

## Frequency of Respiratory Syncytial Virus Among Hospitalized Children with Acute Lower Respiratory Tract Infections

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### ABSTRACT

**Objective:** To determine the frequency of respiratory syncytial virus (RSV) among hospitalized children with acute lower respiratory tract infections (ALRI) and associated risk factors.

**Study Design:** Comparative cross-sectional study.

**Place and Duration of Study:** Pak Emirates Military Hospital, Rawalpindi Pakistan, from Jul 2019 to Aug 2020.

**Methodology:** After approval from the Ethical Review Board, 126 children were included in the study. Nasopharyngeal aspirates were collected from children. The direct immunofluorescence method was utilized to detect intracellular viral antigens of the respiratory syncytial virus. In addition, the presence of symptoms and history for identification of the presence or absence of risk factors was recorded.

**Results:** 57(45.2%) patients were found to be respiratory syncytial virus positive, and 69(54.8%) were respiratory syncytial virus negative. Significant differences were found in symptoms between RSV-positive and negative children ( $p=0.001$ ).

**Conclusion:** Respiratory syncytial virus was among the leading causes of children hospitalized with acute lower respiratory tract infections, with fever and recurrent wheezing as the most common symptoms.

**Keywords:** Acute lower respiratory tract infection, Respiratory syncytial virus, Wheezing.

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### INTRODUCTION

Respiratory tract infections are one of the leading causes of mortality and morbidity around the globe. The most common cause of acute lower respiratory tract infections ALRI is the viruses, which include influenza virus types A and B, adenovirus, parainfluenza virus and respiratory syncytial virus RSV.<sup>1</sup> In both developed and developing countries, the human respiratory syncytial virus is an important etiological factor in developing lower respiratory tract infections, especially in infants, the elderly and people with immunocompromised states.<sup>2</sup>

The respiratory syncytial virus belongs to the paramyxoviridae family and is an RNA virus. It has been documented that the most common causative agent of respiratory tract infections is in children below two years of age.<sup>3</sup> Around 0.5–2% of the cases required hospitalization due to the severity of the respiratory symptoms. Previous studies on children hospitalized with RSV-caused respiratory infection revealed that bronchiolitis and pneumonia were the most common complaints.<sup>4</sup> Preterm birth, low birth weight, history of maternal smoking, positive family history of allergy and no breastfeeding are important

risk factors for developing RSV infections.<sup>5</sup> In addition, underlying medical conditions such as immunosuppression, bronchopulmonary dysplasia, congenital heart disease and cystic fibrosis may predispose to or increase the severity of infection.<sup>6</sup> Uzma *et al.* determined viral aetiology using real-time PCR on the respiratory samples. RSV type A (44%), followed by RSV type B (23%), was the most prevalent among the causative agents.<sup>7</sup> The objective of our study was to determine the prevalence of Respiratory syncytial virus among hospitalized children with acute lower respiratory tract infection and associated risk factors. This study will help us identify the clinical features of respiratory syncytial virus pneumonia that will guide the judicious use of antibiotics.

### METHODOLOGY

This comparative cross-sectional study was carried out at the Department of Paediatrics Pak Emirates Military Hospital, Rawalpindi Pakistan. It is a tertiary care hospital receiving patients from all over the country. The study was completed over one year, from July 2019, to August 2020. This study was started after approval from the Ethical Review Committee Board (Letter number A/28/EC/199/2020). The sample size of 126 was calculated using OpenEpi sample size calculator version 3.0, taking the prevalence of RSV infection as 9%,<sup>8</sup> alpha was set at 0.05,

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power of test at 80% and confidence level of 95%. The non-probability consecutive sampling was employed.

**Inclusion Criteria:** All the children less than five years of age hospitalized with the diagnosis of acute lower respiratory tract infection with the fast breathing ( $\geq 60$  breaths/min at age  $< 2$  months,  $\geq 50$  breaths/min at age 2-12 months and  $\geq 40$  breaths/min at age 12 months-3years) were included in the study.

**Exclusion Criteria:** Children with other co-morbid conditions were excluded from the study.

The detailed history of other symptoms such as fever, rhinorrhoea, cough, wheezing, tachypnea, difficulty in breathing, risk factors like preterm weight  $\geq 2500$ g, duration of breastfeeding, gestational age  $\geq 37$  weeks, family history of allergy, neonatal complications and PICU admission along with presence or absence of symptoms such as fever, wheezing, cough, rhinorrhoea and tachypnoea were recorded. Informed consent was taken from the patients or guardians whose samples were collected and analysed. Nasopharyngeal aspirates were collected from children included in the study. The direct immunofluorescence method was utilized to detect intracellular viral antigens of RSV. The results were screened and confirmed by the virologist.

Statistical Package for Social Sciences (SPSS) version 23:00 was used for the data analysis. Mean and SD were calculated for numerical variables. Percentage and Frequency were calculated for categorical variables. Chi-square test was applied to find out the association. The  $p$ -value lower than or up to 0.05 was considered as significant.

### RESULTS

A total of 126 patients with a mean age of  $12.4 \pm 13.1$  months were included in the study. The age range was 1-59 months. There were 71(56.3%) were males, and 55(43.7%) females. 57(45.2%) patients were found to be RSV positive, and 69(54.8%) were RSV negative as shown in Figure.

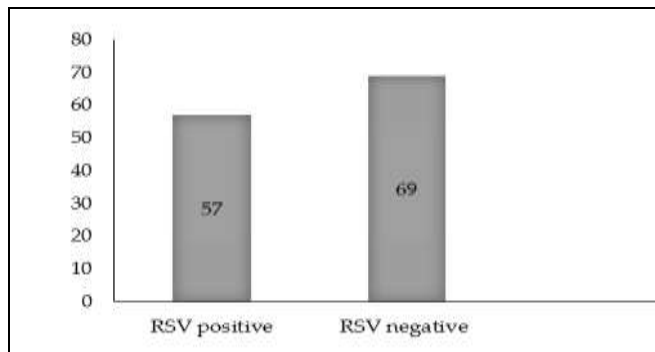


Figure: Frequency of Respiratory Syncytial Virus (n=126)

A comparison of various clinical signs and symptoms in both RSV-positive and negative groups was made. There was a statistically significant difference ( $p < 0.001$ ) among various clinical symptoms in children with acute lower respiratory tract infection with and without RSV, as shown in Table-I.

Table-I: Association of Signs and Symptoms with Respiratory Syncytial Virus Infection (n=126)

Signs & Symptoms		Respiratory Syncytial Virus positive (n=57)	Respiratory Syncytial Virus negative (n=69)	p-value
		Fever	yes 46(80.7%)	
	no 11(19.3%)	48(69.5%)		
Cough	yes	45(78.9%)	16(23.2%)	0.001
	no	12(21.1%)	53(76.8%)	
Rhinorrhoea	yes	36(63.1%)	25(36.3%)	0.002
	no	21(26.9%)	44(63.7%)	
Tachypnoea	yes	43(75.4%)	17(24.7%)	0.001
	no	14(24.6%)	52(75.3%)	
Wheezing	yes	38(66.6%)	23(33.4%)	0.001
	no	19(33.4%)	46(66.6%)	

Association of various risk factors with the presence or absence of RSV infection revealed that children who were born preterm with low birth weight, breastfed for less than three months with a history of admission in PICU and excessive antibiotic use were at an increased risk of developing RSV infection. However, neonatal complications and a family history of allergy or asthma were not among the significant risk factors, as shown in Table-II.

Table-II: Association of Various Risk Factors with Respiratory Syncytial Virus Infection (n=126)

Risk Factors		Respiratory Syncytial Virus positive (n=57)	Respiratory Syncytial Virus negative (n=69)	p-value
		Low Birth weight (<2500g)	Yes 37 (64.9%)	
	No 20 (35.1%)	43 (62.3%)		
Breast feeding for <3 months	Yes	41 (71.9%)	28 (40.6%)	0.001
	No	16 (28.1%)	41 (59.4%)	
Gestational age <37 weeks	Yes	37 (64.9%)	16 (23.2%)	0.001
	No	20 (35.1%)	53 (76.8%)	
Family history of allergies	Yes	23 (40.3%)	28 (40.6%)	0.56
	No	34 (56.2%)	41 (59.4%)	
Paediatric Intensive Care Unit admission	Yes	25 (43.8%)	21 (30.4%)	0.08
	No	32 (56.2%)	48 (69.6%)	
Neonatal complications	Yes	25 (43.8%)	30 (43.5%)	0.55
	No	32 (56.2%)	39 (56.5%)	
Antibiotic use	Yes	43 (75.4%)	13 (18.8%)	0.001
	No	14 (24.6%)	56 (81.2%)	

## DISCUSSION

Around 300,000 deaths each year globally in children below five years of age are due to influenza and respiratory syncytial virus combined.<sup>9</sup> Therefore, timely and accurate diagnosis of these viral pathogens is of paramount importance in initiating appropriate treatment, thus saving many precious lives without unnecessary antibiotics. Viral culture and immunofluorescence assay (direct and indirect) are the conventional diagnostic methods. With the advancements in technology, the diagnosis of the disease process has been revolutionized. Nucleic acid amplification tests are emerging trends in diagnosing viral disease.<sup>9</sup>

The frequency of RSV in our study was 45.2%, comparable to many previous studies. A study in a tertiary care centre in Gilgit revealed RSV genotype in 75 out of 105 children (71.4%).<sup>10</sup> Ali *et al.* revealed that the prevalence of RSV infection was 19%.<sup>11</sup> Halaji *et al.* study on the Iranian population revealed that RSV was the most common causative virus in acute lower respiratory tract infections with a prevalence of 35.9%.<sup>12</sup>

Fever was the most common symptom present (80.7%) in children infected with RSV infection observed in our study, followed by cough (78.9%) and tachypnoea (75%). Rhinorrhoea was present in 63.1% of RSV-positive cases and wheezing in 66.6% of cases. A statistically significant difference was observed in symptoms of positive and negative RSV children with acute lower respiratory tract infections. Farshad *et al.* also reported that children with viral aetiology in acute lower respiratory tract infections were likelier to have a fever and recurrent wheezing.<sup>13</sup> In another study by Yan *et al.* however, the children with RSV infection showed more frequent episodes of wheezing (52%) compared to RSV-negative children (33.52%), with other clinical characteristics showing no statistically significant differences.<sup>14</sup>

Our study revealed that children who were born at a gestational age of fewer than 37 weeks, had low birth weight, exclusively breastfed for less than three months, had a history of prolonged antibiotic use, and PICU admission was at more risk for developing respiratory syncytial virus infections. However, a family history of asthma, allergy and neonatal complications did not play a significant role as risk factors for developing such infections. Hemalatha *et al.* showed contradictory results with children who were well nourished and had normal weight at birth showing more RSV positives.<sup>15</sup> Gupta *et al.* compared children with acute lower respiratory tract infection without

RSV to children with RSV-positive infection and revealed that the latter was less likely to have fever (85% vs 59%) and rhinorrhoea (80% vs 53%).<sup>16</sup> Yoon *et al.* in Korea conducted a study and revealed that the distribution of RSV was not different between low birth weight and normal birth weight children.<sup>17</sup> There is a higher prevalence of morbidity related to RSV infections in preterm infants.<sup>18</sup> Our study reveals that breastfed children for less than three months showed more chances of having RSV infection. Kini *et al.* and Vereen *et al.* revealed similar results, showing a protective influence of breast milk against RSV infection.<sup>19</sup>

At birth, all the babies have passively acquired the antibodies against RSV infection from their mothers.<sup>20</sup> Antibody levels are generally like the maternal levels but start decreasing gradually over the first six months of life. Nevertheless, problems and complications related to RSV infection are massive, and its morbidity and mortality rate is increasing daily. Thus, there is a dire need to increase our knowledge and understanding of the immunopathological background of RSV infection so that further improvements in the treatment modalities and vaccinations can be made.

## CONCLUSION

The respiratory syncytial virus is among the leading cause of children hospitalized with acute lower respiratory tract infections. Fever and recurrent wheezing were the most common symptoms observed with preterm low birth weight children breastfed for less than three months, having a history of admission in PICU and antibiotic use were at greatest risk of acquiring RSV infection.

**Conflict of Interest:** None.

### Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MS & QUM: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

QZK & SM: Conception, Study design, drafting the manuscript, approval of the final version to be published.

MA & JB: Drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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