

Incidence of Respiratory Syncytial Virus Among Young Children in United Arab Emirates

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Abstract

Background: Respiratory syncytial virus (RSV) is the most common cause of acute lower respiratory tract infections among children less than 2 years old. The aim of this study is to determine the incidence of RSV infection in children <2 years old and to evaluate the seasonal variation of this virus in United Arab Emirates (UAE) between 2018-and 2020. **Methods:** This was a retrospective study and data was collected for all patients less than 24 months of age who visited the University Hospital Sharjah (UHS) with acute respiratory tract infections (ARTIs) from 1st January 2018 to 1st January 2020. Seasonal variations were determined by analyzing the monthly RSV-positive isolation cases via time series analysis. **Results:** Of the 2496 children diagnosed with ARTIs, 496 (18.79%) were detected positive for RSV antigen with males being more likely to be infected (53.8%) than females (46.2%). Moreover, higher RSV positive cases were found among infants ≤6-months old (39.7%) than children >6 months old (5.4%). Also, children >6 months of age and who were born by cesarean section were more prone to infection by RSV than other ages. Viral and bacterial co-infections have also been observed among 3.8% of the positive cases. Regarding the seasonality of RSV infection, it was detected in winter and peaked in October to December, while two small peaks were observed in January, April and May. **Conclusions:** The pattern of RSV in the UAE parallels that of tropical countries. These findings may guide in efforts towards healthcare provision, vaccination, and implementation of RSV prevention.

Keywords: Respiratory syncytial viral; Respiratory tract infection; Incidence; Seasonality; United Arab Emirates

INTRODUCTION

Respiratory syncytial virus (RSV) infection is the most common cause of acute lower respiratory tract infections (ALRTIs) among children less than 2 years old.^[1] This virus can cause significant morbidity and mortality in high-risk individuals. Globally, it is estimated that this virus causes approximately 33.8 million new episodes of ALRTIs annually in children aged <5 years. It is also responsible for the mortality of children aged between 1-12 months.^[2,3] In temperate regions of the world, there is a clear seasonal variation of the incidence of RSV infection, with peaks during late fall/winter seasons.^[4] This difference is expected to be less pronounced in the Middle East and other desert climate regions of the world, where there is less ambient temperature fluctuation.

^[5] However, there is evidence that the wave of RSV infection follows a seasonal trend and varies according to the prevailing environment.^[6] The American Academy of Pediatrics recommends prophylaxis for RSV infection in high-risk infants.^[7] The so-called “RSV season” is the key to RSV immunoprophylaxis. Understanding the prevalence, clinical characteristics, and seasonality of RSV infection is essential for promoting the preparedness to establish timely counter-measures to control the pathogen.^[8] Although some studies in the United Arab Emirates (UAE) and nearby

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countries have investigated the seasonality of this virus in children, the information included in these studies is limited. [5,9,10] Therefore, further studies in developing countries including UAE are essential in the prevention, control, and treatment of RSV infection. This study is designed to describe the incidence of ARTIs, clinical characteristics, and seasonality of RSV infection that is considered the main cause of LRTIs among children less than 2 years old.

MATERIALS AND METHODS

Data Collection

Medical reports of infants and young children ≤ 2 years old with ARTIs were reviewed retrospectively. Patients who had visited the pediatric clinic at the University Hospital Sharjah (UHS) between 1st January 2018 and 1st January 2020 were included in this study by using the track care system database. Data of total 2496 patients who were tested with RSV test was included in this study. The data was collected from different hospital clinics including outpatient and emergency departments to detect the RSV positive samples (Table 1).

Table 1: Demographic data and clinical features of positive- RSV cases (n=496)

| Variables | No. of episodes | n(%) |
|---------------------------|-------------------------|-------------|
| Gender | Male | 267 (53.8%) |
| | Female | 229 (46.2%) |
| Age (Months) | 0-6 | 197 (39.7%) |
| | 06-12 | 156 (31.5%) |
| | 12-18 | 116 (23.4%) |
| | 18-24 | 27 (5.4%) |
| Nationality | Emirate | 454 (91.5%) |
| | Non-Emirate | 42 (8.46%) |
| Clinical Features | | |
| Episode's status | Positive RSV | 496(18.79%) |
| | Negative RSV | 2143(81.2%) |
| Diagnosis | Acute Bronchiolitis | 476 (96.0%) |
| | URTIs | 9 (1.8%) |
| | LRTIs | 5 (1.0%) |
| | Bronchopneumonia | 6 (1.2%) |
| | ED* | 289 (58.3%) |
| Management | Outpatient clinic | 94 (19.0%) |
| | Pediatric ward | 113 (22.8%) |
| | NICU | 8 (1.6%) |
| Method of delivery | Normal vaginal delivery | 296 (59.7%) |
| | Caesarean section | 200 (40.3%) |

* Emergency department

The data of patients who were admitted in hospital, had respiratory tract infection symptoms, were less than 24 months of age, and had positive immunofluorescence for RSV in epithelial cells from nasopharyngeal swab, was included in this study. While the data of patients who were born premature and who had any underlying chronic condition like cardiac, neurological, lung diseases, and immunodeficiency was excluded from the study.

The severity of RSV and hospitalization decision was taken following the guidelines by the Integrated Management of Childhood Illnesses (IMCI), and overall judgment by physician at the time of admission.^[11] The data indicated

that nasopharyngeal swabs were collected from children < 24 months old, and who had respiratory symptoms such as cough, breathing difficulties, or flu-like symptoms. Moreover, the specimens for RSV antigen were analyzed with ePlex respiratory pathogen panel system (GenMark Diagnostics, Inc. Carlsbad CA, USA). RSV positive cases that occurred in ≥ 14 days of symptom onset for a previous RSV illness, were considered a new episode.

Frequency of observed reinfection with RSV (repeated RSV infections at least 3 months between 2 episodes of RSV-related illness) and pulmonary viruses in RSV positive infants were calculated during the selected time period of this study. Likewise, the frequency of bacterial co-infection (the incidence and effect of single and multiple pulmonary viral or bacteria infections with the RSV positive infection) was also calculated. Sources of specimens included nasal wash, nasopharyngeal swab, bronchoalveolar lavage, and tracheal aspirate.

Ethics Statement

This study was approved by the ethics and research committee of the UHS (Reference number: UHS-HERC-030-29022020) and was conducted in collaboration with Sharjah institute for medical research.

Statistical Analysis

Statistical analysis was performed using a statistical package for the social sciences version 22.0 (SPSS Inc. Chicago, IL, USA, 2013). Chi-square test was used to assess the significance between categorical variables, while, Fisher exact test was used adjunctively. The p -value < 0.05 was considered statistically significant.

RESULTS

Medical records of total 2496 patients were reviewed retrospectively between 1st January 2018 and 1st January 2020. Of these, 496 cases (18.79%) were found positive for RSV antigen and included in this study. Table 1 presents the demographic characteristics and clinical features of shortlisted patients. More than half of the confirmed RSV positive cases were males ($n=267$, 53.8%), while remaining patients were females. The number of infants ≤ 6 months old ($n=197$, 39.7%) was predominantly higher than children aged (6-12), and (12-18) months. Moreover, children older than 18 months were found less likely to be infected with RSV ($n=27$, 5.4%). The majority of children ($n=454$, 91.5%) were Emiratis, whereas only 8.46% children ($n=42$) were from different nationalities. The clinical summary indicated that most RSV positive cases ($n=476$, 96.0%) were diagnosed with acute bronchiolitis (LRTI that primarily affects the small airways), while 1.8%, 1.0%, and 1.2% of positive cases were diagnosed with upper respiratory tract infections (URTIs), LRTIs and bronchopneumonia respectively. URTIs affect the upper respiratory tract, including nose, sinus, pharynx, larynx, trachea, LRTIs affect the small airways (bronchioles), and bronchopneumonia affects the bronchi of the lungs. Around two-third of RSV positive children ($n=296$, 59.7%) were delivered by normal vaginal delivery (NVD), while

remaining children were delivered through cesarean section. None of the positive cases were either vaccinated against RSV or were found associated with any chronic condition or underlying disease.. Most of the positive cases (n=289, 58.3%) were in emergency department (ED), while others were in outpatient clinic. About 22.8% of cases (n=113) were admitted in the pediatric ward while the neonatal intensive care unit (NICU) received only 1.6% cases (n=8).

Reinfection and Viral or Bacterial Co-Infections

Of the 496 positive cases, 26 (5.2%) infants were found to be reinfected with RSV and about 4 of these cases were hospitalized. As depicted in Table 2, viral or bacterial co-infections were reported in 19 (3.8%) positives cases. Around 7 (1.4%) and 6 (1.2%) of the co-infected cases were infected with Influenza A and Influenza B viruses. While, only 2 (0.4%) cases were infected with both Influenza A and B viruses. Moreover, a single case was found to be co-infected with Rota/Adenovirus. Table 2 also shows that 3 (0.6%) of the cases had bacterial co-infections with three bacteria (1 each) i.e., *Corynebacterium diphtheriae*, *Staphylococcus haemolyticus*, and *Group A streptococcus*.

Table 2: Coinfectious pathogens other than RSV infection

| Confection's pathogens | No. of cases |
|------------------------------------|--------------|
| Viral agent | |
| Influenza A+B | 2 (0.4%) |
| Influenza A | 7 (1.4%) |
| Influenza B | 6 (1.2%) |
| Rotavirus/Adenovirus | 1 (0.2%) |
| Bacterial agent | |
| <i>Corynebacterium Diphtheriae</i> | 1 (0.2%) |
| <i>Staphylococcus Haemolyticus</i> | 1 (0.2%) |
| <i>Group A streptococcus</i> | 1 (0.2%) |

Relation between Two Groups of Children Infected by RSV (≤6 Months vs>6 Months)

Infant patients>6 months old were more likely to get infected with RSV (n=299) than patients≤6 months old (n=197) (Table 3). Hospitalization and ward admission were significantly higher in infants≤6 months old (P

<0.001). Similarly, total 8 infants≤6 months old were admitted to NICU while none of the children>6 months old stayed there (p<0.001). Although acute bronchiolitis was the predominant cause of RSV infection in all ages of patients, neither AURTIs nor ALRTIs significantly affected the infection between the age groups.

Table 3: Relation between RSV infection in two groups of children (<6 months vs>6 months) with the demographic and clinical characteristics (n=496).

| Variable | <6 months of age (n=197) | >6 months of age (n=299) | P value |
|--------------------------------|--------------------------|--------------------------|---------|
| Gender | Male | 106 (53.8%) | 0.993 |
| | Female | 91 (46.2%) | |
| Hospitalization | 54 (27.4%) | 59 (19.7%) | 0.001 |
| NICU stay | 8 (4.1%) | 0 (0%) | 0.001 |
| AURTIs | 3 (1.5%) | 6 (2%) | 0.777 |
| ALRTIs | 1 (0.5%) | 4 (1.3%) | 0.777 |
| Delivery via Caesarian section | 63 (32%) | 135 (45.8%) | 0.002 |

Regarding the method of delivery, children>6 months old who were born by cesarean section tend to be significantly infected with RSV than infants≤6 months old (P <0.002).

Seasonality of RSV Infection in the UAE

The seasonal peak of RSV infection was detected in the winter season as shown in Figure 1. However, the line graph showed that the positivity rate in the year 2019 started to rise from August and continued to December with the highest peak was in November i.e., Aug (n=10, 2%), Sep (n=21, 4%), Oct (n=123, 24%), Nov (n=182, 37%), and Dec (n=36, 7.25%). The same figure shows the number of positive cases in year 2018 as follows: Aug (n=0, 0%), Sep (n=13, 2.6%), Oct (n=24, 4.8%), Nov (n=26, 5.24%), and Dec (n=25, 5%), with the highest peak in November. In addition, two small peaks were found in January 2018 (n=13, 2.6%), January 2019 (n=4, 0.8%), Apr 2018 (n=4, 0.8%) and May 2018 (n=5, 1%), while no positive case was found in April and May, 2019. The Figure 2 presents the distribution of all positive and negative cases in the study period 2018-2019.

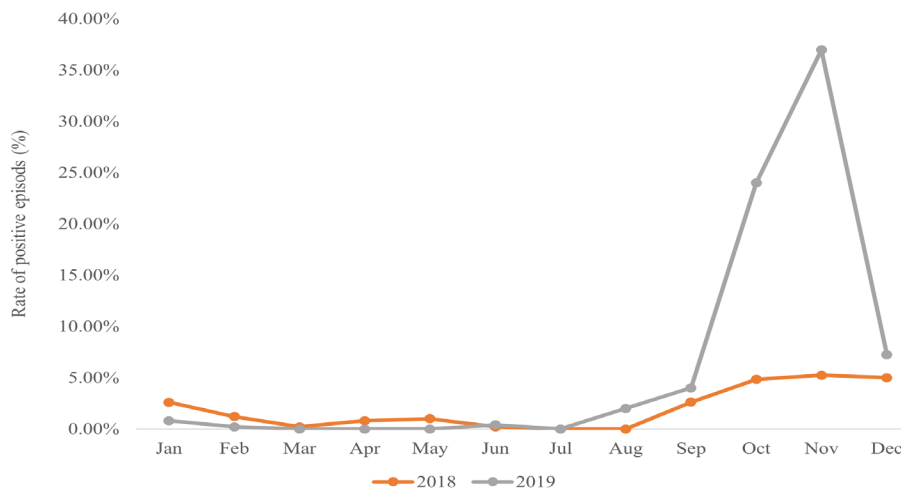


Figure 1: Monthly number and positivity rate of RSV cases between 2018 and 2020

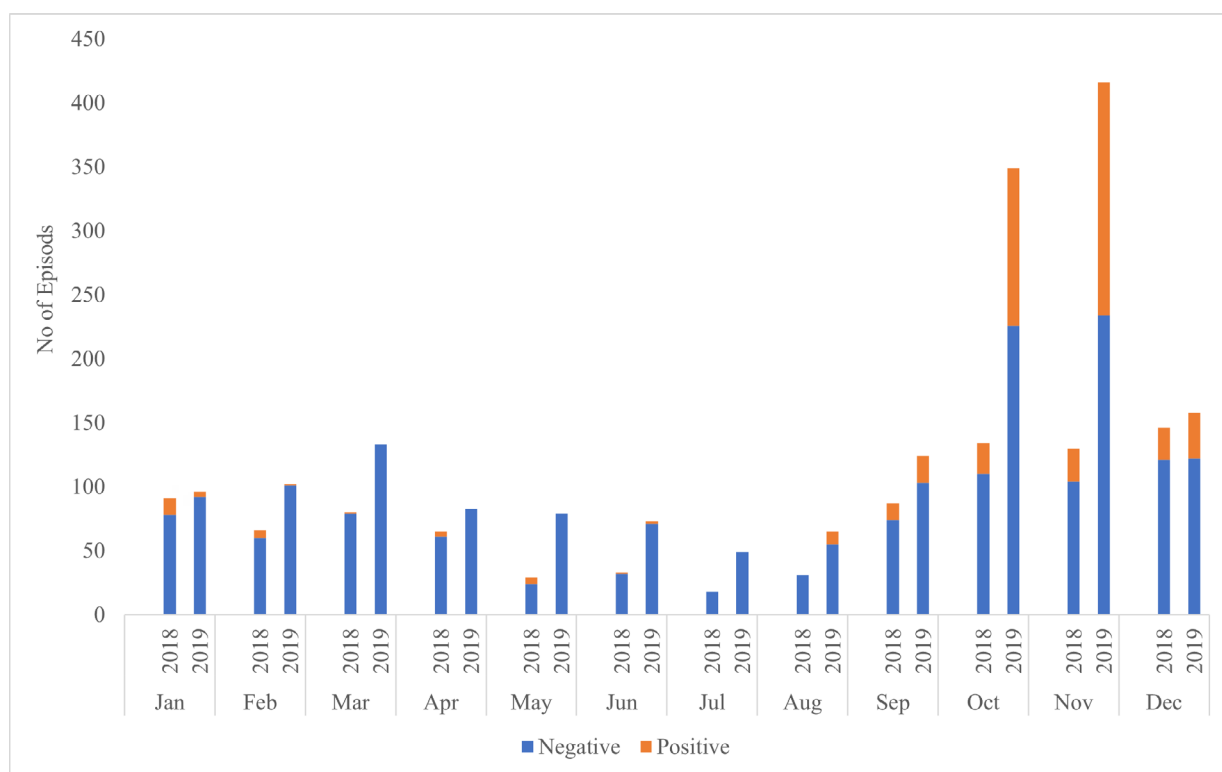


Figure 2: Monthly numbers of positive RSV cases in the study period.

DISCUSSION

RSV infection is highly prevalent and is responsible for a high burden of disease in many countries.^[1] Several studies have been conducted to evaluate the incidence and seasonality of RSV infection in temperate and tropical regions in the world;^[4,12-18] however, there is limited information on the Middle East and other desert climate regions of the world as RSV epidemics appear regularly but with different patterns of seasonality in these regions.^[5,9,10]

In this study, we found that the incidence of RSV positive cases among infants ≤ 2 years was 18.79%, which is lower than that reported in other studies i.e., 67.5% in Kuwait, 43% in Oman, 24% in Riyadh, Saudi Arabia, and 86.8% in northern Taiwan.^[6,10,17,18] However, our results were similar to those reported in countries of tropical Asia, for example, it was 20.1% and 23.0% in Indonesia,^[12,15] while, it was 18.4%, 20.4%, and 18.9% in Malaysia.^[13,19,20] The hot and dry climate of the UAE could be a possible explanation for the low incidence of RSV in this region. This virus is more common during the rainy season in tropical and subtropical areas and is reported to have a low survival rate at high temperatures.^[9,21] Our findings indicated that males were more likely to be infected with RSV than females and these results are consistent with many other studies,^[10,12,18,19,22] yet without convincing explanations so far.^[23] Some studies attribute this to the effect sexual hormones have on the immune response.^[24] Also, RSV was found to be a major cause of hospitalization in children less than 2 years old. Large variations were seen depending on the age group with the highest hospitalization rate among RSV positive children

who were ≤ 6 months old. The rate of admission in our study for this age group was similar to that observed among infants less than 2 months old in Spain, < 3 months old in Denmark, ≤ 3 months old in Dubai, and among 6 months old and below in Kelantan, Malaysia.^[16,22,25,26] In our study, the average hospital and NICU length of stay due to RSV was shorter than that indicated in other studies,^[10,25] however, our results showed that only children ≤ 6 months old stayed in the ICUs.

Delivery by caesarean section was also found associated with an increased risk of hospitalization for RSV infection in this study and these findings are in line with the results of other studies.^[27,28] This could be due to lack of exposure of children delivered by caesarean section, to the cytokines produced during labour.^[29] Also, children born by caesarean section are not exposed to the mother's vaginal microflora which is important not only for development of normal mucosal defence and immunological priming but also for maintaining the normal homeostasis in the host. In addition, the neonatal period is crucial for establishment of the human microbiome.^[22,30]

In our study, we observed that none of the detected cases have been earlier vaccinated against RSV. As RSV vaccination prevents serious RSV-associated LRI, hence, its effectiveness to prevent severe disease and hospitalizations is of paramount importance when weighing pros and cons for the introduction of new vaccines into national immunization programs. There are several obstacles in the development of successful RSV vaccines, including the need to immunize infants, who may respond adequately to vaccination.^[22,31]

As the incidence of hospitalization due to RSV is already

high in infants ≤ 6 months old, therefore, RSV vaccination strategy is necessary. Two possibilities are: either vaccinating the infant shortly after birth or vaccinating the mother before giving birth. Newborn vaccination is challenging due to the immaturity of the newborn's immune system and the negatively received maternal antibodies, which can impair the response. Vaccination of the mother before giving birth may provide more effective protection to the newborn than vaccination of newborns.^[32] A considerable fraction of RSV-associated hospitalizations could likely be avoided per year in the UAE by applying RSV immunization program. In the present study, it was observed that RSV positive children were also exposed to other infectious pathogens especially viral agents such as influenza A or B. Co-infections are likely to be associated with a longer hospital stay, ICU admission or decreased use of supplemental oxygen.^[33] The co-infection rate in this study is compatible with that reported in a previous study.^[34] In the current study, seasonality pattern of RSV was also investigated as this infection is characterized by seasonality that may be associated with the region and the climate.^[6] Our findings showed that most of the incidents of RSV infection occurred in the winter season. Several studies in nearby and Middle East/North Africa (MENA) region countries have also reported that the highest incidence of RSV infection occurs during winter season.^[6,9,25] In this study, most of the RSV positive cases in children were detected from Autumn to Spring. Moreover, the high seasonal peaks were found between August and December with a sharp increase and the highest incidence in October, November, and December in both years 2018 and 2019. Our results were in accordance with several other studies for example, a study reported more than half of the RSV infection-related hospitalization during November and December among infants born at less than 35 weeks in Dubai.^[35] Another study conducted in Northern UAE observed major infection peak in November and December, and a small peak in August.^[9] Similarly, in Oman, 43% of RSV cases were detected between October and March with a high seasonal peak in December.^[10] Likewise, a study in Qatar found that the peak of RSV infection among children < 2 years old was in winter between November and January every year.^[5] Low temperature and low specific humidity during the winter season in the UAE may be the cause of RSV infection peak in winters. In addition, the current study also observed a small seasonal peak in January 2018 which is in contrast with findings of other studies which reported the highest seasonal peak of RSV incidence in January.^[6,17] In Malaysia, the annual peak of RSV infection is in November, December, and January.^[13] Another study in Kuala Lumpur, Malaysia reported the highest peak between September and December, and lowest peak in mid year i.e., April-June.^[20] While a study in Brazil indicated that the highest peak occurred between November and December.^[13] In 2020, an unexpected positive outcome of the coronavirus disease 2019 pandemic is a decline in illnesses associated with respiratory viruses, which is likely due to the extensive use of masks and social distancing.^[36]

LIMITATIONS

The data was collected from single hospital only which may not depict the entire population of the UAE. In addition, this study referred to the severe cases of RTIs only, as 96% of the cases were with bronchiolitis. Moreover, there was a lack of data with respect to the survival status after RSV infection among the infants. More studies are needed to confirm the policies regarding prophylaxis against RSV and these studies need to be based on much wider data regarding populations, children under risk, seasonality and relative cost-benefit relationships.

CONCLUSION

The seasonality of RSV infections in Sharjah, UAE showed a biennial pattern with peaks in October and November and small peaks in January and April to May. The information of this study will provide the guidance to the healthcare provision, vaccination, and implementation of RSV prevention.

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Contributions

Balsam Qubais Saeed: Conceptualization; Methodology; Writing-Original draft preparation, Hanan Abdulgader Sharif: Study design, Methodology, Reviewing and Editing, Ahmed Omer Adrees: Methodology, Reviewing, Proofreading, Rula Al-Shahrabi: Methodology, statistical Analysis; Reviewing, Kubais Saeed Fahady: statistical Analysis, Najeh Rajeh Alsahhi, statistical Analysis, and Methodology, Writing, Review, Rabih Halwani: Writing, Reviewing and Editing.

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Conflicts of Interest

The authors declare no conflict of interest.

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