International Journal of Infectious Diseases 38 (2015) 1–6

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Epidemiological burden of invasive pneumococcal disease in children and adolescents with predisposing risk factors

Luiza Helena Falleiros-Arlant [a,*], Eitan Naaman Berezin [b], Maria Luisa Avila-Aguero [c], Maria Catalina Pirez [d], Angela Gentile [e], Vesta Richardson [f], Jose Brea [g], Cristina Mariño [h]

[a] Faculdade de Medicina da Universidade Metropolitana de Santos, São Paulo, Brazil
[b] Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, Brazil
[c] Hospital Nacional de Niños Dr. Carlos Sáenz Herrera, San José, Costa Rica
[d] Facultad de Medicina, Universidad de la República, Uruguay
[e] Hospital de Niños Ricardo Gutierrez, Ciudad Autónoma de Buenos Aires, Argentina
[f] Secretaría de Salud del Estado de Morelos, Mexico
[g] Centro Medico Universidad Central Del Este, Santo Domingo, Dominican Republic
[h] Universidad Militar Nueva Granada, Bogotá, Colombia

ARTICLE INFO

Article history:
Received 10 April 2015
Received in revised form 12 June 2015
Accepted 23 June 2015

Corresponding Editor: Eskild Petersen, Aarhus, Denmark.

Keywords:
Pneumococcal Vaccines
Child
Adolescent
Latin America
Vaccines
Conjugate

SUMMARY

Objective: Some medical conditions constitute important risk factors for the development of invasive pneumococcal diseases in children and adolescents aged from 5 to 19 years. Conjugate vaccines have potential efficacy in this scenario, but are not available in many Latin American public healthcare systems for this age group. This study aimed to estimate the preventable fraction of invasive pneumococcal diseases among individuals aged from 5 to 19 years with associated risk factors for its development.

Methods: Data regarding the Latin America population, risk factors prevalence and conjugate vaccines efficacy were obtained from the literature.

Results: Total population at risk ranged from 17.3 to 64.6 million of individuals and asthma was the most impacting risk factor. According to SIREVA, PCV13 provided a 62.9% serotypes coverage in individuals from 5 to 29 years in 2012, potentially increasing the covered population from [8,338,457-31,057,620] with PCV10 to [10,906,356-40,622,078] with PCV13. To date, according to available efficacy data, the hypothetically immunized population ranged from 11.4 to 42.4 million, representing 7.0% to 26.0% of the total population in this age group.

Conclusions: Vaccination in risk groups should be encouraged, as it potentially contributes to the reduction in the number of cases of invasive pneumococcal disease.

1. Introduction

Despite the current scenario of population aging and the predominance of chronic degenerative diseases as the main cause of death, invasive pneumococcal diseases (IPD) (meningitis, bacterial pneumonia and bacteremia/sepsis) still constitute a major cause of mortality in Latin America (LA), especially among children and elderly people.[1]

Streptococcus pneumoniae is the most prevalent etiologic agent associated with pneumonia cases in LA, accounting for 11.08% of all disease causes.[2] The average incidence of pneumococcal pneumonia is estimated at 918 cases per 100,000 child-years in the age group of up to five years.[2] Pneumonia associated mortality for any etiologic agent in adults over 50 years is estimated at 17.7%, with 20-60% of cases related to *S. pneumoniae*.[3] In addition, bacteremia may occur in up to 30% of patients with pneumococcal pneumonia, with 20% mortality in children, reaching up to 60% in the elderly.[4]

* Corresponding author. Faculdade de Medicina da Universidade Metropolitana de Santos Campus Bandeirante I, Rua da Constituição, n° 374 Vila Nova – Santos – SP, CEP 11015-470. Tel.: +13 3226-3400; fax: +13 3235-2990.
E-mail address: luizahfc@terra.com.br (L.H. Falleiros-Arlant).

http://dx.doi.org/10.1016/j.ijid.2015.06.016

Pneumococcal meningitis is also a relevant issue in LA. It is estimated that 6.0% of all meningitis are due to pneumococcus. The incidence in this context is an average of 8.34/100,000 in children aged 0-23 months, and 4.62/100,000 in the age group of up to five years. The mortality rate is high among the elderly reaching 80% and ranges from 1.8% to 14.9% among children aged up to 59 months.[4,5]

Serotypes 1, 3, 5, 6A/B, 7F, 9 V, 14, 18C, 19A/F, and 23F are the most frequently found in LA. These serotypes are covered by both conjugate vaccines (PCV7 contains 4, 6B, 9 V, 14, 18C, 19F and 23F serotypes; PCV10 also covers serotypes 1, 5 and 7F in addition to PCV7; and PCV13 contains serotypes 1, 3, 5, 6A, 7F and 19A in addition to PCV7) and the polysaccharide vaccine PPSV23 (serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9 V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F). Thus, despite the high incidence of IPD, available vaccines show potential efficacy in this scenario, setting up a preventable health problem in these countries.

It is known that the incidence of IPD in children and adolescents aged 6 to 17 years is low.[6] Nevertheless, the disease estimation in LA is incipient in this age range due the lack of active surveillance in that particular group. In addition, some medical conditions constitute important risk factors for this age group, such as renal failure, liver failure, chronic lung disease (including asthma), diabetes mellitus, asplenia, cancer, HIV and other diseases.[7,8] Despite this, little research has been carried out in LA and specifically in subjects aged up to 19 years in order to describe the incidence, prevalence, morbidity and additional risk factors for these subgroups. However, research performed in other fields has shown that PD incidence in these individuals is actually higher when compared to those without such conditions.[9] Examples include patients with diabetes, cancer, chronic pulmonary and cardiac diseases having IPD incidence estimated at 34.9 cases per 100,000 people. By comparison, IPD incidence for individuals with same age, but no risk factors was evaluated at 8.8/100,000.[9]

In certain surveys conducted in the United States (US), IPD incidence ranged from 21.1 to 23.0/100,000 in adults with moderate to severe asthma.[10,11] However, in adults without asthma, incidence was estimated at 8.8/100,000.[11] When asthmatic individuals aged 2-49 years were considered, IPD incidence was 42/100,000.[11] This suggests that IPD incidence may be higher among asthmatic children and adolescents when compared to adults with the same condition. Regarding IPD prevalence, the magnitude varied from 17.1 to 17.7% in asthmatic children and adolescents aged 5-17 years vs. 5.5 to 8.1% among subjects with the same age, but without asthma.[10]

Another commonly vulnerable subgroup to pneumococcal infections is end-stage renal disease. Among these patients, IPDs are the second cause of death and the leading cause of hospitalization. This situation takes place, in part, by uremia related to decrease of immune function, and also by exposure to infection through the dialysis catheter. The most common infections among them are urinary tract infections, sepsis and pneumonia.[12]

Subjects with any immunosuppressive condition are also particularly vulnerable to *S. pneumoniae*, including, therefore, positive HIV patients. IPD incidence in HIV positive individuals is estimated at 246/100,000 for those aged 15-44 years and is still higher among patients not using antiretroviral therapy (281/100,000) and those with severe immunosuppression (563/100,000).[13]

Sickle cell disease is also considered a risk factor for IPD development, besides presenting a worse prognosis when compared to individuals without the disease. In a US study with children and adolescents under 18 years old with sickle cell disease, they were more likely to be hospitalized (84%-92% vs. 31%-56%) and had higher risk to die (6%-17% vs. 1%-2%) when compared to children and adolescents with IPD, but without this additional risk factor.[14]

Van Hoek and colleagues reported that among children aged 2 to 15 years the presence of one or more risk factors is associated with a 11.7 times greater probability of developing IPD.[15] Among risk factors, diabetes mellitus incidence in adolescents is an important condition which implies a higher risk for developing bacteremia, invasive forms, and higher mortality. However, studies defining the risk magnitude only in individuals with diabetes are scarce.[16]

Patients with risk factors mentioned above seem to benefit from vaccination against pneumococcus. Immunization of people highly vulnerable to IPD development is not performed in many LA countries. Such intervention represents an important strategy for reducing morbidity and mortality. Thus, this study aims to estimate the preventable fraction of IPD among children and adolescents from 5 to 19 years of age with a risk factor for their development.

2. Material and methods

The total population in LA was estimated from data provided by the Latin American and Caribbean Demographic Center (CELADE) for the year 2014.[17] This included the following countries: Argentina, Plurinational State of Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Ecuador, El Salvador, Guatemala, Haiti, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Dominican Republic, Uruguay and Bolivarian Republic of Venezuela.

Prevalence data (in percentage) for specific risk population was searched in the literature in order to calculate the preventable fraction of IPD in the Latin American population. We sought studies that evaluated the prevalence of pneumococcal disease in patients in high-risk groups. The electronic searches were conducted until July 2014 in the databases MEDLINE via PubMed and LILACS using the following terms combined in a variety of strategies: anatomic asplenia, functional asplenia, kidney diseases, HIV infection, asthma, diabetes mellitus, children and Latin America. Search engines additionally included Google®. Electronic searches were supplemented by manual searches of bibliographic references. Information extracted from abstracts was not considered.

Thus, data on the prevalence of asthma, renal disease (dialysis patients), diabetes mellitus, sickle cell disease and HIV were applied to the total population in LA, and thus the risk population was obtained. When prevalence data were not available for the LA, information from other domains was used.

The vaccine efficacy in specific risk population for each subgroup was used in order to calculate the preventable fraction. Calculations were performed by estimating the use of PCV13 conjugate vaccine, exclusively. Searches were conducted in the databases mentioned above, in the same period, using the following terms: pneumococcal vaccines, children and the diseases mentioned above. Currently, there is no data on PCV13 efficacy in pediatric patients at high-risk in published papers. Therefore, data regarding other conjugate vaccines was used. This scenario considered that all vulnerable population had access to immunization. The impact of herd immunity was not considered. Table S1 provides information of all articles used as a data source.

3. Results

CELADE stratifies individuals into five-year age groups, and therefore the analysis was performed considering the maximum age of 19 years. According to CELADE, 215,197,435 people are aged between 0 and 19 years in LA and 162,950,134 constitute the age group of 5-19 years.

Table 1 shows the prevalence of asthma, renal disease, diabetes, sickle cell disease and HIV in four different age groups (0-4, 5-9, 10-14, and 15-19 years old).[18–22] In this analysis, subjects aged