



Respiratory syncytial virus dominance in pneumonia cases after removal of pandemic restrictions

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Abstract

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Aim: Respiratory syncytial virus is one of the most important causes of lower respiratory tract infections, with high mortality and morbidity in infants and children. It can cause airway inflammation, mucosal edema, and small airway collapse.

Materials and Methods: We evaluated the clinical and demographic characteristics of newborns aged 0-30 days who were hospitalized in Yüziüncü Yil University Neonatal Intensive Care Unit due to lower respiratory tract infections and whose respiratory syncytial virus test was positive between 15/December/2022 and 15/February/2023.

Results: Between the specified dates, 29 patients diagnosed with lower respiratory tract infections were admitted to our neonatal unit. Of the oral/nasopharyngeal swab samples sent from all of these patients, one was positive for SARS-CoV-2, one for adenovirus, one for influenza A/B, and 18 (62%) respiratory syncytial virus. The weeks of the birth of the patients who were found to be positive for respiratory syncytial virus A/B were 36.72 ± 1.48 . The number of days they spent in the hospital was 6.72 ± 1.6 , 2(11.1%) patients required intubation, and 7(38.8%) patients required noninvasive respiratory support. One patient presented with convulsions at home, and cough and fever symptoms appeared on the second day of hospitalization. All patients recovered with oxygen support, hydration, and supportive treatment and were discharged.

Conclusion: The most common cause in neonates was found to be a respiratory syncytial virus. Early diagnosis and treatment are important in patients with suspected lower tract viral infections. Unnecessary antibiotic use and the spread of the disease should be prevented by increasing access to viral tests.



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Introduction

Respiratory syncytial virus (RSV) was explored in 1956 and has since been admitted as one of the very usual reasons of early-life diseases. It produces annual epidemics of respiratory diseases in every age. RSV circulation initiates in the fall and culminates in the winter; however, the intensity and timing of RSV season in a definite society may differ yearly. Researchers are building up alternative vaccines, antiviral treatments, and monoclonal antibodies to lend assistance to defend young children and infants and pregnant and older adults from severe RSV infection [1-3]. Each year in the United States, almost 58,000-80,000 children under five years old are hospitalized for RSV infection [4]. RSV may be risky for many infants. Essentially overall, children catch RSV infection under two years old

[5]. Usually, RSV will have cold-like symptoms, but it can also induce severe illnesses like pneumonia and bronchiolitis [5,6]. Bronchodilators and corticosteroids have not shown a benefit for managing RSV bronchiolitis and, therefore, are not recommended [3].

In the last twenty years, progressively passive immunoprophylaxis has been performed for high-risk children utilizing palivizumab, a monoclonal antibody, but there is recently no licensed vaccine to avoid RSV contamination. Premature infants, especially babies younger than six months, cases under two years old with chronic lung disease or congenital heart disease, children with slight immune response, and cases with a neuromuscular disorder are among the significant risks for RSV [4]. Palivizumab decreased the risk of RSV-related LRTI (lower respiratory tract infection) hospitalizations for these infants [2, 7, 8]. Blanken et al. declared that implementing palivizumab for RSV interception diminished the whole number of wheez-

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ing days in the first year of life among preterms with a gestational age of 33-35 weeks [9]. Ghazaly and Nadel have shown that using agents such as palivizumab has decreased the loading of hospitalization and mortality in bronchiolitis cost-effectively [10]. A study from Scotland of over 740,000 neonates followed to 18 years of age published that children hospitalized for RSV infections throughout the first two years of life had a triple higher risk of hospitalization for asthma and used notably more anti-asthmatic drugs [11].

Materials and Methods

We performed a retrospective observational study in the Neonatal Intensive Care Unit (NICU) at Yuzuncu Yil University, a tertiary referral center with approximately 950 admissions per year after Yuzuncu Yil University ethics committee approval (no:15032023-01). Informed consent was submitted by all subjects when they were enrolled.

After recording the clinical and demographic characteristics of newborns aged 0-30 days who were hospitalized in Yüzüncü Yil University NICU due to lower respiratory tract infection (LRTI) and whose RSV RT-PCR (real-time reverse transcriptase-polymerase chain reaction) test was positive in oral/nasopharyngeal swab sample between 15/December/2022 and 15/February/2023.

We reviewed all identified babies' medical records to obtain clinical data, including the pre-hospitalization disease, the initial presentation to the hospital, and the babies' inpatient course process to NICU admission, vital signs, laboratory results, medical management, and NICU outcome. We particularly noted certified risk factors for severity, admission data, demographic data, family history, microbiology, and outcome. RSV and other RT-PCR viral infection tests have been studied at the Ministry of Health's Public Health laboratory.

Descriptive statistics for continuous variables; was expressed as Mean, Standard Deviation, Minimum, and Maximum values; for categorical variables, it was expressed as numbers and percentages. A chi-square test in determining the relationships between categorical variables and, where necessary, rate comparisons were made. Independent t-test was used in comparisons to be made according to categorical variables in terms of continuous variables. The statistical significance level was taken as 0.05 in the calculations SPSS (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp) statistical package program was used for calculations.

Results

We performed a retrospective observational study in neonates admitted to the NICU at Yuzuncu Yil University Hospital, Van, Türkiye. Twenty-nine patients diagnosed with LRTI were admitted to our NICU between the specified dates. Of the oral/nasopharyngeal swab samples sent from all of these patients, one was positive for SARS-CoV-2, one for adenovirus, one for influenza A/B, one for rhinovirus, and 18 (62%) for RSV A/B RT-PCR. Demographic features of the cases are in Table 1. Table 2 shows which parameters affect the need for mechanical ventilation.

Fifteen (83.3%) neonates lived in the same household with at least one person with acute respiratory infection symptoms. Two (11.1%) patients required intubation, and 7 (38.8%) required respiratory support with nCPAP. While cough was the first complaint in 16 (88.8%) patients, one patient presented with afebrile convulsion at home, and cough and fever symptoms appeared on the second day of hospitalization. Indirect hyperbilirubinemia was detected in 5 (27.7%) patients, which required phototherapy. All patients recovered with oxygen support, hydration, and supportive treatment and were discharged. There were no specific blood parameters results of RSV cases.

Discussion

The respiratory syncytial virus is the primary reason of pneumonia and bronchiolitis. It is related to disease epidemics and simultaneous infections contaminating respiratory contexts worldwide [12] and a lasting occasion of hospitalization in early childhood [13]. The most widespread clinical finding came across RSV infection is an upper respiratory infection; however, RSV usually comes into being in young children as bronchiolitis, an LTRI with small airway obstruction, and can uncommonly advance to pneumonia, apnea, respiratory failure, and death [14].

RSV is outspread with the respiratory droplet. The incubation period following inoculation with RSV sets from 2 to 8 days, with an average incubation of 4 to 6 days. It is attached to host determinants like the patient's age and whether the patient has a primary infection with RSV. Some weak immune people can maintain to disseminate the virus likewise after they quit representing signs for all four weeks [14,15]. In our study, the time from onset of symptoms to hospitalization was 3.16 ± 1.9 (1-8) days.

Maternal smoking, low birth weight, being male, history of atopy, non-breastfed, siblings, and crowding (defined as five or more people in the household) have been traced to be crucially associated with LTRI due to RSV [16]. Breast milk has a preventive effect against RSV infection in terms of hospitalization of children younger than two years in recent and previous studies [17]. Being younger than six months augments the threat of RSV hospitalization during RSV season [18,19]. Male gender has everlastingly been a threat determinant for serious RSV LRTI, and researchers reported the risk ratio of boys to girls being almost 1.4:1 [17]. In our study, thirteen (72.2%) infants were male. Twelve (66.6%) babies were born by cesarean section, and thirteen (72.2%) patients were fed only breast milk (Table 1).

Living in a crowded family and siblings attending school were counted as a risk group for hospitalization. Siblings of school and preschool-age enforce an increased incidence of RSV infection in the young infant [17]. The Spanish study reported that only siblings who were school-aged and more than four further residents at the same home were risk components mainly related to hospitalization due to RSV [18]. The Canadian researchers declared that the entity of preschool-aged siblings was substantially and severally correlated with a raised threat for RSV-associated hospitalization, and a poorer association was shown with the entity of school-aged siblings [19]. Risk factors for RSV

Table 1. Demographic features of RSV-positive neonates.

RSV A/B positive patients n=18(%62)	Mean±SD	Min-Max
Birth weeks (week)		
34-35 gestation weeks (n=4)		
36-37 gestation weeks (n=7)	36.72±1.48	34-39
38-39 gestation weeks (n=7)		
Birth weight (g)	2845±606	1600-4000
Symptoms appeared on postnatal day (day)	15.94±7.05	5-29
Postnatal day of hospitalization (day)	19.11±7.5	7-32
The time between the onset of symptoms and hospitalization (day)	3.16±1.9	1-8
length of spent in the hospital (day)	6.72±1.6	5-10
people living in the same house	4.88±1.67	3-8
siblings attending school	2.27±0.75	1-4

Table 2. Results according to the need for mechanical ventilation.

			Mean±SD	Min-Max	t	p-value
Gestation week	Mechanical Ventilation	Required (n=9)	35.6±1.22	34-37	-4.275	0.001**
		Non- required (n=9)	37.7±0.8	37-39		
Oxygen required day	Mechanical Ventilation	Required (n=9)	6±1.7	4-9	-1.20	0.244
		Non- required (n=9)	5.1±1.3	3-7		
Length of hospital	Mechanical Ventilation	Required (n=9)	7.2±1.8	5-10	-1.35	0.19
		Non- required (n=9)	6.2±1.2	5-8		

infection comprise more children in the household and day-care center admission [17]. In our study number of siblings of the neonates who attended school was 2.27 ± 0.75 (1-4), and several people living with neonates hospitalized in our NICU were 4.88 ± 1.67 (3-8). In addition to our study, fifteen newborns lived in the same household with at least one person with lower or upper respiratory infection symptoms.

The length of hospital stay is correlated with the disease's severity and respiratory failure's presence [15,17]. In addition, chemokines, proinflammatory cytokines, and more viral replication in nasal washes of experimentally infected adults enounce a correlation between disease severity and host immune response [20]. We have shown that; in terms of hospitalization time, although the hospitalization period of the babies (7.2 ± 1.8) who needed mechanical ventilation was not statistically significant, it was longer than those who did not need mechanical ventilation (6.2 ± 1.2) ($p > 0.05$) (Table 2).

Children admitted to the hospital due to RSV infection get better with no sequelae in general. They could be discharged in 3 or 4 days. Major risky children have prolonged hospitalizations and advanced rates of mechanical ventilation and entry to the intensive care unit [14]. No statistical significance was found when the number of days requiring oxygen in infants requiring mechanical ventilation (6 ± 1.7) was compared with the number of days receiving oxygen in infants not requiring mechanical ventilation (5.1 ± 1.3) ($p > 0.05$). We think this result is due to the small number of patients (Table 2).

The diagnosis of RSV and following bronchiolitis is clini-

cal and does not suppose imaging or confirmative testing. Utilizing test methods for RSV is discouraged unless the reality of its entity will replace medical decisions. Radiographic findings in RSV are generally similar to bronchiolitis, non-certain, and supposed commentary on the status of the illness. Chest x-ray results of RSV bronchiolitis may comprise hyperinflation and peribronchial condensation, but these can be inconvenient to allocate from bacterial pneumonia [14]. Since this is the first winter season after the COVID-19 pandemic restrictions were entirely revoked, we tested all patients to determine the etiological agent with nazo/oropharyngeal swabs. None of our patients have specific radiographic findings.

There are two subtypes of RSV, type A and type B, with variations in the envelope proteins on the viral shell [21]. The very frequently utilized kind of RSV laboratory assay is real-time reverse transcriptase-polymerase chain reaction (rRT-PCR), which is more susceptible than culture and antigen testing that is extremely sensible in children [14]. While both subtypes of the virus are evenly contagious, the occurring argument suggests that type A can induce more serious illness [21]. Since the laboratory restrictions, we could not differentiate between RSV subtypes A and B with tests.

Infants who have RSV infection commonly represent signs. In young infants younger than six months old, the only symptoms of RSV infection may be irritability, decreased activity, and lack of appetite. Fever may not appear at any time [4]. The acute illness generally proceeds for nearly 5–10 days, but the cough may be prolonged for a few weeks [22]. We have declared that while cough was the first complaint in 16 (88.8%) patients, one patient presented with

afebrile convulsions at home, and cough and fever symptoms appeared on the second day of hospitalization in our research. Only two (%11.1) neonates had a fever. Indirect hyperbilirubinemia was detected in 5 (27.7%) patients, which required phototherapy.

Histopathology of serious illness contains numerous airway edema, respiratory epithelial cell death, and infiltration of immune cells, primarily polymorphonuclear initial in the disease and subsequently in the disease, lymphomononuclear [14]. We could not analyze our patient's airways, and there are no specific laboratory results in our patients.

The cornerstone of therapy for cases with RSV is supportive maintenance. The supportive maintenance comprises nasal suction and lubrication to maintain comfort from nasal congestion, antipyretics, and oxygen for patients with existing hypoxia. Nevertheless, a hospitalized infant can not take on oral feedings owing to a high respiratory rate (>60 breaths/minute). In that case, a nasogastric tube can be accommodated to renovate sufficient hydration and feeding [6,23]. Patients with severe illness and respiratory failure can suppose ventilatory assistance through a high-flow nasal cannula, CPAP (Continuous Positive Airway Pressure), or intubation and mechanical ventilation. Admission to the hospital is suggested for cases who are obtaining or are at hazard for moderate to severe illness, cases calling for supplemental fluids, and/or respiratory support [17]. The difference between the weeks of the birth of the patients who needed mechanical ventilation (35.6 ± 1.22) and the weeks of the birth of the babies who did not need mechanical ventilation (37.7 ± 0.8) was statistically significant ($p < 0.05$). While all newborns at 34-35 gestation weeks needed mechanical ventilation, none of the newborns at 38-39 gestation weeks were followed up with mechanical ventilation. All patients recovered with oxygen support, hydration and supportive treatment and were discharged. None of them were fatal (Table 2). Oseltamivir and azithromycin treatment, hypertonic inhalation was initiated for the patients whose samples were sent via nasal swabs. The treatment of the patients whose RT-PCR results were positive was discontinued and continued as a supportive treatment and hypertonic inhalation for our neonates.

Conclusion

LRTI is a significant cause of death under the age of five worldwide. RSV is a common cause of morbidity and mortality, especially in neonates and infants associated with LRTI. It causes higher morbidity and mortality, especially in premature babies, infants with chronic lung diseases, children with chronic heart diseases, and neuromuscular retardation. Complications can be prevented in the risky group or healthy infants by expanding the availability of diagnostic tests, reducing unnecessary antibiotic use, and vaccine or other treatment methods to be developed with future research.

Conflict of interest

There is no conflict of interest between the authors.

Author contributions conception

Nur A. Serap K Design: Nur A. Serap K, Oğuz T. Supervision: Nur A, Serap K, Eyyüp Y Materials: Ali A, Emel NT, Eyyüp Y Data collection and/or Processing: Ali A, Emel NT Analysis and/or Interpretation: Nur A, Emel NT, Ali A, Eyyüp Y. Literature review: Nur A, Ali A, Serap K, Eyyüp Y, Emel NT, Oğuz T. Writing: Nur A, Eyyüp Y, Serap K, Oğuz T Critical Review: Oğuz T, Ali A.

Ethical approval

Yuzuncu Yil University Ethics Committee approval was obtained (no:15032023-01).

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