The male-female ratio was 1.625:1. The study population comprised of pediatric and adult participants, with ages ranging from 6 months to 86 years.

The FilmArray ME Panel identified pathogens in 14 of the 147 samples, resulting in a positivity rate of 9.52% (Figure 1). Pathogens detected included Cytomegalovirus (03), *Streptococcus pneumoniae* (03), HSV1 (02), *E. coli* K1 (01), Enterovirus (01), *Haemophilus influenzae* (01), HHV6 (01), Parechovirus (01), and Varicella Zoster Virus (01). The distribution of various pathogens detected is shown in Table 1 and Figure 2.

In contrast, traditional culture methods detected pathogens in only 7 cases. Out of three cases where the BioFire panel detected

Streptococcus pneumoniae, whereas only 33% (1 out of 3) could be detected by culture. Additionally, *Haemophilus influenzae* and *Escherichia coli* K1 were not detected by culture. The patient with *E. coli* K1 had a concurrent culture growth of *Acinetobacter baumannii*, which is not included in the BioFire panel. Another case identified HSV-1 along with *Acinetobacter baumannii*. Furthermore, of the BioFire-negative cases, cultures revealed the presence of *Pseudomonas aeruginosa* in two instances and *Acinetobacter baumannii* in two additional cases. The comparison of BioFire FilmArray ME Panel and conventional culture is shown in Table 2.

DISCUSSION

Traditional microbiological methods, including routine bacterial cultures, Gram staining, and phenotypic identification, are essential tools for guiding the treatment of bacterial meningitis. However, these methods have limitations, including a low positive rate in clinical diagnosis. CSF cultures are time-intensive, restricted to bacteria that grow on specific media, and may not always align with findings from microscopy. For example, only 25% of cases with bacterial concentrations $<10^3$ CFU/mL yield positive

Table 2. Comparison of Pathogen Detection between BioFire ME Panel and Culture Results

Organism	Filmarray ME Panel Result	No. of detections	Culture Result	Remark
<i>Streptococcus pneumoniae</i>	Positive	3	Only in 1 out of 3 samples detected by Filmarray ME panel	67% missed by culture
<i>Hemophilus influenzae</i>	Positive	1	No Growth	100% missed by culture
<i>E. coli</i> K1	Positive	1	Concurrently detected <i>Acinetobacter baumannii</i>	<i>E. coli</i> K1 missed by culture <i>Acinetobacter baumannii</i> : off-panel target for Film Array ME panel
HSV-1	Positive	1	Concurrently detected <i>Acinetobacter baumannii</i>	<i>Acinetobacter baumannii</i> : off-panel target for Film Array ME panel
<i>Pseudomonas aeruginosa</i>	Negative	2	Positive	<i>Pseudomonas aeruginosa</i> : off-panel target for Film Array ME panel
<i>Acinetobacter baumannii</i>	Negative	2	Positive	<i>Acinetobacter baumannii</i> : off-panel target for Film Array ME panel

microscopy results, while 60% are detected when concentrations range from 10^3 to 10^6 CFU/mL.²³ A 27-year study also found that CSF culture could miss bacterial meningitis diagnoses in more than 10% of cases.^{3,24}

CSF culture remains the gold standard, showing 70-85% positivity in patients who have not received prior antibiotic treatment. While antibiotics typically do not alter CSF cell counts, glucose, or protein, they reduce Gram stain sensitivity to 40-60% and culture positivity to below 50%. Administering antibiotics before CSF sampling can significantly hinder diagnosis by reducing microbial load or eliminating pathogens entirely, resulting in sterile CSF samples.^{25,26}

Sulaiman *et al.* identified the etiology in only about 32% of cases, with similar findings reported in other studies. This limited detection is likely due to the low sensitivity of CSF cultures for non-bacterial pathogens and the underuse of molecular and serologic testing for viral agents.^{15,27,28}

This diminished sensitivity due to the aforementioned factors complicate timely diagnosis and optimal treatment. Consequently, clinicians often face a diagnostic dilemma when CSF cultures return negative despite a high suspicion of infection, particularly in patients who have received prior antimicrobial therapy.

The introduction of multiplex PCR-based assays, such as the BioFire FilmArray Meningitis/Encephalitis (ME) Panel, has significantly enhanced the diagnostic landscape for CNS infections by offering rapid, sensitive, and comprehensive pathogen detection. These tools enable early and targeted therapy, which is crucial for life-threatening conditions like meningoencephalitis.^{5,22}

The FilmArray ME Panel, which is US FDA approved, provides a comprehensive, accurate, and time-efficient solution for pathogen detection.

Despite certain challenges, such as small sample volumes, the FilmArray ME Panel demonstrated robust diagnostic performance by utilizing just 200 μ L of CSF, significantly enhancing pathogen detection through multiplex PCR. Its rapid turnaround time and comprehensive pathogen coverage facilitate early therapeutic interventions in critical clinical settings and also in antimicrobial stewardship.^{21,29,30}

In this study, the BioFire FilmArray ME panel detected *Streptococcus pneumoniae* in three cases, with a culture-confirmed detection rate of only 33%, highlighting the superior sensitivity of the BioFire panel over traditional culture methods.^{30,31} Additionally, culture methods failed to detect *Haemophilus influenzae* and *Escherichia coli* K1, further underscoring the limitations of conventional microbiological techniques in identifying pathogens in CSF samples.^{32,33}

Notably, one patient with *E. coli* K1 also exhibited concurrent growth of *Acinetobacter baumannii* in culture, a nosocomial pathogen not included in the BioFire panel's repertoire. This case emphasizes the need for a comprehensive diagnostic approach, integrating both the BioFire panel and conventional culture methods, particularly for nosocomial pathogens like *Acinetobacter* and *Klebsiella* species, which are not part of the panel's design.³⁴

Additionally, certain studies have highlighted the FilmArray ME Panel's superior diagnostic yield compared to traditional methods. For example, a study conducted at the Kerala Institute of Medical Sciences found a 23.6% positivity rate with the FA-ME panel, compared to just 3% with standard culture methods.⁵ Other studies similarly reported that enteroviruses were the most commonly detected pathogens, corroborating the findings of this study.^{5,13}

In line with Infectious Diseases Society of America (IDSA) guidelines, which recommend the use of molecular diagnostics in the evaluation of encephalitis, this study supports the integration of rapid molecular diagnostics into routine clinical practice for optimal management of CNS infections.³

The enhanced performance of PCR-based diagnostics over conventional microbiological testing, including patients who have already received antibiotics, where traditional culture-based methods may not be diagnostic, further solidifies the role of these rapid diagnostics in clinical microbiology.

While CSF culture is considered the gold standard to determine antimicrobial susceptibility, WHO also strongly recommended CSF be assayed using PCR-based molecular tests for relevant pathogens in individuals with suspected acute

meningitis. This guideline was supported by an extensive meta-analysis of CSF molecular testing.^{5,22,35,36}

Finally, the minimal CSF volume requirement (200 µL) and rapid turnaround time (approximately 1 hour) of the FilmArray ME Panel make it a valuable tool in clinical practice, particularly in scenarios requiring prompt diagnosis and intervention.

CONCLUSION

The FilmArray ME Panel significantly outperformed traditional culture methods in detecting a broad spectrum of pathogens in cerebrospinal fluid (CSF) samples, demonstrating its superior sensitivity even with minimal sample volumes of just 200 µL. This rapid and accurate diagnostic capability enhances early diagnosis and improves patient management in cases of meningoencephalitis, allowing for timely interventions and potentially better clinical outcomes. Furthermore, the integration of the BioFire panel into routine clinical practice aligns with antimicrobial stewardship efforts by facilitating targeted therapy and reducing unnecessary broad-spectrum antibiotic use. This is particularly crucial in a clinical landscape where misdiagnosis and delays can lead to detrimental patient outcomes. As we continue to face the challenges of central nervous system infections, ongoing research and investment in rapid and innovative diagnostic technologies like the FilmArray ME Panel are essential. Such advancements not only promise to enhance the diagnostic landscape but also aim to improve the yield and overall clinical outcomes for patients affected by CNS infections.

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None.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

PB, VS, JT, SK conceptualized the study. PB, VS, JT performed literature review. PB, VS, JT performed experiments. PB, VS, JT, SK performed

results analysis. PB, VS, JT wrote the manuscript. PB, SK reviewed the manuscript. All authors read and approved the final manuscript for publication.

FUNDING

None.

DATA AVAILABILITY

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

This study was approved by the Institutional Ethics Committee, Army Hospital (R & R), Delhi Cantt., vide regn. no. 14/2025.

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