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ORIGINAL ARTICLE

Epidemiology of invasive pneumococcal disease in Saudi Arabian children younger than 5 years of age



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Abstract This study evaluated the incidence, serotype distribution, and antimicrobial susceptibility of invasive pneumococcal disease (IPD) in Saudi Arabian children. This multicenter, prospective, clinical surveillance study included children under 5 years of age, residents of one of the seven study health areas, who were brought to a study hospital with suspicion of IPD. Bacterial isolates from sterile site samples, collected less than 24 h after hospital visit/admission, were identified, serotyped, and tested for antibiotic susceptibility. Between June 2007 and January 2009, 631 episodes of suspected IPD were recorded, and 623 were included in the analysis. One child (0.2%) had previously received one dose of a pneumococcal vaccine. Forty-seven episodes were positive for *Streptococcus pneumoniae* and three for *Haemophilus influenzae*. The incidence of confirmed IPD cases was estimated to be 2.5–21.6 per 100,000 children (<5 years). Among the 46 *S. pneumoniae* isolates serotyped and tested for antibiotic susceptibility, the most common serotypes were 5 and 23F (20% each), 6B (17%), and 1 and 14 (11% each). Sixty-three percent of isolates were multidrug-resistant. Vaccination of Saudi Arabian children with expanded-coverage conjugate pneumococcal vaccines containing serotypes 1 and 5 could have a substantial impact to prevent IPD in this population. © 2015 Ministry of Health, Saudi Arabia, Production and hosting by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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1. Introduction

Invasive pneumococcal disease (IPD) caused by *Streptococcus pneumoniae* is a major cause of morbidity and mortality worldwide, especially in young children and elderly people; its most severe manifestations include bacteremia, septicemia, bacteremic pneumonia, and meningitis [1,2]. A previous study conducted in 1999–2003 in Saudi Arabia has estimated an average annual IPD incidence of 17.4/100,000 children younger than 5 years of age, a case fatality rate of 12.2%, and an almost fourfold higher incidence of IPD in the 1st year of life compared with the next 4 years [3]. That study may underestimate the true IPD burden in Saudi Arabia since only microbiologically confirmed IPD cases (meningitis or bacteremia) were included in the analyses [3]. Additionally, as the study focused only on hospitalized children, outpatient bacteremia was not assessed and blood cultures from pneumonia were frequently not performed [3].

Currently, more than 90 pneumococcal serotypes have been identified based on differences in capsular polysaccharides. The serotype distribution varies somewhat between different geographical regions, especially regarding the relative prominence of serotypes 1 and 5 [4,5]. In a study conducted in 2000–2004 on 350 isolates collected from children in different regions of Saudi Arabia, the most common invasive *S. pneumoniae* serotype was 14, followed by serotypes 23F, 6B, and 19F. These serotypes were shown to account for 80% of the invasive pneumococcal isolates resistant to widely used antibiotics (penicillin, erythromycin, and cefotaxime); in Saudi Arabia, different antibiotics are prescribed against these pathogens as there are no national guidelines [6].

Other studies conducted in Saudi Arabia have shown a high and increasing prevalence of multidrug-resistant *S. pneumoniae* isolates [6–14]. The emergence of antimicrobial resistance among pneumococcal isolates is a major health problem in many other countries and is mainly due to the extensive and inappropriate use of antibiotics [15].

Since certain serotypes occur with different frequencies due to outbreaks, temporal variability in serotype distribution can be observed. The existing data need to be updated and the relative value of expanded serotype conjugate vaccines needs to be understood. Moreover, the true IPD incidence rate in Saudi Arabia remains unclear, as does the geographical representativeness of previous studies. The current clinical study assesses the

incidence per health area (except Riyadh and Jeddah) of IPD in Saudi Arabian children younger than 5 years of age, along with the distribution of pneumococcal serotypes and antibiotic susceptibility of *S. pneumoniae* isolates, in both inpatient and outpatient populations that had not yet benefited from the introduction of pneumococcal conjugate vaccination. Additionally, this study attempted to provide information on other bacterial pathogens causing invasive disease in Saudi Arabian children, such as *Haemophilus influenzae* and *Neisseria meningitidis* and to describe antimicrobial drug resistance patterns of these pathogens in Saudi Arabian children suspected of having IPD.

2. Materials and methods

2.1. Study design and participants

This multicenter, prospective, national, clinical surveillance study was conducted in 12 hospitals located in seven health areas (Al Gassim, Al Baha, Al Jouf, Al Madeenah, Al Qateef, Riyadh City, and Jeddah City), to represent the epidemiology and disease burden across Saudi Arabia. The selected study hospitals from Riyadh and Jeddah do not accurately represent the catchment area for these two cities because of other private and public healthcare centers not included in this study; for this reason the two areas were excluded from the incidence calculation. The recruitment period was longer than 1 year to take seasonal variations into account (June 2007–January 2009). The study was conducted according to Good Clinical Practice, the Declaration of Helsinki, and the local rules and regulations of the country. The study protocol and the consent form were reviewed and approved by the Ministry of Health or the National Independent Ethics Committee. Before enrollment, informed consent was obtained from the parents/guardians of each study participant.

This study included children younger than 5 years of age suspected of having IPD, who were residents of the study areas and were brought to one of the study hospitals. Suspected IPD cases were identified by the local physicians according to their individual clinical judgment. IPD was suspected if at least one of the following pulmonary symptoms was present: dyspnea, chest discomfort, pleuritic pain, chest splinting, cough productive of purulent or blood-tinged sputum, tachypnea, or tachycardia. Other symptoms included fever (axillary temperature $>37.5^{\circ}\text{C}$), elevated white blood cells ($>15,000$), suspicion of meningitis, or systemic complaints. At each study hospital, attempts were

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