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Original Research

Evaluation of Etiological Causes and Factors Affect Length of Hospitalization in Neonates Hospitalized with Lower Respiratory Tract Infection

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Abstract

Objectives: This study aims to determine the risk factors by examining the sociodemographic characteristics of infants hospitalized in the neonatal intensive care unit (NICU) due to lower respiratory tract infection (LRTI), to determine the factors that affect the duration of hospitalization, and to determine the underlying microbial factors and evaluate them in the light of the literature.

Methods: This study evaluated the data of newborns hospitalized with LTRI between 01 October 2022 and 31 March 2023. Demographic characteristics of the patients detected viral agents, duration of hospitalization and risk factors were recorded in the study form. Babies divided viral LRTI and non-viral LRTI, and then compared with each other. Additionally, the facts that might affect the duration of hospitalization were investigated.

Results: The study included 57 babies. Viral agent was detected in 50.9% of the babies, the most frequently viral agent was respiratory syncytial virus (RSV) (48.2%). Other viral factors, in order of frequency; Adenovirus, SARS-CoV-2, Influenza A and B. There is no demographic difference between the viral agent positive and negative groups. The patients were evaluated according to length of hospitalization, it was seen that the hospital stay was longer in babies who were found to be viral positive and needed oxygen therapy (p=0.02, p=0.03, respectively). The male gender ratio was higher in the group with longer hospital stays, but this difference was not statistically significant. Although the rate of exclusive breastfeeding was higher in the group with a short hospitalization period, this difference was not statistically significant (p>0.05).

Conclusion: RSV is currently the most frequently detected viral agent in lower respiratory tract infections in newborns. The hospital stay of babies diagnosed with RSV is longer than those with non-RSV viral agents. So struggling with RSV is important in preventing lower respiratory tract infections in newborns. It is necessary to develop a vaccine or immunoglobulin application against RSV infection not only for preterm babies but also for all newborn babies.

Keywords: Lower respiratory tract infection, neonatal intensive care unit, newborn, RSV

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Acute lower respiratory tract infections (LRTIs) in newborns and infants significantly cause mortality and morbidity, especially in underdeveloped and developing countries.[1,2] LRTI agents in the infant period are frequently viruses, and the most common types are reported to be Respiratory syncytial virus (RSV), Parainfluenza virus (PIV), Influenza A, B, and Adenoviruses.[3] Prematurity, low birth weight, bronchopulmonary dysplasia (BPD), crowded life

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and smoking exposure are known as risk factors for LRTI in newborns.

Observational studies have shown inconsistent results on the associations of respiratory tract infections in early life with the risk of wheezing or asthma in later life, which ranges from a 1.5- to 10-fold increased risk.[4,5] Relatively few observational studies focused on lung function as an outcome, which showed that early-life respiratory tract infections were associated with a lower lung function in childhood or adulthood.[6,7] Because LRTI in early life can cause morbidities that can negatively affect the whole life, prevention and appropriate treatment of neonatal LRTI is very important.

Literature data on community-acquired lower respiratory tract infection in newborns is minimal. However, in this outpatient group, it is crucial to evaluate the etiology and risk factors to prevent long-term hospitalizations, avoid unnecessary antibiotic use and prevent transmission to other infants. This study aims to determine the risk factors by examining the sociodemographic characteristics of newborns hospitalized in the neonatal intensive care unit (NICU) due to LRTI, to determine underlying microbial factors and the factors that affect the length of hospitalization.

Methods

This study evaluated the data of babies hospitalized due to LRTI between 01 October 2022 and 31 March 2023 in the Neonatal Intensive Care Unit of the hospital. Approval for the study was received from the local Ethics Committee (number: 79, date: 07/06/2023). This study was conducted in accordance with the Declaration of Helsinki. (The babies' data were accessed from their files.) Data about the babies were obtained from hospital files. The data form of the study included the sociodemographic characteristics of the newborn, complaints of hospital admission, need for oxygen and/or non-invasive respiratory support, length of hospitalization, detected viral agents, history of hospitalization due to respiratory system diseases in the postnatal period and hospitalization month.

In the study protocol of our clinic, the diagnosis of LRTI is made based on examination findings and/or the presence of infiltration in the chest X-ray. All babies admitted to NICU due to LRTI: blood count, C-reactive protein, blood culture and nasopharyngeal viral swab samples (RSV, Influenza A, B, Parainfluenza, Adenovirus and SARS CoV-2) are tested. It may be a risk factor for LRTI in the neonatal period; the gender, premature birth history, delivery method, feeding pattern, maternal age, smoking exposure and hospitalization for respiratory problems in the early postnatal period were noted.

Study Design

Babies with detected viral agents (Group 1) and undetected (Group 2) were compared regarding sociodemographic characteristics, duration of hospitalization, hospitalization history in the early postnatal period, and need for respiratory support. We divided the babies into two groups according to the length of hospitalization. Two groups were created and determined according to the median hospitalization time of the babies. Babies with a hospital stay of ≤7 days (Group A) and >7 days (Group B) were compared for sociodemographic characteristics, presence of viral agent, type of viral agent and need for respiratory support. Also, babies diagnosed with RSV and babies diagnosed with other viral etiological causes were compared in terms of duration of hospitalization stay.

Statistical Analysis

The SPSS-26 (Armonk, Newyork, IBM Corp.) program was used for statistical analysis. While evaluating the study data, in addition to descriptive statistical methods (mean, median, standard deviation, frequency), an independent sample t-test was used to compare normally distributed parameters, and the Pearson chi-square test was used to compare categorical variables. Significance was evaluated at the $p<0.05$ level.

Results

Two hundred fifty-seven babies were hospitalized in the neonatal intensive care unit between 01 October 2022 and 31 March 2023, and 62 (24.1%) were followed up with lower respiratory tract infections. Since five babies had missing data in their files, they were excluded from the study, and the study included 57 babies. The average birth weight of the babies was 3221±456 g, the gestational age was 38.2±1.5 weeks, and 52.6% were born with normal spontaneous vaginal birth. The median age of hospitalization was 20 days, and the average length of hospitalization was 7.8 days.

Conditions that may be risk factors for LRTI are examined; 10.6% of babies were late preterm, 49.1% were boys, 52.6% were born via C/S, 50.9% were exposed to smoking, and 47.4% were fed formula. It was observed that a history of NICU admission due to respiratory diseases such as transient tachypnea of the newborn and congenital pneumonia in the postnatal period was detected in 8.8% of the babies.

Viral agents were detected in 29 (50%) of the babies so 14 had RSV, 4 had Adenovirus, 3 had SARS-CoV2, 2 had Influenza A, 2 had Influenza B, and 2 had Influenza A and B, RSV and Influenza A co-infections in one newborn, and Influenza B and Adenovirus co-infections in one newborn (Fig. 1). None of the patients had positive blood culture.

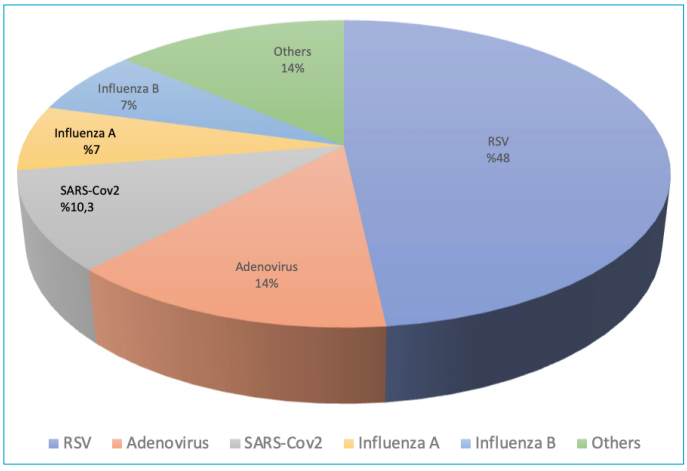

Figure 1. Viral agents.

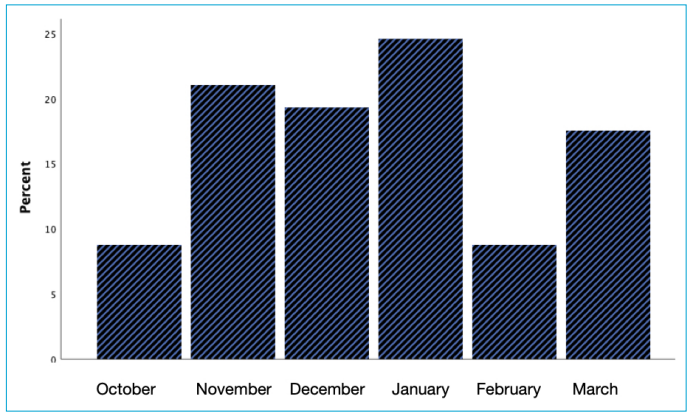

Figure 2. Distrubution of patients according to months of hospitalization.

We observed the distribution of babies' hospitalization month; it was seen that the highest hospitalization rate was in January at 24.6% (Fig. 2).

Group 1 and Group 2, which were created according to the presence of viral agents, were compared in terms of demographic data, age at hospitalization, duration of hospitalization, oxygen therapy and cigarette exposure. There is no statistically significant difference was detected (Table 1).

The groups formed according to the duration of hospitalization are evaluated. Although male gender and the rate of viral agent detection were higher in group B, this difference was not statistically significant. Oxygen therapy and non-invasive respiratory support in group B were statistically significantly higher than in group A ($p<0.05$). The ratio of exclusive breastfeeding was higher in Group A, but this difference was not statistically significant. It was observed that the patient's mode of birth, history of hospitalization due to postnatal respiratory problems, smoking exposure and the patient's nationality did not affect the duration of hospitalization (Table 2). In addition, RSV-positive babies and babies with other viral etiology were compared regarding hospitalization times. It was determined that 71.4% of the babies found positive for RSV had an extended hospital stay, and only 26.6% of the babies found positive for any of the other viral factors had an extended hospital stay ($p<0.05$).

Discussion

In our study, it has been shown that viral factors are the most common etiology (50.9%), and the most frequently detected virus is RSV (48.2%). Okulu et al.[8] reported detecting viral etiology in 69% of the cases, and 87.5% were RSV. A study from Turkey examining the clinical and viral characteristics of babies admitted to the neonatal intensive care unit due to LRTI determined that the most common etiological cause was viral factors, and 30% of them were reported to be RSV.[9] Cho et al.[10] detected 87% of viral factors as the cause of LRTI in newborns and reported that 53% were RSV.

Table 1. Characteristics of patients viral agent positive (group 1) and negative (group 2)

	Group 1 (n=29)	Group 2 (n=28)	p
Birth weight, (g) *	3218±403	3224±513	0.96
Gestational age, (week) *	38.2±1.6	38.2±1.5	0.95
Sex, (ratio of female %)	51.7	50	1
Vaginally birth, (%)	50	51	1
Duration of hospitalization, (day)	7.4±2.6	8.2±3.3	0.33
Patients receiving oxygen therapy and/or non-invasive respiratory support, (%)	10	14	0.7
Hospitalization age, (day) **	20.2±9	19.9±5.3	0.90
Smoking exposure, (%)	44.8	53.5	0.6
Maternal age, (year) *	27.2±6.8	25.7±5.5	0.37

* Mean±SD; ** Median (IQR).

Table 2. Comparison of groups according to duration of hospitalization

	Group A (≤7 days) (n=33)	Group B (>7 days) (n=24)	p
Birth weight (g) *	3119±415	3361±481	0.06
Gestational age (week) *	37.9±1.7	38.7±1.1	0.06
Male, (%)	42	58	0.28
Vaginally birth, (%)	51	54	1
Viral agent positive (%)	15 (45.4)	14 (58.3)	0.42
RSV positive n (%)	4 (28.6)	10 (71.4)	0.02
Non-RSV viral agent positive n (%)	11 (73.3)	4 (26.6)	
Hospitalization history, n (%)	3 (9)	2 (8)	1
Oxygen therapy, n (%)	1 (3)	6 (25)	0.03
Hospitalization age, day**	20.3	19.7	0.7
Smoking exposure, (%)	54	41	0.42
Breastfeeding, (%)	60	41	0.18
Maternal age, (year) *	26.6±6	26.3±6.6	0.8
Race			
Turkish, n (%)	22 (66.6)	17 (71)	0.7
Others, n (%)	11 (33.3)	7 (29)	

* Mean±SD; ** Median (IQR).

Bilgin et al.[11] detected viral etiology in 119 of 243 infants diagnosed with LRTI and reported that 78% had RSV. The same study detected Rhinovirus, Coronavirus, Parainfluenza, Influenza A/B, Metapneumovirus, Enterovirus and Adenovirus as viral agents. In their study, Celik et al.[9] found Rhinovirus, Parainfluenza and Adenovirus as the most common etiological factors among non-RSV viruses. In our study, in order of frequency, Adenovirus, SARS-CoV2, Influenza A/B, and Parainfluenza virus were found in viral etiology other than RSV.

In the literature, situations in which viral factors coexist are defined as co-infection or codetection, and different rates from 7.1% to 29% have been reported.[8, 10, 12-14] In our study, the coexistence of viral factors was detected in 14%, consistent with the literature. Okulu et al.[8] reported that they detected Rhinovirus and Coronavirus codetection with RSV. Another study reported the coexistence of Parechovirus and Rhinovirus.[9] Our study observed the coexistence of Influenza A and B, RSV and Influenza A, Influenza B and Adenovirus. Rhinovirus and Enterovirus, found in other studies, may not have been detected in our study because no tests were available in our hospital.

Babies were grouped and examined according to the duration of hospitalization period, and it was seen that the rate of babies fed only breast milk was higher in the group with a hospital stay of ≤7 days. It was thought that this situation might be due to the protective antibodies contained in breast milk. It was observed that the duration of stay was longer in the male gender, in babies with viral agents detected, and in babies receiving oxygen and/or non-invasive respiratory support. Kasap et al.[15] reported in their study that the hospitalization period of the cases where they detected RSV was longer. Cho et al.[10] also reported that the hospitalization period of newborns in whom RSV was detected was more extended, and their oxygen requirement was higher. In our study, consistent with the literature, viral LRTI cases with RSV were significantly more common in the group with extended hospital stays compared to non-RSV viral factors. No information was found in the existing literature regarding other factors that may affect the length of hospitalization.

Previous studies have reported prematurity, male gender, crowded life and the presence of viral infection at home, inadequate breastfeeding and exposure to smoking as risk factors for LRTI in newborns.[14,16] Because the neonatal intensive care unit is the second level in our hospital, highly preterm babies are not monitored, so it was thought that the hospitalized babies were not premature. There were only 10.6% of late preterm babies. Unlike other studies, no difference was detected between genders. Although smoke exposure is seen in half of the babies, it is slightly higher in cases where viral etiology is not detected.

This study was planned for six months, covering the months of October and March, and it was observed that most patients were hospitalized in January. RSV-related LRTI studies in our country reported that the most common infection period was February.[8,15] Such a difference may be seen because not only babies with RSV infection

were included in our study. Additionally, the fact that our study was conducted after the SARS CoV-2 pandemic suggests that the pandemic may cause changes in the months when viral infections peak.

There are few studies on community-acquired LRTI in healthy newborns under one month old.[17,18] Most studies have focused on newborns with underlying risk factors like premature. But RSV and other viral agents can cause LRTI in healthy term neonates.

Conclusion

Lower respiratory tract infections in newborns continue to be expected, especially in winter months. RSV maintains its first place in viral etiology. Exclusive breastfeeding can shorten the length of hospitalization. Some strategies are needed to protect and prevent lower respiratory tract infection in term newborns.

Disclosures

Ethics Committee Approval: Gaziosmanpasa Training and Research Hospital Ethics Committee (Number: 79, Date: 07/06/2023).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – D.A.; Design – A.B.; Supervision – H.A.; Materials – D.A.; Data collection &/or processing – DA., H.A.; Analysis and/or interpretation – A.B.; Literature search – H.A., A.B.; Writing – D.A.; Critical review – D.B., A.B.

References

1. Duke T. Neonatal pneumonia in developing countries. Arch Dis Child Fetal Neonatal Ed 2005;90:F211–9. [CrossRef]
2. Williams BG, Gouws E, Boschi-Pinto C, Bryce J, Dye C. Estimates of world-wide distribution of child deaths from acute respiratory infections. Lancet Infect Dis 2002;2:25–32. [CrossRef]
3. Hatipoğlu S, Arıca S, Çelik Y, Öztora S, Şevketoğlu E, Erkum T. The frequency and clinical features of rsv infection among babies hospitalized with the diagnosis of lower respiratory tract infection. Duzce Med J [Article in Turkish] 2009;11:38–44.
4. Balekian DS, Linnemann RW, Hasegawa K, Thadhani R, Camargo CA Jr. Cohort study of severe bronchiolitis during infancy and risk of asthma by age 5 years. J Allergy Clin Immunol Pract 2017;5:92–6.
5. Jackson DJ, Gangnon RE, Evans MD, Roberg KA, Anderson EL, Pappas TE, et al. Wheezing rhinovirus illnesses in early life predict asthma development in high-risk children. Am J Respir Crit Care Med 2008;178:667–72. [CrossRef]
6. Chan JY, Stern DA, Guerra S, Wright AL, Morgan WJ, Martinez FD. Pneumonia in childhood and impaired lung function in adults: a longitudinal study. Pediatrics 2015;135:607–16. [CrossRef]
7. Bui DS, Lodge CJ, Burgess JA, Lowe AJ, Perret J, Bui MQ, et al. Childhood predictors of lung function trajectories and future COPD risk: a prospective cohort study from the first to the sixth decade of life. Lancet Respir Med 2018;6:535–44. [CrossRef]
8. Okulu E, Akduman H, Tunc G, Ciftci E, Ince E, Erdeve O, et al. The epidemiological and clinical features of neonates hospitalized with lower respiratory tract viral infections. Turk J Pediatr Dis [Article in Turkish] 2018;1:31–5. [CrossRef]
9. Celik IH, Arslan Z, Unal S, Mollamahmutoglu L, Bas AY, Demirel N. Clinical and virological characteristics of neonates admitted with acute lower respiratory tract infections. Turk J Womens Health Neonatol 2021;3:33–8. [CrossRef]
10. Cho HJ, Shim SY, Son DW, Sun YH, Tchah H, Jeon IS. Respiratory viruses in neonates hospitalized with acute lower respiratory tract infections. Pediatr Int 2013;55:49–53. [CrossRef]
11. Bilgin SB, Yazici A, Ozkaya Parlakay A, Unal S. Acute lower respiratory tract infections caused by PCR proven RSV and non-RSV viruses in the NICU. Turk J Pediatr Dis 2020;14:168–175.
12. García-Garcia ML, González-Carrasco E, Quevedo S, Muñoz C, Sánchez-Escudero V, Pozo F, et al. Clinical and virological characteristics of early and moderate preterm infants readmitted with viral respiratory infections. Pediatr Infect Dis J 2015;34:693–9.
13. Smit PM, Pronk SM, Kaandorp JC, Weijer O, Lauw FN, Smits PH, et al. RT-PCR detection of respiratory pathogens in newborn children admitted to a neonatal medium care unit. Pediatr Res 2013;73:355–61. [CrossRef]
14. Kumar P, Medigeshi GR, Mishra VS, Islam M, Randev S, Mukherjee A, et al. Etiology of acute respiratory infections in infants: a prospective birth cohort study. Pediatr Infect Dis J 2017;36:25–30.
15. Kasap T, Takcı Ş, Özcan P. Evaluation of babies with viral lower respiratory tract infections in neonatal intensive care unit. J Curr Pediatr [Article in Turkish] 2021;19:106–12. [CrossRef]
16. Rossi GA, Medici MC, Arcangeletti MC, Lanari M, Merolla R, Paparatti UD, et al. Risk factors for severe RSV-induced lower respiratory tract infection over four consecutive epidemics. Eur J Pediatr 2007;166:1267–72. [CrossRef]
17. Nair H, Nokes DJ, Gessner BD, Dherani M, Madhi SA, Singleton RJ, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. Lancet 2010;375:1545–55. [CrossRef]
18. Houben ML, Bont L, Wilbrink B, Wilbrink B, Belderbos ME, Kimpen JL, et al. Clinical prediction rule for RSV bronchiolitis in healthy newborns: prognostic birth cohort study. Pediatrics 2011;127:35–41.