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Original Research Article

Exploring pneumonia in less than two-year-olds: comparing respiratory syncytial virus and pneumonia due to other pathogens

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ABSTRACT

Background: The purpose of this study is to compare the clinical characteristics and outcomes of RSV and non-RSV pneumonia in children less than two years weighing less than 10kg admitted to the Pediatric Intensive Care Unit (PICU) and also study the differences in efficacy of bubble Continuous Positive Airway Pressure (bCPAP) between the two groups.
Methods: Children with severe pneumonia (World Health Organization criteria) and moderate to severe distress (PRESS- Pneumonia Risk Emergency Score Severity criteria) were participants of this cross-sectional comparative study. They were tested for RSV and grouped. Both groups received bCPAP. Data collection included demographic details, clinical findings and outcomes.
Results: 70 children had pneumonia 18 had RSV pneumonia and 52 were non-RSV pneumonia cases. Suprasternal ($p<0.05$) and xiphoid retractions ($p=0.034$) were more prevalent in RSV pneumonia and it also required longer duration of bCPAP (50 hours versus 28 hours; $p=0.023$). bCPAP showed improvement in most of the cases in both groups (RSV-88.9%, non-RSV-80.8%). RSV cases demonstrated better improvement in saturation and respiratory rate within the first four hours of administration of bCPAP. Mortality was comparable between the two groups (RSV-5.6%, non-RSV-11.5%, $p=0.14$).
Conclusions: RSV pneumonia is associated with more severe respiratory distress and longer bCPAP support but final clinical outcomes of bCPAP were similar in both groups. This is the first study to report a higher prevalence of suprasternal and xiphoid retractions in RSV pneumonia and a significantly better initial response to bCPAP.

Keywords: Continuous positive airway pressure, Intensive care unit, Pneumonia, Respiratory syncytial virus

INTRODUCTION

The leading infectious cause of death worldwide among children younger than five years of age is pneumonia. It attributes to almost one-third of all under five deaths with infectious etiology.[1] The mortality burden due to pneumonia is mainly borne by low and middle-income countries in Africa and South Asia. One of the United Nations Millennium Development Goals is to reduce global mortality in children younger than five years. Pneumonia stands as a major hindrance to achieving this.[2] During the first few months of life the pulmonary anatomy, depleting maternally acquired antibody levels and the lack of mature immune system make children more vulnerable to pneumonia.[3]

The most frequently observed viral pathogen causing lower respiratory tract infections (LRTI) in children less than two years of age is respiratory syncytial virus (RSV).[1] Comorbidities like congenital heart disease and chronic neurological conditions complicate the management of pneumonia. Children suffering from RSV pneumonia often have more severe respiratory distress and require more advanced management.[4] Even babies

who were previously healthy and lacked any comorbidities were admitted to the hospital with severe pneumonia.[5]

The severity of pneumonia is possibly determined by genetic susceptibility of the host, viral genotype and viral load.[6] Some studies have identified links between severe RSV disease and development of asthma and wheezing later on.[7-10] RSV is responsible for 15.6% of all admissions to the intensive care unit. This is indicative of the prominence of RSV as a viral pathogen in severe acute lower respiratory tract infections in children.[11] There is no evidence- based treatment for RSV, only supportive care. Even though there is a market-approved long-acting monoclonal antibody that can be used as a vaccine, its high-cost limits widespread use.[12]

The literature on RSV in children from India reveals a significant gap in comprehensive research, detailing the epidemiology, risk factors and clinical outcomes of RSV infections in this population. There is minimal evidence of the efficacy of bubble continuous positive airway pressure (bCPAP) in pneumonia caused by RSV. The degree of improvement in oxygen levels seen with bCPAP in patients with RSV pneumonia may differ from non-RSV cases and needs to be probed further.

Additionally, it remains unclear whether the augmentation of oxygen levels achieved through bCPAP leads to varied final clinical outcomes in those with RSV pneumonia. It is important to address these gaps for developing effective prevention and management strategies designed according to the needs of the Indian population.

This study aimed to investigate the characteristics, clinical course and outcomes of pneumonia in young children admitted to our PICU, comparing these parameters between patients with pneumonia due to RSV and non-RSV pneumonia cases, as well as assessing the efficacy of bCPAP in both groups.

METHODS

Study type

This was a cross-sectional comparative study.

Study place

The study was conducted in the PICU of the Department of Pediatrics, Mysore Medical College and Research Institute.

Study duration

The study duration was from August 2023 to June 2024.

This study took place in an eight bedded ICU and was approved by the Institutional Ethics Committee. The procedures used in this study adhere to the tenets of the declaration of Helsinki. Informed written consent was obtained from parents or guardians of all children after the purpose of study was clearly explained to them and they were given enough opportunity to clarify any doubts they had regarding the study.

Inclusion criteria

Eligible children were those, who weighed less than 10 kg, were not immunized against RSV and met the criteria for pneumonia as defined by the World Health Organization (WHO) and who were admitted to the PICU with moderate to severe respiratory distress measured by the PRESS (Pneumonia Risk Emergency Score Severity) criteria.[13,14]

Exclusion criteria

Respiratory distress due to other causes and children who had congenital malformations of the lungs were excluded.

Treatment protocol

bCPAP in addition to standard WHO recommended treatments were given to all children with severe pneumonia who had moderate to severe respiratory distress. Strict aseptic precautions were observed throughout the study and continuous monitoring of vitals such as heart rate, respiratory rate and oxygen saturation was done. The children were transitioned from bCPAP to free flow oxygen delivered by nasal prongs once their respiratory distress improved and they were ultimately weaned off all respiratory support once the PRESS score reached 0. In cases where bCPAP failed, patients were intubated and mechanically ventilated without any delay.

Data collection

Data was collected using a predesigned proforma which collected baseline demographic details, presenting symptoms and their duration, antenatal, natal and postnatal histories, dietary and immunization records and vital signs. Patient records were also reviewed for data on clinical improvement and outcomes. Nasopharyngeal swabs were obtained from all patients with pneumonia and subjected to Reverse Transcription Polymerase Chain Reaction (RT-PCR) for the detection of RSV. Blood cultures were collected with other routine lab investigations.

Statistical analysis

Data was entered in Microsoft Excel and analysis was conducted with SPSS Version 26. Numerical data was presented as mean values with standard deviation. Intergroup differences were assessed using Mann-Whitney and Wilcoxon rank-sum tests. Categorical variables were displayed as counts and percentages and have been analyzed using Pearson's chi-square test and

Fisher exact tests (when the expected count of 20% of cells was less than 5). A p value which was less than 0.05 was considered statistically significant for all analyses.

RESULTS

The study included 70 children admitted to the PICU with pneumonia, of whom 18 had pneumonia attributable to RSV while 52 had pneumonia due to other etiologies. Age and sex distribution have been reported in table 1. They were not statistically significant. Additionally, two bacterial co-infections were noted in the RSV group, Klebsiella and Methicillin-resistant *Staphylococcus aureus*. The co-infections were diagnosed through blood culture reports.

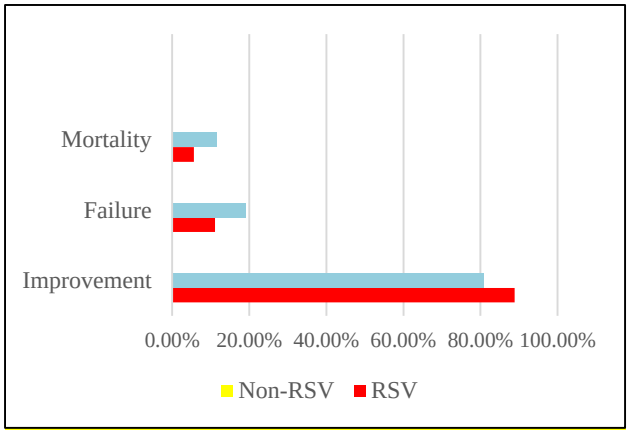

Figure 1: Comparison between RSV and non RSV cases on the basis of mortality, failure and improvement on bCPAP.

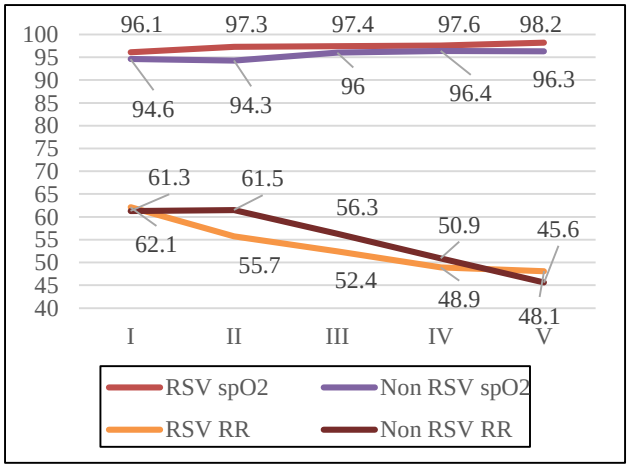

Figure 2: Comparison of changes in oxygen saturation among the study groups.

Presenting complaints and clinical examination findings

The analysis of presenting complaints and examination findings revealed differences between the two groups. The only statistically significant difference between the groups was related to suprasternal ($p<0.00002$) and xiphoid retractions ($p=0.03$), both of which were more prevalent in the RSV group. These findings suggest that RSV pneumonia may manifest with more severe respiratory distress as evidenced by the higher frequency of these specific type of retractions.

Despite this, both groups had similar PRESS scores because the study was conducted in an intensive care unit where one of the criteria for admission is respiratory distress, according to the score. The presenting complaints in both groups and examination findings are depicted in Table 2.

CPAP and respiratory support outcomes

CPAP was administered to both groups. It yielded improvement in 16 out of 18 RSV cases (88.9%) and 43 out of the 52 non-RSV cases (80.8%) with no statistically significant difference ($p=0.44$). However, children with RSV required significantly longer duration of bCPAP support with a mean duration of 50 hours (SD 36 hours) compared to 28 hours (SD 18 hours) in the non-RSV group ($p=0.02$).

This suggests that RSV pneumonia may be associated with significantly longer respiratory distress necessitating extended bCPAP support. Despite this there was no statistically significant difference in the requirement for mechanical ventilation between the two groups (RSV 11.1% versus non-RSV 19.2%, $p=0.72$). Mortality rates were 5.6% in the RSV group and 11.5% in the non-RSV group ($p=0.14$). This is illustrated in figure 1.

Sepsis was the significant risk factor for mortality in both groups. ($p=0.03$). This underscores the importance of early identification of sepsis in pneumonia and its prompt management. Post bCPAP initiation, both groups showed improvement in oxygen saturation, heart rate and respiratory rate.

Figure 2 demonstrates the initial faster improvement in SpO2 and respiratory rate. These vitals were measured at 4 hours intervals. Statistically significant difference was not found in the final outcome and overall extent of improvement. Overall, the findings suggest that while both RSV and non-RSV pneumonias present with respiratory distress, RSV-associated pneumonia tends to require longer respiratory support but shows quicker initial improvement.

Table 1: Demographic details of both groups.

Parameter	RSV pneumonia	Non-RSV pneumonia
Age (in months), mean (SD*)	6.4 (4.2)	8.3 (5.4)
Male: Female ratio	11:7	8:5

Table 2: Presenting complaints and examination findings.

Presenting complaint	RSV (n=18)	Non-RSV (n=52)	P value
Wheezing	2 (11.1%)	4 (7.7%)	0.643
Accessory muscle use	8 (44.4%)	19 (36.5%)	0.553
Feeding difficulties	0	6 (11.5%)	0.327
Nasal flaring	4 (22.2%)	22 (42.3%)	0.129
Hurried breathing	9 (50%)	28 (53.8%)	0.778
Grunting	2 (11.1%)	1 (1.9%)	0.16
Stridor	2 (11.1%)	0	0.063
Lethargy	1 (5.6%)	3 (5.8%)	>0.99
Convulsions	1 (5.6%)	7 (13.5%)	0.670
Intercostal retractions	10 (55.6%)	16 (30.8%)	0.061
Suprasternal retractions	12 (66.7%)	6 (11.5%)	0.00002
Xiphoid retractions	11(61.1%)	17 (32.7%)	0.034
Cyanosis	1 (5.6%)	1 (1.9%)	0.451
Hypoxia (based on spO2)	4 (22.2%)	21 (40.4%)	0.166
Tachypnea	11 (61.1%)	34 (65.4%)	0.744
Moderate to severe pneumonia at presentation (based on PRESS scores)	9 (50%)	29 (55.8%)	0.179

DISCUSSION

This study examined children with pneumonia admitted to the PICU, distinguishing between those with pneumonia owing to RSV and those with non-RSV pneumonia. On average, children in the RSV group were younger compared to the non-RSV group, had more severe respiratory distress with significant higher occurrence of suprasternal and xiphoid retractions. Children with RSV pneumonia required longer bCPAP support with a mean duration of 50 hours compared to 28 hours in the non-RSV group (p=0.02).

RSV cases demonstrated better improvement in terms of oxygen saturation and respiratory rate within the first four hours of bCPAP initiation. Despite this efficacy of bCPAP, in terms of final positive outcome, findings in both groups were congruous. There was no significant difference in mortality rates between the groups. Sepsis was the prominent risk factor for mortality in our study.

RSV was identified as one of the most frequently detected viruses in children consistent with findings from other studies originating from low-income countries.[15] Over the past decade pneumonia etiology studies in the USA, South Africa and GABRIEL multisite study have highlighted RSV as a key pathogen.[16-19] In our study RSV was responsible for 18 out of the 70 pneumonia cases admitted to the PICU accounting for 26% pneumonia cases, making it one of the few pathogens with high etiological attribution. This finding allies with results from the PERCH multi country case-control study.[20]

Throughout the analysis more boys than girls were admitted with pneumonia, this could be indicative of boys being more severely affected by airway infections. A 2015 study from China reported a boy to girl ratio of 2.3:1 for children admitted to the intensive care units with RSV infection.[21] Additionally studies from Denmark and Sweden have shown that boys were more likely to develop asthma-like post infection sequelae as compared to girls.[22-24] In our study, the boy to girl ratio was 1.6:1. While the reasons for this disparity between the two sexes remain ambiguous, anatomical, physiological and inflammatory factors could play a role in this difference.

In comparison to their non-RSV counterparts, RSV infected children had more severe respiratory distress, consistent with the study conducted in Malawi.[25] Seasonal variability in infection rates has been noted in several studies, but our study spanning over 10 months was not able to appreciate any seasonable variability. This is indicative of the need for further investigations into the patterns of RSV pneumonia in different months compared to other causes of pneumonia. In particular following the COVID-19 pandemic there have been changes observed in the seasonal distribution of several diseases. In conjunction to this, long-term research extending beyond one year is needed to elucidate the factors contributing to RSV pneumonia- host, environmental and pathogen specific.

Some studies suggest that co-infections may increase the severity of RSV with reports indicating longer hospital stays and a greater need for supplemental oxygen in cases.[26-28] However, other studies have not confirmed these results.[29,30] In our study there were only 2 cases of co-infection both requiring CPAP support for an average of 30 hours which is shorter than the 50 hours average for the RSV group.

Due to the small sample size these findings are not conclusive. The frequency of co-infections with other pathogens in RSV lower respiratory tract infections is considerably different across studies, ranging from 19% to 38%.[27,30] The co-infection rate in our study was 2 out of 18 cases (11.1%). This variation may be due to differences in study populations, seasonal variations and the range of pathogens being checked.

The limitations of this study include the small sample size which may affect the generalizability of the findings and the relatively short observation period limiting the ability to assess long-term complications and seasonal

variations. Furthermore, the lower number of co-infections limits conclusions on the impact of co-infecting pathogens. More studies with larger sample sizes, extended observation periods and consideration of seasonal and geographical factors are warranted to strengthen the findings and explore the broader implications of RSV pneumonia.

In spite of these limitations, to our knowledge no prior studies have specifically reported a significant higher incidence of suprasternal and xiphoid retractions in RSV pneumonia nor have they demonstrated initial faster improvement in respiratory rate and saturation with CPAP in RSV pneumonia. These observations suggest unique clinical and therapeutic characteristics in the RSV related respiratory distress. This observation along with the high prevalence of RSV as an etiological agent among young children underscores the clinical relevance of our study.

CONCLUSION

This study highlights the distinct clinical characteristics and prolonged CPAP support required for children suffering from RSV pneumonia in comparison to pneumonia due to other infectious agents. Our study sheds light on the novel clinical differences in the presentation and management of RSV, specifically the increased frequency of suprasternal and xiphoid retractions and the initial faster respiratory improvement with CPAP suggests that RSV has features not observed in other pneumonia. The shortcomings of this study suggest the need for further research spanning over a longer period of time, nevertheless, our findings emphasize the importance of early CPAP intervention in the management of respiratory distress in pediatric RSV pneumonia contributing to valuable insights into its clinical management.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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