ORIGINAL ARTICLE

Evolution of antimicrobial resistance and serotype distribution of *Streptococcus pneumoniae* isolated from children with invasive and noninvasive pneumococcal diseases in Algeria from 2005 to 2012

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Abstract

Pneumococcal infections are a major cause of morbidity and mortality in developing countries. The introduction of pneumococcal conjugate vaccines (PCVs) has dramatically reduced the incidence of pneumococcal diseases. PCVs are not currently being used in Algeria. We conducted a prospective study from 2005 to 2012 in Algeria to determine antimicrobial drug resistance and serotype distribution of *Streptococcus pneumoniae* from children with pneumococcal disease. Among 270 isolated strains from children, 97 (36%) were invasive disease; of these, 48% were not susceptible to penicillin and 53% not susceptible to erythromycin. A high rate of antimicrobial nonsusceptibility was observed in strains isolated from children with meningitis. The serotype distribution from pneumococci isolated from children with invasive infections was (by order of prevalence): 14, 1, 19F, 19A, 6B, 5, 3, 6A and 23F. Multidrug resistance was observed in serotypes 14, 19F, 19A and 6B. The vaccine coverage of serotypes isolated from children aged <5 years was 55.3% for PCV7, 71.1% for PCV10 and 86.8% for PCV13. Our results highlight the burden of pneumococcal disease in Algeria and the increasing *S. pneumoniae* antibiotic resistance. The current pneumococcal vaccines cover a high percentage of the circulating strains. Therefore, vaccination would reduce the incidence of pneumococcal disease in Algeria.

Keywords: Algeria, antibiotics, burden of disease, children, pneumococcal conjugate vaccines, pneumococcal diseases, serotype distribution, *Streptococcus pneumoniae*

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Introduction

Streptococcus pneumoniae is a leading respiratory pathogen that is responsible for infections such as pneumonia, meningitis, bacteremia and otitis media. In 2003, the World Health Organization (WHO) estimated that pneumococcal disease is responsible for 1 million deaths annually, most of which occur in children <5 years of age in the developing world [1]. Although pneumococcal meningitis is relatively rare, it is strongly associated with mortality or subsequent neurologic damage [2].

Pneumococcal resistance to penicillin was first described in 1967, and since the 1990s an increasing rate of resistance has been reported worldwide [3,4]. This resistance makes the treatment of serious pneumococcal infections difficult, and many antibiotic treatment failures have been reported [5].

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In Algeria, several reports have shown an increase in antibiotic resistance from 1996 to 2010, especially among children [6–9]. Although epidemiologic surveillance data for invasive pneumococcal infections are available, clinical data are lacking. Moreover, since the introduction of *Haemophilus influenzae* type b vaccination in 2008 in Algeria, *S. pneumoniae* has become the predominant pathogen in bacterial meningitis (unpublished data).

The *S. pneumoniae* polysaccharide capsule is a major virulence factor; more than 90 serotypes have been identified, and their distribution differs in different regions and between developing and developed countries [10]. This highlights the importance of having national data before implementation of a pneumococcal vaccine. The aim of the study was to investigate the evolution of antibiotic resistance and serotype distribution of *S. pneumoniae* in infections in children in Algeria.

Material and methods

From January 2005 to June 2012, a total of 270 unique *S. pneumoniae* isolates were collected from children aged 0 to 16 years with invasive and noninvasive infections; about 89% were from Algiers and 11% from Oran, a town located in the western part of the country. The hospital clinical laboratories were asked to send all their viable isolates. Every year, the centers isolate between 15 and 50 *S. pneumoniae* strains from children who are diagnosed by physicians with invasive pneumococcal disease (IPD) and non-IPD (NIPD). *S. pneumoniae* isolates were identified by colony morphology, Gram staining, catalase reaction, optochin susceptibility and bile lysis. Antibiotic susceptibilities for oxacillin, erythromycin, clindamycin, tetracyclin, chloramphenicol and cotrimoxazole were determined following the Clinical and Laboratory Standards Institute (CLSI) recommendations [11,12]. Minimum inhibitory concentrations (MICs) for penicillin, amoxicillin and cefotaxim were determined using the E-test following the manufacturer's instructions (Solna, Sweden) for all strains. The *S. pneumoniae* ATCC 49619 strain was used for quality control.

Serotyping was performed by latex agglutination for determining pools, and serotypes were identified using the Neufeld test (Pneumo test latex; Statens Serum Institute, Copenhagen, Denmark). A total of 127 isolates were serotyped, 85 from invasive samples and 42 from noninvasive samples. The isolates that were serotyped were selected on the basis of the clinical data, with priority given to IPD and the number of viable isolates. Isolates were stored in 10% glycerol broth at −80°C after primary isolation.

Results

From the 270 isolates collected (IPD *n* = 97, NIPD *n* = 173), 197 (73.0%) were from children <5 years, of whom 151 (76.7%) were <2 years. Among the isolates from children with IPD, 78.4% were collected from children <5 years of age, of whom 76.3% were <2 years old. The IPD isolates were collected from children with meningitis (*n* = 53), pneumonia and pleuropneumonia (*n* = 25), bacteremia (*n* = 11), arthritis or peritonitis infections (*n* = 8). The non-IPD isolates were from ear, nose and throat infections (*n* = 91), bronchopulmonary infections (*n* = 77) and other suppurative infections (*n* = 5). Among the isolates from children with NIPD, 69.9% were from children <5 years of age; 53.8% were <2 years old (Table 1).

Nonsusceptibility to penicillin was detected in 48% of the *S. pneumoniae* isolates (MICs ranged from 0.016 μg/mL to 4 μg/mL); 2.6% of isolates had intermediate resistance to amoxicillin; 7% and 1.7% of isolates had intermediate and full resistance to cefotaxime, respectively. For the IPD isolates, the MIC90s were 2 μg/mL for penicillin and amoxicillin and 1.5 μg/mL for cefotaxime. The highest rate of cefotaxim resistance was observed in isolates from meningitis: 20.8% intermediate and 3.8% resistant (Table 2).

The percentages of isolates that were resistant to non-β-lactam antibiotics were 53.0% for erythromycin and cotrimoxazole; 43.7% for clindamycin; 42.0% for tetracycline; and 5.3% for chloramphenicol. According to the new breakpoints suggested by CLSI, whereby meningitis and nonmeningitis isolates have different breakpoints, 49.0% of the meningitis isolates were resistant to penicillin (MIC ≥0.12 μg/mL), among which 26.9% had a MIC of ≥2 μg/mL.

TABLE 1. Number of *Streptococcus pneumoniae* isolates by sample origin and patient age

Sample	Patient age			Total
	<2 years	2–5 years	>5–16 years	
Invasive samples				
CSF	30	10	13	53
Blood culture[1]	15	4	2	21
Puncture fluids[2]	13	4	6	23
Total	58	18	21	97
Noninvasive samples				
Lower respiratory tract samples	57	8	12	77
Auricular swabs	31	7	9	47
Sinus and nasal aspirates	5	10	29	44
Other samples[3]	0	3	2	5
Total	93	28	52	173
Overall total	151	46	73	270

[1]Pneumonia (*n* = 10), bacteremia (*n* = 11).
[2]Pleural (*n* = 15), joint (*n* = 5), peritoneal (*n* = 3).
[3]Conjunctive (*n* = 4), genital sample (*n* = 1).