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A population-based assessment of the disease burden of consolidated pneumonia in hospitalized children under five years of age

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Summary
Background: Population-based studies on childhood community-acquired pneumonia are scarce in Latin America. Pneumococcal epidemiology is poorly defined, hence the World Health Organization recommended standardized chest radiograph interpretation to improve the approach to bacterial pneumonia. Therefore, our study aimed to estimate the burden of pneumonia in hospitalized children.
Methods: A three-year surveillance study was carried out in four hospitals covering a population of 229 128 inhabitants of whom 10.2% were under five years of age. Clinical records and digitization of their chest radiographs were obtained. A pediatrician and a pediatric radiologist blinded to the clinical diagnosis interpreted the digital images.
Results: Of 2034 patients, 826 (40.6%) had consolidated pneumonia, 941 (46.3%) had non-consolidated pneumonia, and 267 (13.1%) had no pneumonia. Children under two years of age predominated (66.9%). The average annual incidence rate for consolidated pneumonia over the three-year study period was $1175/10^5$. Eighteen invasive *Streptococcus pneumoniae* were isolated from patients with consolidated pneumonia and two from those with non-consolidated pneumonia. Respiratory syncytial virus was evenly distributed between both X-ray groups.
Conclusions: Patients younger than two years of age predominated, being the main targets for anti-pneumococcal conjugated vaccines. Incidence rates provided evidence of the burden of consolidated pneumonia for childhood, estimating the potential benefits of vaccination.

Introduction

Pneumonia is the major cause of morbidity and mortality from pneumococcal infection, especially in developing countries.[1] Population-based studies on community-acquired pneumonia

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in childhood are scarce in Latin America and *Streptococcus pneumoniae* epidemiology is poorly defined due to the low sensitivity of bacteriologic diagnostic methods. To overcome this problem the World Health Organization (WHO) recommended standardized chest radiograph interpretation as an epidemiological tool to provide a reasonable approach to bacterial pneumonia.[2] In addition, to assure comparability of data among population-based studies on pneumonia burden and results from vaccine field trials performed in different countries, a generic protocol was proposed by the WHO in collaboration with the Communicable Disease Center (CDC). This protocol was adopted in several Latin American countries, including Uruguay, in order to assess the burden of consolidated pneumonia in hospitalized children under five years of age, and the proportion preventable by vaccination with a *S. pneumoniae* conjugated vaccine.[3] In Uruguay, this estimation was facilitated because ten years of anti-*Haemophilus influenzae* type b (Hib) vaccination had dramatically controlled Hib pneumonia, and consequently it was possible to assume that most of the remaining bacterial pneumonia cases were due to *S. pneumoniae*.[4,5] Also, bacteremic pneumonia has been monitored since 1994, providing data on serotype frequency and antibiotic susceptibility of invasive isolates.[6,7]

Methods

A three-year population-based prospective study (June 2001—May 2004) was carried out in the municipalities of Paysandú and Salto in Uruguay, covering a population of 229 128 inhabitants of whom 23 445 (10.2%) were under five years of age. These populations represent 7.1% and 8.3% of the total national population, respectively.

Patients were enrolled in four hospitals (two public and two private). Those eligible for enrollment were patients with acute lower respiratory tract infections for whom a chest X-ray was performed on admission to confirm a clinically suspected case of pneumonia. Excluded from the study were bronchiolitis and asthma/bronchial hypersensitivity cases for whom no X-ray was ordered.

A research nurse checked the pediatric ward admission book daily looking for children under five years of age. The medical charts of the patients were reviewed and relevant data were abstracted onto a standardized form including age, sex, previous hospitalizations, recent antibiotic-treated episodes, underlying conditions, selected respiratory signs and symptoms, antibiotherapy, duration of hospitalization, and outcome.

Digitization of the analog chest X-rays was also performed. A pediatrician and a pediatric radiologist, blinded to the patients' clinical diagnoses, interpreted the digital images according to the WHO criteria: alveolar consolidation or pleural effusion, non-consolidated pneumonia with mild interstitial/perihilar changes, and no pneumonia. By a table of random numbers, 10% of the digitized chest X-rays were identified and referred to an international panel of experts for quality evaluation.

Selected variables from the standardized form were compared between children with consolidated and non-consolidated pneumonia.

Bacterial and viral etiologies were routinely investigated during three winter months, three days per week. During the three study years, blood or pleural fluid specimens were cultured by standard methods for isolation of invasive pneumococci. At the National Reference Laboratory, identification of *S. pneumoniae* isolates was confirmed, serotypes determined by 'quelling' reaction, and susceptibility to antibiotics (penicillin, third generation cephalosporins, trimethoprim—sulfamethoxazole, vancomycin) assessed according to the National Committee for Clinical Laboratory Standards. Viral antigens for five respiratory viruses (respiratory syncytial virus (RSV), influenza A and B, parainfluenza 3, and adenovirus) were investigated by direct immunofluorescence (Light Diagnostics, Respiratory Panel, CA, USA) in cells of nasopharyngeal aspirates during the last two study years.

Data were entered into Epi Info 6.4, which was also employed for statistical analysis.

To calculate the annual incidence rate of chest X-ray documented consolidated pneumonia cases, the number of cases enrolled in one year (numerator), was divided by the number of population at risk in the area (denominator), and the result multiplied by 100 000. Non-parametric variables were evaluated by Chi-square test and results were considered significant when $p < 0.05$. The kappa coefficient was used to measure the degree of agreement between the interpretation of the local readers and the reference panel of experts. This project was approved by the Pediatric Committee of Ethics from the Pediatric Institut Prof L.A. Morquio.

Results

Between June 2001 and May 2004, 2034 children were eligible for enrollment: 668, 662, and 704 patients per year. The majority of the inpatients were cared for at public hospitals, while a minority were admitted to private services, 97.1% and 2.9%, respectively. Most of the families lived in urban areas (82.2%), but their homes were located in areas where dwelling conditions and poverty predisposed the children to illness. Only 363 patients lived in rural areas (17.8%).

Table 1 shows the age distribution of all the enrolled patients. Of these 54.5% were male. Their median age was one year (range 0—4) with predominately children younger than 24 months (66.9%), of whom 38.3% were aged less than 12 months.

The standardized radiograph interpretation of 2034 patients indicated that 826 (40.6%) had consolidated pneumonia, 941 (46.3%) had non-consolidated pneumonia, and 267 (13.1%) had no pneumonia. Agreement between the interpretation of the local readers and those of the panel of experts showed a kappa coefficient of 0.58, which validated the study results.

Table 1 Age distribution of children aged less than five years hospitalized with community-acquired pneumonia

Age (in months)	Cases (*n*)	%	Accum. %
0—5	381	18.7	18.7
6—11	399	19.6	38.3
12—23	581	28.6	66.9
24—35	312	15.3	82.2
36—59	361	17.8	100.0
Total	2034	100.0	