Respiratory Syncytial Virus-Associated Hospitalizations in Louisiana

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Respiratory syncytial virus (RSV) is the most common cause of bronchiolitis and pneumonia in children under one year of age worldwide. Records indicative of RSV cases were pulled from The Louisiana Inpatient Hospital Discharge Data based on RSV diagnosis codes to describe the burden of RSV infections in Louisiana from 1999 to 2010. Two thousand to three thousand hospitalized RSV cases occurred each year, with rates ranging from 37.2 to 71.4 hospitalizations per 100,000 population and the majority of cases (79%) being diagnosed with bronchiolitis. The vast majority of cases occurred in children under one year of age, and within that group, 44% of the cases occurred in children ages 0 to 3 months. The RSV season was found to occur from November to March, and immunoprophylaxis for high-risk infants should be given according to that season. Hospital-acquired versus community-acquired infections were also examined and most (96.1%) cases were community-acquired.

INTRODUCTION

Respiratory syncytial virus (RSV) is recognized as the most common cause of bronchiolitis and pneumonia in children under one year of age worldwide.[6] It is estimated that 75,000 to 125,000 infants are hospitalized each year with RSV in the United States, and RSV infection has been associated with 43% to 74% of bronchiolitis cases and 19% to 54% of pneumonia cases.[1]

RSV is primarily transmitted through contact with respiratory secretions deposited on fomites or droplets from the respiratory tract of the source hitting the mucous membranes of the recipient. The virus can survive on hard surfaces for up to six hours.[2] Symptoms of RSV infection vary widely depending on age, comorbidities, environmental exposures, and previous infections; however, infants often experience upper and lower respiratory symptoms.[2] Risk factors for developing severe RSV infections have been widely studied, pointing to chronic lung disease of prematurity, congenital heart disease, and prematurity; however, a majority of RSV hospitalizations have been found to occur among children with no underlying high-risk conditions.[3]

Transmission of RSV is a concern in healthcare settings, and outbreaks have occurred in a number of both pediatric and adult healthcare settings.[4] Studies have shown secondary attack rates of 19% to 45% among patients when limited or no infection control measures were utilized.[4] It has also been shown that 15% to 20% of asymptomatic infected personnel shed RSV.[4] Studies evaluating various control measures have shown mixed results for the use of gowns, gloves, and masks, which may be in part due to the prolonged survival of RSV on surfaces including gowns and gloves.[4] Studies that included isolation of patients and handwashing in addition to PEP yielded better results.[4]

Diagnostic methods for RSV detect the virus, viral antigens, or virus-specific nucleic acid sequences in respiratory secretions. Methods that are currently available include virus isolation in tissue culture, direct or indirect immunoflourescent staining (DFA/IFA), enzyme-linked immunosorbent assays (EIA), and nucleic acid amplification assays, including reverse transcription polymerase chain reaction (RT-PCR).[5] The most sensitive and specific methods are nucleic acid tests; studies comparing diagnostics demonstrated a two-fold increase of detection rates compared to isolation in cell culture and antigen detection techniques.[5]

Respiratory syncytial virus infections are not reportable to the state of Louisiana. Nationally, surveillance is conducted on RSV through The National Respiratory and Enteric Virus Surveillance System (NREVSS), which is a laboratory-based system that monitors temporal and geographic patterns associated with the detection of certain diseases including RSV.[6] In Louisiana, RSV surveillance is conducted by using the Louisiana Inpatient Hospital Discharge Data (LaHIDD).

METHODS

For the purposes of this study, the data used was obtained from LaHIDD, although this only represents a minute fraction of the RSV disease burden because most cases of RSV are never severe enough to be hospitalized.

Records of patients were extracted from LaHIDD us-

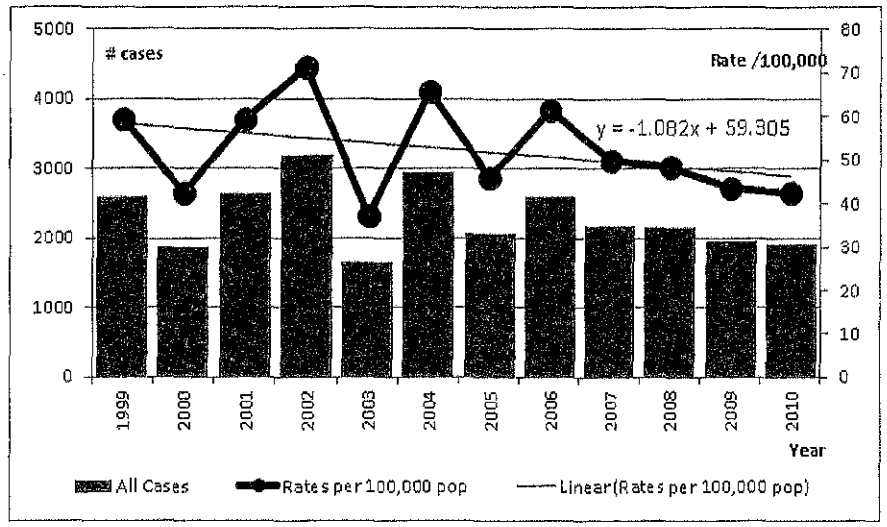

Figure 1: Hospitalized case rates (All RSV) per 100,000 population - Louisiana, 1999-2010

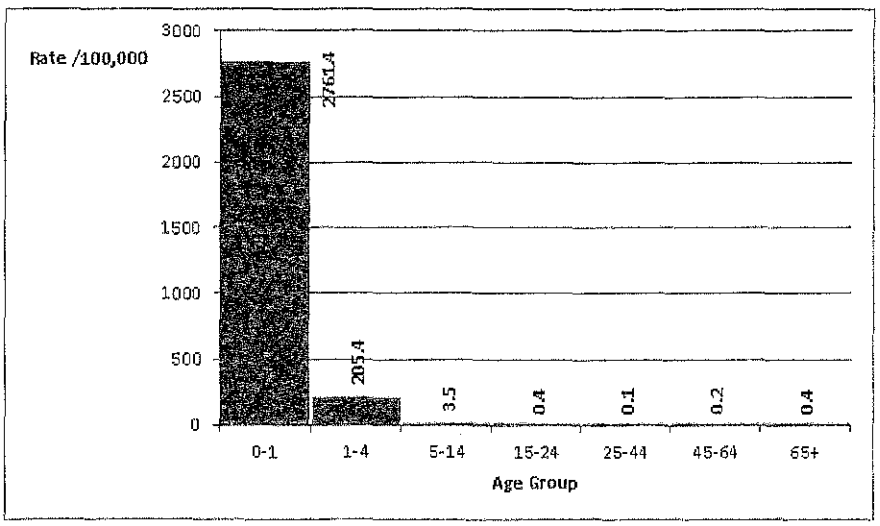

Figure 2: Age group distribution - Louisiana, 1999-2010

ing the three ICD-9 codes indicative of RSV cases, whether in the main diagnosis or in the eight additional secondary diagnoses. The code of 079.6 represents a diagnosis of RSV; the code of 480.1 represents a diagnosis of pneumonia due to RSV; and the code of 466.11 represents a diagnosis of acute bronchiolitis due to RSV. The following statistics are based on unduplicated patients. The data is based on the years from 1999 to 2010.

Hospitalizations were categorized as having a main diagnosis of RSV or a secondary diagnosis (Diagnosis 1 to 8) of RSV and also categorized as having an admit diagnosis of respiratory condition or other condition compatible with RSV (fever, dehydration, viral infection). These categories were used to estimate the importance of hospital-acquired RSV infections. Patients missing an admit diagnosis were excluded from these statistics.

RESULTS

There were 2,000 to 3,000 RSV cases every year of the study period, including 200 to 400 cases of pneumonia due to RSV, 1,000 to 2,000 cases of bronchiolitis due to RSV, and 100 to 200 unspecified cases of RSV. The majority of cases are in the bronchiolitis category (79% of all cases); this proportion remained fairly constant throughout the period of study.

Overall trend

Figure 1 shows the hospitalized case rates per 100,000 population for all RSV diagnoses. For the entire period, the yearly rates for all RSV-associated hospitalizations ranged from a high of 71.4 hospitalizations to a low of 37.2 hospitalizations per 100,000 population and show a significant decreasing trend (Cochran-Armitage chi-square test for trend=145.9, p=0.000) with an annual rate of decrease of 1.93%, with a 95% Confidence Interval [CI] = -4.9 to +1.1%.

Rates by Age

The rates of hospitalization for RSV over the study period are significantly higher for infants under one year (2,761.4 per 100,000, ranging from 2,139 to 3,737 per 100,000), as well as those in the one to four-year age group (205.4 per 100,000). The rates drop off dramatically after those ages, with the remaining age group rates falling between 0.1 and 3.47 per 100,000 population (Figure 2). The rate ratio between the age groups 0 to 1 and 1 to 4 was 13.4 with a 95% CI=13.1 to 13.8.

In the infant group (0-1), there is a steady decline in number of cases with age (Figure 3), with 44% of cases for ages zero to three months, 29% for three to six months, 16% for six to nine months, and 11% for 9 to 12 months.

Rates by sex

Figure 4 shows the hospitalized case rates by sex. The rates of RSV hospitalizations among males for the entire period was 62.87 per 100,000 population and 47.18 per 100,000 population for females. Male rates were consistently higher than those of females except for in 2008. For the period 2006 - 2010, the stratified Mantel-Haenszel rate ratio for M/F=1.23, p<0.000, 95% Cornfield CI=1.18 to 1.28. This more recent period was selected because of the limitations of the statistical test package used.

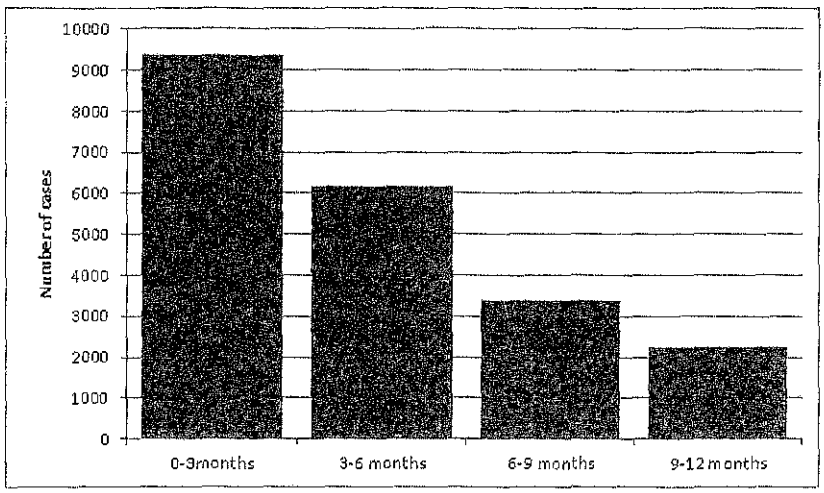

Figure 3: Distribution of cases between the ages of 0 to 1 - Louisiana, 1999-2010

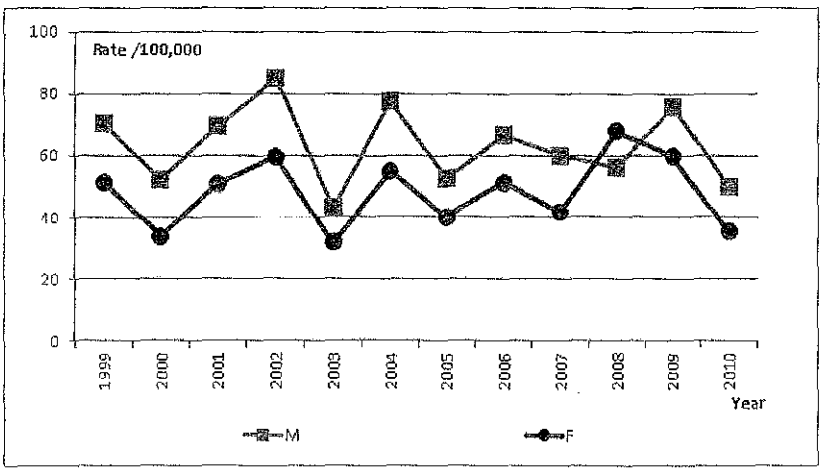

Figure 4: Hospitalized case rates (all RSV) per 100,000 population by sex - Louisiana, 1999-2010

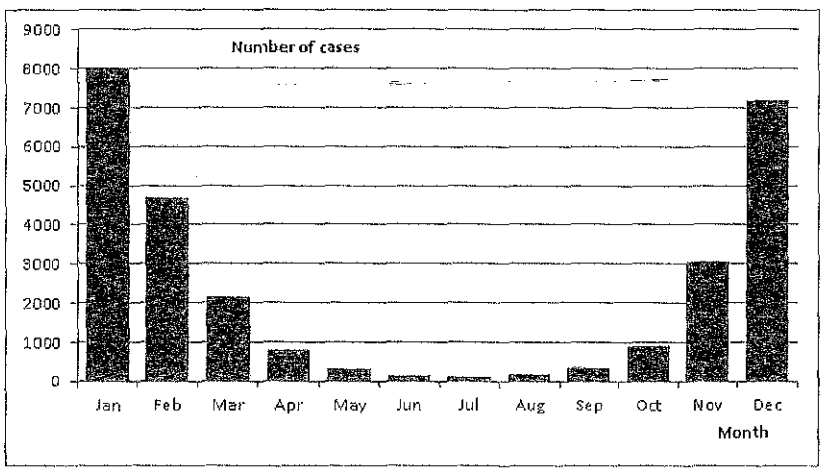

Figure 6: Seasonality of RSV - Louisiana (1999-2010)

Rates by Race

Figure 5 shows the hospitalized case rates by race. The rates of RSV hospitalizations among African-Americans for the entire period was 41.82 per 100,000 population and 34.83 per 100,000 population for Caucasians. For the period 2006-2010 the stratified Mantel-Haenszel rate ratio for AfAm/C = 1.28, p<0.000, 95% Cornfield CI = 1.22 to 1.34.

Seasonality

There is a significant trend in seasonality of RSV, with the majority of cases occurring in December, January, February, and March (Figure 6). The peak occurs in January. Cases decrease in the spring, very few cases occur in the summer months, and cases then rise into the winter months. The five-months peak from November to March is significant (Hewitt's rank sum test = 42, p = 0.013).

Table 1 depicts the seasonality of RSV, which varies very little from year to year. The table displays the months of the year in columns and the years in rows. The months with more than 100 cases are shaded. For most of the years, the period November to March shows consistently high numbers. For only two of the 12 years, the start of the season was in October, and in only one year, the season continued until April.

RSV Mortality

The mortality rate among RSV-associated hospitalizations is very low, with 18 deaths (0.06% of all RSV hospitalizations) occurring from 1999 to 2010 (Table 2).

Hospital-acquired versus community-acquired RSV infections

Main and secondary RSV diagnoses were compared with admit diagnosis to speculate possible hospital-acquired versus community-acquired infections (Table 3). It is reasonable to assume that:

- if a patient has a main diagnosis of RSV and a respiratory admit diagnosis, the infection is community-acquired,
- if a patient has a secondary diagnosis of RSV and a non-respiratory admit diagnosis, the infection could very well be hospital-acquired.

The majority of all RSV-related hospitalizations had a respiratory cause for admission, and RSV was also listed as the primary discharge diagnosis (Box 1: 83.9%), which are the most likely community-acquired infections.

Table 1: Seasonality of RSV - Louisiana (1999-2010)

YR	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept
1999	124	383	760	577	363	179	70	32	17	23	18	43
2000	33	158	474	666	321	112	63	24	3	8	7	15
2001	46	118	439	730	722	382	111	40	17	6	16	26
2002	126	350	572	865	698	333	96	51	22	12	18	45
2003	67	128	346	484	307	182	80	16	4	7	15	29
2004	78	400	788	806	558	225	37	16	10	6	10	17
2005	49	165	590	635	321	149	92	20	11	9	9	16
2006	121	448	763	689	303	136	35	13	5	11	26	52
2007	84	279	732	610	258	116	44	17	7	1	6	21
2008	74	324	731	661	174	77	39	20	12	3	16	32
2009	53	198	618	568	246	105	57	21	13	15	24	36
2010	38	104	365	717	415	154	55	24	16	9	12	16

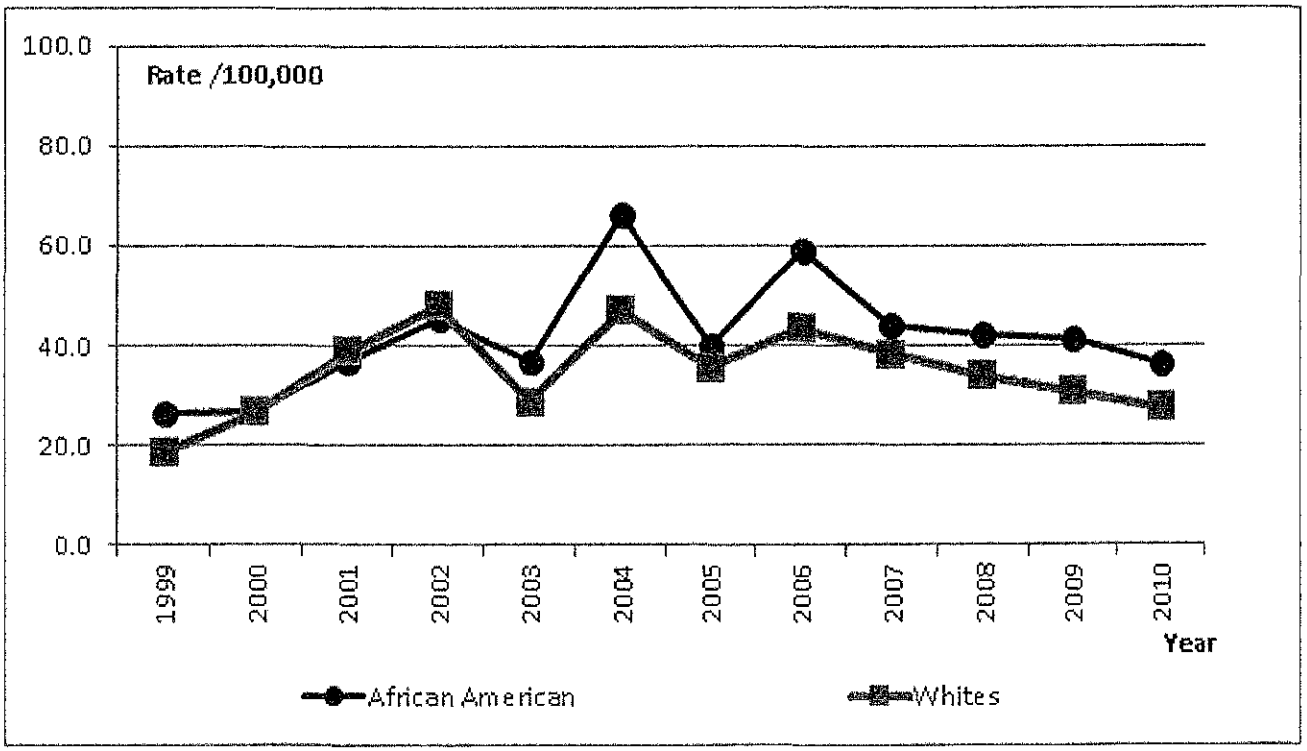

Figure 5: Hospitalized case rates (all RSV) per 100,000 population by race - Louisiana (1999-2010)

Table 2: RSV mortality - Louisiana (1999-2010)

Year	All RSV-associated Hospitalizations	Deaths	% Deaths
1999	2,595	1	0.04
2000	1,884	0	0
2001	2,653	1	0.04
2002	3,188	2	0.06
2003	1,665	0	0
2004	2,950	3	0.10
2005	2,066	1	0.05
2006	2,602	2	0.08
2007	2,175	2	0.09
2008	2,163	2	0.09
2009	1,954	1	0.05
2010	1,925	3	0.16
Total	27,820	18	0.06

The category including a compatible RSV admit diagnosis and a secondary RSV diagnosis seems to be, upon careful review of the diagnoses, consisting of mostly community-acquired cases (Box 2: 12.2%).

The categories with a non-respiratory admit diagnosis and a primary RSV diagnosis (Box 3: 1.1%) or a secondary RSV diagnosis (Box 4: 2.8%) appear to consist of hospital-acquired RSV infections after thorough inspection of the admit diagnosis, main diagnosis, and secondary diagnosis.

DISCUSSION

Since the great majority of cases occurred in the 0-1 age group, it was felt to be unnecessary to calculate age-adjusted case rates. The proportion of the population under 1 year of age has been hovering around 1.45% of the population during the entire study period.

The rates of hospitalizations observed in Louisiana (2,721/100,000) are within the same order of magnitude as the rates observed in the USA (3,120/100,000 in 1996).[1] This statewide data is representative of the state hospitalizations; however, it is important to note that rates of outpatient office visits for RSV among children under 5 years of age are much higher than rates of hospitalizations,[8] and therefore this data does underrepresent the true burden of RSV infections in the population.

RSV bronchiolitis-associated rates are much higher than both RSV pneumonia-associated and RSV non-specified associated hospitalizations. Coding practices, availability of laboratory tests, and indications for laboratory testing may explain this distribution of cases. Variations observed from year to year may also be the result of variations in RSV strain virulence, seasonal variations, and access to healthcare.

Table 3: RSV Diagnosis by Respiratory or Non-Respiratory Admit Diagnosis - Louisiana (1999-2010)			
	Main RSV	Secondary RSV	Total
Admit Dx = Respiratory Plus	22,976	3,328	26,304
Admit Dx = Not Respiratory	301	766	1,067
Total	23,277	4,094	27,371
Admit Dx = Respiratory Plus	84%	12%	96%
Admit Dx = Not Respiratory	1%	3%	4%
Total	85%	15%	100%

Seasonality of RSV infections has been often studied, and it is well documented that the South has an earlier onset and longer duration than the rest of the country,[3] beginning late November and ending mid-March.[9]

Current methods of prevention of RSV include hand hygiene and contact precautions, both in healthcare settings and in the community.[3] Immunoprophylaxis is also used to protect against severe complications of RSV infection, particularly in infants and young children who are at high risk.[10] Considering the substantial cost of immunoprophylaxis and the limited protection it provides, it has been recommended to give doses in a timely and efficient manner based on the RSV season.[10] The first RSV vaccine trials were conducted in the mid-1960s with a formalin-inactivated vaccine for children aged 2 months to 9 years; however the children who received the vaccine were more likely to develop severe RSV than those who received the placebo.[3] Currently, there are a few candidate vaccines under development.[3]

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