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■ Research Article

Determination of the long term prognosis in children hospitalized with lower respiratory infection due to respiratory syncytial virus

Respiratuar sinsityal virüse baęlı alt solunum yolu enfeksiyonu nedeniyle hastanede yatmış çocukların uzun dönem prognozunun belirlenmesi

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Abstract

Aim: Respiratory infections, notably Respiratory Syncytial Virus (RSV), significantly affect young children globally, causing mortality and long-term respiratory issues. Early severe infections can lead to chronic conditions like asthma and impaired lung function in adulthood. This study aims to determine the long-term health outcomes of children who have suffered from RSV-related lower respiratory tract infections.

Material and Methods: The study was conducted as a retrospective study at the Pediatric Health and Diseases Clinic. It investigated children aged 1 month to 5 years treated for lower respiratory tract infections caused by RSV between January 2007 and December 2014. Patients' families were reached via phone, and provided with information, and their verbal consent was obtained. Subsequently, surveys focusing on the period after RSV infection were conducted with these families. Logistic Regression was used to identify hospital admission risk factors, with statistical significance set at $P < 0.05$.

Results: In this study, out of 215 patients with respiratory infections associated with RSV, 151 agreed to participate in the study. Post-discharge, 47.6% of these children had to applied emergency depermant due to respiratory distress, and 29.1% needed rehospitalization. Strong correlation was found between application emergency department and the probability of rehospitalization.

Conclusion: The results of this study reveals that children recovering from RSV-related respiratory infections frequently require ongoing inhaler treatment and risk of emergency visits and rehospitalization, emphasizing the need for continuous patient monitoring. The study urge further research into long-term management and prevention strategies for respiratory complications post-RSV infection.

Keywords: Pediatrics, Respiratory Syncytial Virus, Respiratory Tract Infection, Wheezing.

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ÖZ

Amaç: Solunum enfeksiyonları, özellikle Respiratuvar Sinsityal Virüs (RSV), küresel olarak genç çocukları önemli ölçüde etkilemekte, ölümlere ve uzun süreli solunum sorunlarına neden olmaktadır. Erken yaşta ciddi enfeksiyonlar, yetişkinlikte astım ve bozulmuş akciğer fonksiyonu gibi kronik durumlara yol açabilir. Bu çalışma, RSV kaynaklı alt solunum yolu enfeksiyonu geçiren çocukların uzun vadeli sağlık sonuçlarını belirlemeyi amaçlamaktadır.

Gereç ve Yöntemler: Çocuk Sağlığı ve Hastalıkları Kliniği'nde retrospektif gözlemsel bir araştırma olarak yapılan bu çalışmada, RSV kaynaklı alt solunum yolu enfeksiyonları nedeniyle Ocak 2007 ile Aralık 2014 yılları arasında tedavi edilen 1 ay ile 5 yaş arası çocuklar incelenmiştir. Hastaların aileleri telefonla ulaşılarak bilgilendirilmiş ve sözlü onamları alınmıştır. Ardından, bu ailelerle RSV enfeksiyonundan sonraki döneme odaklanan anketler yapılmıştır. Hastaneye yatırılma risk faktörlerini belirlemek için lojistik regresyon analizi kullanılmış, istatistiksel anlamlılık $p < 0.05$ olarak belirlenmiştir.

Bulgular: Bu çalışmaya RSV ile ilişkili solunum enfeksiyonu olan 215 hastanın çalışmaya katılmayı kabul eden 151'i dahil edildi. Taburculuktan sonra, %47,6'sı solunum sıkıntısı nedeniyle acil servise başvurmuş ve %29,1'i benzer enfeksiyonlar için yeniden hastaneye yatırılmıştır. Acil servise başvurma ile tekrar hastaneye yatış olasılığı arasında güçlü bir ilişki bulundu.

Sonuç: Çalışmanın sonuçları, RSV ilişkili solunum yolu enfeksiyonları sonrasında çocuklarda sıklıkla devam eden inhaler tedavisi gerektiği ve yineleyen acil servis ziyaretleri ile yeniden hastaneye yatırılma riski taşıdığını ortaya koymaktadır ve sürekli hasta takibinin gerekliliğini vurgulamaktadır. Bulgular, RSV enfeksiyonu sonrası solunum komplikasyonlarının uzun vadeli yönetimi ve önlenmesi stratejilerine yönelik daha fazla araştırma yapılmasını desteklemektedir.

Anahtar Kelimeler: Hışıltı, Pediatri, Respiratuvar Sinsityal Virüs, Solunum Yolu Enfeksiyonu.

Introduction

Respiratory infections are a significant health concern globally, commonly affecting children and contributing to both morbidity and mortality (1). Acute respiratory infections severely affect life quality due to their morbidities and are responsible for the annual deaths of approximately 1.9 million children in developing countries. (2). Common symptoms of these illnesses include coughing and increased respiratory rate (3). Viruses are the primary cause of lower respiratory tract diseases in infants and young children, posing a serious public health challenge in this age group. Among these viruses, Respiratory Syncytial Virus (RSV) is the most prevalent cause (3,4).

Early childhood respiratory diseases are recognized as the starting point for many chronic respiratory conditions, with increasing evidence suggesting that lung events during this period have lasting effects on adult lung function. Particularly, the first two years of life are critical for parenchymal lung growth, with significant increases in the number of alveoli occurring during this time. Hence, severe lower respiratory tract infections during this critical period may have long-term adverse effects, potentially leading to pulmonary dysfunction in adults (5,6). Studies have shown that infants exposed to RSV-related lower respiratory tract infections often experience recurrent wheezing and have a heightened risk of developing asthma (3,7). Bronchiolitis caused by RSV, particularly in children under

five years of age, significantly increases mortality rates and has long-term impacts on respiratory health (8).

The aim of this study is to characterize the clinical course and long-term health outcomes of children who have suffered from RSV-related lower respiratory tract infections. The research will examine the frequency and duration of wheezing episodes post-infection in children, and their impact on the need for inhaler therapy. Additionally, the rates and characteristics of hospital admissions and emergency department visits due to lower respiratory tract infections in these patients will be analyzed.

Material and Method

Design

This study was designed as a retrospective observational study. It was conducted at the Dokuz Eylul University Pediatric Health and Diseases Clinic. From January 2007 to December 2014, patients aged between 1 month and 5 years who were identified with and assessed for lower respiratory tract infections associated with RSV were included in the study. Patients who had antigen detection and/or PCR (Polymerase Chain Reaction) positivity from nasopharyngeal lavage fluid at the time of hospital admission were accepted as having RSV infection. Patient data was recorded from the Dokuz Eylul University Hospital Electronic Hospital Information Management System. Families of the patients included in the study were contacted by phone, and informed, and verbal consent was obtained.

Following this process, a survey study related to the post-RSV infection period was conducted with the families.

Patient Selection

The study included patients aged between 1 month and 5 years who were treated for lower respiratory tract infections at the Dokuz Eylul University Pediatric Diseases Clinic. Eligibility required positive results from antigen detection and/or PCR test in nasopharyngeal lavage fluid during the infection period. Additionally, only children whose families agreed to participate and gave consent were included.

Exclusion criteria encompassed a history of premature birth, infants born with low birth weight, patients who required mechanical ventilation after birth, and the presence of bronchopulmonary dysplasia.

Statistical Analysis

The SPSS 20.0 (IBM Corp., Armonk, NY) program was used for data analysis. Whether the data followed a normal distribution was evaluated with the Shapiro-Wilk test. Patients' ages, the number of years they continued to receive inhaled treatment, and the annual number of emergency department visits were presented as median (range). The Logistic Regression Test was applied to determine the risk factor for hospital admission with Nagelkerke R2 utilized as a metric to assess the model's goodness of fit. The p-value<0.05 was considered statistically significant.

Ethical Consent

The study received approval from the Dokuz Eylul University ethics committee with the decision number 2016/17-31. This study was conducted in accordance with the Declaration of Helsinki Principles. All participants involved in the study have given their consent to participate.

Results

A total of 215 patients were identified as being treated inpatient for lower respiratory tract infections due to respiratory syncytial virus. Out of these patients, 151 who were reached and gave consent were included in the study. There were 84 (55.6%) male and 67 (44.4%) female patients. The median age (range) was 77.2 (52.3-101.8) months. The number of children with at least one parent having an allergy history was 61 (40.4%), and 90 (59.6%) had no such history. The number of children with at least one parent smoking at home was 41 (27.2%), while 110 (72.8%) families reported no smoking at home.

After discharge from the hospital, 72 (47.6%) patients had emergency department visits due to respiratory distress (figure1). 71 patients needed inhaled medication in subsequent years, continuing for a median (range) of 1 (1-6)

years. 42 patients (27%) needed inhaled treatment in the first year, 16 (10.6%) in the second year, and 14 (9.4%) for three years or more. The median (range) number of emergency department visits within one year was 2 (1-6). The number of children who had lower respiratory tract infections requiring inpatient treatment again after the infection was 44 (29.1%), with a median (range) of 1 (1-10) hospital admissions.

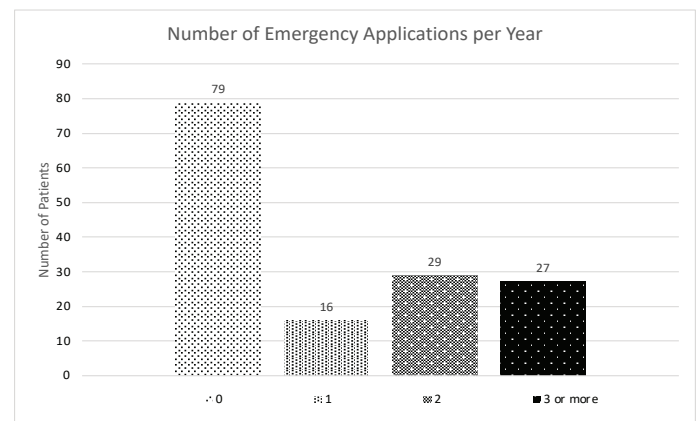


Figure 1. Annual Emergency Department Application Frequencies after Discharge

Risk factors were evaluated for their association with the likelihood of hospital readmission. In this context, variables such as age, gender, exposure to cigarette smoke within the home, and the presence of a family history of atopy were examined. Statistical analysis did not reveal a significant difference among these risk factors. However, a strong correlation was observed between emergency department visits and the likelihood of hospital readmission (Table 1).

| | Odds ratio | p-value | 95% CI interval |
|----------------------------------|------------|---------|-----------------|
| Gender | 1,11 | 0,82 | 0,42-2,93 |
| Age | 0,99 | 0,48 | 0,98-1 |
| Exposure to smoking at home | 0,77 | 0,65 | 0,25-2,36 |
| Family history of atopy | 1,08 | 0,86 | 0,41-2,85 |
| Emergency department application | 116,34 | <0,01 | 15,23-888,52 |

Nagelkarke R²: 0.56, X² (Chi-Square): 75,3. p-value of <0.05 is considered statistically significant.

Discussion

This study aimed to determine the clinical course following discharge of children who suffered from severe lower respiratory tract infections due to RSV infection. Therefore, post-discharge emergency visits due to respiratory distress,

hospitalizations for lower respiratory tract infections, and durations of continued inhaler treatment were examined.

In our study, the most significant result we have considered, nearly half of the patients required inhaler therapy and had emergency department visits due to respiratory distress. It is believed that lower respiratory tract infections in children, especially during infancy, significantly impact the development of asthma and recurrent wheezing. Among these infections, those associated with RSV are particularly notable. Children who had undergone viral lower respiratory tract infections, particularly those infected with RSV, had a risk for recurrent wheezing and asthma (9,10). In a study by Kneyber et al. on children who had RSV-related bronchiolitis, it was found that 40% of the patients in the RSV bronchiolitis group experienced recurring wheezing over a five-year follow-up, compared to 11% in the control group, a statistically significant difference. In the five to ten-year follow-up, 22% of the RSV bronchiolitis group and 10% of the control group had wheezing (11). Also another research and analyses have identified a correlation between early-life RSV infections and the later emergence of wheezing and asthma. (12). These findings indicate that RSV infections, particularly in young children, are a significant factor in the progression of respiratory diseases.

After infections of the lower respiratory tract caused by RSV, there is a risk of recurrent hospital admissions (13). Our study's data shows that 29.1% of patients with RSV infection required hospital readmission and treatment even after recovering from the disease. This highlights the need for close monitoring of patients not only in the post-discharge period but also in subsequent years. These findings underscore the importance of awareness regarding the long-term effects of RSV infection. Even with appropriate treatment during the acute infection phase, some patients may continue to face long-term health issues.

The risk factors evaluated for hospital admission, gender, exposure to cigarette smoke, and family history of atopy were not found to be statistically significant. However, emergency department visits were identified as a statistically significant risk factor for hospital readmission. It is commonly expected that children who are hospitalized will have made a prior application to the emergency department. However, these applications often indicate a significant deterioration in the patient's clinical condition. Nevertheless, this situation may suggest that with close monitoring after discharge, patients can be treated early without serious clinical deterioration, highlighting the importance of post-discharge follow-up. This

underscores the importance of patient follow-up in the post-discharge period. Early detection and timely intervention can be made for potential clinical deterioration.

This study is retrospective and relies on data reported by families, introducing subjectivity into the data and posing a significant limitation. Particularly in areas like cigarette smoke exposure, the possibility of families providing incorrect or misleading information can complicate the accurate identification of risk factors. Additionally, the fact that this study was conducted at a single center limits the generalizability of its findings. Limitations should be considered when interpreting the results of the study.

Conclusion

This study examined the clinical developments of children with lower respiratory tract infections due to RSV infection in the post-discharge period. Our findings indicate that children may continue to require inhaler therapy after discharge. Additionally, these children carry a risk of emergency department visits and hospital readmission due to respiratory distress. This highlights the importance of patient monitoring. In conclusion, this study presents significant findings about the long-term effects of RSV infection and emphasizes the need for prolonged monitoring of these patients. Future research should validate these findings with larger sample groups and focus on developing strategies for the prevention and management of chronic respiratory diseases in children following RSV infection.

Funding and Conflict of Interest

There was no Funding. No Conflict of Interest has been declared by the authors.

Ethical Statement, Funding and Conflict of Interest

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References

1. Greenbaum AH, Chen J, Reed C, et al. Hospitalizations for severe lower respiratory tract infections. *Pediatrics*, 2014; 134.3: 546-554.
2. Taneja J, Malik A, Malik A, Rizvi M, Agarwal M. Acute lower respiratory tract infections in children. *Indian Pediatrics*, 2009; 46.6.
3. Boloursaz MR, Lotfian F, Aghahosseini F, et al. Epidemiology of lower respiratory tract infections in children. *Journal of Comprehensive Pediatrics*, 2013; 4.2: 93-8.

4. Van Woensel JBM, Van Aalderen WMC, Kimpen JLL. Viral lower respiratory tract infection in infants and young children. *Bmj*, 2003; 327.7405: 36-40.
5. Chang AB, Chang CC, O'Grady K, Torzillo PJ. Lower respiratory tract infections. *Pediatric Clinics*, 2009; 56.6: 1303-1321.
6. Galobardes B, McCarron P, Jeffreys M, Davey-Smith G. Association between early life history of respiratory disease and morbidity and mortality in adulthood. *Thorax*. 2008;63(5):423-429.
7. Steiner RWP. Treating acute bronchiolitis associated with RSV. *Am Fam Physician* 2004; 69:325-330
8. Mazur NI, Martín-Torres F, Baraldi E, et al. Lower respiratory tract infection caused by respiratory syncytial virus: current management and new therapeutics. *The Lancet Respiratory Medicine*, 2015; 3.11: 888-900.
9. Wennergren G, Kristjansson S. Relationship between respiratory syncytial virus bronchiolitis and future obstructive airway diseases. *Eur Respir J* 2001;18:1044- 1058.
10. Openshaw PJM, Dean GS, Culley FJ. Links between respiratory syncytial virus bronchiolitis and childhood asthma: clinical and research approaches. *Pediatr Infect Dis J*, 2003;22:58-65
11. Kneyber MCJ, Steyerberg EW, De Groot R, Moll HA. Long-term effects of respiratory syncytial virus (RSV) bronchiolitis in infants and young children: a quantitative review. *Acta Paediatrica*, 2000, 89.6: 654-660.
12. Binns E, Tuckerman J, Licciardi PV, Wurzel D. Respiratory syncytial virus, recurrent wheeze and asthma: A narrative review of pathophysiology, prevention and future directions. *Journal of Paediatrics and Child Health*, 2022, 58.10: 1741-1746.
13. Wong K, Robinson JL, Hawkes MT. Risk of repeated admissions for respiratory syncytial virus in a cohort of > 10 000 hospitalized children. *Journal of the Pediatric Infectious Diseases Society*, 2021, 10.3: 352-358.