

# RSV Versus Non-RSV Bronchiolitis at Haykal Hospital between January 2016 and December 2018

Farah Rida<sup>1</sup>, Bassem Abou Merhi<sup>1</sup>, Laudy Abi Rida<sup>1</sup>, Joelle Azzi<sup>2</sup>, Manal Dahrouj<sup>1</sup>, Ghaiss Makkoul<sup>3</sup>

<sup>1</sup>Department of Pediatrics, Faculty of Medical Sciences, Lebanese University, Beirut, Lebanon, <sup>2</sup>Department of Public Health, Faculty of Public Health, Lebanese University, Beirut, Lebanon, <sup>3</sup>Department of Neonatology, Haykal Hospital, Tripoli, Lebanon

## ABSTRACT

**Introduction:** Bronchiolitis is a clinical syndrome that occurs in children <2 years, characterized by upper respiratory symptoms followed by lower respiratory tract infection that results in wheezing and/or crackles and other complications. Its typically caused by a viral infection, among which, respiratory syncytial virus (RSV) is the most common cause. **Objective:** The aim of this study is to determine whether RSV is the most common cause of acute bronchiolitis in North Lebanon and to determine the most common age, season for RSV bronchiolitis, whether it is more prevalent in preterm patients and whether it is a more serious infection. Our study is the first one conducted in North Lebanon that provides information related to RSV versus non-RSV bronchiolitis. **Materials and Methods:** A retrospective study was conducted at Haykal hospital in North Lebanon over a period of 3 years; a total of 368 medical records of cases younger than 2 years who presented with complaints related to bronchiolitis, admitted based on clinical presentation, with evidence of an International Classification of Diseases, 10<sup>th</sup> Revision codes and in whom the RSV nasal swab test was done, were all reviewed. **Results:** Among 368 cases enrolled in the study, 211 (57.3%) were RSV positive bronchiolitis. RSV was mostly found among younger ages <3 months with  $P = 0.014$ . Cases with RSV bronchiolitis had a longer hospital stay and more oxygen requirement compared to cases with non-RSV bronchiolitis with  $P \leq 0.001$  and  $P = 0.028$ , respectively. Both RSV and non-RSV bronchiolitis peaked in December and being reported throughout the whole year  $P < 0.001$ . Prematurity was the only risk factor studied  $P = 0.010$ , but our data did not show significantly higher rates of hospitalization for RSV versus non-RSV bronchiolitis among preterm infants. City of residence was associated with more intensive care admissions, increased rates of RSV infection in higher regions (Akkar and Dinieh) and more crowded cities (Tripoli) compared ( $P = 0.013$ ). **Conclusion:** RSV is the most common cause of hospitalization for bronchiolitis in North Lebanon, it has a more severe course in all parameters, and thus, physicians should emphasize on the use of palivizumab for the prevention of RSV infections in children at high risk as recommended by guidelines.

**Key words:** Bronchopulmonary dysplasia, congenital heart disease, respiratory syncytial virus

## INTRODUCTION

**B**ronchiolitis is defined as a clinical syndrome that occurs in children <2 years of age that is characterized by upper respiratory symptoms followed by lower respiratory tract infection (LRTIs) which in turn results in wheezing and/or crackles, retractions, and cyanosis as well as other complications. Its typically caused by a viral infection, among

which, respiratory syncytial virus (RSV) is the most common cause.<sup>[1]</sup> RSV causes seasonal outbreaks throughout the world.<sup>[2]</sup> It appears to be greatest in infants younger than 3 months of age and in those with risk factors, especially prematurity.<sup>[3]</sup> RSV bronchiolitis is considered to be a more severe illness compared to that caused by other viruses; infected patients had a longer length of hospital stay, had more oxygen requirements, and other comorbidities (atelectasis/condensation and acute otitis

### Address for correspondence:

Bassem Abou Merhi, Department of Pediatrics, Faculty of Medical Sciences, Lebanese University, Beirut, Lebanon.  
E-mail: bassemaboumerhi@gmail.com

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media). These findings suggest that RSV bronchiolitis is a more severe illness compared to that caused by other viruses.<sup>[4]</sup>

## OBJECTIVES

### Primary objective

The aim of this study is to determine whether RSV bronchiolitis is the most common cause of acute bronchiolitis in hospitalized children <2 years old in North Lebanon and to examine RSV and non-RSV bronchiolitis hospitalization rates from 2016 to 2018 among infants less 2 years.

### Secondary objectives

The objectives of the study were to assess the hospitalization trends for RSV and non-RSV for children <2 years with or without higher-risk medical conditions, to determine: At what age in the first 2 years of life, children mostly got infected with RSV/non-RSV bronchiolitis? (To determine the age and duration of an RSV/non-RSV bronchiolitis admission), when during the year does RSV bronchiolitis mostly occur (Monthly distribution)? If preterm infants are more susceptible to RSV compared to term babies? The length of hospitalization for RSV bronchiolitis is longer than non-RSV bronchiolitis. Which is proportionate to the cost of hospitalization; thereafter is RSV bronchiolitis a more severe disease than that caused by other viruses?

## MATERIALS AND METHODS

### Ethical information's

This study was done in a manner that ensures the confidentiality of patients. Data collected were identified and stored at the principal investigator's office that was locked as a measure of security.

### Study design

This study is a retrospective study conducted at Haykal hospital in North Lebanon over a period of 3 years, from January 1, 2016, to December 31, 2018.

### Study population

After board approval, 368 medical records were retrieved from the hospital's archive; all of them included cases younger than 2 years old who presented with a chief complaint related to bronchiolitis; more specifically based on the ICD10 codes for those who were treated for bronchiolitis.

### Inclusion criteria

Infants and children up to 24 months of age and in whom the RSV nasal swab test was done that has a sensitivity and a specificity of 80% and 97% respectively.

### Exclusion criteria

We excluded those admitted for bronchiolitis in whom the RSV swab test was not done and those born at the hospital

in whom the RSV was isolated in the 1<sup>st</sup> week suggesting hospital-acquired infection.

### Procedures of data collection and measurements

Data were collected from medical records and entered into a Microsoft Excel spreadsheet which was designed specifically for this study. After that, data were transferred into IBM SPSS, version 22, which was used for data cleaning and analyses.

### Statistical analysis

All statistical analyses were performed using the Statistical Package of the Social Science (IBM SPSS, version 22.0). Continuous variables were reported as mean and standard deviation, while categorical variables were summarized as frequency and percentage. Categorical variables were compared using the Chi-square test. The mean of quantitative variables was compared using the Student's *t*-test. All tests were two-sided and  $P < 0.05$  was considered to be statistically significant.

## RESULTS

This is a retrospective study done in a tertiary medical center in Tripoli-Lebanon. Records of 368 patients admitted to the hospital for bronchiolitis were collected. Demographic information was gathered. Age and gender groups: The mean age of patients was 4.23 months. Of all those cases, 219 (59.3%) cases were males while 149 (40.4%) were females with a similar mean of age in both groups (4.09 months in males vs. 4.44 months in females). The cases were classified into three groups according to age. The results are summarized in Figure 1. Those between 1 and 3 months constituted the largest group.

### Month of hospitalization

The cases were classified according to the month of admission to the hospital; the results are summarized in Figure 2. December and January had the highest number of admissions for bronchiolitis.

### Length of hospitalization

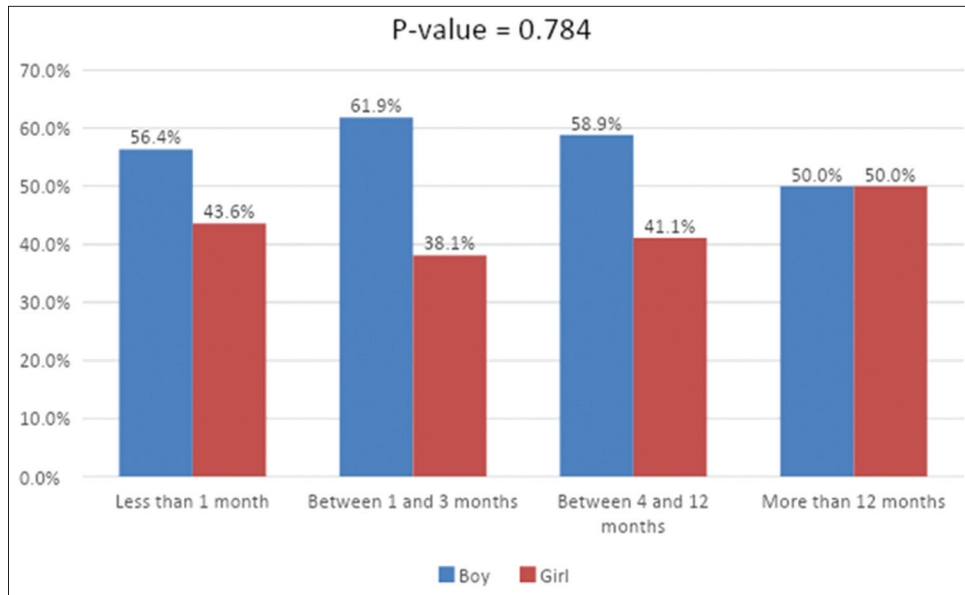
The cases were classified according to the length of hospitalization; the results are summarized in Table 1. The median length of hospitalization for bronchiolitis was 5 days.

### Resident region

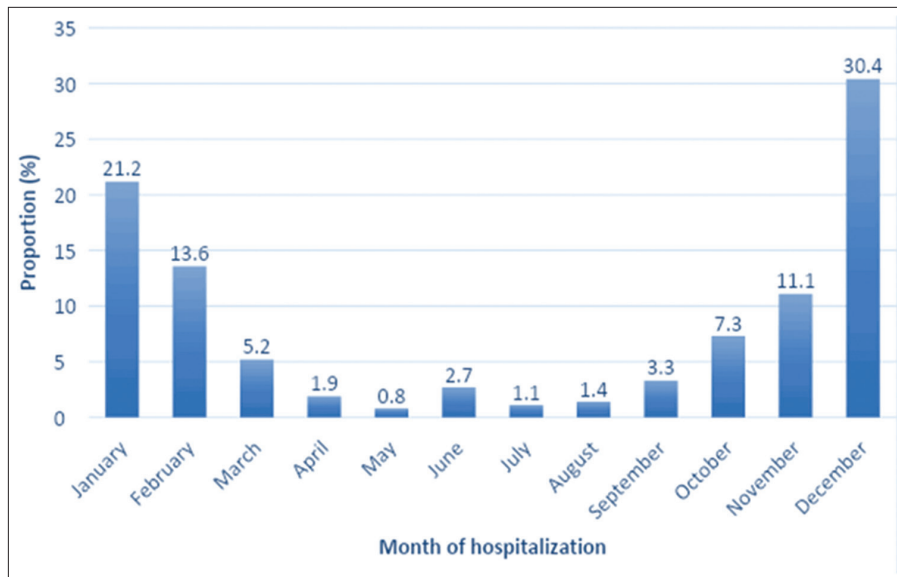
Our cases were grouped according to their living city or region, Figure 3 shows that most of our patients were from the Northern part of Lebanon. The highest ones were Tripoli and Akkar.

### Term versus preterm

The cases were divided between those born at term and those born prematurely; there was no enough data on those



**Figure 1:** Distribution of gender by age groups



**Figure 2:** Month of hospitalization distribution

**Table 1:** Length of hospitalization distribution

Length of hospitalization	n (%)
Valid answers	368
Mean±SD	5.8±4.1
Median	5.0
Min-Max	1–44

born prematurely (small number of preterm patients and no available gestational age) also in a few patients, the neonatal history was missed in the medical records and we could not even reach the family. The results are shown in Figure 4.

### Oxygen requirement

The cases were classified if they required or not oxygen during hospitalization. The results are shown in Figure 5.

### ICN/ICU admission

The cases were divided whether they required intensive care unit admission. The results are shown in Figure 6.

### RSV versus non-RSV bronchiolitis

The cases were divided into two groups: The first group included 158 cases that had non-RSV bronchiolitis, and the second one included 211 cases that had RSV bronchiolitis. The results are shown in Figure 7.

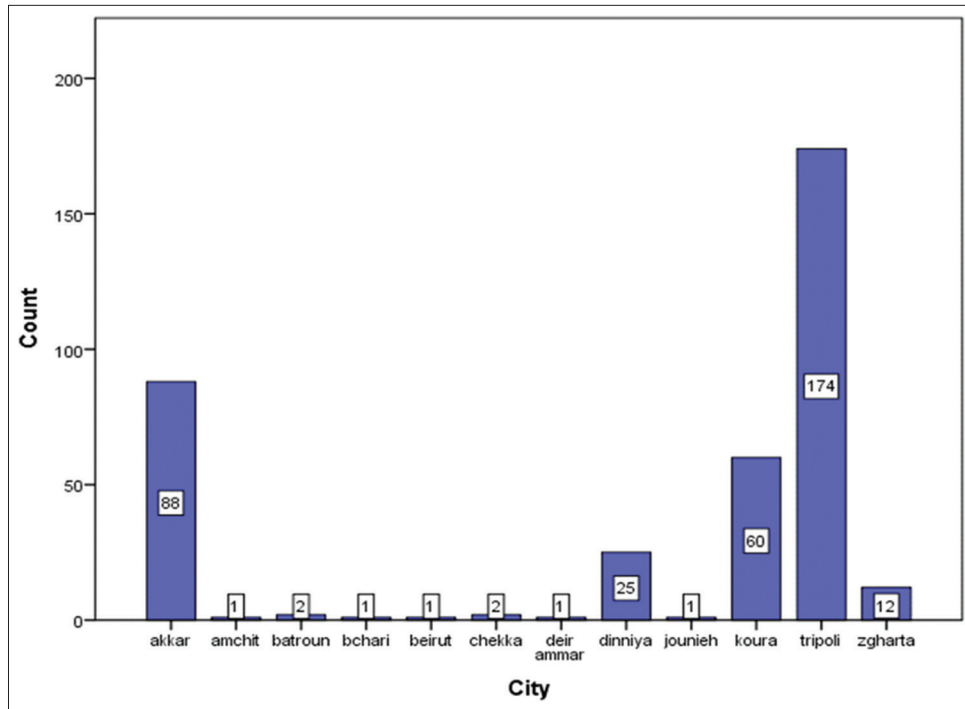


Figure 3: Living region or city distributions

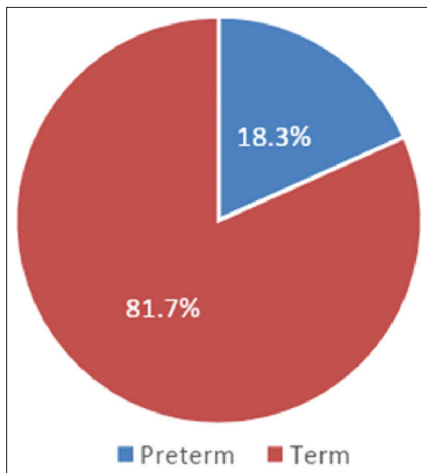


Figure 4: Term versus preterm distribution

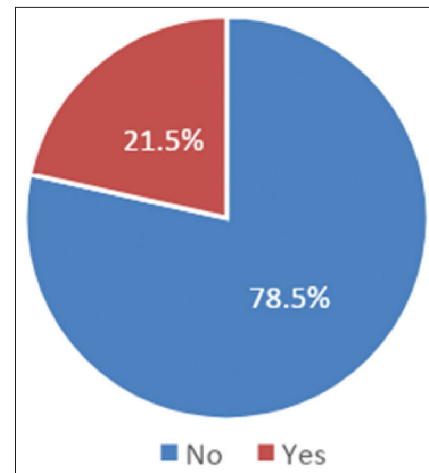


Figure 5: Oxygen requirement distribution

## DISCUSSION

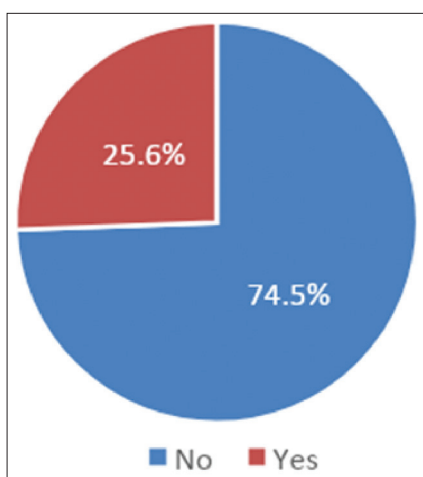
### Other studies conducted in Lebanon

Three other studies on RSV were done in Lebanon; one of them “Respiratory Syncytial Virus: Prevalence and Features among Hospitalized Lebanese Children “conducted at Makassed General Hospital, Beirut, Lebanon (MGH) reported by Assaf-Casals *et al.* between 2012 and 2014, published on December 15, 2014, included infants and children from 0–13 years,<sup>[5]</sup> the second one “Etiology, Seasonality, and Clinical Characterization of Viral Respiratory Infections Among Hospitalized Children in Beirut, Lebanon” also done at Makassed General Hospital, Beirut, Lebanon (MGH) published on May 19, 2016, included children <16 years, and the third one “Bronchiolitis Admissions in a Lebanese

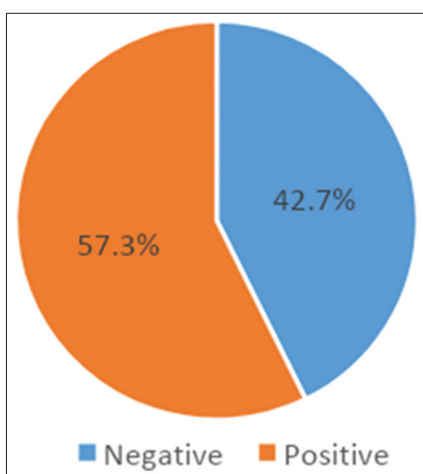
Tertiary Medical Center: A 10 Years’ Experience” done at AUBMC reported by Zeina Naja, between October 2004 and October 2014 published on May 17, 2019, included children <5 years.<sup>[6]</sup> None of them fit with the definition of bronchiolitis “the first episode of wheezing in a child younger than 12–24 months”,<sup>[7,8]</sup> also the second study examined the viral etiology of acute respiratory infection and their epidemiology and not the severity. Thus, none of the above studies compared between “RSV bronchiolitis” and “non RSV bronchiolitis.”

### Overall results

Our study is the first one done in North Lebanon in a tertiary medical center: “Haykal hospital.” It is a retrospective,



**Figure 6:** ICN/ICU distribution



**Figure 7:** RSV versus non-RSV distribution

comparative study that includes all cases admitted for bronchiolitis (up to 24 months) over a period of 3 years (January 2016 to December 2018), and compared between RSV positive versus RSV negative bronchiolitis. Our study yielded to a total of 368 patients. About 57.3% were RSV positive bronchiolitis; this value was higher than the one reported by Assaf-Casals *et al.* at another tertiary care center (MGH) in Beirut (22.1%),<sup>[5]</sup> and to those published in neighboring countries: About 16.9% in Turkey<sup>[9]</sup> and 22.9% in Egypt.<sup>[10]</sup> However, our results were almost similar to the one reported by Zeina Naja at AUBMC in Beirut (61%).<sup>[6]</sup> The seasonality patterns for RSV and non-RSV bronchiolitis hospitalizations were almost the same; both subgroups peaked in December, which coincides with the one described by Assaf-Casals *et al.*<sup>[5]</sup> while the study described by Zeina Naja<sup>[6]</sup> showed that RSV hospitalizations were most common during the first 3 months of the year, in accordance with the previous studies conducted in Turkey<sup>[9]</sup> and Jordan.<sup>[11]</sup> We reported RSV cases throughout the whole year with RSV being a lot more common than non-RSV in the months of June and July. Thus, in North Lebanon, the RSV outbreak

season seems to start near October, peaks in December, continues throughout the winter, spring, and summer season and does not end at all. Which somehow again coincides with the one described by Assaf-Casals *et al.*<sup>[5]</sup> that reported RSV cases throughout the whole year except in August. A variety of risk factors and demographic features were associated with a higher likelihood of acquiring RSV bronchiolitis. Our study revealed male predominance in both subgroups (RSV and non-RSV), which is expected, since male infants are suspected to have decreased pulmonary function compared to female infants<sup>[12]</sup>. A result that came in accordance with a recent US multicenter prospective cohort study of 1836 pediatric patients with bronchiolitis where 60% of the patients were males,<sup>[13]</sup> and in the one reported by Zeina Naja.<sup>[6]</sup> In our study, RSV bronchiolitis peaked in the age group between 1 and 3 months and was more common than non-RSV in the age group of <1 month while non-RSV bronchiolitis peaked in the age group between 4 and 12 months. This repartition was different from the one reported by Zeina Naja<sup>[6]</sup> that showed an older mean age at the admission of 7 months for both RSV and non-RSV subgroups. Although prematurity is a risk factor for RSV bronchiolitis, as mentioned in literature, “RSV has the potential to cause severe LRTI in certain high-risk groups: Young, premature infants with chronic lung disease or congenital heart disease (CHD), patients with significant asthma, and patients who are immunocompromised;”<sup>[3]</sup> our data did not show significantly higher rates of hospitalization for RSV and non-RSV bronchiolitis among preterm infants similar to the ones reported by Assaf-Casals *et al.*<sup>[5]</sup> and Zeina Naja<sup>[6]</sup> (No data on the other risk factors for RSV bronchiolitis). In agreement with previous studies, we found that RSV infections led to a longer hospital course compared to non-RSV (mean days of hospitalization 6.6 vs. 4.8, respectively) and that the patients in the RSV group required more oxygen during their hospitalization and more ICN/ICU admissions; a result that is expected since RSV bronchiolitis is a more severe illness compared to that caused by other viruses.<sup>[4]</sup> Thus, physicians should emphasize on the use of palivizumab which is a humanized monoclonal antibody against the RSV F-Glycoprotein, licensed for the prevention of serious RSV lower respiratory tract disease in children at high risk of RSV disease;<sup>[14]</sup> among them: Bronchopulmonary dysplasia (BPD), prematurity without BPD < 28 weeks.<sup>[15]</sup> The role of breastfeeding in protecting against RSV bronchiolitis and preventing hospitalization and death has been very well-established.<sup>[16]</sup> Thus, again all mothers should be encouraged to breastfeed for at least 6 months to prevent LRTIs according to the 2014 American Academy of Pediatrics guidelines for the management of bronchiolitis,<sup>[17]</sup> and all families should be warned about the consequences of the second-hand smoke exposure that was associated with an increase in the severity of RSV infection by several studies.<sup>[18]</sup> But unfortunately, there were no data on the availability of breastfeeding or on the exposure to a second-hand smoke to support these findings. In our study, inhaled bronchodilators, inhaled, and



systematic corticosteroids and antibiotics were frequently used in the management of RSV and non-RSV bronchiolitis. However, due to the retrospective nature of our study, it was difficult to assess whether the usage of those therapies was warranted. Regardless of that, based on guidelines, physicians should not regularly prescribe bronchodilators, antibiotics, and/or corticosteroids to children with bronchiolitis.<sup>[17]</sup> City of residence was associated with more ICN admission, with higher rates of RSV infection in higher regions (Akkar and Dinieh), and more crowded cities (Tripoli). However, this result is biased, because this study enrolled patients from only one tertiary care center in North Lebanon (Albert Haykal Hospital) and not multiple ones ( $P = 0.013$ ). This result may lead to the fact that in one side, these mentioned regions (Akkar and Dinieh) are poor in facilities: Absence of electricity during many hours of the day and night, limitation in the ways of warmth in Winter, limitation in the number of hospitals or medical centers and even a total absence of hospitals in Dinieh. Moreover, on the other side, an important number of families belong to the poor socio-economic status in these regions. Do not these regions need to be more supervised by our Ministry?! Doesn't the population there deserve all the appropriate facilities for their children?

### Study limitations and perspectives

It is a retrospective study that limited our ability to collect data on the following: The exact gestational age of the child, also in some records the neonatal history is missing, and we could not reach the family to know it. No data on other risk factors for RSV (CHD, immunocompromised, smoking, etc.). No data on the availability of breastfeeding or on second-hand smoking exposure. In some records, we could not find if the child required oxygen. We did not find data on the use of palivizumab in high-risk patients. Some of the non-RSV bronchiolitis might have had RSV since they were tested with the RSV antigen swab test, and not with the polymerase chain reaction diagnostic technologies. The cases of bronchiolitis in whom the RSV swab test was not done, were missed. This study was done in North Lebanon; it enrolled patients from only one tertiary care center in Lebanon and not multiple ones.

## CONCLUSION

Our study showed that more than half of cases with bronchiolitis were RSV positive thus; it showed that RSV is the most common cause of bronchiolitis among hospitalized infants and children up to 24 months. Both RSV and non-RSV bronchiolitis were more common in boys with the younger cases being more affected by RSV bronchiolitis. It also showed that RSV is associated with a more severe course compared to non-RSV bronchiolitis, because RSV cases had a longer hospital stay, required more oxygen during their stay, and the ICN/ICU admissions were more common in the RSV group.

## Recommendations

For sure, all mothers should be encouraged to breastfeed for at least 6 months to prevent LRTIs. All families should be warned about the consequences of the second-hand smoke exposure that was associated with an increase in the severity of RSV infection. Parent's education for preventive hygiene measures is easy and worth to perform, to limit the virus's transmission. All parents should be aware that a minor cold to them may cause life-threatening illness in a young infant or a high-risk child. Physicians should emphasize on the use of palivizumab for the prevention of serious RSV lower respiratory tract disease in children at high risk of RSV disease as recommended by guidelines. Regions in the North Lebanon with the low facilities (Akkar and Dinieh) were the ones with a prevalent number of ICN/ICU admissions with higher rates of RSV bronchiolitis. Our ministry should reconsider to assure all the appropriate needs for this population.

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