Eur J Pediatr (2010) 169:861–866
DOI 10.1007/s00431-009-1132-8

ORIGINAL PAPER

The epidemiology of hospitalized children with pneumococcal/lobar pneumonia and empyema from 1997 to 2004 in Taiwan

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Received: 7 May 2009 / Accepted: 9 December 2009 / Published online: 6 January 2010

Abstract Pneumococcal/lobar pneumonia and empyema have an important impact on the health of children worldwide. There has been no epidemiological study of pneumococcal/lobar pneumonia and empyema in Taiwan, a middle-income Asian population. Using Taiwan's National Health Insurance database, we collected and analyzed data obtain from medical care claims related to pneumococcal/lobar pneumonia and empyema for children below the 18 years old from 1997 to 2004. We found the annual population-based incidence to have significant year to year increases and the average annual incidences of pneumococcal/lobar pneumonia and empyema in children under five to be 44.9 and 10.5 episodes per 100,000 children-year, respectively. About 64% of children with pneumococcal/lobar pneumonia and empyema were under 5 years old. Children 4 to 5 years old had the highest incidences of both pneumococcal/lobar pneumonia and empyema. Incidence was the highest each spring. The odds ratio of the case fatality among pneumococcal/lobar pneumonia patients complicated with empyema to those without was 118 (95% confidence interval 28–492). In conclusion, the population-based incidences of pneumococcal/lobar pneumonia and empyema among children under five in Taiwan were 44.9 and 10.5 episodes per 100,000 children-year, respectively, and 4- to 5-year-old children had the highest incidences of both pneumococcal/lobar pneumonia and empyema. This population might benefit from a universal pneumococcal vaccination program which might cover about 70% of invasive pneumococcal diseases in Taiwanese children under 5 years old.

Keywords Pneumococcus · Pneumonia · Empyema · Children · Annual incidence · Seasonality

Abbreviations

PCV	Pneumococcal conjugated vaccine
NHI	National Health Insurance
ICD-9	International Classifications of Diseases, Ninth
CM	Revision, Clinical Modification
SARS	Severe acute respiratory syndrome
IPD	Invasive pneumococcal diseases

Introduction

Pneumococcal/lobar pneumonia is a serious worldwide pediatric health issue because the disease often occurs with complications and drug resistance, especially in cases infected by *Streptococcus pneumoniae*. According to the World Health Organization, *S. pneumoniae* is the leading cause of severe pneumonia worldwide in children younger than 5 years old, causing more than one million deaths in

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children each year [19]. Empyema, one of the most severe complications of bacterial pneumonia, has been reported in 20% to 30% of all cases in Utah of USA [2]. Although the incidence of invasive pneumococcal disease has decreased since the use of pneumococcal conjugated vaccine (PCV) [4], developed countries such as USA have seen an emergence of empyema and necrotizing pneumonia episodes caused by nonvaccine serotypes [1, 3]. In Taiwan, the represented pneumococcal serotypes in hospitalized children with invasive pneumococcal diseases (IPD) were serotypes 14, 19F, 3, 6B, and 23F, and the seven-valent pneumococcal conjugate vaccines covered 73% of IPD cases in children aged between 2 and 4 years and 65% of cases in children aged <2 years [11, 12]. To date, little research has been done into the epidemiology and population-based incidence of pneumococcal/lobar pneumonia and empyema in the Asian and subtropical areas.

In Taiwan, the medical care of 98% of the population is covered by a universal national health care system of National Health Insurance (NHI) established in 1995 [8]. Using the NHI database, we calculated the age-specific incidences and mortality rates of children hospitalized for pneumococcal/lobar pneumonia and empyema in Taiwan over an 8-year period, from 1997 to 2004. The findings of such a study might provide important information relevant to future universal PCV vaccination policies there

Materials and methods

Taiwan has a population of 22.9 million people, and the NHI covered most of the health care costs for 98% of its population in 2006 [8]; the remaining 2% of its population is living in the foreign countries or in families with monthly household incomes less than US $1,000 [18]. Taiwan's NHI database includes health care data collected from over 95% of Taiwan's hospitals caring for 98% of its population.

Using the NHI claims database, we collected the data of children under 18 years old hospitalized for lobar pneumonia or pneumococcal pneumonia and empyema, as defined by the International Classifications of Diseases, Ninth Revision, Clinical Modification (ICD-9 CM) codes. We included those classified as ICD-9 CM code 481 for pneumococcal/lobar pneumonia, 510 for empyema, 510.0 for empyema with fistula, 510.9 for empyema without fistula, and 511.1 for pleurisy with bacterial causes. ICD-9 code 481 was for both pneumococcal pneumonia and lobar pneumonia, and not all of them were pneumococcal pneumonia.

Among these hospitalized children with the above ICD-9 CM diagnoses, we also collected the data of whether they received the procedures used to manage complicated pneumonia, including ICD-9 CM code 32 for excision of lung and bronchus; 34 for operations on chest wall, pleura, mediastinum, and diaphragm; 96.05 code for other intubations of respiratory tract; and 96.7 for continuous mechanical ventilation. Because intensive care unit and general wards are different categories in NHI claims database, the rate of requiring intensive care among patients was obtained by analyzing the categories of the wards.

We analyzed the pneumococcal/lobar pneumonia and empyema-associated hospitalizations and the need of intensive care by age group, gender, and month of hospitalization. The annual age-specific pneumococcal/lobar pneumonia episodes were divided by the midyear age-specific gender-specific population [9] to calculate the annual age-specific pneumococcal/lobar pneumonia incidence, and the annual age-specific empyema episodes were divided by the midyear age-specific gender-specific population to calculate the annual age-specific empyema incidence. The mortality due to pneumococcal/lobar pneumonia or empyema was also analyzed. In our analysis of seasonal distribution, the months February to April were considered spring, May to July summer, August to October autumn, and November to the following January winter.

Statistics

The category variables were tested by χ^2 test. The difference of annual incidence among various age groups, the difference of annual incidences in different years, and the difference in seasonal distribution were measured with goodness-of-fit χ^2 test. A P value of <0.05 was considered significant.

Results

The incidence of pneumococcal/lobar pneumonia

Pneumococcal/lobar pneumonia (ICD-9 CM code 481) accounted for 1.3% (range 0.7–2.1%) of all children hospitalized for pneumonia during the 8-year study period. An average of 1,009 (range 420 to 1,775) episodes of pneumococcal/lobar pneumonia was reported yearly. The male-to-female ratio was 1.09:1. In children below the age of 18 year old, the annual population-based incidence of children hospitalized for pneumococcal/lobar pneumonia averaged 16.6 episodes per 100,000 children-year (range 6.4–31.4 episodes per 100,000 children-year). The annual population-based incidence of pneumococcal/lobar pneumonia increased significantly year by year ($p<0.01$; Fig. 1). Figure 1 shows the annual population-based incidence of hospitalized pneumococcal/lobar pneumonia in children under 2, 2–5, and 5–18 years old from 1997 to 2004.

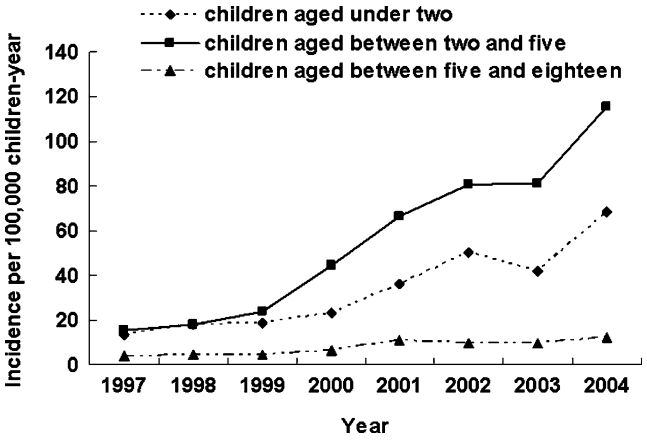

Fig. 1 The annual population-based incidence of pneumococcal/lobar pneumonia in children under 2, 2–5, and 5–18 years old from 1997 to 2004 in Taiwan

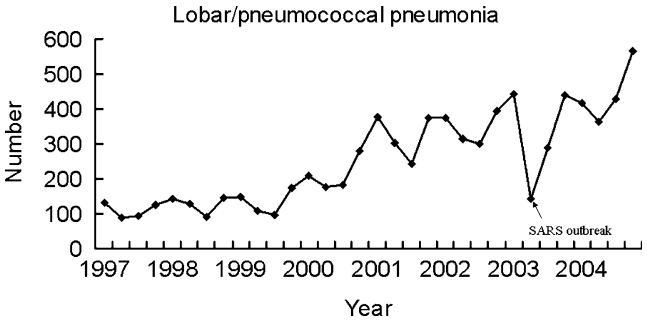

Fig. 3 The seasonal distribution of pneumococcal/lobar pneumonia from 1997 to 2004 in Taiwan. The peak consistently occurred in the spring (February to April) and the nadir in the autumn (August to October) annually except for 2003 when SARS epidemic occurred in Taiwan

Children aged between 2 and 5 had the highest incidence, and there is a significant difference of population-based incidence between these three age groups ($P<0.01$).

Children under 5 years old were the most susceptible to pneumococcal/lobar pneumonia (64.7% of all cases). The overall annual population-based incidence of pneumococcal/lobar pneumonia in children in that age group was 44.9 episodes per 100,000 children-year. The age-specific incidence increased gradually, peaking at 4 to 5 years old. After the age of 5, incidence decreased yearly (Fig. 2).

The seasonal distribution of pneumococcal/lobar pneumonia

We analyzed the seasonal distribution of hospitalizations for pneumococcal/lobar pneumonia (Fig. 3). Incidence was significantly higher in the spring and winter seasons ($P<0.01$). Peak incidence occurred in the spring every year and the nadir usually in the autumn except the year 2003. During the 8-year study period, the lowest incidence of hospitalizations for pneumococcal/lobar pneumonia was in the summer of 2003, the year Taiwan had a large outbreak of severe acute respiratory syndrome (SARS).

The incidence of empyema

The average annual number of empyema (ICD-9 CM code 510.0, 510.9, or 511.1) was 237 episodes per year (range 138–341 episodes). Male-to-female ratio was 1.14:1. The overall population-based incidence of empyema in children below the age of 18 years old was 3.9 episodes per 100,000 children-year (range 2.1 to 5.8 episodes per 100,000 children-year). Incidence increased significantly from year to year, peaking in 2002 and slightly declining in 2003 and 2004 (Fig. 4). Figure 4 shows the annual population-based incidence of empyema in children under 2, 2–5, and 5–18 years old from 1997 to 2004. Again, children aged between 2 and 5 had the highest incidence of empyema among these three age groups ($P<0.01$).

About 64% (63.8%) of empyema episodes occurred in children 5 years old or below. In this population, the annual incidence of empyema was 10.5 episodes per 100,000 children-year (range 4.9 to 15.5 episodes per 100,000 children-year). The age-specific incidence of empyema increased in these children up to 5 years old. As was found with lobar pneumonia hospitalizations, incidence of empyema decreased with age after 5 years old, too (Fig. 5).

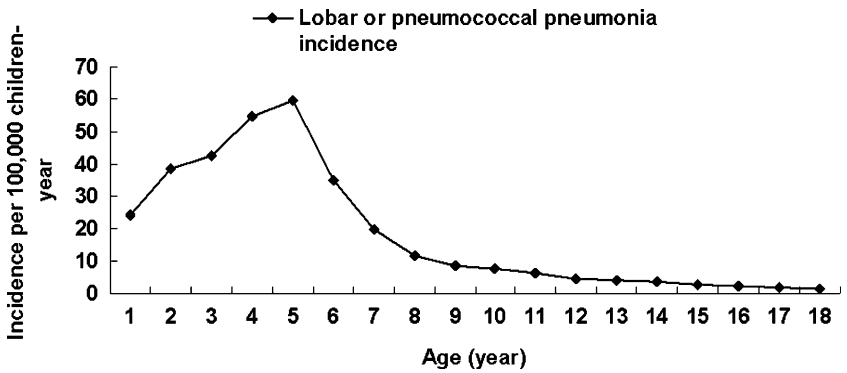

Fig. 2 The age-specific incidence of pneumococcal/lobar pneumonia from 1997 to 2004 in Taiwan

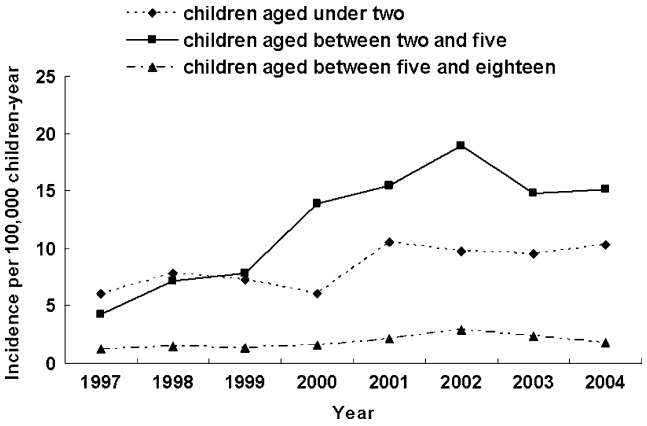

Fig. 4 The annual population-based incidence of empyema in children under 2, 2–5, and 5–18 years old from 1997 to 2004 in Taiwan

The morbidity and case fatality rate of children with pneumococcal/lobar pneumonia and empyema

In total, 2.3% of the children with pneumococcal/lobar pneumonia required mechanical ventilation and 34% required intensive care. Of those with pneumococcal/lobar pneumonia complicated with empyema, 12.0% require mechanical ventilation and 58.1% required intensive care, which were significantly higher rates than those found for children with pneumococcal/lobar pneumonia alone ($p<0.01$). Furthermore, 63.4% of those complicated with empyema also received invasive procedures of chest tube insertions and/or thoracotomies. Of 1,169 patients with empyema, 66 (5.6%) cases received lung excision and bronchus. Children with pneumococcal/lobar pneumonia and those children with empyema had a crude case fatality rate of 0.43% (range 0.19–0.61%) and 2.74% (range 1.02–5.07%), respectively. In general, cases complicated with empyema had a significantly higher case fatality rate than those without this complication (odds ratio (OR) 118; 95% confidence interval (CI) 28–492; $P<0.001$).

Discussion

In this first study of the population-based incidence of pneumococcal/lobar pneumonia and empyema in Taiwan, we found the average annual population-based incidence of pneumococcal/lobar pneumonia in children under 5 to be 44.9 episodes per 100,000 children-year and the disease complicated with empyema in the same age group to be 10.5 episodes per 100,000 children-year. The majority (about 64%) of episodes of pneumococcal/lobar pneumonia and empyema occurred in children under 5 years old, peaking at 4 to 5 years old. Children with empyema had a higher case fatality rate than those without (OR 118; 95% CI 28–492).

Evaluating the population-based incidence of pneumococcal pneumonia was difficult because the blood and pleural effusion culture yield rates of *S. pneumoniae* were very low in these cases [20]. A rapid diagnostic tool, the urine pneumococcal antigen test (Binax NOW, Binax, USA), was introduced to Taiwan in 2000. This test is reported to be useful for diagnosing pneumococcal pneumonia cases due to its high specificity, though it has also reported to have a 15% false-positive rate in younger children [15, 16]. Since this test was introduced, there has been a significant increase in the annual population-based incidence of pneumococcal/lobar pneumonia. We were not sure whether this increasing trend is due to this better and more convenient diagnostic tool.

In a previous nationwide population study, we reported the incidence of pneumonia to be the greatest in children younger than 1 year old in Taiwan [21]. The current study, however, found incidence of pneumococcal/lobar pneumonia to reach a peak between the ages of 4 and 5 years old. The age distribution pattern of empyema cases was similar to that of pneumococcal/lobar pneumonia. The difference in age distribution may be due to the greater number of virus etiologies causing pneumonia in younger children [14, 17] as well as the higher colonization rates of pneumococci in kindergarteners [13]. One 1998 study reported pneumococcal carriage rate to be 19.9% in northern Taiwan population and the isolation rate to be higher in children aged between

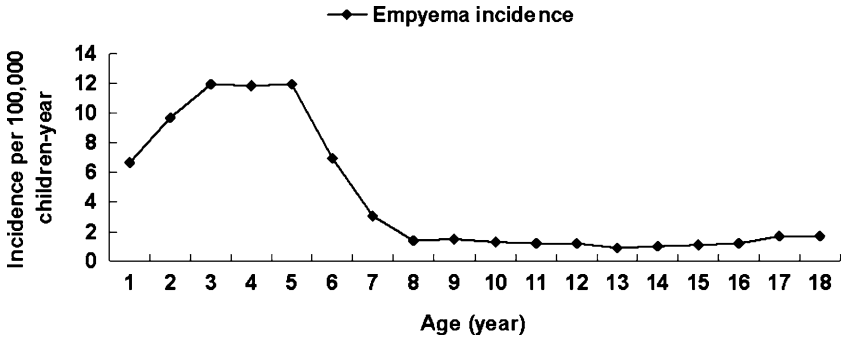

Fig. 5 The age-specific incidence of empyema from 1997 to 2004 in Taiwan

2 and 5 years [13]. Therefore, it is reasonable to hypothesize that high pneumococcus colonization rate may contribute to peak in incidence of lobar/pneumococcal pneumonia and empyema in this age group. Furthermore, this population might benefit from a universal pneumococcal vaccination program since seven-valent conjugated vaccine can cover about 70% of IPD cases in this age group in Taiwan [12].

The seasonal distribution of pneumococcal/lobar pneumonia was prominent in winter and spring seasons in Taiwan in this 8-year study. This seasonal distribution is similar to that of influenza because the viral surveillance of Taiwan Centers for Disease Control between 2002 and 2004 demonstrated that influenza A and influenza B viruses had a obvious seasonal variation, with peak incidence from the fifth to 14th week every year during our study period in Taiwan [6], and it was compatible to the peak pneumococcal/lobar pneumonia incidence in the spring (February to April) in this study. It suggests that both are seasonal diseases and may be interrelated in Taiwan.

In our previous study [21], the nadir of hospitalized pneumonia occurred in the summer of 2003, so did lobar/pneumococcal pneumonia in this study. The incidence decrease in the summer of 2003 may be related to SARS outbreak [5], which kept people away from hospitals for fear of nosocomial SARS infections. In addition, the hygiene campaign for SARS may have universally reduced the transmission of infections and thus decreased the incidence or episodes of pneumonia of all causes.

This study found that annual population-based incidence of empyema among children under 5 increased year by year, reaching a peak in 2002 (from 4.94 to 15.55 episodes per 100,000 children-year). From 1995 to 2002, one medical center in Taiwan also reported an increase in percentage of pneumococcal pneumonia complicated with necrotizing pneumonia and/or empyema (from 25% to 70%) [10]. In our study, the rate (34%) of requiring intensive care was relatively high, which could be explained by some less severe cases who were admitted to intensive care unit for just close monitoring of vital signs. According to another study of pediatric empyema receiving thoracoscopic management in Taiwan, 32.7% of cases also required the preoperative intensive care [7], which was similar to our results.

One of the major limitations of the study is that it only presents data based on ICD-9 coding and we could not provide actual patient clinical data and microbiologic data that would be important in determining the true incidence of disease and its clinical outcome and the possible impact of vaccine on disease burden. The other weak point of this study is that patients with ICD-9 codes for pneumococcal pneumonia and those for lobar pneumonia were combined, and we have to clarify that all patients with lobar pneumonia do not have pneumococcal disease. For the purpose of clinical data and microbiologic data, a prospective cohort study to investigate the etiology of lobar pneumonia and serotypes of pneumococci in Taiwan is mandatory in the near future.

In summary, this study found the population-based incidences of pneumococcal/lobar pneumonia and empyema among children 5 years old or younger in Taiwan to be 44.9 and 10.5 episodes per 100,000 children-year, respectively. The morbidity and case fatality rates of children with pneumococcal/lobar pneumonia were significantly higher because of empyema complications. To date, Taiwan has no universal PCV inoculation program for younger children, a population that this study finds most susceptible to pneumococcal pneumonia and empyema. A universal inoculation of PCV may be able to provide maximum protection from this disease and prevent most episodes of pneumococcal/lobar pneumonia and empyema across the region in the future.

Acknowledgment This study is based in part on data from the National Health Insurance Research Database provided by the Bureau of National Health Insurance, Department of Health and managed by National Health Research Institutes. The interpretation and conclusions contained herein do not represent those of Bureau of National Health Insurance, Department of Health or National Health Research Institutes.

Conflict of interest The authors declare no conflicts of interest.

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