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ORIGINAL ARTICLE

FilmArray® meningitis/encephalitis (ME) panel, a rapid molecular platform for diagnosis of CNS infections in a tertiary care hospital in North India: one-and-half-year review

Bansidhar Tarai[1] · Poonam Das[1]

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Abstract

Background Acute meningitis and encephalitis (AME) is a syndrome of central nervous system (CNS) infections, which could lead to neurological damage and fatality. This study evaluates the multiplex FilmArray® ME Panel which is aimed to diagnose agents causing suspect CNS infections in north India.

Methods A total number of 969 cerebrospinal fluid (CSF) samples collected between August 2016 and January 2018 from patients who showed clinical symptoms of CNS infections were analyzed using the FilmArray® ME Panel. Also a comparison of molecular diagnosis and various laboratory and radiological findings for *Streptococcus pneumoniae*, Enterovirus and *Cryptococcus neoformans* positive cases was done.

Result Out of the 969 CSF samples, 101 cases were found to be positive for viral ($n = 55$), bacterial ($n = 38$), fungal ($n = 7$), and poly-microbial ($n = 1$) agents. Out of the 55 viral positive cases, the most detected pathogen was Enterovirus ($n = 23$) with predominance in the age group of 2–17 years, followed by Varicella Zoster virus ($n = 14$) and HSV1($n = 9$) cases. *Streptococcus pneumoniae* ($n = 26$) was found to be the predominant bacterial pathogen, of which 17 were detected in the age group above 35 years. *Cryptococcus neoformans* was found in 7 cases.

Conclusion The FilmArray® ME Panel aids in rapid detection of 14 pathogens directly from CSF. When compared to gram stain, culture, antigen detection, and CSF biochemical analysis, the FilmArray® ME Panel has detected more cases, some of which are difficult to diagnose by conventional methods. This rapid technology will help the clinicians in case of early patient management, outcomes and provide aid in antimicrobial stewardship.

Keywords Meningitis · Encephalitis · FilmArray · Streptococcus pneumonia · Enterovirus

Introduction

Infections of the central nervous system (CNS) are associated with significant morbidity and mortality and often lead to serious consequences. In order to establish a timely diagnosis, it is important for physicians to be familiar with the signs and symptoms of CNS infections. The patients who survive the CNS infections may have to face lifelong penalties including loss of limbs, problems with hearing and vision, and cognitive defects [1].

✉ Bansidhar Tarai
bansisss@gmail.com

[1] Institute of Lab Medicine, Max Superspeciality Hospital, Saket, New Delhi 110017, India

Approximately 4100 cases of bacterial meningitis are diagnosed in the USA each year, including 500 deaths [2]. *Streptococcus pneumoniae*, *Streptococcus agalactiae* (group B Streptococcus), *Neisseria meningitis*, *Haemophilus influenzae*, and *Escherichia coli* (particularly the K1 serotype) are the most common bacterial pathogens of acute CNS infections.

CNS infections are clinically significant because of the endemicity of many pathogens, the fact that many of the pathogens also colonize the human body, the emergence and re-emergence of new infectious pathogens, the heavy burden they impose on the health care system, the relatively large numbers of causative pathogens involved, the difficulties in correct microbiological diagnosis, and the significant mortality and morbidity rates in the affected patients. This is particularly true for Asia. The epidemiology of CNS infection in Asia exhibits significant differences from global epidemiology. Although the causes of bacterial meningitis are relatively

uniform in many parts of the world, in some parts of Asia, gram negative bacilli and tuberculosis, not globally found to be important as causes of bacterial meningitis, assume far greater importance. The spread of enterovirus 71 and Japanese encephalitis virus from their previously geographically limited locations exemplifies the dynamics of the changes in epidemiology induced by interaction between ecological factors, human activities, and climatic changes. Yet there is a disconcerting lack of epidemiological data from these regions. More epidemiological studies and cooperation between centers to facilitate disease surveillance, detection of pathogen transmission, and formulation of improved clinical management are urgently needed in Asia.

In order to provide timely treatment, it is essential to detect and identify the microbial pathogens [3]. The non-specific symptom of CNS infections in the initial phase poses challenges in establishing a correct diagnosis. Patients with CNS infections mostly present similar symptoms of headache, fever, and neurological conditions. It is challenging to establish a differential diagnosis of meningitis and encephalitis as the patient presents with overlapping symptoms [4, 5]. Due to lack of targeted testing, the etiology is mostly not easily recognized. Routinely used methods involving Gram stain, culture, antigen detection, and biochemical and cellular analysis lack sensitivity and specificity and are time consuming [6, 7]. Routine microbial diagnosis can now be performed using nucleic acid amplification-based molecular methods. These nucleic acid in vitro amplification-based molecular techniques have higher sensitivity and specificity, and they show greater detection rates in comparison to conventional methods. Molecular techniques can enable a more rapid diagnosis thanks to a time to result significantly reduced [8, 9]. There are four rapid molecular assays which are FDA cleared for the detection of pathogens from cerebrospinal fluid (CSF). The Xpert EV assay (Cepheid) for the detection of enteroviruses, Simplexa HSV 1 & 2 Direct (Focus Diagnostics) and MultiCode RTx HSV 1&2 kit (Luminex Corporation) to detect herpes viruses 1 and 2, and the FilmArray® ME Panel (BioFire, bioMerieux, Salt Lake City, USA) which is currently the only FDA cleared multiplex assay for the simultaneous detection of bacteria, viruses, and fungi in CSF. This study evaluates the FilmArray® ME Panel to assess the suspected CNS infections with clinical symptoms of bacterial meningitis, maculo-vesicular rashes, and altered mental status. The FilmArray® ME Panel uses a multiplexed PCR platform for the simultaneous detection of 14 pathogens from CSF specimens.

Materials and method

Study design

A prospective study was conducted during the period of August 2016 to January 2018 in the Microbiology Department of a tertiary care hospital in New Delhi, India. A total number of 969 CSF samples of patients who showed symptoms of CNS infections were analyzed.

Clinical specimens

CSF was collected by lumbar puncture and sent to the laboratory in three different aliquots: for biochemistry, hematology/cytology, and microbiology.

Microbiology

CSF samples were first processed for culture, gram strain, bacterial and cryptococcal antigen detection, and India Ink smear preparation. The residual volume of un-centrifuged CSF (≥ 500 μL) left over was further processed by the FilmArray® test (ME).

FilmArray® ME Panel testing

Approximately 200 μl of specimen was subject to FilmArray® ME Panel testing according to manufacturer's instructions. The FilmArray® ME Panel test consists of automated sample homogenization and nucleic acid extraction, reverse transcription, nucleic acid amplification, and results analysis in approximately 1 h per run (i.e., per specimen).

The FilmArray® ME Panel identifies 14 common agents of community-acquired ME: *Escherichia coli* K1, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Streptococcus agalactiae*, cytomegalovirus (CMV), enterovirus (EV), herpes simplex virus type 1 (HSV-1), herpes simplex virus type 2 (HSV-2), human herpesvirus type 6 (HHV-6), human parechovirus (HPeV), varicella zoster virus (VZV), and *Cryptococcus neoformans/gattii* from CSF.

Detailed biochemical and microbiological analysis was done for the commonest found bacterial pathogens, i.e., *Streptococcus pneumoniae* (26 all positive cases), *Cryptococcus neoformans* (7 all positive cases), and for the commonest found viral pathogens, i.e., Enterovirus positive patients (23 all positive cases).

Results

Demographics A total of 969 clinical cerebrospinal fluid specimens were tested using the FilmArray® ME Panel, out of which 588 (60.7%) were from male patients and 381(39.3%) were from female patients. Of all the 969 cases, 157 (16.2%) were of the age group < 17 years, 507 (52.3%) were 18–64 years, and 305 (31.5%) were > 65 years. Out of 969 cases, 101 were positive and 868 were negative (Table 1). The demographic characteristics collected on all patients were sex,

Table 1 Positivity rate for the FilmArray ME Panel for all samples and by age group

Parameter	No. of samples	% of total						
Total samples tested	969							
Negative samples	868	89.6%						
Positive samples	101	10.4%						
Analyte		% of the positive samples	No. of positive detections by age group					
Bacteria			< 2 months	2–23 months	2–17 years	18–34 years	35–64 years	> 65 years
Streptococcus pneumoniae	26	25.7	0	1	6	2	9	8
Haemophilus influenzae	6	5,.9	0	0	1	3	1	1
Listeria monocytogens	3	3.0	0	0	0	0	2	1
Streptocococcus agalactiae	1	1.0	0	0	0	0	1	0
Neisseria meningitidis	1	1.0	0	0	0	1	0	0
E.coli K1	1	1.0	0	0	0	1	0	0
Viruses								
Enterovirus	23	22.8	1	2	18	1	1	0
Varicella Zoster virus	14	13.9	0	0	1	3	2	8
HSV 1	9	8.9	0	0	1	1	3	4
HSV 2	4	4.0	0	0	1	1	2	0
HSV 6	4	4.0	0	0	0	3	1	0
CMV	1	1.0	1	0	0	0	0	0
Yeast								
Cryptococcus neoformans	7	6.9	0	0	0	1	6	0
Polymicrobial								
VZV + Streptococcus pneumoniae	1	1.0	0	0	0	1	0	0
Total	101		2	3	28	18	28	22

age group, and patient location (emergency department [ED], PICU, NICU, ICU, HDU, IPD) at time of sample collection. Out of the 101 positive cases, 26 positive cases were found to be *S. pneumoniae* by the FilmArray® technology. Table 2 shows the comparison of theses 26 positive cases with other diagnostic tests for meningitis such as CBC, glucose, CSF TLC, gram staining, antigen test, and culture findings. Out of these 26 positive cases, only 1 case of a 4-year female with a glucose < 5, protein 208, and CSF TLC of 7 had the gram stain, the antigen test, and the culture positive for *S. pneumoniae* (see Table 2). In this study, the other bacterial pathogens detected were *Haemophilus influenzae* (3 cases), *Listeria monocytogenes* (1 case), *Streptococcus agalactiae* (1 case), *E. coli K1* (1 case), and *Neisseria meningitidis* (1 case). Twenty-three cases of *Enterovirus* were identified during this study (Table 3), and seven positive cases of *Cryptococcus neoformans/gattii* as well (Table 4).

Positivity rate The FilmArray® ME Panel detected at least one pathogen in 101 of the 969 specimens that were tested, yielding an overall positivity rate of 10.4%, as shown in Table 1. The highest detection rates were in the pediatric (2–17 years) and 35–65 age groups. The most prevalent organisms detected during this study were *S. pneumoniae* ($n = 26$), *Haemophilus influenzae* ($n = 6$), *Listeria monocytogenes* ($n = 3$), Enterovirus ($n = 23$), Varicella Zoster Virus ($n = 14$), HSV 1 ($n = 9$), HSV 2 ($n = 4$), HSV 6 ($n = 4$), and *Cryptococcus neoformans* ($n = 7$). Co-detections were observed in a single specimen for VZV and *Streptococcus pneumoniae*. This is a case of a male patient with HIV infection whose spinal fluid was also positive for *S. pneumoniae* by FilmArray® along with the VZV (co-infection detected, Table 1).

Statistical analysis

Statistical analysis was done for age, gender, and location. Chi-square of age/gender cross tabulation and age/location cross tabulation were not valid because of low frequency.

Discussion

Meningitis and encephalitis often present with similar symptoms and the causative agents underlying the disease cannot be identified based on the clinical symptoms alone [2]. Diagnosis of meningitis and encephalitis has always been a challenge to laboratory managers and clinicians. Currently

Table 2 *Streptococcus pneumoniae* cases

				CSF						
S no.	Age/ sex	Location	Blood TLC (ltr)	Glucose (mg/dl)	Protein (mg/dl)	TLC (cells /cumm)	Neutrophils %	Gram stain	Antigen	Culture
1	71 M	Medical ICU	16	51	548	25	80	Negative	Negative	Negative
2	55 F	Medical ICU	12.1	19	235	8550	75	Negative	Negative	Negative
3	4 F	Pediatric ICU	16	< 5	208	7	80	Positive	Positive	Positive
4	65 M	Medical ICU	1.3	10	1907	260	75	Negative	Negative	Negative
5	68 F	Neurosurgical ICU	7.7	91	584	11,264	90	Negative	Negative	Negative
6	41 F	Medical ICU	14.4	29	431	360	85	Negative	Negative	Negative
7	7 M	Pediatric ICU	15.9	23	302	450	80	Negative	Negative	Negative
8	76 M	Neurosurgical ICU	16.9	50	445	510	85	Negative	Negative	Negative
9	35 M	Neurosurgical ICU	16.8	< 3	801	1620	90	Negative	Negative	Negative
10	53 F	Neurosurgical ICU	25.6	42	813	2600	85	Negative	Negative	Negative
11	67 F	Neurosurgical ICU	11.6	37	234	1500	80	Negative	Negative	Negative
12	3 M	Pediatric ICU	11.6	12	165	120	30	Negative	Negative	Negative
13	56 M	Ward	12.0	54	19	5	100	Negative	Negative	Negative
14	61 M	Ward	10.5	53	138	100	55	Negative	Negative	Negative
15	75 F	Ward	27.5	56	622	880	60	Negative	Negative	Negative
16	66 M	Ward	12.3	6	1491	30	70	Negative	Negative	Negative
17	64 M	Ward	11.4	85.8	53	10	70	Negative	Negative	Negative
18	63 F	Ward	20.3	30	175	850	60	Negative	Negative	Negative
19	13 M	Ward	16.2	12	262	590	15	Negative	Negative	Negative
20	41 F	Ward	13	47	132	2250	10	Negative	Negative	Negative
21	13 M	Ward	16	50	55	25	100	Negative	Negative	Negative
22	72 M	Ward	?	17	176	80	20	Negative	Negative	Negative
23	29 M	Ward	22.4	25	435	2000	10	Negative	Negative	Negative
24	82 F	Ward	42.7	24	1801	1000	15	Negative	Negative	Negative
25	16 M	Ward	15.6	5.6	728	15,000	10	Negative	Negative	Negative
26	27 M	Ward	9.1	72	49	28	92	Negative	Negative	Negative

available testing methods are time-consuming and lack sensitivity and specificity. They are technically complex technologies and also require scientific expertise. Their accuracy may be affected by antibiotic administration prior to the testing, which is overcome by the FilmArray® technology. Also the small volumes of CSF obtained lead to a major challenge in the testing laboratory. Differentiation between bacterial, viral, or fungal meningitis/encephalitis is another challenge for clinical laboratories. While pleocytosis in the CSF is a sensitive marker of inflammation, several studies have shown that cell counts may be normal in both adult and pediatric patients despite an ensuing diagnosis of bacterial meningitis [10, 11]. It is relevant to identify the etiologic agent in patients suffering from CNS infections. This would facilitate in identifying the most likely causative organisms. Diagnosis based on nucleic acid in vitro amplification-based molecular methods has a broader and superior application in clinical microbiology practice.

In India, children under the age of 15 are the worst placed, with acute encephalitis syndrome (AES) usually affecting children under five who are often also severely malnourished. Of those affected, the ones who pull through rarely do so without some degree of disability. About one in three suffer permanent intellectual, behavioral, or neurological problems, including partial paralysis, recurrent seizures, and the inability to speak. India is a vast country with diverse weather and terrain patterns, resulting into tremendously divergent ecological presentations. The variant monsoon seasons, agricultural and animal husbandry practices, and socio-economic and cultural differences give rise to an intricate mixture of clinical situations [12]. For the purpose of surveillance, WHO has introduced a broad definition of AES [13]. Clinically, a case of AES is defined as a person of any age, at any time of year, with acute onset of fever, and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) and/or

Table 3 *Enterovirus* cases

S no.	Age /sex	Location	CSF				Brain MRI
			Glucose (mg/dl)	Protein (mg/dl)	TLC (cells/ cumm)	Lymphocytes %	
1	9 F	ICU	63	30	35	60	Negative
2	5 M	ICU	67	46	560	20	Negative
3	6 F	ICU	68	24	250	20	Negative
4	> 1 F	ICU	66	87.4	80	30	Negative
5	4 M	ICU	54	34.33	375	91	Negative
6	> 1 M	ICU	90	53	325	60	Negative
7	8 M	ICU	60	78.3	1500	15	Negative
8	7 F	ICU	61	59	280	40	Negative
9	4 F	ICU	65	46	24	20	Negative
10	5 M	ICU	54	31	50	20	Negative
11	> 1 M	ICU	47	60	250	30	Negative
12	8 F	Ward	67	34	150	70	Negative
13	9 M	Ward	56	37	35	90	Negative
14	8 M	Ward	57	21	100	85	Negative
15	24 M	Ward	51	129	10	95	Negative
16	8 F	Ward	78	22	70	35	Negative
17	16 F	Ward	58	36	50	60	Negative
18	7 F	Ward	45	64	350	90	Negative
19	> 1 M	Ward	56	32	120	80	Negative
20	4 F	Ward	47	26	90	60	Negative
21	1 M	Ward	69	12	2	100	Negative
22	6 M	Ward	47	23	125	90	Negative
23	55 M	Ward	105	59.4	10	20	Negative

new onset of seizures (excluding simple febrile seizures) [14, 15]. The different surveillance systems in our country such as the National Vector Borne Diseases Control Program (NVBDCP), State Government Laboratories, and Indian Council of Medical Research (ICMR) through its network laboratories also contribute in tracking AES. The major data compilation is carried out by NVBDCP and according to its website, large numbers of AES cases with or without definitive diagnosis are reported from Assam and Uttar Pradesh [16].

The Filmarray® ME Panel is an US-FDA approved de novo technology, based on the principle of multiplex PCR with detection by melting curve analysis. It adequately detects significant number of targets and has high sensitivity and specificity compared to conventional techniques [17].

In this study, the overall positivity rate observed with the FilmArray® ME Panel was similar to those described in other studies [17, 18], but there were a significant number of bacterial species detected. The majority of meningoencephalities

Table 4 *Cryptococcus neoformans/gattii* cases

S no.	Age/ sex	Location	CSF						
			Glucose (mg/dl)	Protein mg/dl	CSF TLC	Lymphocyte %	Gram stain	Antigen	Culture
1	50 F	M	88	69	2	L-100	Negative	Negative	Negative
2	60 M	MICU	69	147	25	L-80	Negative	Positive	Negative
3	37 M	NSICU	34	57	< 5	L-100	Positive	Positive (1:32)	Positive
4	60 M	NSICU	51	144	280	L-80	Negative	Positive (1:16)	Negative
5	37 M	NSICU	40	101	25	L-90	Negative	Positive (1:32)	Negative
6	30 F	IPD	53	62	35	L-90	Negative	Negative	Negative
7	47 F	IPD	39	48	10	L-80	Negative	Negative	Negative

seen by the clinicians are postinfectious neurologic syndromes [19, 20], due to immune-mediated tissue damage caused by host immunity. Mast cells which are part of the immune and neuroimmune systems play a key role in defense against pathogens and in the inflammatory process. Activated mast cells generate inflammatory cytokines including TNF and inflammatory IL-1 family members which could be harmful for the host [21]. Postinfectious neurologic syndromes should be treated by steroid therapy and immune therapies, once the infectious nature has been excluded. The definitive diagnosis of bacterial meningitis has been historically based on isolation in culture. The sensitivity of culture on average is approximately 80% or greater [22]. Culture was therefore used as the comparator technique for this study. The sensitivity of culture does vary by pathogen, and pretreatment with antibiotics lowers the sensitivity [7].

Among the hundred and one positive cases, the most prevalently detected bacterial organisms were *Streptococcus pneumoniae* (25.7%), *Haemophilus influenzae* (5.9%), and *Listeria monocytogenes* (3.0%). In the elderly population of up to 60 years of age, *Streptococcus pneumoniae* is responsible for about 60% of cases of acute bacterial meningitis [23]. Splenectomy is an important cause for bacterial infections especially caused by *Streptococcus* pneumoniae [24, 25]. Due to the rapid development of meningitis, the cerebrospinal fluid in this kind of patients could be clear, without cells or with a small number of cells, causing diagnostic confusion. The *Haemophilus influenzae* has been seen prevalently in the age group of 4-week infants to 50-year adults. In these cases, the predisposing conditions may be otitis or sinusitis, diabetes, immune deficiency, or head trauma with CSF leakage. In the temperate regions, it has bimodal distribution with first peak in the month of June and second in September to October. The CT/MRI of the brain edema or hydrocephalus may reveal subdural effusions or empyemas, cerebritis, or brain abscess. *Haemophilus* colonization can be quite high (up to 25%) and in children even higher, although Hib vaccines have considerably reduced the incidence of infection.

The meningitis caused by *Listeria monocytogenes* differs from other types of bacterial meningitis, especially in treatment and prognosis. These cases of meningitis have a significantly lower incidence of meningeal signs compared to others. Ampicillin is considered the drugs of choice as *Listeria monocytogenes* is inherently resistant to third-generation cephalosporins and vancomycin has limited antimicrobial activity as well.

Enterovirus is the most common viral agent (22.8%) in this study, predominantly in the age group of 2–17 years. Infants retain trans-placental immunity for the first 4–6 months of life. Enteroviruses are the causative factor in a large number of cases of aseptic meningitis [26]. Studies from India, Kuwait, and European countries report the prevalence of EV in encephalitis cases to be as high as 21–22% in encephalitis in endemic areas [27]. As per the study conducted by Beig et al. in 2010, they reported in children from Uttar Pradesh with viral encephalitis caused by Enterovirus was found to be 42.1% [28]. In enterovirus encephalitis cases, MRI shows characteristic lesions in the posterior portions of the medulla oblongata and pons [29]. However, in this study, all of the enterovirus positive cases showed normal MRI findings.

Among the positive cases, 12.9% were positive for HSV-1 or HSV-2. The complexity in the viral genome of Herpes simplex virus which usually persists as a latent infection in trigeminal ganglions, and reactivation could be caused by a number of stimuli including febrile illnesses, menstruation, sunlight, stress, and immunosuppression. The virus has a predilection for temporal lobes of the brain, but extra temporal involvement could be found in a majority of patients. Focal changes can be identified especially in older patients. Sometimes the unusual clinical course of bacterial meningitis sometimes could indicate a concurrent viral infection. Herpes encephalitis can cause up to 75% mortality in the absence of therapy, or severe neurological damages despite the therapy with intraveneous acyclovir [30]. Prompt diagnosis facilitates timely and appropriate therapy and can minimize the risks of mortality and severe adverse outcomes. Techniques for the detection of the other herpesviruses (CMV, VZV, and HHV-6) in the CNS are not routinely available in most evaluations of acute infectious ME. They are critical pathogens in certain populations, including immunosuppressed patients [31], and are best detected in the CNS by molecular methods [32]. All of the herpesviruses included in the FilmArray® ME Panel are known to create latency so detection may represent a recent primary infection, reactivation with disease, reactivation without disease, or latent detection in cells present in the CSF. This is particularly important with evidence of a bloody, traumatic tap, and contamination of the CSF with peripheral blood cells. Therefore, careful correlation of the clinical presentation would be needed for interpretation of a positive result with any of these viruses.

In this study, VZV infections were detected in 13.9% of the positive cases. Meningitis/encephalitis caused by VZV is predominantly seen in immunocompromised patients who are affected by reactivation of this virus with primary clinical features of rash and neurological symptoms. However, even young immunocompetent patients without rash might present with VZV meningitis.

The FilmArray® ME Panel can detect both the HHV-6 variants A and B. However, it does not discriminate between them [33]. In this study, HHV-6 was detected in 4.0% of the positive patients. The majority of detections were in adult patients; two detections were also confirmed in blood samples.

In this study, *Cryptococcus neoformans* was detected in 6.9% of the positive cases, with the majority in the age group of 35–65 years. Out of these 7 cases, only one case of 37-year

male with biochemical findings of glucose 34, protein 57, CSF TLC < 5, which had a gram stain positive and positive antigen test had the culture positive. The remaining 6 positive cases had negative cultures.

With reference to all the tables, the analysis of other diagnostic tests (biochemical) indicates the clinical correlation with suspected CNS infection patients.

Limitation of the study

In India, the state of UP has been a constant focus of JEV activity every year. The second half of 2005 saw one of the largest outbreaks of JE in three decades that has occurred in Northern India in recent years [34]. In UP, after the vaccination drives since 2006, overall incidence of JE has decreased (7.1% of AES). However, in Assam, the percentage of JE remains high (37.8% of AES) [14]. Average mortality due to JE has been estimated to be between 14 and 16% [8]. The FilmArray® ME Panel does not have the JE virus, which is a limitation.

Another major infection with CNS involvement, tuberculosis (TB), may be devastating. It is noted in 5 to 10% of extrapulmonary TB cases and accounts for approximately 1% of all TB cases. Definitive diagnosis of tuberculous meningitis (TBM) depends upon the detection of the tubercle bacilli in the CSF. The causative organism for TB, M*ycobacterium tuberculosis*, is also not part of the FilmArray® ME Panel. This again causes a setback to this technology.

Similarly, the panel lacks the Chikungunya and Dengue viruses and Plasmodium species. These are the most prevalent pathogens in the Indian subcontinent.

Conclusion

The FilmArray® ME is one of the latest technologies, which detects rapidly a broad range of infectious agents associated with the CNS infections. The data in this study depicts that the FilmArray® ME Panel is able to detect 14 pathogens directly in the CSF with excellent performance relative to culture and other laboratory reference methods. In cases of immune-compromised and transplant patients, the FilmArray® ME Panel will be of critical importance. For pediatric patients, the ability to test for both bacterial and viral agents will be tremendously useful and potentially allow more targeted use of antiviral and antibacterial drugs. The FilmArray® ME Panel takes an hour, which can reduce the time taken to diagnose the clinical cases.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval from institute Approved.

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