Short Research Article

CLINICAL PROFILE, SEVERITY AND INTENSIVE CARE NEEDS OF CHILDREN ADMITTED WITH RESPIRATORY SYNCYTIAL VIRAL INFECTIONS IN PICU: POST COVID TREND

Abstract

Aims: Epidemiology of RSV infection have shown changing trends in the post covid times. Changing pattern in its seasonality have been reported following relaxation of lockdown measures after SARS COVID. Literature describing severity and intensive care needs of pediatric RSV infections are scarce. Our study aims to describe the clinical profile, severity and intensive care needs of pediatric RSV infections requiring PICU admission in post COVID period.
Study design: Retrospective Study
Place and Duration of Study: Paediatric Intensive Care Unit of a tertiary care teaching hospital in south India. Study period was from May 2022 and October 2022, over 6 months.
Methodology: All children with clinical diagnosis of viral pneumonia or bronchiolitis were screened. RSV positive cases were taken for the study. The data including age, gender, symptoms, duration of each symptom, respiratory support, duration of oxygen requirement, number of days of PICU stay and outcome of all the children was entered into a structured proforma and data was analysed. The primary objective was to see clinical profile, severity and intensive care needs of RSV affected children aged 1month-12 years admitted in PICU with RSV infections. The secondary objective was to see mortality and length of PICU stay among them.
Results: Out of 36 children with clinical diagnosis of viral pneumonia or acute bronchiolitis, 21 tested positive for respiratory virus, out of which 11 were RSV positive. There was a slight male preponderance. All children were aged less than 18 months. All had respiratory failure and required oxygen support (n=11, 100%). Intensive care needs were high flow nasal cannula requirement in 9 patients (n=9,81%), oxygen via nasal prongs (n=3,27%) and mechanical ventilation (n=1, 9%). Median (IQR) duration of oxygen requirements was 6 (5,9) days. Median (IQR) duration of PICU stay was 6(5,8) days. All 11 children survived.
Conclusion: In the Post Covid era, RSV was the most identified viral etiology behind viral pneumonia or bronchiolitis in our PICU. All children had respiratory failure, which improved with High Flow Nasal Cannula in majority of the children.

Keywords: Pediatric Respiratory Syncytial Virus infection, High Flow nasal cannula, Bronchiolitis, Viral Pneumonia

1. INTRODUCTION

Globally, respiratory syncytial virus (RSV) is the leading cause of bronchiolitis and pneumonia in children less than 2 years, and the association between severe RSV

disease and later recurrent wheeze and asthma is well established (1,2). Clinical manifestations may vary from mild disease to a severe form of infection with requirement of hospitalization and eventually pediatric intensive care unit (PICU) admission (3,4). Complications necessitating admission to intensive care units in children with RSV are typically respiratory failure due to severe bronchiolitis in young infants (aged <3 months) and older children with comorbidities (5). Epidemiology of RSV infection have shown changing trends in the post covid times. There has been a changing pattern in its seasonality following relaxation of lockdown measures after SARS Covid. The number of paediatric RSV hospital admissions and children who had mechanical ventilation was shown to have doubled in the interseasonal RSV epidemic in 2021–22 compared with the pre-COVID-19 seasons. Higher morbidity and mortality for viral lower respiratory infections have been reported in association with respiratory syncytial virus (RSV) globally (6). A few studies were done globally which documented seasonality shift in the occurrence of RSV infection and also increasing PICU admissions of RSV pneumonia or bronchiolitis following the relaxation of COVID public health measures which they explained as a result of absence of natural immunity to the virus in a cohort of young children during the lockdown period (7,8). However, limited data is available across our country regarding the seasonality changes and intensive care needs in RSV infections in the post COVID times. Only one study was found in Indian literature regarding the intensive care needs of pediatric RSV infections and the impact on RSV infections following SARS COVID period (9).There were no studies done in Southern India regarding the same. Therefore, studying the severity of RSV infection along with its seasonality patterns in the post COVID era is particularly crucial for planning appropriate treatment strategies and preventive measures. Hence, our study aims to describe the clinical profile, severity, intensive care needs and outcome of pediatric RSV infections requiring PICU admission in the post COVID times.

2. MATERIAL AND METHODS

A retrospective study was done over 6 months in Pediatric Intensive Care Unit between the months of May 2022 and October 2022 after the COVID public health precaution measures were relaxed. An overall surge in respiratory infections were observed in hospitals around that time. Case records of all children aged 1 month to 12 years of age admitted in the PICU with viral pneumonia or bronchiolitis between the months of May to October were screened, out of which RSV positive cases were enrolled for the study. There was no exclusion criteria. The primary objective was to see clinical profile, severity and intensive care needs of RSV affected children aged 1month-12 years admitted in PICU with RSV infections. The secondary objective was to see mortality and length of PICU stay among them. Clinical profile of these children which included signs and symptoms of fever, cough, breathlessness, crepitations, wheeze and hypoxemia were collected from hospital records. Lab parameters like complete Blood Counts(Hemoglobin, Total count, Differential count, and Platelet counts), C Reactive Protein, ESR, Liver transaminases and radiology investigations like Chest X Ray, CT and MRI were also recorded. To see disease severity, data of organ dysfunctions like respiratory failure, shock, encephalopathy, myocarditis or cardiac dysfunction or any other

organ dysfunction were collected. Intensive care needs like respiratory support requirements
(HFNC, Continuous Positive Airway Pressure, Non-Invasive Ventilation and Mechanical Ventilation), requirement of inotropic support and other organ support and total duration of oxygen requirement were also entered into structured proforma. Other outcome measures like duration of PICU stay and mortality were also recorded. We also looked for number of previous RSV infections in our PICU 6 months prior to study period.

In our Centre, Viral pneumonia or bronchiolitis is treated as per hospital protocol. All children with suspected viral etiology are screened for viral pathogens by quantitative nasopharyngeal swab PCR. Respiratory specimens of children with suspected viral pneumonia or bronchiolitis are routinely sent for molecular PCR based viral diagnostic studies. Specimen sites included nasopharyngeal swab and throat swab. We do Respiratory Panel 1(RIPER) test, which is a nested PCR analysis that detects 14 different viral targets including Adenovirus, H1N1, Human Metapneumovirus A/B, Human Rhinovirus-HRV, Enterovirus, influenza virus A, influenza virus B; Parainfluenza 1, 2, 3, 4; Respiratory Syncytial Virus-RSV and Mycoplasma pneumonia.

Statistical Analysis: The data collected was entered into Microsoft Excel. Analysis was carried out using SPSS 21 version. Quantitative variables were described by their position (median) and dispersion (standard deviation, extremes) parameters. The study was approved by the hospital ethics clearance committee.

3. RESULTS AND DISCUSSION

36 children with clinical diagnosis of viral pneumonia or acute bronchiolitis were admitted in PICU during the study period. 21 tested positive for respiratory virus, out of which 11 were RSV positive, of which 2 were diagnosed as acute bronchiolitis and 9 as viral pneumonias. All children were aged less than 18 months. Eight children were less than 12 months of age (72%). Six were boys (n= 6, 54.5 %) and 5 were girls (n=5, 44.4%). Two of them were Multitrigger wheezers, one had congenital laryngeal stridor and one had prematurity. Shortness of breath [11(100%)] was the most common symptom followed by cough [10(90.9%)] and fever [8(72.7%)]. Median (IQR) duration of symptoms at admission was 4(3,7) days. All children presented in respiratory failure (n=11,100%). All admitted children had wheeze (n= 11,100%) and Crepitations were present in 10(90.9%). CRP was positive in majority of the children (n=7,63.6%). Three had leucocytosis (n=3,27%), 5 had lymphocytic predominance (n=5,45.4%). Liver transaminases were elevated in one child. Seven children had associated anaemia (n=7,63%), which was microcytic hypochromic anaemia. Co- infection was present in 2 children (11%) of which one was bocavirus and another was influenza B virus. All of them had bilateral interstitial infiltrates (n = 11,100%) on chest radiography. Six had associated hyperinflation and features of collapse (n=6,60% (Table1).

All children had respiratory failure, and 1 child had encephalopathy. No other organ dysfunctions were noticed. Nine required high flow nasal cannula support (n=9,81%) and three required oxygen via nasal prongs (n=3,27%). One child required mechanical ventilation (n=1,9%). Only one child had ARDS. No children

required inotropic support or other organ support. Median (IQR) duration of oxygen requirements was 6(5,9) days. Median (IQR) duration of PICU stay was 6(5,8) days. All 11 children survived (Table 2). One child in whom mechanical ventilation was required was later found to have CVID (Common variable immunodeficiency).

In our study majority of RSV infections were seen from the month of May to October 2022, predominantly during summer and rainy season and we had zero cases of RSV in 6 months prior to the study period.

Table 1. Clinical Profile and Severity of respiratory syncytial virus

CLINICAL PROFILE & SEVERITY	%(n)
Age in months (Mean± SD)	15 ± 3
CLINICAL FEATURES ▪ Fever ▪ Cough ▪ Breathlessness	 72%(n=8) 90%(n=9) 100%(n=11)
LABORATORY AND RADIOLOGICAL FINDINGS ▪ Anemia ▪ Leukocytosis ▪ Lymphocytic predominance ▪ CRP Positivity ▪ Elevated transaminases ▪ Co- Infection ▪ Bilateral infiltrates and hyperinflation	 63%(n=7) 27%(n=3) 45%(n=5) 64%(n=7) 9%(n=1) 18%(n=2) 100%(n=11)
SEVERITY OF ILLNESS ▪ Respiratory failure ▪ Oxygen requirement ▪ Encephalopathy ▪ Other organ dysfunction	 100%(n=11) 100%(n=11) 9%(n=1) 0%(n=0)

Table 2: Intensive care needs and outcomes

INTENSIVE CARE NEEDS	**%(n)**
Nasal prongs	9% (1)

HFNC	82% (9)
Mechanical Ventilation	9% (1)
OUTCOME MEASURES	
Duration of PICU stay in days [Median (IQR)]	6(5,8)
Mortality	0%(0)

DISCUSSION

Respiratory Syncytial Virus is an RNA virus that causes respiratory tract infections in children.
It is common in children aged less than 2 years. Symptoms include cough, coryza, and wheezing. Treatment of an RSV infection is supportive. Children younger than 60 days and those with severe symptoms may require hospitalization (10). All children in our study were aged between 1- 18 months. This was in line with other studies which documented the majority of severe RSV infection below 2 years of age or younger (10,11). Only Indian study on RSV infections in PICU by **Mandal B et al,** done in 36 pediatric RSV infections in PICU also reported higher proportion of infants (88.9%) similar to our study (9). Shortness of breath was the most common symptom followed by cough and fever and there was a high proportion of anemia in our study. This was similar to a study by Singh C et al, where the majority of the children with RSV presented with cough and breathlessness and anemia was seen in 65% of children. Majority of the children in their study also had lymphocytic predominance and raised CRP which was comparable with our laboratory data (12). Co-infection was present in 2 children (11%) of which one was detected with bocavirus and another with influenza virus. In a study by Ghazaly et al, 45% of children with RSV had coinfection (13). All children in our study had respiratory failure and we didn't find any other organ dysfunction except encephalopathy. Study by Mandal B et al and a study done in Southern China by Q Zhang et al also reported respiratory failure in all the children admitted with RSV pneumonia with no other apparent organ dysfunction(9,11).

There are scarce data regarding pediatric RSV infections and the impact on RSV infections following SARS COVID period. Therefore, our study aimed to describe intensive care needs of pediatric RSV infections requiring PICU admission in the post COVID times. Mandal et al's study reported maximum respiratory support requirements of HFNC in 38.9%, non-invasive ventilation in 27.8% and mechanical ventilation in 25%(9). Zhang et al on their study on 171 children with RSV requiring PICU admission, reported respiratory failure in all the children with 22% of them requiring mechanical ventilation(11). We had lesser number of mechanical ventilation and most of the children responded to HFNC (82%) and zero mortality. Our data showed similar patient profile and PICU duration of stay consistent with previous studies which showed PICU length of stay less than a week in pediatric RSV infections (11). Studies have reported higher incidence of acute respiratory distress syndrome (ARDS) in RSV, whereas only one child had ARDS in

our study who was later found to have immunodeficiency (9,13). Our study population didn't require organ support other than respiratory support which is comparable with other similar studies where majority of the children recovered with respiratory support(9,11). In our study Respiratory Syncytial Viral Pneumonia showed favourable outcome with appropriate respiratory support irrespective of the severity at presentation. Only one child required prolonged mechanical ventilation, later diagnosed with CVID (Common variable immunodeficiency).

In India, many studies report rise in positive cases of RSV during rainy and early winter season (July to November) and smaller spikes in infection from December to February (12).We had all cases between May to October which is different from the usual trend. Our 6 months prior to current study data shows zero RSV cases. **M Bardsley et al**. in their retrospective study (2020-2021) on Epidemiology of respiratory syncytial virus in children younger than 5 years in England during the COVID-19 pandemic, interpreted that the extraordinary absence of RSV during winter 2020-21 resulted in a cohort of young children without natural immunity to RSV, which raised the potential for increased RSV incidence when SARS-CoV-2 transmission restriction measures were relaxed (7). **Domínguez et al** (2022) suggested an upward trend of RSV cases, observed six to nine months after the usual time of the winter RSV epidemic, coinciding with the relaxation of the preventive public health measures of COVID (8). Chuang Chuan et al, in their study showed significant resurgence of Respiratory syncytial viral infection in the post COVID era with a seasonal delay compared to the previous studies which is mostly due to viral interference (14). More cases in May to October in our study also shows a slight shift in the seasonality of RSV infections in contrast to usual prevalence of RSV infection in winter months in India before COVID times.

4. CONCLUSION

RSV infection is considered as a major concern among viral infections requiring PICU admission. All the children were less than 18 months of age. All patients had respiratory failure with majority of cases requiring HFNC and other advanced respiratory support indicating the severity of illness. Outcome is favourable with good supportive care. There has also been a slight shift in the seasonality of RSV infections following relaxation of public health measures after SARS COVID which is in line with other studies in literature.

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CONSENT

As per international standard, parental written consent has been collected and preserved by the authors.

ETHICAL APPROVAL
The study was reviewed and approved by Ethics Committee of our hospital.

REFERENCES

1. Binns E, Tuckerman J, Licciardi PV, Wurzel D. Respiratory syncytial virus, recurrent wheeze and asthma: A narrative review of pathophysiology, prevention and future directions. J Paediatr Child Health. 2022 Oct;58(10):1741-1746.
2. Ohuma EO, Okiro EA, Ochola R, Sande CJ, Cane PA, Medley GF et al. The natural history of respiratory syncytial virus in a birth cohort: the influence of age and previous infection on reinfection and disease. Am J Epidemiol. 2012 ;176(9):794-802.
3. Azzari C, Baraldi E, Bonanni P, Bozzola E, Coscia A, Lanari M et al. Epidemiology and prevention of respiratory syncytial virus infections in children in Italy. Ital J Pediatr. 2021 Oct 2;47(1):198.
4. Bozzola E, Ciarlitto C, Guolo S, Brusco C, Cerone G, Antilici L et al. Respiratory Syncytial Virus Bronchiolitis in Infancy: The Acute Hospitalization Cost. Front Pediatr. 2021 Jan 18;8:594898.
5. Chaw PS, Hua L, Cunningham S, Campbell H, Mikolajczyk R, Nair H; RESCEU Investigators. Respiratory Syncytial Virus-Associated Acute Lower Respiratory Infections in Children With Bronchopulmonary Dysplasia: Systematic Review and Meta-Analysis. J Infect Dis. 2020 Oct 7;222(7):S620-S627
6. Nygaard U, Hartling UB, Nielsen J, Vestergaard LS, Dungu KHS, Nielsen JSA, et al. Hospital admissions and need for mechanical ventilation in children with respiratory syncytial virus before and during the COVID-19 pandemic: a Danish nationwide cohort study. Lancet Child Adolesc Health. 2023 Mar;7(3):171-179.
7. Bardsley M, Morbey RA, Hughes HE, Beck CR, Watson CH, Zhao H et al. Epidemiology of respiratory syncytial virus in children younger than 5 years in England during the COVID-19 pandemic, measured by laboratory, clinical, and syndromic surveillance: a retrospective observational study. Lancet Infect Dis. 2023;23(1):56-66
8. Reyes Domínguez AI, Pavlovic Nesic S, Urquía Martí L, Pérez González MDC, Reyes Suárez D, García-Muñoz Rodrigo F. Effects of public health measures during the SARS-CoV-2 pandemic on the winter respiratory syncytial virus epidemic: An interrupted time series analysis. Paediatr Perinat Epidemiol. 2022;36(3) :329-336
9. Mandal B, Roychowdhoury S, Barui P, Konar MC, Bhakta S, Nandi M et al. Outbreak of respiratory syncytial virus infection in Eastern India during COVID-

19 pandemic: An observational study from a single pediatric intensive care unit. J Pediatr Crit Care 2022;9:124-30

10. Dawson-Caswell M, Muncie HL Jr. Respiratory syncytial virus infection in children. Am Fam Physician 2011; 83(2):141-6
11. Zhang Q, Guo Z, Langley JM, Bai Z. Respiratory syncytial virus-associated intensive care unit admission in children in Southern China. BMC Res Notes. 2013 Nov 8;6:447.
12. Singh C, Angurana SK, Bora I, Jain N, Kaur K, Sarkar S. Clinico demographic profiling of the *Respiratory syncytial virus* (RSV) infected children admitted in tertiary care hospital in North India. J Family Med Prim C.2021;10(5):1975-1980.
13. Ghazaly M, Nadel S. Characteristics of children admitted to intensive care with acute bronchiolitis. Eur J Pediatr.2018;177(6):913-920.
14. Chuang YC, Lin KP, Wang LA, Yeh TK, Liu PY. The Impact of the COVID-19 Pandemic on Respiratory Syncytial Virus Infection: A Narrative Review. Infect Drug Resist. 2023 ;16:661-675.