

# Respiratory Syncytial Virus Infection in Young Children Hospitalized with Respiratory Illness in Riyadh

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## Summary

The occurrence of respiratory syncytial virus (RSV) infection among young children hospitalized with lower respiratory tract illness, at King Khalid University Hospital in Riyadh, was examined during the autumn-winter season between September 1991 and February 1992. Sixty-nine cases were diagnosed by immunofluorescent antibody staining of viral antigen in nasopharyngeal aspirates from 127 children, constituting 54 per cent of these patients. Virus culture was attempted only in a few cases, yielding two isolates. Most children were < 1 year of age (median 2 months). Bronchiolitis and bronchopneumonia were the major diagnoses on admission. Hospitalization was for an average of 5 days (range 1-36 days). Treatment was supportive but most children received antibiotic therapy. There was no mortality. Few other bacterial or viral pathogens could be identified from RSV-positive or -negative patients. These results indicate that, during the season of infection, RSV may be the main pathogen of lower respiratory tract illness in hospitalized young children in this region.

## Introduction

Respiratory syncytial virus (RSV) is considered to be the most important cause of lower respiratory tract infections in infants and young children.<sup>1-3</sup> Respiratory syncytial virus was found in 40-80 per cent of infants hospitalized with bronchiolitis and in 20-25 per cent of infants hospitalized with pneumonia.<sup>4</sup> Normal children usually recover, but fatal infections can occur. An overall mortality rate has been estimated at 0.5-2.5 per cent.<sup>5</sup> Children with congenital heart disease can experience particularly severe infections, with mortality reaching 37 per cent.<sup>6</sup> Severe infections are also observed in immunosuppressed children.<sup>7</sup> Abnormalities in pulmonary function may occur and can commonly persist for several years after RSV infection.<sup>8</sup> Respiratory syncytial virus is a major cause of nosocomial infections,<sup>9</sup> with rates of 26-47 per cent in newborn units.<sup>2</sup> It can also infect older children and adults, usually causing milder infections, although severe infections among the elderly can occur.<sup>10</sup> There are two antigenically distinguishable

main sub-groups of RSV, subgroups A and B.<sup>11-15</sup> Re-infection by a different or the same subgroup can occur, although the severity is diminished in the latter case.<sup>15</sup> Respiratory syncytial virus is labile to conditions of transport and storage, which makes diagnosis by virus isolation difficult. However, the availability of sensitive antigen-detection techniques have made the study of RSV infections much easier.

Most studies on RSV infection have been carried out in Western countries, but several studies have revealed its importance in other regions of the world, including many developing countries.<sup>16-22</sup> However, information on the extent of RSV infection and its effect on the health of young children in our region of the world is still limited. We have therefore attempted to study the effect of this virus on the hospitalization of young children at the King Khalid University Hospital in Riyadh, Saudi Arabia, during the winter season of 1991-2.

## Materials and Methods

### Patients

The patient population included all children below 3 years ( $n=127$ ) who were hospitalized at the pediatric ward at King Khalid University Hospital with severe respiratory illness (bronchiolitis, bronchopneumonia, bronchial asthma, croup, and upper respiratory tract infection) during the period from August 1991 to March 1992.

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*Specimen collection and processing*

Nasopharyngeal aspirates were collected using disposable mucous extractors. Collected specimens were diluted by adding 2 ml of viral transport medium where a sufficient quantity was present and virus culture attempted. The sample was split into two parts: one for virus culture, the other for direct antigen detection by immunofluorescent antibody staining.

*Immunofluorescent antibody staining*

The portion used for antigen detection was further diluted in 10 ml of phosphate buffered saline (PBS) and centrifuged at 1000 *g* for 10 min. The pellet was resuspended and washed three times in 10 ml of PBS. Finally, it was resuspended in a small amount of PBS, spotted on Teflon-coated slides, fixed with cold acetone, and stained with fluorescein-conjugated anti-RSV conjugates using either the direct method with reagents from Kallestad (Germany) or Novo Nordisk Diagnostics Ltd (UK), or the indirect method with reagents from Pasteur Diagnostics (France).

Antigen detection by immunofluorescent antibody staining was similarly used for detecting infection by the following respiratory viruses: influenza A and B, parainfluenza 1, 2, and 3, and adenoviruses. The conjugate for these tests were obtained from Pasteur Diagnostics. A report of 'few cells present' was given if less than 30 cells were observed.

*Virus culture*

For virus isolation, the split part of the specimen was disrupted by vortexing in the presence of glass beads, allowing it to settle, and plating 0.1 ml on Hep-2 cells obtained from Flow Laboratories (UK). The culture was observed for up to 2 weeks for characteristic syncytia formation. Cells from the culture flasks were also checked for viral replication after 2-3 days of infection by staining with fluorescent anti-RSV conjugate. The isolate of adenovirus was identified by immunofluorescent staining after the appearance of cytopathic changes in Hep-2 cells.

**Results**

Figure 1 shows the total number of nasopharyngeal aspirates examined from different patients together with those found positive for RSV antigen by immunofluorescent staining during the period from August 1991 to April 1992. The period from September to February represents the coldest months of the year. Of eight specimens processed for virus culture, two were positive by both culture and antigen detection, while six were negative by both techniques. Five patients yielded repeat-positive samples for RSV by immunofluorescence.

The age distribution of positive children ranged from 15 days to 2.5 years, with a median of 2 months. The ratio of male to female was 1.52 (41/27) in RSV-

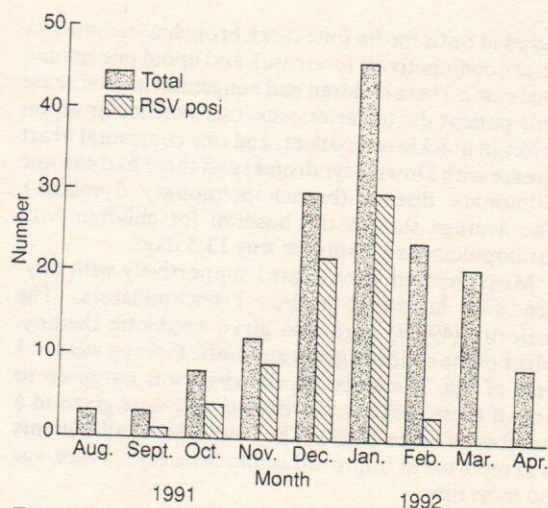


FIG. RSV infections in hospitalized children—Riyadh.

positive cases and 1.2 (32/26) in RSV-negative cases (no significant difference ( $=0.65$ )).

During the latter part of the study, a search was added routinely for influenza A and B viruses, parainfluenza 1, 2, and 3, and adenovirus. Two RSV-negative specimens were found positive for influenza A virus by immunofluorescence, while one specimen yielded an isolate of adenovirus. One child was initially positive for RSV. A month later, she became negative for RSV but was found positive for influenza A. The three influenza A-positive samples were all obtained in February 1992.

Bacterial cultures yielded few possible respiratory pathogens from either RSV-positive or RSV-negative patients. From the former, the following were obtained: B-haemolytic group A *Streptococcus* (one case) and type B *Haemophilus influenzae* (two cases); from the latter: *Haemophilus influenzae* (three cases), *Klebsiella pneumoniae* (two cases), and *Streptococcus pneumoniae* (one case).

The period of hospitalization of RSV-positive patients ranged from 1 to 36 days, with a median of 5 days. Hospitalization of RSV-negative cases also had a median of 5 days.

A history of allergic respiratory disease in a family member was frequently present in both RSV-positive cases (33/69) and RSV-negative cases (23/40).

Among the 69 RSV-positive patients, the diagnosis on admission was as follows: bronchiolitis (36), bronchopneumonia (24), bronchial asthma (4), other (5). Among the 40 RSV-negative patients, the diagnosis was: bronchiolitis (16), bronchopneumonia (9), bronchial asthma (6), other (9). Six of the RSV-positive patients were managed at the paediatric intensive care unit. However, four of these patients had an associated cardiopulmonary disorder.

Associated symptoms in RSV-positive cases



included otitis media (one case), bronchial asthma (six cases), conjunctivitis (one case), and lipoid pneumonia (one case). Three children had congenital heart disease (one patient ductus arteriosus, one ventricular septal defect in a sickle cell patient, and one congenital heart disease with Down's syndrome) and three had chronic pulmonary disease (bronchopulmonary dysplasia). The average stay in the hospital for children with cardiopulmonary disorders was 13.5 days.

Most children were treated supportively with oxygen and humidity, and/or bronchodilators. The majority (49/69) were also given antibiotic therapy. Most of the children given antibiotic therapy were < 1 year of age. The antiviral, ribavirin, was not given to any of these patients. Corticosteroids were given in a number of cases (9/69). The condition of all patients was reported as improved before discharge. There was no mortality.

#### Discussion

The results of this study indicate that RSV is a major cause of bronchiolitis and bronchopneumonia in hospitalized young children in Saudi Arabia. The pattern of RSV disease in this region exhibits a clear seasonality during the colder months of the year, which is a similar situation to that in other countries with a temperate climate. The age distribution is also similar to that observed in most earlier studies.<sup>4</sup>

Community-based studies are needed to evaluate the overall involvement and disease pattern caused by this virus in our community. As only severely affected children are usually hospitalized, a higher incidence of milder infections may be expected, especially among older children and adults. The involvement of RSV in respiratory disease of hospitalized patients of other age categories, especially the elderly, deserves further investigation as this virus is not routinely considered.

The fragility of RSV to transport and storage conditions and the slow growth of the virus make antigen detection the preferred method for rapid diagnosis in routine laboratories. The sensitivity and specificity of this technique is comparable to virus culture.<sup>23</sup> However, culture remains valuable for definitive diagnosis and subgroup identification.

The present study may not accurately reflect the involvement of other viruses in respiratory disease in our patient population as a longer period of study is needed. This is especially true for viruses such as influenza A, which occur in outbreaks.

Hospital cross-infection by RSV was considered unlikely among the infected children in this study because all patients exhibited lower respiratory tract disease on admission and because specimens were obtained within 24 hours of admission. Moreover, the duration of hospitalization for most patients (median 5 days) was too short to allow cross-infection.

In spite of the fact that most of our patients were given antibiotics, our results would favor the restric-

tion of antibiotic usage to cases where a strong clinical suspicion of a bacterial infection exists or where a bacterial pathogen has been identified. Instead, consideration may be given to the use of aerosolized ribavirin, particularly in children with special risk (e.g. with cardiopulmonary disease, with immunosuppression, or of very young age). This antiviral was shown to be of benefit in diminishing the severity of illness and is approved for the treatment of infants hospitalized with RSV lower respiratory tract disease.<sup>24-26</sup>

The outcome of our study does not necessarily reflect the situation of RSV infection in other settings. Conditions that are prevalent in developing countries, such as overcrowding and malnutrition, may lead to heightened susceptibility to severe disease-making RSV infections, among other major pathogens of acute respiratory disease, a major cause of mortality in these countries.<sup>3</sup>

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