ELSEVIER

Journal of Clinical Epidemiology 66 (2013) 36−43

Journal of Clinical Epidemiology

Invasive pneumococcal disease associated with high case fatality in India

Kurien Thomas[a,*], Lalitha Mukkai Kesavan[b], Balaji Veeraraghavan[b], Sudha Jasmine[a], John Jude[b], Mitra Shubankar[a], Poorva Kulkarni[c], Mark Steinhoff[c], and IBIS Study Group IndiaCLEN Network[1]

[a]*Department of Medicine, Christian Medical College, Vellore 632004, India*
[b]*Department of Microbiology, Christian Medical College, Vellore 632004, India*
[c]*Johns Hopkins Bloomberg School of Public Health, Baltimore, MD 21287, USA*

Accepted 9 April 2012

Abstract

Objective: To study the seroepidemiology and antimicrobial resistance pattern of invasive pneumococcal disease (IPD) in older subjects who are admitted to hospitals in India.

Study Design and Setting: Prospective surveillance of IPD in patients older than 18 years in seven large academic teaching hospitals in India from 1993 to 2008. All subjects who had *Streptococcus pneumoniae* isolated from normally sterile body fluids or were antigen positive in cerebrospinal fluid, ascitic fluid, and pleural fluid were identified as IPD cases in the study. Serotype/group (STG) and minimum inhibitory concentration for penicillin, chloramphenicol, co-trimoxazole (trimethoprim−sulfamethoxazole), erythromycin, and cefotaxime were determined.

Results: A total of 1,037 adult subjects with suspected invasive bacterial infection were recruited in the study. *S pneumoniae* was identified from normally sterile body fluids in 449 (43.3%) subjects. Meningitis (34.3%) and pneumonia (33.9%) were the most common clinical conditions associated with IPD. The case fatality was 25−30% across all age groups. Penicillin resistance was low at 2.7% overall. Resistance to co-trimoxazole was noted to be high and increasing in the study period from 42.9% in 1993 to 85.2% in 2008 ($P = 0.001$). The most common STG was serotype 1, which accounted for 22.9% of all isolates. The 23-valent pneumococcal polysaccharide vaccine covered 83.3% of the STGs (49/54; 95% confidence interval: 79.7, 96.9) for patients older than 60 years.

Conclusion: IPD continues to be a problem in India and is associated with high case fatality in spite of treatment in the hospital setting. Penicillin resistance is currently low in India. More than 80% of invasive STGs causing disease in the elderly in India are included in the formulation of polysaccharide pneumococcal vaccine.

Keywords: Surveillance; Invasive pneumococcal disease; Antimicrobial resistance; Serotype group; 23-valent pneumococcal polysaccharide vaccine; PPV23; *S pneumoniae*; STG

1. Introduction

The population of older people in the community is increasing [1] in India as the country goes through demographic transition. Globally, invasive pneumococcal disease (IPD) continues to have high case fatality rate and contributes significantly to morbidity and mortality, particularly in the older population above 60 years of age [2]. Although there is some controversy on the usefulness of polysaccharide pneumococcal vaccine (PPV23) in adult population [3,4], administration of PPV23 is recommended in populations at high risk for pneumococcal infection, including those older than 65 years in the United States and Europe. Reports suggest that PPV23 has 60−80% efficacy in reducing the burden of IPD and also decreases hospitalization and health care expenditure [5,6]. We have limited data on antimicrobial resistance (AMR) of IPD in India and the distribution of invasive pneumococcal serotype/groups (STGs) in the country to develop treatment guidelines and preventive policies. Although the Geriatric Society of India has recommended routine use of PPV23 in the elderly [7], The Expert Group of the Association of Physicians of India on Adult Immunization has recently stated that the available evidence is insufficient to

[1] The members of the network were Dr Kurien Thomas (Vellore), Dr Ramesh Ahuja (Lucknow), Dr Amita Jain (Lucknow), Dr A.K. Niswade (Nagpur), Dr Vandana Agarwal (Nagpur), Dr Bimal Das (New Delhi), Dr Rajmohan Pillai (Trivandrum), and Dr Kavita Raja (Trivandrum).

* Corresponding author. Tel.: +96824181055.
E-mail address: kurien123@gmail.com (K. Thomas).

0895-4356/$ - see front matter
http://dx.doi.org/10.1016/j.jclinepi.2012.04.006

recommend its routine use in the older population [8]. Currently, immunization rates with pneumococcal vaccine are very low in India. Lack of information on STG causing invasive disease may be one reason, so it was decided to review adult data from the Invasive Bacterial Infection Surveillance (IBIS) study. The present study describes the characteristics of IPD in hospitalized adult patients over a 15-year period in seven tertiary care centers across India with special reference to AMR pattern and the distribution of STGs.

1.1. Study objectives

The objectives were to study the STG and AMR pattern of IPD in India and assess the potential coverage offered by PPV23 in older subjects who are admitted to hospitals in India.

2. Methods

The study design was a prospective 15-year hospital surveillance.

2.1. Participating centers

Prospective hospital surveillance for suspected IPD was undertaken in seven large academic referral hospitals of the Indian Clinical Epidemiology Network (IndiaCLEN) by the IBIS study group from 1993 to 2008. The participating institutions include All India Institute of Medical Sciences (AIIMS), New Delhi; King George Medical College, Lucknow (KGMC), Lucknow; Government Medical College (GMC), Nagpur; Madras Medical College, Chennai; Christian Medical College, Vellore; Medical College, Trivandrum; Lokmana Thilak Medical College, Mumbai (LTM). Adult subjects were recruited in the study during 1993–1997 (phase 1) and 1999–2008 (phase 2). Geographic distribution of the study centers in India is given in Fig. 1. A report on phase 1 of the study primarily dealing with childhood disease (IBIS-1) was published earlier [9]. The study protocol was reviewed and approved by the institutional review boards of the seven participating hospitals as well as Johns Hopkins Bloomberg School of Public Health and the Institutional Review Board of International Clinical Epidemiology Network (INCLEN).

2.2. Study subjects

Adult patients older than 15 years attending the outpatient and inpatient setting from the network hospitals with the following syndromes were recruited: clinical evidence of pneumonia with or without radiographic evidence; clinically suspected pyogenic meningitis with suggestive cerebrospinal fluid (CSF) (>10 white blood cells/mL); and fever at a temperature of at least 39°C for 5 days or less, with hypotension, without definite urinary or gastrointestinal focus (hospital-based recruitment). Informed written consent was obtained from all recruited subjects before study-related procedures. Exclusion criterion was admission to the hospital during the 10 days before presentation to avoid hospital-acquired infections. In addition, hospital and laboratory records of the network hospitals were scrutinized every day and patients with isolates of *Streptococcus pneumoniae* from normally sterile sites were included, if they met the study criteria and the patient was available for follow-up in the ward prospectively (laboratory-based recruitment).

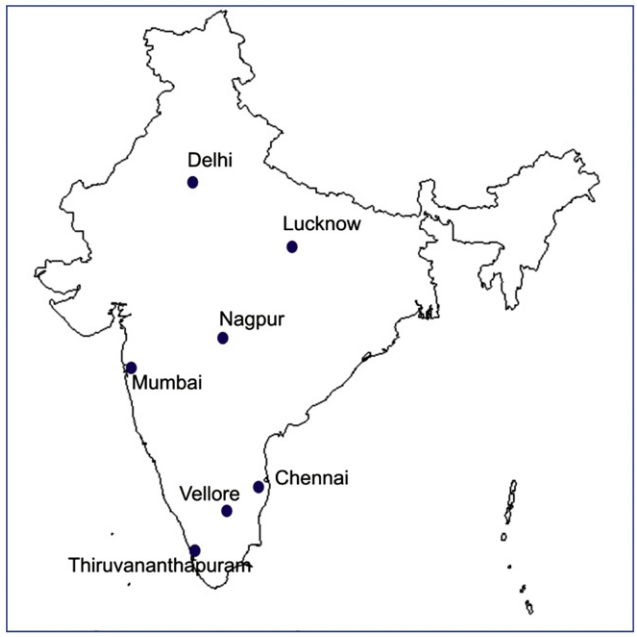

Fig. 1. Geographic distribution of study centers in India.

Adult subjects were recruited in the study during 1993–1997 (phase 1) and in 1999–2008 (phase 2). Information on the history, course, and outcome of illness was recorded on standardized study data forms. Subject recruitment was similar in the two phases of the study. The difference was primarily in the source of funding and minor variation in microbiology technique (described in laboratory methods).

2.3. Laboratory

During both phases of the study, 5–10 mL of normally sterile body fluids were collected for bacteriologic identification. In phase 1 of the study, blood samples were collected in trypticase soy broth and subcultured according to the World Health Organization (WHO) manual for AMR [9]. For detailed laboratory methods during phase 1, refer to the IBIS-1 report [10]. During phase 2, blood samples were inoculated on standard commercial HiMedia primary culture blood agar plates (HiMedia Laboratories, Mumbai). At the reference laboratory, blood was collected in BacT/ALERT automated blood culture media (bioMerieux Inc, Durham, NC) for primary culture. In presence of any growth after 12–24 hours, subculture was done and held for 7 days on