

Trends of Respiratory Syncytial Virus Infections in Children under 2 Years of Age in Puerto Rico

Israel Matías, MD*; Inés García, MD*; Lourdes García-Fragoso, MD*; Gilberto Puig, MD†; Lourdes Pedraza, MD†; Luis Rodríguez, MD‡; Alvaro Santaella, MD§; Sylvia Arce, MD**; Marilyn Toledo, MD††; Edwin Soto, MD††; Marta Valcárcel, MD*

Objective: The respiratory syncytial virus (RSV) is the most significant viral pathogen causing bronchiolitis and pneumonia in infants, today. In tropical climates the RSV infection may occur throughout the year. The purpose of this study was to assess RSV infections during the 2009–2010 RSV season in children under 2 years of age and to evaluate the trend of positive RSV tests in the period of 2007 to 2009.

Methods: A retrospective review of data collected from 6 hospitals in Puerto Rico was performed. Patients with confirmed RSV bronchiolitis were included in the study.

Results: A total of 4,678 patients were included. The mean age of the patients was 7 months. Data showed that RSV infection occurred throughout the studied months.

Conclusion: Data confirms a year-round presence of RSV in Puerto Rico. The RSV surveillance system needs to be reinforced to establish and understand the epidemiology of RSV and to review the current immunoprophylaxis guidelines. [*PR Health Sci J* 2015;34:98-101]

Key words: Respiratory syncytial virus, Bronchiolitis, Hospitalizations, Puerto Rico

The respiratory syncytial virus (RSV) is the most significant viral pathogen causing bronchiolitis and pneumonia in infants, today (1). There is a high risk of serious RSV illness in infants who were born prematurely or who have bronchopulmonary dysplasia (BPD), congenital heart disease (CHD), congenital abnormalities of the airway or neuromuscular disease, or certain immunodeficiencies. Up to 90% of infant hospitalizations in the United States are related to RSV, and most of them occur in infants under 6 months of age (1), and it is estimated to cause 40,000 to 125,000 hospitalizations each year in infants younger than 1 year old (1, 2, 3).

The mortality rate in children hospitalized with RSV infection is less than 1%, with fewer than 500 deaths per year attributed to RSV (4). However, in high-risk infants, there is higher mortality and significant morbidity associated with RSV. An example of this is the 3 to 5% mortality rate reported in infants with chronic lung disease of infancy (i.e., bronchopulmonary dysplasia) or congenital heart disease or who are markedly premature when hospitalized for RSV (4).

Palivizumab, an antibody that is given by intramuscular injection, is licensed in the United States as an immunoprophylaxis and is recommended for infants and children who are at increased risk for severe RSV disease. The American Academy of Pediatrics (AAP) has developed guidelines for palivizumab administration using data from previous RSV seasons to suggest a period for administration. However, specific dates for palivizumab administration have not been clearly established (5).

Since 2004, eligible infants in Puerto Rico have been receiving up to 9 doses of palivizumab during the RSV season, which has been established to run from July through March of the following year. In 2009, the revised AAP guidelines recommending a decrease in the number of palivizumab doses in all geographical areas were published (5, 6). After taking these new recommendations into account, the Puerto Rico Health Department decreased RSV prophylaxis with palivizumab to 3 doses or, in some patients, 5 doses, depending on eligibility criteria. No new consensus, surveillance system reports or epidemiologic data of RSV infections supporting these changes have been reported in Puerto Rico. The purpose of this study was to assess RSV infections during the 2009–2010 RSV season (July 09 to March 10) in children under 2 years of age in Puerto Rico and evaluate the trend of positive RSV tests in the period of 2007 to 2009, based on information from 6 hospitals from around the island, so as to provide data to review the current immunoprophylaxis guidelines.

*Department of Pediatrics, Neonatology Section, University of Puerto Rico Medical Sciences Campus, San Juan, PR; †San Jorge Children's Hospital, San Juan, PR; ‡University of Puerto Rico Hospital Dr. Federico Trilla, Carolina, PR; §Interamerican Hospital for Advanced Medicine, Caguas, PR; **San Antonio Hospital, Mayagüez, PR; ††Manatí Medical Center Hospital, Manatí, PR

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Address correspondence to: Israel Matías, MD, Department of Pediatrics, Neonatology Section, University of Puerto Rico Medical Sciences Campus, PO Box 365067, San Juan, PR 00936-5067. Email: israel.matias@upr.edu

Methods

A retrospective review of data collected from 6 Puerto Rico hospitals during the 2009-2010 season (from July 2009 to March 2010) was performed. Only patients who were under 2 years of age and had confirmed RSV bronchiolitis were included in the study. The 6 hospitals that participated provide service to patients around Puerto Rico who have medical insurance, either private or that offered by the government. The data from all the hospitals included the mean age of the subjects and the total number of patients with RSV bronchiolitis (confirmed by an RSV rapid test).

Retrospective data from 2007 through 2009 were available year round for 2 hospitals. We examined RSV trends represented by the cases drawn from the participating hospitals. Data analysis was performed by using frequency, mean, median, and range of collected data. Each institution approved the use of its data for this study. The study was approved by the University of Puerto Rico Medical Sciences Campus Institutional Review Board.

Results

At the 6 participating institutions, 4,678 patients with respiratory symptoms were evaluated. Table 1 shows the number of patients that were at each hospital. The mean age of the patients with RSV bronchiolitis was 7 months of age (range, 0 to 15 months). During the 2009-2010 RSV season, 77% of patients with a positive RSV test were hospitalized with bronchiolitis in the participating institutions.

Table 1. Subjects with respiratory symptoms reported by each hospital

| Hospital | Subjects N (percent) |
|----------|-------------------------|
| A | 128 (2.7%) |
| B | 210 (4.5%) |
| C | 159 (3.4%) |
| D | 279 (6.0%) |
| E | 3,710 (79.3%) |
| F | 192 (4.1%) |
| Total | 4678 |

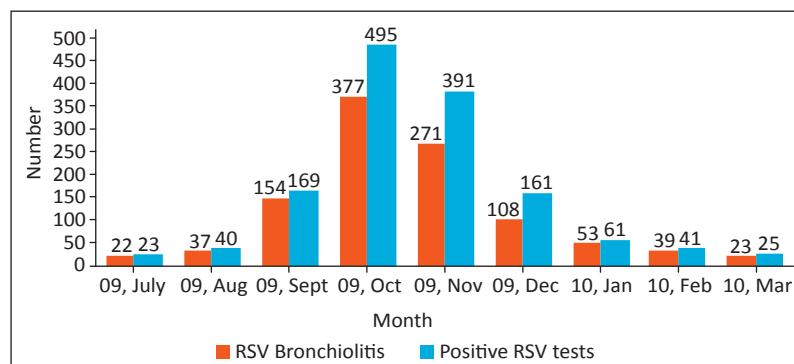


Figure 1. Positive RSV tests and hospitalized patients with RSV bronchiolitis in the participating hospitals during the 2009-2010 season

Figure 1 shows the total number of positive RSV tests per month in the participating hospitals during the 2009-2010 RSV season and the number of patients hospitalized with RSV bronchiolitis. This information demonstrates that RSV infections occur throughout the season (from July to March of the following year).

Data from 3 years, covering from 2007 through 2009, from hospitals E and F (n = 3,778) show the occurrences of RSV infection throughout the year, with an increase in the number of occurrences being reported from September through December (Figures 2 and 3). In addition, the data show that there was an increase in positive RSV cases in both hospitals (that is, E and F) during the first 6 months of the 2009-2010 RSV season compared to what had occurred in previous seasons.

Discussion

RSV is the only respiratory virus that produces important outbreaks every year (7). Reinfection with this virus is common. It has been reported that by 2 years of age, 99% of all children will experience at least 1 infection, and 50% of them will experience at least 2 infections (7). Different geographical regions have different specific seasons, and the outbreak length (for each region) is also subject to variation. In the United States, typical outbreaks last an average of 5 months, although there are regions where year-round infections have been reported. In tropical climates, such as that of Puerto Rico, the pattern of RSV infection is less predictable, and outbreaks may occur throughout the year (8).

RSV activity is considered widespread, that is, at epidemic or outbreak level, when at least half of the participating laboratories report having detected RSV for at least 2 consecutive weeks or when more than 10% of all specimens test positive for the virus (9). Prior to 2004, because of the lack of an RSV surveillance system, health care workers in Puerto Rico used Florida data to determine when the local RSV season had started and, subsequently, when prophylaxis should be implemented; the season generally lasted from August to December of any given year and patients were prescribed Synagis (palivizumab). In 2004, after a consensus was reached by experts in Puerto Rico, and in the face of evidence confirming the year-round incidence of RSV infection, the Puerto Rico Health Department established the RSV season as covering from July through March of the subsequent year, thereby ensuring that eligible infants would be offered prophylaxis for 9 months (8).

In 2009, the American Academy of Pediatrics (AAP) guidelines for the use of palivizumab for the prevention of RSV infections were updated. Recent descriptions from the Centers for Disease Control and Prevention (CDC) regarding RSV seasonality in different geographic locations were used to recommend new initiation and

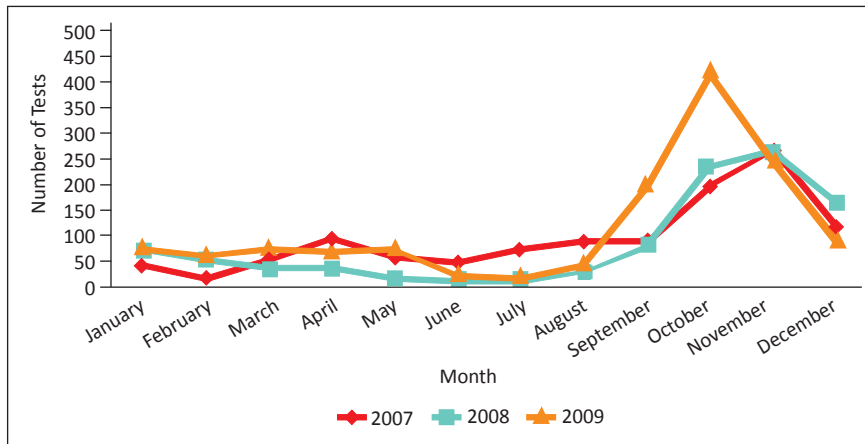


Figure 2. Positive RSV test cases from 3 seasons in hospital E (2007 to 2009)

termination periods for prophylaxis. For all locations, a maximal number of 5 doses was recommended (without regard to the month of prophylaxis initiation) for infants with significant congenital heart disease or chronic lung disease (CLD) or who had been born before 32 weeks, 0 days, of gestation. A maximal number of 3 doses was recommended for infants with a gestational age (GA) of 32 weeks, 0 days, to 34 weeks, 6 days, and without significant CHD or CLD (5).

These new recommendations have created concerns among physicians in the US and other countries. Recommendations for infants at a GA of 32 to 35 weeks were the most divergent. The Canadian guidelines recommended that localized policies be implemented in each (Canadian) province and territory, with each region considering its own particular risk factors and then implementing a specific and appropriate risk-scoring tool. Canadian authors stated that the use of 1 to 3 doses of palivizumab over the course of an entire RSV season is a strategy untested in randomized controlled trials and that such use is not supported by the pharmacokinetics and therapeutic efficacy of the drug, as evidenced in the earlier phases 1 and 2 of the IMPact trials (10, 11). In an analysis of infants under 1 year of age and who had been hospitalized for RSV infection in 9 hospitals around the US, it was found that a GA of 33 to 35

weeks was a significant risk factor for mechanical ventilation, a longer stay in the ICU (7.7 vs. 5.8 days for <32 weeks GA), and longer hospitalization (8.4 vs. 6.8 days for <32 weeks GA) (12).

Other aspects that need to be taken into consideration are the long-term effects of RSV infection. Investigators in Arizona demonstrated that children with RSV bronchiolitis early in life had a significantly higher risk of wheezing until they reached 6 years of age. The majority of these children did not require hospitalization and yet developed a subsequent post-bronchiolitis wheeze. Studies conducted in Sweden showed

that children hospitalized because of RSV bronchiolitis had an increased risk of wheezing and asthma until reaching the age of 18. Study investigators concluded that interventions directed at preventing RSV bronchiolitis could provide long-term benefits by reducing recurrent wheezing episodes in childhood (13).

Data from our study confirm the year-round presence of RSV in Puerto Rico, with increased activity occurring from September through December. This pattern correlates with the one reported in the southeastern region of Florida, which pattern usually takes place of a period of 11 to 12 months (1, 14, 15). This study is limited by the retrospective nature of the analyzed data. The demographic characteristics of the patients in the study population and the clinical courses followed for those patients were not available for analysis. RSV infections seen in private offices or in other settings are not included in this study, and not all the institutions collect the same surveillance data or parameters. Furthermore, the data are presented as number of cases instead of as percent of positive tests, precluding the interpretation of epidemic levels throughout a given year. A prospective study would help us analyze age groups and preexisting risk factors associated with RSV infections in Puerto Rico. Nevertheless, the impact of these data reinforces the importance of the implementation of a prospective and accurate surveillance system

in all the institutions that provide pediatric care in Puerto Rico, to understand and monitor the epidemiology of RSV infections. In addition, such a system would allow us to set priorities in the form of RSV immunoprophylaxis guidelines and so further guide public health policy and strategies.

Resumen

Objetivo: El Virus Respiratorio Sincitial (VRS) es el patógeno viral más importante que causa bronchiolitis y pulmonía en infantes. En climas tropicales la infección por el VRS puede ocurrir durante todo el año. El

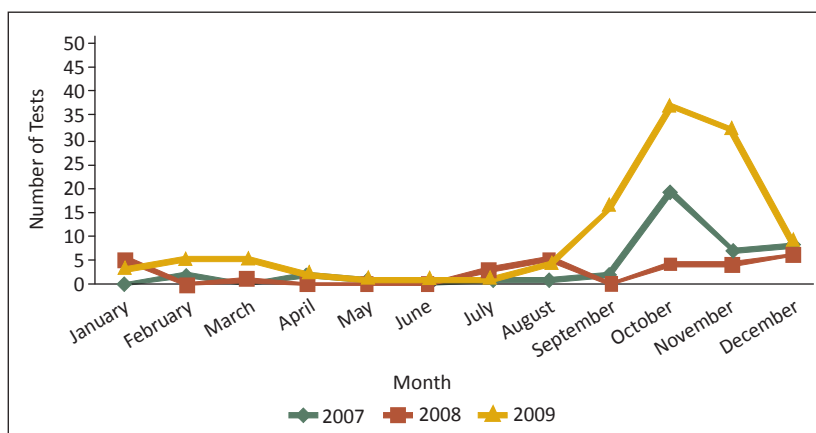


Figure 3. Positive RSV test cases from 3 seasons in hospital F (2007 to 2009)

propósito de este estudio es revisar las infecciones por el VRS durante la temporada 2009-2010 en niños menores de 2 años de edad, y evaluar la tendencia de las pruebas positivas para el VRS en el período de 2007 a 2009. Métodos: Se realizó una revisión retrospectiva de los datos de 6 hospitales en Puerto Rico. Se incluyeron en el estudio a los pacientes con bronchiolitis confirmada por el VRS. Resultados: Un total de 4,678 pacientes fueron incluidos en el estudio. La edad media de los pacientes fue de 7 meses. Los datos demostraron que la infección por el VRS ocurrió a través de todos los meses estudiados. Conclusiones: Los datos confirman la presencia del VRS a través de todo el año en Puerto Rico. La vigilancia del VRS necesita ser reforzada para poder establecer y entender mejor su epidemiología, y para reevaluar las guías de inmunoprofilaxis.

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