

NEONATOLOGY

Respiratory Syncytial Virus-Related Bronchiolitis in Puerto Rico

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Background. Respiratory syncytial virus (RSV) is an important cause of respiratory tract disease in infants and young children. Immunoprophylaxis is available for high-risk infants. This study reviews infants with bronchiolitis at three primary care hospitals to describe the epidemiology of RSV infection in Puerto Rico.

Methods. We analyzed data from 2 hospitals by obtaining the number of infants diagnosed with bronchiolitis and estimating the percentage of cases due to RSV. A third hospital included patients with

confirmed RSV infection.

Results. There were 4,557 patients in the study. RSV infection occurred throughout the year. Data shows a progressive decrease in RSV-positive infections.

Conclusions. Data confirms year-round incidence of RSV in Puerto Rico. A standardized surveillance system in Puerto Rico is imperative to determine RSV epidemiology. The decrease in positive RSV infections may be due to the introduction of immunoprophylaxis to high-risk patients.

Key words: RSV, Bronchiolitis, Prematurity, Puerto Rico

Respiratory syncytial virus (RSV) is an important cause of severe lower respiratory tract disease in infants and young children and is an important cause of recurrent upper and lower respiratory infections in the community. It is responsible for 45-75% of cases of bronchiolitis, 15-25% of childhood pneumonias and 6-8% of cases of croup (1). Usually, it is associated with moderate to severe cold-like symptoms but severe lower respiratory tract disease may occur. RSV is the major cause of bronchiolitis and pneumonia among infants under 1 year of age. Eighty percent of hospitalized patients under 6 months of age with the diagnoses of bronchiolitis or pneumonia have RSV positive cultures (2).

RSV is the only viral respiratory pathogen that regularly produces an important outbreak each year and due to its strain variability, reinfection is common. By two years of age, 99% of children will experience at least one infection and 50% of them will experience at least two infections (3). Outbreaks may vary in length and season depending on the geographical region. Throughout most of the U.S.,

outbreaks typically last an average of five to six months. (November-April) although there are regions where year-round epidemics have been reported (3). In tropical climates the pattern of RSV infection is less predictable and may occur throughout the year.

In Puerto Rico, there is significant RSV infection, but there is no surveillance system to determine its incidence or its epidemic levels. RSV activity is considered widespread, at "epidemic" or "outbreak" levels, when at least half of the reporting laboratories announce RSV detection for two consecutive weeks or when more than 10% of all specimens tested are positive (4). Data from Florida has been traditionally used to determine and implement local season and thus immunoprophylaxis for high-risk patients in Puerto Rico. Based on this data, prophylaxis for RSV consisted of five doses of Synagis (*Palivizumab* Med Immune Inc.) that started on August and lasted until December. On September 2004, after a scientific session related to RSV prophylaxis, the Puerto Rico Health Department established the RSV season in Puerto Rico from July through March. Consensus was established based on data submitted by individual institutions demonstrating apparent year-round incidence. In addition, the Puerto Rico Health Department started efforts to improve RSV vigilance by the creation of a surveillance system (5). The purpose of this study is to describe the epidemiology of RSV infection in Puerto Rico based on data from three hospitals representing infants and young children from around the island.

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Methods

A retrospective cross-sectional study was performed at three institutions from August 2002 to May 2004. Patients with confirmed RSV infection and estimates of RSV positive infection in patients two years or younger admitted with the diagnosis of bronchiolitis were reviewed. These institutions included patients from all regions of the island. Hospital A, the University Childrens Hospital in Carolina is located in the east of the island, Hospital B (Dr. Pila Hospital in Ponce) in the south and Hospital C (San Jorge Children's Hospital in San Juan) in the Metropolitan Area (north).

Data from Hospital A was obtained by collecting the total number of patients under two years of age admitted to the hospital with the diagnosis of bronchiolitis. Estimates of the percentage of RSV-related bronchiolitis were done based on literature stating that 33% or 1/3 of all patients under two years of age with bronchiolitis have RSV positive infection (2). Hospital B included all cases of emergency room evaluations diagnosed with bronchiolitis in patients less than two years of age and estimated the percentage of RSV related infections. Hospital C obtained data by revision of all positive RSV nasopharyngeal viral cultures in patients diagnosed with bronchiolitis in the emergency room. Directigen RSV antigen detection test confirmed RSV in cultures obtained by nasopharyngeal lavage.

Results

A total of 4,557 patients were included in the study. Of these, 4% represented cases selected from hospital A, 11% from hospital B, and 85% from hospital C. All these patients had either a confirmed diagnosis of RSV infection or were less than two years of age with the clinical diagnosis of bronchiolitis. Hospital A included 245 cases and Hospital B included 604 cases sorted by month and year. We estimated and attributed 33% of monthly cases to RSV positive bronchiolitis. Hospital C evaluated 4,718 patients with the diagnosis of bronchiolitis of which 1,723 patients (37%) had confirmed RSV infection.

Figure 1 shows the total number of new cases of bronchiolitis per month of the three institutions. This data shows bronchiolitis occurrence throughout the year as well as peak incidence from August to March. Figure 2 shows the total number of cases with confirmed RSV cultures from hospital C plus the estimated cases of RSV-related bronchiolitis showing a similar pattern of year-round incidence. We estimated the monthly percent of RSV-related infections showing approximately 20% of bronchiolitis to be caused by RSV every month (Figure 3).

Data from hospital C (Table 1). showed a progressive decrease in the annual percent of positive RSV infections since 2002.

Table 1. Data from hospital C

Month	Positives	Negatives	Total Tests	%Positives
May-Dec 2002	575	738	1313	44%
Jan-Dec 2003	811	1285	2096	39%
Jan-Oct 2004	541	1313	1854	29%

Figure 1. New cases of bronchiolitis in hospitals A, B, and C (August 2002 to May 2004)

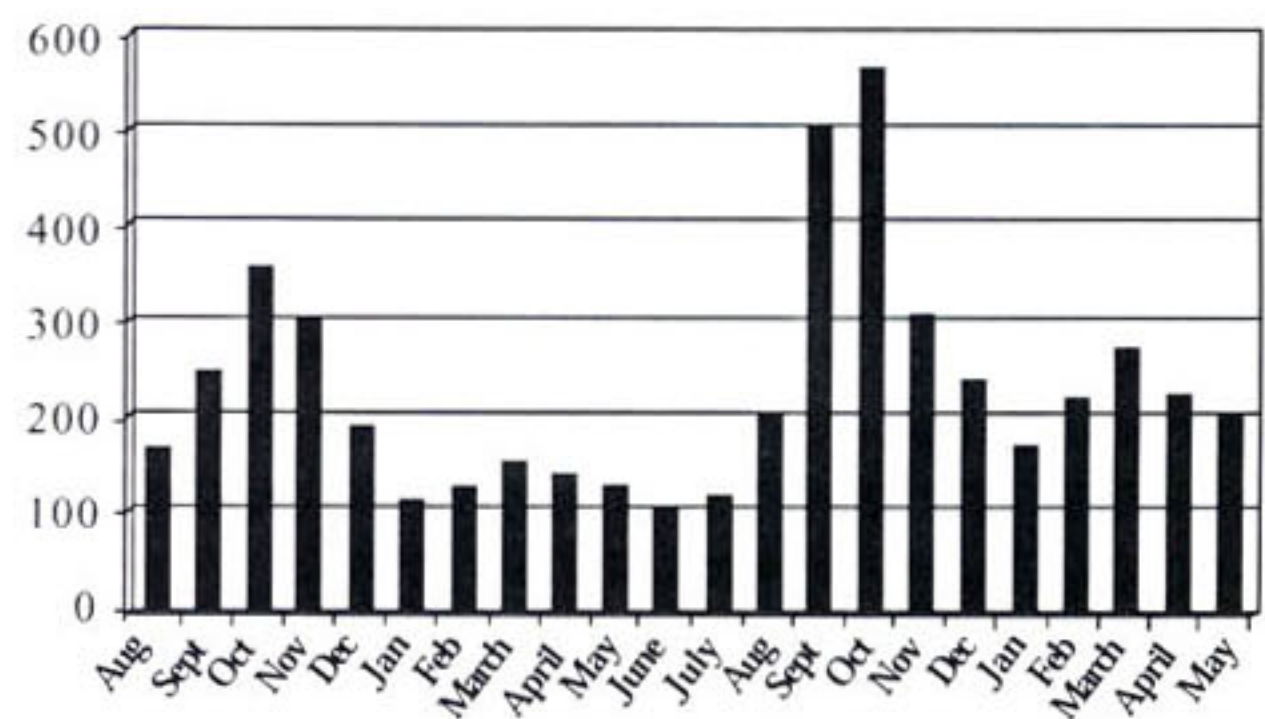


Figure 2. Estimated RSV-related infections in hospital A, B and C. (August 2002 to May 2004)

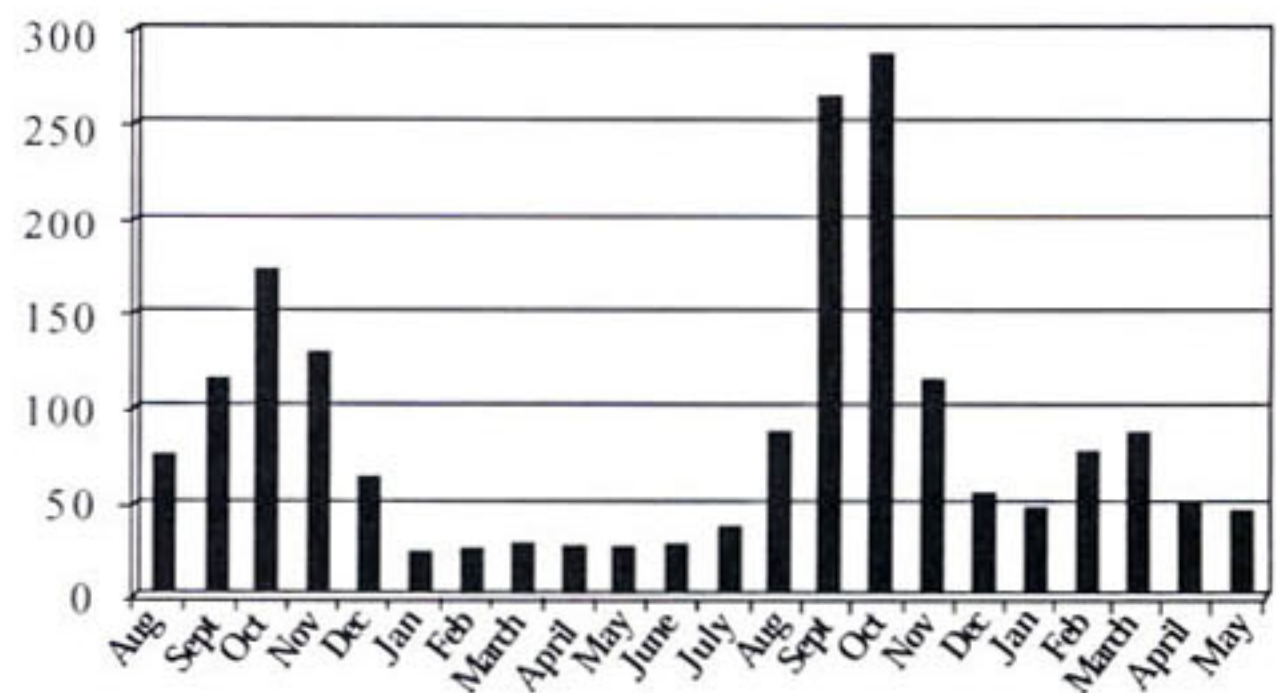
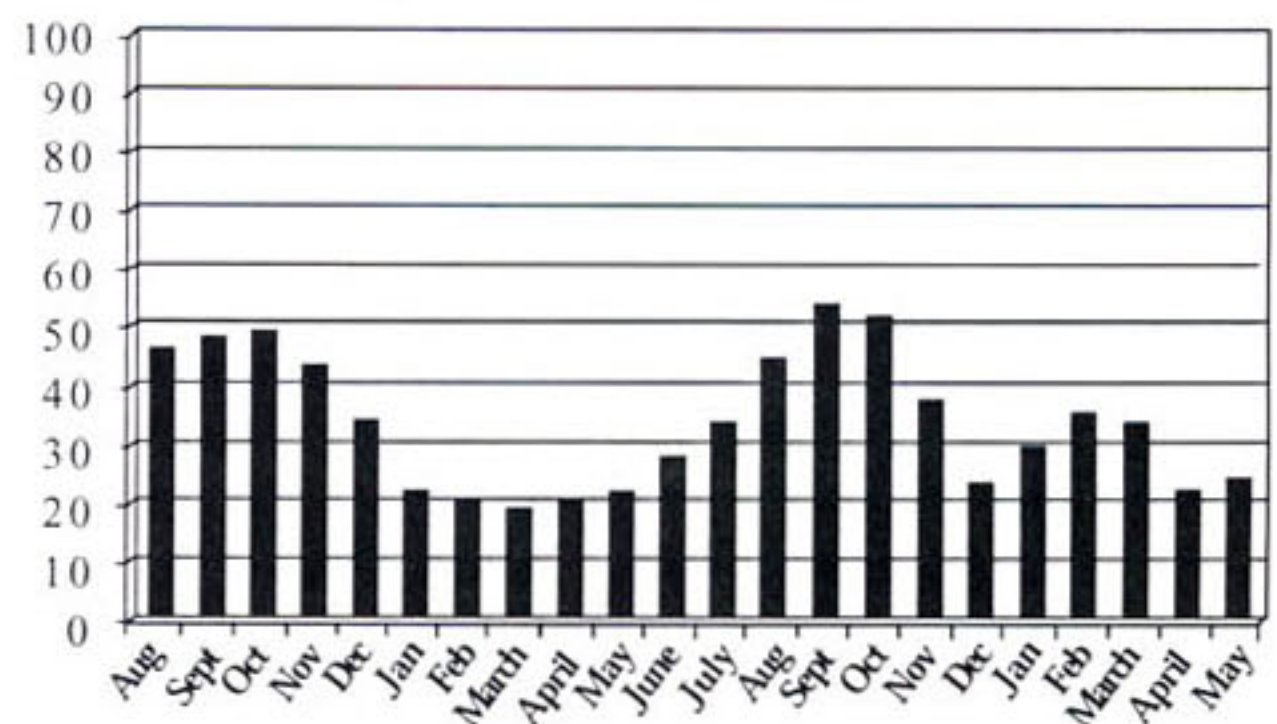


Figure 3. Estimated monthly percent of RSV-related bronchiolitis. (August 2002 – May 2004)



Discussion

High-risk infants exposed to RSV infection are susceptible to develop severe and fatal disease as well as long-term disability (6). The mortality of hospitalized infants with RSV infection of the lower respiratory tract is 2%. Almost all deaths occur in young, premature infants or those with underlying disease of the neuromuscular, pulmonary, cardiovascular or immunological system (1). Immunoprophylaxis is available but should be reserved only for infants and children at greatest risk for severe RSV infection.

The American Academy of Pediatrics issued a policy statement with recommendations for immunoprophylaxis of high-risk infants for the prevention of RSV transmission (7). It includes infants born premature, and those with chronic lung disease, neuromuscular disorders, and congenital heart disease among others.

In Puerto Rico high-risk patients considered for prophylaxis are the same as those recommended by the American Academy of Pediatrics and include:

- Preterm infants born of ≤ 28 weeks of gestation ≤ 12 months chronologically at the beginning of the season.
- Preterm infants born of 29-32 weeks of gestation ≤ 6 months chronologically at the beginning of the season.
- Preterm infants born of 32-35 weeks of gestation ≤ 6 months chronologically at the beginning of the season with 2 or more of the following risk factors
 - child care attendance
 - has school-aged siblings
 - exposure to environmental contaminants
 - has congenital abnormalities of the respiratory tract
 - has severe neuromuscular disease
- Infants and children younger than two years of age (chronologically) at the beginning of the season with chronic lung disease who have required medical therapy within 6 months.
- Infants or children younger than two years of age (chronologically) at the beginning of the season with hemodynamically unstable/significant congenital heart disease (cyanotic), moderate to severe pulmonary arterial hypertension (PAH) or on medications for cardiac failure or hemodynamically stable congenital heart disease who is preterm, has chronic lung disease or is in medications for congestive heart failure.

Currently there is no consensus on medical treatment for this condition, only supportive measures are recommended and emphasis is given to prevention. A critical aspect of RSV prevention is parent or caregiver education on the importance of decreasing exposure to and transmission of RSV (6). Preventive measures including avoiding exposure to contagious settings and emphasizing on hand hygiene in all settings is imperative. In addition, prevention through immunoprophylaxis for high-risk patients is the standard of care. Two products are available to prevent RSV infection: respiratory syncytial virus immune globulin intravenous (RSV-IVIG) and intramuscular *palivizumab*. Because RSV-IGIV and *palivizumab* are not effective in the treatment of RSV disease, neither is an approved indication (6).

In Puerto Rico, there is year-round RSV infection with peak incidence from August to March. We could not establish epidemiologic values because part of the data of positive RSV infection was estimated, do to lack of confirmatory testing in most of the local institutions in Puerto Rico. The estimate that 20% of bronchiolitis cases seen monthly are caused by RSV shows year-round epidemic levels in Puerto Rico. The decrease in positive RSV infections in hospital C may be explained by the introduction of immunoprophylaxis to high-risk patients. The impact of this data stresses the importance of the implementation of a surveillance system in our community so that accurate assessment of epidemiologic levels of RSV infection can be established leading to an informed revision of season and immunoprophylaxis guidelines.

Resumen

El virus sincitial respiratorio (RSV) es una causa importante de enfermedad de tracto respiratorio en infantes y niños. Hoy en día existe inmunoprofilaxis contra este virus para niños de alto riesgo. Este estudio revisa casos de pacientes con bronquiolitis por RSV en tres hospitales de cuidado primario en Puerto Rico y describe la epidemiología del virus en estas instituciones. **Métodos.** Se analizó data de dos instituciones obteniendo el número de infantes con bronquiolitis y estimando el porcentaje de casos infectados por RSV. Los resultados del tercer hospital se obtuvieron mediante evaluación de pacientes con pruebas confirmatorias de infección por RSV. **Resultados.** Se incluyeron 4,557 pacientes en el estudio y hubo evidencia de infección por RSV durante todo el año. Nuestra data demostró una disminución progresiva de infección por RSV. **Conclusión.** La data confirma la incidencia de RSV durante todo el año. Se señala la necesidad de implementar un sistema de vigilancia estandarizado para determinar la epidemiología del virus

sincitial respiratorio en Puerto Rico. La disminución de bronquiolitis por RSV en nuestra data podría ser resultado de la introducción de inmunoprofilaxis a pacientes de alto riesgo en Puerto Rico.

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