

**Original Articles**

## A study on aetiology and outcomes of viral lower respiratory tract infections in hospitalized children from South India

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### Abstract

**Introduction:** Viral respiratory infection is a common cause of morbidity and mortality in children, especially those less than 5 years old.

**Objectives:** To study the aetiology and seasonal variation of viral lower respiratory tract infection (LRTI) in hospitalized children and to assess the morbidity and mortality.

**Method:** A retrospective cohort study was done on children, aged 1 month to 16 years, admitted in G. Kuppaswamy Naidu Memorial Hospital, a tertiary care hospital in Coimbatore, South India. Case records of children hospitalized with features of LRTI, for whom a respiratory viral panel was sent, were retrospectively reviewed and were analysed from July 2017 to June 2018. The aetiology of viral infection, age wise distribution, severity of illness and seasonal variation were studied. Multiplex PCR panel was done from either throat swab or nasopharyngeal aspirate in 69 children admitted with a clinical diagnosis of LRTI.

**Results:** Respiratory viruses were identified in 33 (47.8%) of the 69 children. Respiratory syncytial virus (RSV), influenza viruses A and B, parainfluenza virus and boca virus were the common viruses isolated from hospitalized children with LRTI. RSV and bocavirus were common among children less than 2 years old. RSV infection began in July, peaked during September and October and continued till January. Influenza virus was common among children more than 2 years and occurred between September and March.

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**Conclusions:** RSV, influenza A and B viruses, parainfluenza virus and bocavirus were the common viruses isolated from hospitalized children with LRTI. RSV infection peaked from September to October whilst influenza virus infection peaked from January to March.

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(Key words: Respiratory viruses, lower respiratory tract infection, seasonal variation)

### Introduction

Lower respiratory tract infection (LRTI) is an acute illness, commonly with cough as the chief symptom, with a minimum of one other lower respiratory tract symptom such as fever, breathlessness, wheeze, and no alternative explanation such as sinusitis or asthma<sup>1</sup>. It includes acute bronchitis, bronchiolitis, pneumonia and tracheitis. LRTI is a common cause of morbidity and mortality in children, especially those less than 5 years old. Viral infections contribute to a significant proportion and predispose to various complications<sup>2</sup>. Acute respiratory infections (ARIs) account for 1.9 million childhood deaths per annum in developing countries, 20% of them occurring in India<sup>3</sup>. However, the exact incidence of viral respiratory infection in India is not known. Western studies have noted significant mortality and morbidity in children associated with different respiratory viruses<sup>4</sup>.

### Objectives

The primary objective was to assess the aetiology and seasonal variation of viral LRTI over a one year period in hospitalized children using molecular polymerase chain reaction (PCR). The secondary objective was to assess the severity of illness, morbidity and mortality in the cohort.

### Method

We performed a retrospective cohort study of children, 1 month to 16 years old, admitted in G. Kuppaswamy Naidu Memorial hospital, a tertiary care hospital in Coimbatore, South India. Case records of children hospitalized with features of LRTI, for whom a respiratory viral panel was sent, were retrospectively reviewed and were analysed from July 2017 to June 2018. The aetiology of viral

infection, age wise distribution, severity of illness (duration of hospital stay and respiratory supports required) and seasonal variation were studied. Multiplex PCR panel was done from either throat swab or nasopharyngeal aspirate (whichever was feasible for that age group) in 69 patients who were admitted with a clinical diagnosis of LRTI.

Samples were collected in 3ml of HiViral™ transport medium. DNA/ RNA extraction was done with QIAAsymphony SP. The extracted DNA/ RNA was further amplified by multiplex PCR using fast track diagnostics kit. The kit detected 18 respiratory viruses (RSV, influenza A, B, parainfluenza A, B, corona, boca, human metapneumovirus (hMPV), adenovirus,

enterovirus, rhinovirus, parechovirus and H1N1. It was analysed in the platform- Real time PCR in Rotor gene Q 5plex from Qiagen or in CFX96 thermal cycler from Biorad.

*Statistical analysis:* Chi-squared test or Fisher's exact test was used for categorical variables. A p value less than 0.05 was considered statistically significant.

**Results**

A total of 69 samples were analysed from children 1 month to 16 years old. Age wise distribution of various respiratory viruses is shown in Table 1.

**Table 1: Age wise distribution of various respiratory viruses**

Age (years)	Positive for at least 1 virus	hRSV	Inf A	Inf B	PIV	AdV	HboV	EV/ Parecho/ Rhino	Coinfection
<2	16	10	0	0	01	01	06	02	03
2-5	08	02	0	03	0	02	01	04	03
>5	09	03	02	02	01	01	01	01	02
Total	33	15	02	05	02	04	08	07	08
%	47.8%	45.5%	06%	15.2%	06%	12.1%	23%	21.2%	81%

*hRSV- human respiratory syncytial virus, Inf A- influenza A, Inf B- influenza B, PIV- parainfluenza virus, AdV- adenovirus, HBoV- human Boca virus, EV- enterovirus*

Of the total samples analysed, 33 (47.8%) were positive for at least one virus. Boys (57.6%) were affected more than girls (42.4%). A greater proportion (72.7%) were less than 5 years of age and positive for at least one virus.

*Seasonal Variation*

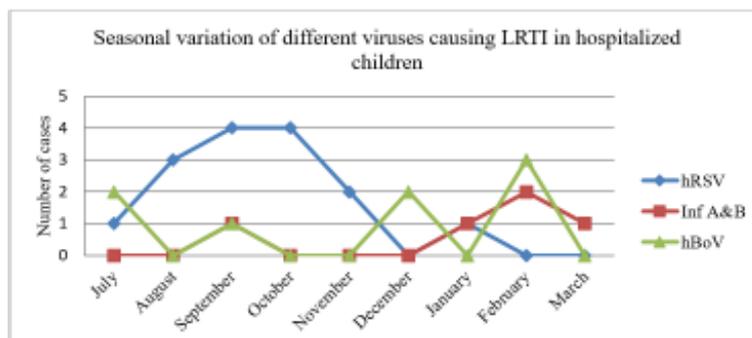
Overall, samples were sent from July to March and there were no samples sent from April to June. Number of samples sent was highest (33) from January to March. Percentage of positive samples

was highest (92.3%) from July to September. The percentage of co-infection was also highest (66.7%) from July to September (Table 2).

As seen in Figure 1, respiratory viruses showed seasonal distribution. RSV infection began in July, peaked during September and October and continued till January. Influenza infection was seen between September and March.

**Table 2: Number and percentage of positive viral infections among various months**

	July - September	October - December	January - March
No. of samples	13	23	33
No. of positive samples	12	09	12
% of positive samples	92.3	39.1	36.4
% of co infection	66.7	0.0	07.7



**Figure 1: Seasonal variation of individual viruses**

*Aetiology*

Common viruses isolated were RSV, influenza viruses A and B, parainfluenza virus and boca virus in that order. RSV and boca virus infection were common in children less than 2 years old whilst influenza viruses A and B and parainfluenza virus were common among children more than 2 years of age.

*Co-infection*

Co-infection was found in all age groups. However, no statistically significant difference was obtained between the age groups. The prevalence was highest among 1 month to 5 years (75%, n=6). The co-infection among various viruses is highlighted in table 2. Co-infection rates were high with RSV and were found in 6 out of the 8 samples. RSV infection was associated with boca virus and parecho virus.

**Table 2: Co-infection among various respiratory viruses**

	RSV	Adeno	Inf A/B	Boca	Entero	Rhino	Parecho
RSV	-----			++		+++	+
Adeno		-----	+		+		
Inf A/B		+	-----				
Boca	++			-----	+		
Entero		+		+	-----		
Rhino	+++					-----	
Parecho	+						-----

*Severity*

The mean duration of hospital stay was 6.8 days and the median was 4.0 days. A total of 15 (45.5%) children warranted paediatric intensive care unit (PICU) admission of which 10 were less than 2 years of age. Invasive ventilation was required for 2 children (1 child less than 2 years old) and 11 children (9 children less than 2 years old) were managed on high flow nasal cannula (HFNC). There was one death (11 year old boy) which was due to influenza ‘A’ virus along with Moraxella infection.

**Discussion**

Data on patterns of viral respiratory infections in children are available in Western literature<sup>5</sup>. However, there is a paucity of data on the seasonality and viral aetiology in India. Availability of multiplex PCR has facilitated early detection of viral respiratory infection in hospitalized children<sup>6</sup>. Common viruses isolated in our study were RSV, influenza virus, parainfluenza virus and boca virus. However, the proportion of boca virus accounting for LRTI was more compared to the metanalysis on aetiology of common respiratory viruses by Shi T *et al.*<sup>7</sup>. Boca virus is an established cause of severe LRTI in children in recent years. In the study by Moesker *et al.* boca virus was responsible for severe LRTI as an isolated agent but it also had a high rate of co-infection with RSV<sup>8</sup>. Adenovirus, enterovirus and parecho virus were also established causes of LRTI in children. However, the exact proportion and their significance need further study<sup>9</sup>.

It is possible that colonisation of mucosal tissue can have an impact on the immune system and can affect the severity of viral infection. Colonisation can either increase or lower the severity of viral

RTI present in *S. pneumonia* and *H. influenza*<sup>10,11</sup>. Staphylococcal colonisation has been found to be beneficial in some studies<sup>12</sup>. Adenovirus infection in children present more commonly with fever than with respiratory symptoms and at a higher age group<sup>13-15</sup>. Enterovirus has been known to cause severe respiratory infection in children<sup>16</sup>. Human metapneumovirus was also detected in a good proportion of infants and children<sup>17</sup>. The persistence of infection following respiratory infection was identified by Jartti *et al.*<sup>18</sup>. Enterovirus persisted up to 2-3 weeks and rhinovirus up to 5-6 weeks following infection. However, colonization in asymptomatic children was not explored<sup>18</sup>.

Children are more vulnerable to viral respiratory infections compared to adults. Viral LRTI are more common in children less than 5 years old and the severity of infections is inversely proportional to the age<sup>19</sup>. Similar to Western literature, RSV and boca virus infection were common in children less than 2 years old, while influenza and parainfluenza viruses were common in children older than 2 years<sup>5</sup>. Co-infection rates are high in young children and are commonly associated with RSV, boca virus and parecho virus similar to western studies<sup>8</sup>.

Severity of infection was assessed in terms of duration of hospital stay, requirement of intensive care monitoring and mode of ventilation. Children under 2 years are vulnerable due to their naive immune system which correlates with the high risk of hospitalization<sup>19</sup>. Among the children monitored in intensive care, 2/3rds were less than 2 years of age and required high flow nasal cannula in our study. Exact data on the severity of infections caused by various viruses is lacking in the

literature. RSV infection is more severe in children less than 2 years old, similar to other studies<sup>20</sup>.

The data with regard to the seasonal distribution of viruses in the tropical countries is limited<sup>21</sup>. We observed seasonal variation in the incidence of viral infections in our study. RSV infection was seen from July to January and peak infection occurred during September and October. Western studies have documented a peak incidence around the same time (November). Infection with influenza virus was first isolated in September which extended into the month of March. The incidence peaked from January to March in the current study. Similarly, highest influenza infection incidence occurred during the coldest months in western countries (January to March)<sup>6</sup>. Larger multi-centric longitudinal follow-up studies to assess the seasonality may provide better understanding of the same in future.

### Conclusions

RSV, Influenza A and B viruses, parainfluenza virus and bocavirus were the common viruses isolated from hospitalized children with LRTIs. RSV infection peaked during September and October whilst influenza virus infection peaked from January to March.

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