



The Brazilian Journal of INFECTIOUS DISEASES

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Original article

Clinical and microbiological implications of invasive pneumococcal disease in hospitalized patients (1998–2013)[☆]



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ARTICLE INFO

Article history:

Received 2 October 2015

Accepted 25 January 2016

Available online 16 April 2016

Keywords:

Streptococcus pneumoniae

Serotypes

Death

Comorbidity

ABSTRACT

Introduction: Infections caused by *Streptococcus pneumoniae* (pneumococcus) still represent a challenge for health systems around the world.

Objective: The objective of this study was to assess microbiological and clinical aspects in hospitalized patients with invasive pneumococcus disease between 1998 and 2013.

Materials and methods: This was a retrospective study that analyzed the results of pneumococcus identification, serotyping, and susceptibility testing found in the Adolfo Lutz Institute databank. Personal variables, medical history and clinical outcome of patients admitted with invasive pneumococcal disease were analyzed. These were obtained from records of a public teaching hospital – Hospital das Clínicas Faculdade de Medicina Ribeirão Preto.

Results: The sample comprised 332 patients. Patient age ranged from less than one month to 89 years old (mean 20.3 years) and the sample was predominately male. Pneumonia (67.8%) was the most common disease, accounting for 18.2% of deaths. Serotypes 14, 1, 3, 9V, 6B, 6A, 23F, 19A, 18C, 19F, 12F, and 4 were the most common (75.3%). Most patients, or 67.5%, were cured without any complication (success), 6.9% had some type of sequela (failure), and 25.6% died (failure). In the case of deaths due to meningitis, strains of fully penicillin resistant pneumococcus were isolated. Furthermore, 68.2% of patients who died presented some type of comorbidity. The 60 and older age group presented the most significant association (Odds Ratio = 4.2), with outcome failure regardless of the presence of comorbidity. Serotype 18C was the most significant risk factor both in raw analysis (Odds Ratio = 3.8) and when adjusted for comorbidity (Odds Ratio = 5.0) or age (Odds Ratio = 5.4). The same occurred with serotype 12F (respectively, Odds Ratio = 5.1, Odds Ratio = 5.0, and Odds Ratio = 4.7)

[☆] Part of a doctoral thesis “Serotypes and antimicrobial resistance profile of *Streptococcus pneumoniae*: clinical implications for invasive disease and the national immunization program” (1998–2013).

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<http://dx.doi.org/10.1016/j.bjid.2016.01.011>

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Conclusion: The present findings highlight the importance of IPD among young adults and older adults. In the era of conjugate vaccines, monitoring serotypes in different age groups is essential to assess the impact and adequacy of immunization.

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Introduction

Even with the possibility of immunoprevention of several serotypes, the World Health Organization has indicated and estimated 1.6 million deaths per year due to pneumococcus disease. The data demonstrate greater prevalence in developing countries and 0.7–1 million children less than five years of age.¹ In countries with immunization for *H. influenzae* serotype b, pneumococcus has become the most common cause of invasive disease.² Based on data from the Hospital Information System (HIS), Novaes, Sartori, and Soárez³ found that there were 34,217 hospitalizations due to pneumococcal disease in the Brazilian Unified Health System (SUS) between 2006 and 2014. This figure represented 0.1% of the total of admissions, of which 64.8% were pneumococcal pneumonia. A study on the clinical and epidemiological profile of patients with pneumonia acquired in the community observed among individuals under the age of 60 an elevated percentage of the disease, in addition to worsened clinical outcomes. Lethality was low (4.9%) and concentrated among the youth. In Brazil, these patients are usually hospitalized in order to ensure access to medication and clinical follow-up, especially in the case of older adults and individuals with underlying chronic diseases.⁴ According to the Brazilian Ministry of Health,⁵ between 2000 and 2008 pneumococcal meningitis represented 11% of bacterial meningitis recorded in the Notifiable Diseases Information System (SINAN), with an average of 1218 cases per year and 30% lethality. In order to minimize the impact of pneumococcal disease, in 2009 the National Agency of Health Surveillance (ANVISA) approved the use of conjugate pneumococcal polysaccharide vaccine (PVC) with 10 specific serotypes (PVC10) in children under the age of two. Thus, Brazil was one of the first countries to include the VPC10 in the immunization schedule of the National Immunization Program (PNI).^{6,7} The objective of this study was to analyze clinical and microbiological aspects of people hospitalized with IPD between 1998 and 2013, and therefore evaluate the outcome of cases in relation to the serogroups.

Materials and methods

This was a retrospective cross-sectional study that analyzed records from 1998 to 2013. These records contained the results of 332 isolated pneumococcal strains in patients with invasive pneumococcus disease (IPD) hospitalized in the Ribeirão Preto School of Medicine Teaching Hospital–University of São Paulo (HCRP-USP), Brazil. The pneumococcus samples included in this study were isolated in the HCRP laboratory and sent to Adolfo Lutz Institute in Ribeirão Preto (IAL-RP) in order to

confirm the species, and then forwarded to the National Laboratory of Public Health (Adolfo Lutz Institute in São Paulo) for serotyping and to determine the antimicrobial susceptibility profile. Toward this end, microbiological information was obtained from the IAL-RP archives and the clinical aspects of patients retrieved from the surveillance system of HCRP-USP epidemiological center.

Analysis and inference of results

The information gathered was saved on an MS Excel XP spreadsheet and then exported to SPSS (Statistical Package for the Social Sciences), version 19.0 for statistical analyses: descriptive analysis through absolute and relative frequencies and then means, standard deviations, medians, and minimum and maximum values were calculated. Possible associations between outcomes: success (cure with no complications) or failure (cure with complications or death). The studied variables (gender, age, presence of comorbidity, and the most common serotypes) were analyzed using chi-square test and univariate (raw OR) and multiple (adjusted OR) logistic regression. Level of significance was set at $p \leq 0.05$. This was a retrospective study, with limitations associated with the nature of information in quantitative and qualitative terms. The present study was approved by the human subject research ethics committee, protocol CAAE: 26759714.80000.5393.

Results

Among the 332 patients with IPD, age ranged from less than a month to 89 years old, with mean age of 20.3 (standard deviation = 25.5 years, median 4 years), with a predominance of male patients (61.1%). The most common clinical diagnoses were pneumonia (67.8%), followed by meningitis and bacteremia (22.9%). After 2010, there was a significant reduction in the number of pneumococcus cases sent for identification (Table 1). Forty-two different serotypes of *S. pneumoniae* were identified, of which 75.3%, in decreasing order, were serotypes 14, 1, 3, 9V, 6A, 6B, 23F, 19A, 18C, 19F, 12F, and 4 with at least 10 isolates. Furthermore, there was a progressive increase of serotypes 3 and 6A, which were present in the 13-valent conjugate pneumococcal vaccine, and serotypes 12F and 18C (non-vaccine). There was a reduction in serotypes 14, 1, and 23F included in VPC10 (Table 2). The prevalence of the serogroups varied according to age of the patients. Serogroup 14 was the most common in children younger than five years of age, and serogroup 3 was the most common in the age range greater than five years old (Table 3). In children younger than five years of age, in the period prior to the VPC10, there

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