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Short Report

Immunochromatography in CSF improves data on surveillance of *S. pneumoniae* meningitis in India

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ABSTRACT

Introduction: Streptococcus pneumoniae is a significant cause of childhood bacterial meningitis in India. The United States Food and Drug Administration has licensed an immunochromatographic (ICT) test, Binax® NOW™, to detect the C polysaccharide antigen of *S. pneumoniae* in cerebrospinal fluids (CSF). Accurate etiological diagnosis of bacterial meningitis in India is essential for effective treatment strategies and preventive interventions.

Materials and methods: CSF samples from 2081 children admitted, with clinically suspected bacterial meningitis at 11 sentinel sites of hospital based sentinel surveillance network for bacterial meningitis in India between September 2009 and December 2016 were tested with ICT. Concurrent CSF cultures were processed using standard procedures.

Results and discussion: S. pneumoniae was detected thrice the number of times by ICT than by CSF culture, with a sensitivity and specificity of 100% and 95.3% respectively. This rapid ICT test proves to be of immense use as a diagnostic test for meningitis patients with/without prior antibiotic treatment, especially in facilities with limited laboratory infrastructure in resource limited settings.

Introduction

The World Health Organization (WHO) estimates that nearly 1 million children below 5 years of age die of invasive disease due to *Streptococcus pneumoniae* every year. A significant proportion of them live in developing countries, including India [1]. Ironically, part of this mortality can be prevented using available vaccines [2], while rapid and early diagnosis are crucial for effective treatment. Unfortunately, conventional diagnostic tests to detect Invasive

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Pneumococcal Disease (IPD), including bacterial meningitis are often not rapid or sensitive enough to help in making decisions on initiating antimicrobial therapy. *S. pneumoniae* are isolated and identified by culture, but overnight culture and recovery are compromised due to the production of autolysin, a cell wall enzyme responsible for its own lysis. Autolysis may distort the appearance of pneumococci in Gram stain and prevent growth in culture. Hence, antigen and nucleic acid detection are the other alternative common laboratory tests used to detect *S. pneumoniae*. The above mentioned diagnostic methods have some disadvantages: (1) culture may fail due to antimicrobial therapy before admission and lumbar puncture, (2) antigen detection methods lack sensitivity and (3) the molecular methods are relatively expensive and require substantial expertise [3,4]. Despite the global importance of pneumococcal disease, very limited developments have occurred in the area of laboratory diagnosis of *S. pneumoniae*. One of the rapid test for detecting *S. pneumoniae* is *S. pneumoniae* BinaxNOW®, an immunochromatographic (ICT) test that detects the C polysaccharide antigen of the pneumococcus cell wall. It has been licensed for use on cerebrospinal fluid (CSF) samples by the United States Food and Drug Administration. We report here our experience with the comparative performance of ICT to the standard culture in detecting pneumococcal meningitis as part of hospital based sentinel surveillance for bacterial meningitis in India.

Material and methods

CSF samples of children below 15 years of age who were suspected cases of bacterial meningitis with >10 WBC/mm^3 in CSFs were collected at hospitals under hospital based sentinel surveillance for bacterial meningitis in India (HBSSBM) network. The work was funded by Ministry of Health and Family Welfare, New Delhi. The study was coordinated by ICMR National Institute of Epidemiology (NIE), Chennai. The ICT kits were kindly provided by WHO, Geneva, to strengthen pneumococcal surveillance in India. The sites included in this study were: Government Medical College, Thiruvananthapuram, Government Medical College, Alapuzha, Institute of Child Health, Chennai, Stanley Medical College, Chennai, Kilpauk Medical College, Chennai, Madurai Medical College, Madurai, Christian Medical College, Vellore, Kasturba Medical College and Hospital, Manipal, Regional Medical Research Centre, Bhubaneswar, Indira Gandhi Institute of Medical Sciences, Shimla and Chacha Nehru Bal Chikitsalaya Hospital, New Delhi. We evaluated pediatric CSF samples from September 2009 through December 2016. CSF specimens were subjected to ICT testing (*S. pneumoniae* BinaxNOW®; Binax, Inc., Scarborough, Maine, USA). Concurrent CSF cultures were performed using standard routine microbiological procedures [5]. The ICT was performed according to the manufacturer's instructions. The ICT kit had been tested to rule out cross-reaction to organisms that are known to cause meningitis. We pre-evaluated CSF culture positive specimens for *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus viridans*, *Enterococcus faecalis*, *Neisseria meningitidis*, *Moraxella catarrhalis*, *Haemophilus influenzae* and *Klebsiella pneumoniae* and found no cross-reaction. Results of Binax test and CSF culture were compared by baseline characteristics. Chi Square test was used and 95% confidence intervals were calculated. STATA 13.1 I/C software was used for data analysis.

Results

A total of 12,850 CSF samples were collected from the study network. Based on >10 WBC/mm^3 count and availability of ICT test kits, 2081 specimens were subjected to ICT testing. One hundred and twenty-nine (6.1%) of the 2081 CSF samples were positive for *S. pneumoniae* by one or more of the following: either culture, ICT or together (clinical characteristics of Binax test and/or CSF culture positive cases were distributed in Tables 1 and 2). Of these, 33 (1.5%) were positive for *S. pneumoniae* by both culture and ICT and 96 (4.6%) were positive by ICT alone (see Table 3).

Discussion

For timely and effective diagnosis of bacterial meningitis, the staff in clinical microbiology laboratories has to be on call around the clock to process and interpret the Gram stain smears and initiate cultures in suspected cases. They have to be familiar with techniques to detect bacterial antigens in CSF and also must under-

Table 1
Characteristics of meningitis cases confirmed by Binax test and CSF culture.

	Total no. tested (*n = 2081*)	Positive by Binax (*n = 129*) (6.1%)	Positive by Binax and CSF culture (*n = 33*) (1.5%)	*P* value
Gender distribution				
Male	1135	59 (5.1%)	15 (1.3%)	0.60
Female	719	36 (5%)	7 (0.9%)	
Age distribution				
0–12 months	1076	51 (4.7%)	11 (1%)	0.76
13–24 months	272	9 (3.3%)	3 (1.1%)	
25–59 months	412	22 (5.3%)	6 (1.4%)	
59–179 months	97	16 (16%)	2 (2%)	
Diagnosis at time of admission				
Suspected meningitis	947	32 (3.3%)	13 (1.3%)	0.28
Acute CNS infections/encephalitis	102	7 (6.8%)	2 (1.9%)	
Meningitis	30	13 (43.3%)	2 (6.6%)	
Seizures/fever	256	7 (2.7%)	0 (0%)	
Diagnosis at discharge				
Acute CNS infections/meningitis/partially treated meningitis	584	33 (5.6%)	15 (2.5%)	0.03
Antibiotic usage				
Antibiotic prescribed for present illness	1231	41 (3.3%)	16 (1.3%)	0.33
Antibiotic not prescribed for present illness	177	3 (1.6%)	2 (1.1%)	
Antibiotic administered before LP	775	40 (5.2%)	11 (1.4%)	
Antibiotic not administered before LP	465	13 (2.7%)	5 (1%)	
<4 h of antibiotic before LP	258	10 (3.8%)	7 (2.7%)	
>4 h of antibiotic before LP	517	30 (5.8%)	4 (0.7%)	
Antibiotic/treatment in the last 48 h	458	20 (4.3%)	7 (1.5%)	

CNS – central nervous infections, LP – lumbar puncture.

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