



Comparison of clinically related factors and treatment approaches in patients with acute bronchiolitis

Akut bronşiolitli olgularda klinik ilişkili faktörler ve tedavi yaklaşımlarının karşılaştırılması

Özlem Üzüm¹, Ali Kanık², Kayı Eliaçık¹, Hacer Örsdemir Hortu¹, Yavuz Demirçelik¹, Mehmet Yan¹, Mehmet Helvacı¹, Belde Kasap Demir³

¹Department of Pediatrics, Tepecik Training and Research Hospital, İzmir, Turkey

²Department of Pediatrics, İzmir Katip Çelebi University Faculty of Medicine, İzmir, Turkey

³Division of Pediatric Nephrology and Rheumatology, Department of Pediatrics, İzmir Katip Çelebi University Faculty of Medicine, İzmir, Turkey

The known about this topic

It has been reported that the most common agent in acute bronchiolitis is a respiratory syncytial virus, but rates of rhinovirus have increased in recent studies. Low birth weight, preterm birth, congenital heart disease, and a history of atopy have been considered risk factors in studies in the literature, and hospitalization rates in these cases have been reported to be prolonged. According to the American Academy of Pediatrics recommendations, use of nebulized salbutamol and intravenous steroid is not needed in the treatment of acute bronchiolitis.

Contribution of the study

In our study, the most common causative agent was found to be rhinovirus. In our study, the hospitalization time was found to be longer in patients with acyanotic congenital heart disease compared with those without. Need for HFNC was found with a higher rate in patients who were positive for respiratory syncytial virus compared with those who were negative. When the patients who received intravenous hydration and/or oxygen treatment alone were compared with the patients who received nebulized salbutamol and/or intravenous steroid in addition to these therapies, no difference was found in terms of the need for HFNC and intensive care, whereas the hospitalization time was found to be longer in the group that received nebulized salbutamol and/or intravenous steroid.

Abstract

Aim: Acute bronchiolitis is a lower respiratory tract infection caused by viral agents in children aged under two years. Treatment includes hydration, oxygen, nebulized salbutamol, and intravenous steroids. This study aimed to determine the clinically related factors, the effect of viral agents on the clinical picture, and the efficacy of treatment methods in patients admitted with acute bronchiolitis.

Material and Methods: Patients aged under two years of age who were hospitalized with a diagnosis of moderate/severe acute bronchiolitis between March 2015 and March 2019 were included in the study. Demographic data, hospitalization time, body temperature, presence of congenital heart disease, history of atopy, acute-phase reactants, mean platelet volume values, and respiratory virus panel results were recorded. The treatment modalities, length of hospitalization, intensive care hospitalization, and high-flow nasal cannula oxygen therapy (HFNC) were recorded.

Results: Four hundred twenty-two patients were included in the study. The duration of hospitalization was found to be significantly longer in

Öz

Amaç: Akut bronşiolit iki yaş altı çocuklarda, viral ajanlar ile oluşan alt solunum yolu enfeksiyonudur. Tedavisinde hidrasyon, oksijen, nebulize salbutamol, damar içi steroid gibi yaklaşımlar bulunmaktadır. Çalışmamızda akut bronşiolit ile yatırılan olgularda klinik ilişkili etmenlerin belirlenmesi, viral ajanların kliniğe etkisi ve tedavi yöntemlerinin etkinliklerinin karşılaştırılması amaçlanmıştır.

Gereç ve Yöntemler: Çalışmamıza Mart 2015–Mart 2019 tarihleri arasında orta/ağır akut bronşiolit tanısı ile yatarak tedavi gören iki yaş altı olgular alındı. Olguların demografik verileri, yatış zamanı, vücut sıcaklığı, doğuştan kalp hastalığı olup olmaması, atopi öyküsü, akut faz reaktantları, ortalama trombosit hacmi, solunum virus panel sonuçları kaydedildi. Uygulanan tedavi yöntemleri, hastanede yatış süreleri, yoğun bakım yatışları ve yüksek akışlı nazal kanül oksijen tedavisi (YANKOT) alıp almadığı kaydedildi.

Bulgular: Çalışmaya 422 hasta alındı. Bir yaş altı olguların ve asiyanotik

Cont. ➡

Cite this article as: Üzüm Ö, Kanık A, Eliaçık K, et al. Comparison of clinically related factors and treatment approaches in patients with acute bronchiolitis. Turk Pediatr Ars 2020; 55(4): 376–85.

Corresponding Author/Sorumlu Yazar: Özlem Üzüm E-mail/E-posta: baspinarozlemm@hotmail.com

Received/Geliş Tarihi: 25.10.2019 **Accepted/Kabul Tarihi:** 18.05.2020

©Copyright 2020 by Turkish Pediatric Association - Available online at www.turkpediatriarsivi.com

©Telif Hakkı 2020 Türk Pediatri Kurumu Derneği - Makale metnine www.turkpediatriarsivi.com web adresinden ulaşılabilir.

DOI: 10.14744/TurkPediatriArs.2020.46144

OPEN ACCESS This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.



patients aged under one year and in patients with acyanotic congenital heart disease. A single viral agent was detected in 69 (51.9%) patients. Rhinovirus was detected in 70 patients and RSV was detected in 37. The duration of hospitalization was found to be significantly shorter in patients who received only oxygen and/or intravenous fluid treatment compared with those who received nebulized salbutamol and/or intravenous steroids. In addition, and there was no significant difference between the groups in terms of HFNC and hospitalization in the intensive care unit.

Conclusion: Rhinovirus was the most common cause of acute bronchiolitis in our study. It was observed that congenital heart disease prolonged the length of hospitalization. In the treatment approaches, it was observed that hydration and oxygen therapy were sufficient treatment methods for the patients, in accordance with the recommendations of the American Academy of Pediatrics, and giving nebulized therapy prolonged the hospitalization period due to the treatment discontinuation steps.

Keywords: Bronchiolitis, rhinovirus, salbutamol, steroid

doğuştan kalp hastalığı olan olguların yatış süreleri anlamlı olarak uzun saptandı. Olguların 69'unda (%51,9) tek viral etken saptandı. Olguların 70'inde Rinovirüs, 37'sinde respiratuar sinsityal virüs saptandı. Sadece oksijen ya/ya da damar içi sıvı tedavisi alanların yatış süreleri, bu tedavilerin yanında nebulize salbutamol ya/ya da damar içi steroid alanlarda anlamlı düzeyde kısa olduğu, YANKOT ve yoğun bakım yatış için iki grup arasında anlamlı fark olmadığı görüldü.

Çıkarımlar: Çalışmamızda akut bronşiolit etkenleri arasında en sık Rinovirüs saptandı. Doğuştan kalp hastalığının yatış süresini uzattığı görüldü. Tedavi yaklaşımlarında ise Amerikan Pediatri Akademisi önerileri ile uyumlu olarak, hidrasyon ve oksijen tedavisinin olgular için yeterli tedavi yöntemi olduğu ve nebulize tedavi vermenin tedavi kesme basamakları nedeni ile yatışı süresini uzattığı görüldü.

Anahtar sözcükler: Bronşiolit, rinovirüs, salbutamol, steroid

Introduction

Acute bronchiolitis is a lower respiratory tract infection characterized by inflammation and edema in the small airways that occur frequently in children younger than 2 years (1–3). Viral agents are most commonly involved in the etiology, and respiratory syncytial virus (RSV) is responsible for 50% of the cases (1, 4, 5). The clinical picture may be more severe in patients with immune deficiency, chronic lung disease, congenital heart disease, and a history of preterm birth. It was found that laboratory tests [increased white blood cell count, C-reactive protein (CRP) values, mean platelet volume (MPV)] and respiratory virus typing did not affect predicting the severity of clinical picture (1, 6, 7).

There are different approaches in the treatment of bronchiolitis. In the latest guidelines published by the American Academy of Pediatrics (AAP), the mainstay of treatment includes oral/intravenous hydration and oxygen support (1). Although it has been reported that nebulized salbutamol, nebulized adrenaline, nebulized steroid or intravenous steroid treatment do not affect the duration or severity of the clinical picture, these therapies are used in many centers and continued, if a response is obtained (1, 8–10).

In this study, we aimed to examine the demographic characteristics, symptoms, acute-phase reactants, and treatments in patients hospitalized because of acute bronchiolitis, to determine clinically related factors and the effect of viral agents on the clinical picture, and to retrospectively compare the efficiencies of different treatment modalities.

Material and Methods

Patients aged under two years who presented with symptoms of cough, tachypnea, wheezing and dyspnea, who were hospitalized with a diagnosis of moderate/severe acute bronchiolitis between March 2015 and March 2019 were included in our study. The clinical data were retro-

spectively obtained from patient registries. The demographic data, hospitalization seasons and years, presence of fever and cough, presence of acyanotic heart disease and atopy, family history of atopy, and the presence of a sibling who was followed up with a diagnosis of wheezy infant, were recorded. White blood cell count, neutrophil count, lymphocyte count, CRP, MPV values, and viruses detected in a respiratory virus panel among laboratory tests, treatment methods performed, hospitalization durations, if high-flow nasal cannula oxygen therapy (HFNC) was performed, and intensive care hospitalizations were recorded. Patients who had cyanotic congenital heart disease, received treatment with a diagnosis of recurrent acute bronchiolitis (patients who had been followed up with a diagnosis of acute bronchiolitis for ≥ 3 times), were being followed up because of wheezing for longer than one month, and had chronic lung disease, were not included in the study.

Patients with a diagnosis of moderate and severe acute bronchiolitis who have tachypnea and need intravenous/oral hydration are followed up in our clinic. These patients are discharged when full oral feeding is achieved and when there is no need for oxygen. Before the guidelines and recommendations have been published by the American Academy of Pediatrics (AAP) in 2014, treatment was based on the Turkish Thorax Association's 'Consensus Report on the Diagnosis and Treatment of Acute Bronchiolitis,' and nebulized salbutamol and intravenous steroid treatments were used intensively (1, 10). After 2014, treatment amendments came to the forefront following the AAP recommendations (1). Between March 2015 and March 2019, the period in which the study was conducted, treatments were adjusted according to clinicians' preference of guideline, independent of the severity of the clinical picture. In our study, the patients were divided into two groups as patients who received nebulized salbutamol and/or intravenous steroid in addition to oxygen and/or intravenous fluid treatment (group 1) and those who received oxygen and/or intravenous fluid treatment alone

Table 1. Demographic data of the subjects

Sex, n (%)	
Female	166 (39.3)
Male	256 (60.7)
Age (months), Mean ($\pm$ SD)	8.04 ($\pm$ 5.33) months
Patients younger than 1 year (n=326), Mean (Min.–Max.)	5.83 ay (1–11) months
Patients older than 1 year (n=96), Mean (Min.–Max.)	16.00 (12–24) months
Birth weight (grams)	
<2500 g (n=109), Mean (Min.–Max.)	2053 (890–2460) g
$\geq$ 2500 g (n=313), Mean (Min.–Max.)	3335 (2500–4800) g
Patients with acyanotic congenital heart disease, n (%)	37 (8.7)
Patients with a history of atopy, n (%)	8 (1.8)
Patients with a history of familial atopy, n (%)	77 (18.2)
Patients with a history of sibling with a diagnosis of wheezy infant, n (%)	48 (11.3)
SD: Standard deviation; Min.: Minimum; Max.: Maximum	

(group 2). The effect of the AAP guideline on hospitalization duration, need for HFNC, and need for hospitalization in the intensive care unit (ICU), was evaluated. HFNC treatment is initiated in patients hospitalized in our ward with a diagnosis of moderate/severe bronchiolitis whose respiratory distress persists, oxygen saturation is below 93% or who have respiratory acidosis despite treatment methods preferred by physicians. The study was conducted in accordance with the principles of the Helsinki Declaration and approval was obtained from the local ethics committee (10.04.2019, decision No: 2019/6–13). The data were obtained from patient records. Therefore, informed consent was not obtained.

Statistical Analysis

Analyses of the present data were performed using the IBM Statistical Package for the Social Sciences Ver. 24 program (SPSS, Chicago, IL, USA) according to group characteristics. Before analysis of the data related to the variables included in case form, their compatibility with normal distribution was examined considering the number of cases using primarily the Shapiro-Wilk and Kolmogorov-Smirnov tests, and subsequently using Skewness and Kurtosis values. After the assumption was provided that the data were distributed normally, the Fisher's exact, Chi-square and Student t-tests were used in the comparison of the mean values of two independent groups. The Mann-Witney U test was used for variables that did not have normal distribution. In all statistical tests, a p-value of 0.05 was considered statistically significant.

Results

Four hundred twenty-two patients were included in the study. It was observed that 60.7% of the subjects were

male and the mean age was 8.04 ($\pm$ 5.33) months (Table 1). There was no significant difference between the male and female subjects in terms of hospitalization duration, HFNC treatment, and hospitalization in the ICU. When the subjects were evaluated in two groups as those aged under and over one year of age, the hospitalization duration was found to be significantly longer in the group aged under one year (Table 2). It was found that 213 (50.6%) of the subjects presented in winter months and 95 (22.3%) presented in autumn months. It was observed that 74.2% of the subjects had a birth weight of 2500 g and over and 18.2% had a family history of atopy. The subjects' clinical and demographic data are summarized in Table 1. The subjects who had a history of preterm birth, low birth weight (LBW), acyanotic heart disease, atopy, a family history of atopy, and had a sibling who had been followed up with a diagnosis of wheezy infant, were compared in terms of hospitalization duration, need for HFNC and hospitalization in the ICU. Among the clinically related factors, only subjects who had congenital heart disease were observed to have longer hospitalization duration and more prolonged need for HFNC (Table 2).

It was observed that 188 (44.5%) of the subjects had a body temperature above 38°C at the time of the first presentation and 389 (92.1%) had cough. No significant difference was observed between the subjects who did and did not have fever in terms of hospitalization duration, need for HFNC and hospitalization in the ICU. In the classification made according to oxygen saturation, it was observed that the need for HFNC was significantly higher in the subjects who had an oxygen saturation below 93% (Table 2).

Table 2. Comparison of hospitalization duration, need for HFCN and need for hospitalization in ICU by demographic characteristics

	Hospitalization duration (days) (mean±SD)	p	HFCN n (%)	p	Hospitalization in the ICU (mean±SD)	p	Total
Sex n (%)							
Female	5.70±2.38	0.126 ^a	41 (24.6)	0.606 ^c	5 (3.0)	0.676 ^c	166
Male	6.12±2.95		69 (26.9)		6 (2.3)		256
Age n (%)							
<1 year	6.11±2.80	0.033^a	86 (26.3)	0.787 ^c	9 (2.7)	0.714 ^c	326
≥1 year	5.43±2.48		24 (25.0)		2 (2.1)		96
Gestational week n (%)							
≤37+6 weeks	6.51±3.31	0.098 ^a	21 (28.3)	0.983 ^c	2 (2.7)	0.095 ^c	74
<37+6 weeks	5.83±2.59		88 (25.2)		9 (2.6)		348
Birth weight n (%)							
<2500 g	6.31±3.04	0.126 ^a	29 (26.6)	0.647 ^c	5 (4.6)	0.101 ^c	109
≥2500 g	5.84±2.59		78 (24.9)		5 (1.6)		313
Acyanotic congenital heart disease n (%)							
Yes	7.43±4.1	0.023^b	16 (43.2)	0.025^c	2 (5.4)	0.206 ^d	37
No	5.80±2.5		91 (23.6)		8 (2.1)		385
History of atopy n (%)							
Yes	6.88±2.69	0.338 ^a	2 (25)	0.652 ^d	1 (12.5)	0.192 ^d	8
No	5.93±2.74		108 (26)		10 (2.4)		414
Famiy history of atopy n (%)							
Yes	5.83±2.68	0.688 ^b	19 (24.6)	0.759 ^c	—	0.228 ^d	77
No	5.98±2.76		91 (27.2)		11 (3.2)		334
Presence of sibling with a diagnosis of wheezy infant n (%)							
Yes	5.98±2.76	0.715 ^b	17 (35.4)	0.117 ^c	3 (6.2)	0.118 ^d	48
No	5.95±2.74		93 (24.8)		8 (2.1)		374
Fever n (%)							
Yes	5.84±2.23	0.437 ^b	51 (27.1)	0.657 ^c	103 (54.7)	0.951 ^c	188
No	6.04±2.76		59 (25.2)		7 (2.9)		234
Oxygen saturation n (%)							
<93%	5.71±2.7	0.085 ^a	71 (32.1)	0.003^c	3 (1.3)	0.226 ^d	221
≥93%	6.17±2.7		39 (19.4)		8 (3.9)		201

SD: Standard deviation; ICU: Intensive care unit; HFCN: High-flow nasal cannula oxygen therapy; a: Student's t-test; b: Mann-Witney U Test; c: Chi-square Test; d: Fisher's Exact Test

The subjects' white cell counts, CRP, and MPV values were compared. No significant difference was found between the subjects who had high acute-phase reactants and high MPV values and the those who had normal values in terms of the need for HFCN and hospitaliza-

tion in the ICU. When the subjects' neutrophil/lymphocyte ratios (NLR) and white blood cell/MPV ratios were compared, no significant difference was found between subjects who did and did not need hospitalization in the ICU or HFCN.

Table 3. Viral agents detected in respiratory samples

Single viral agents	n	HFCN (n=27)	ICU (n=4)	Hospitalization duration (mean days)
Rhinovirus	36	14	4	6.4 days
RSV A	13	7		6.1 days
Metapneumovirus	5	2		6.6 days
Bocavirus	4	1		7.6 days
RSV B	3	0		5 days
Parainfluenza virus	3	1		5 days
Influenza B virus	2	0		10.5 days
Adenovirus	2	1		7 days
Influenza A virus	1	1		10 days
Multiple viral agents	n	HFCN (n=19)	ICU (n=2)	Hospitalization duration (mean days)
Rhinovirus, RSV A	11	7	2	7.2 days
Rhinovirus, Bocavirus	9	4		5.9 days
Rhinovirus, Parainfluenza virus	5	1		7.4 days
RSV B, Bocavirus	4	1		6.3 days
Rhinovirus, RSV B	4	3		10.3 days
Rhinovirus, Adenovirus	4	1		5 days
Rhinovirus, Metapneumovirus	3	1		5.7 days
Rhinovirus, Coronavirus	2	0		9 days
Adenovirus, Influenza A virus	2	1		12 days
RSV A, Adenovirus	1	0		7 days
RSV A, Bocavirus	1	0		7 days
RSV A, Influenza A virus	1	0		6 days
Parainfluenza virus, Influenza B virus	1	0		7 days
Parainfluenza virus, Adenovirus, Bocavirus	1	0		5 days

HFCN: High-flow nasal cannula oxygen therapy; RSV: Respiratory syncytial virus; ICU: Intensive care unit

It was observed that respiratory virus panel was obtained from 133 (32%) of the subjects and no viral agent was found in 15 subjects. A single viral agent was found in 69 subjects (59%), and multiple viral agents were detected in 49 (36.8%) subjects. The most common viral agent was found to be rhinovirus (77 subjects, 44%). Respiratory syncytial virus was found in 38 subjects (22.6%) (Table 3). Among the subjects in whom a viral agent was found in the respiratory virus panel, six were hospitalized in the ICU; rhinovirus was found in four of these subjects and RSV A and rhinovirus were found in two subjects (Table 3). HFCN, hospitalization in the ICU, and hospitalization durations related to the viral agents detected are shown in Table 3. Hospitalization duration and HFCN were evaluated between single viral agents and multiple viral agents, and no significant difference was found between the two groups (Table 4). The subjects were divided into two groups as patients in whom RSV and non-RSV viral agents were found and those in whom rhinovirus and non-rhinovirus viral agents were found, and need for

HFCN was observed to be significantly higher in subjects in whom RSV was found (Table 4). These subjects were not compared in terms of hospitalization in the ICU because these subjects were those in whom rhinovirus and RSV were found.

When the treatment performed to the subjects was evaluated, it was observed that all subjects received intravenous fluid therapy at the time of hospitalization, 252 subjects received oxygen treatment, 212 subjects received nebulized salbutamol treatment, and 87 subjects received both nebulized salbutamol and intravenous steroid treatment. The subjects were divided into two groups as the those who received nebulized salbutamol and intravenous steroid treatment in addition to oxygen and/or intravenous fluid therapy (group 1) and patients who received oxygen and/or intravenous fluid therapy alone (group 2). When evaluated by years, it was observed that the AAP treatment approaches in our clinic (oxygen and/or intravenous fluid treatment) increased from 12.3% to 62.3% in four years.

Table 4. Comparison of single/multiple viral agents and treatment groups

	Single viral agent (n=69) (%)	Multiple viral agents (n=49) (%)	p			
HFCN, n (%)	27 (39.1)	19 (38.7)	0.969 ^a			
Hospitalization duration (days), (mean±SD)	6.64 (±3.2)	7.06 (±3.7)	0.510 ^b			
	Group 1 n=299	Group 2 n=123	p			
HFCN, n (%)	73 (24.4)	37 (30.1)	0.272 ^a			
ICU, n (%)	7 (2.3)	4 (3.2)	0.737 ^c			
Hospitalization duratio (days), (mean±SD)	6.21 (±2.9)	5.33 (±2.2)	0.001^b			
	RSV (+) patients (n=37) (%)	RSV (–) patients (n=95) (%)	p	Rhinovirus patients (n=70) (%)	Rhinovirus patients (n=62) (%)	p
HFCN, n (%)	18 (48.6)	28 (29.5)	0.001^a	31 (44.3)	14 (22.6)	0.317 ^a
Hospitalization duration (days), (mean±SD)	7.08±3.49	6.67±3.38	0.541 ^b	6.69±3.67	6.95±2.99	0.689 ^b

Group 1: The patients who received nebulized salbutamol and/or intravenous steroid treatment in addition to oxygen and/or intravenous fluid therapy. Group 2: The patients who received oxygen and/or intravenous fluid therapy alone; HFCN: High-flow nasal cannula oxygen therapy; ICU: Intensive care unit; a: Chi-square Test; b: Student's t-test; c: Fisher's Exact Test

Gestational week, birth weight, association with acyanotic congenital heart disease, history of atopy, family history of atopy, and history of a sibling who had been followed up with a diagnosis of wheezy infant, were compared to evaluate the groups' distribution and no significant difference was found between the groups. HFCN therapy, hospitalization in the ICU, and hospitalization durations were evaluated between the groups. It was observed that the hospitalization duration was significantly shorter in group 2 and no significant difference was found between the two groups in terms of HFCN and hospitalization in the ICU (Table 4).

Discussion

In our study, the subjects were compared in terms of hospitalization duration, need for HFCN, and need for hospitalization in the ICU by risk groups. It was observed that being aged under one year or the presence of congenital heart disease significantly prolonged hospitalization duration, and the presence of congenital heart disease, RSV positivity, and oxygen saturation below 93% at the time of presentation significantly increased the need for HFCN. Also, it was found that there was no difference between the subjects who did and did not receive nebulized salbutamol and/or intravenous steroid treatment in terms of the need for HFCN or the need for hospitalization in the

ICU, and hospitalization duration prolonged significantly in subjects who received these additional therapies.

In our study, the number of male patients was significantly higher and no difference was found between the sexes in terms of hospitalization duration, need for HFCN, and need for hospitalization in the ICU. Acute bronchiolitis affects children aged younger than two years and most frequently peaks between 2 and 12 months (11). The AAP reported that acute bronchiolitis occurred more frequently in children aged younger than 12 months in its reviews and guidelines, and recommended close monitoring in this group because it carried risk (1). In our study, the hospitalization duration was found to be longer in children aged younger than 1 year. Studies in the literature have reported that acute bronchiolitis occurred more frequently in boys, but no difference has been reported between the sexes in terms of clinical severity. Some studies reported that the higher frequency in boys might be explained by the fact that the ratio of airway lumen diameter to lung volume is smaller in boys compared with girls (12, 13).

When LBW babies were compared with babies with normal birth weight in our study, but no significant difference was found in terms of hospitalization duration, need for hospitalization in the ICU, and need for HFCN. In the literature, children with a history of preterm birth, car-

diopulmonary disease or immunodeficiency have been specified as the group in whom acute bronchiolitis has a severe clinical course (1, 11, 14). Apnea may develop and high mortality/morbidity rates may be observed, especially in babies with a history of preterm birth (15). Low birth weight is among the risk factors for acute bronchiolitis, and many studies have reported that hospitalization duration is prolonged and disease severity is higher in this group (16, 17). In a study conducted by Turan et al. (13), however, no significant difference was found between LBW babies and babies with normal birth weight in terms of the number of acute bronchiolitis episodes.

In our study, it was observed that two-thirds of the subjects presented in winter months. Respiratory viruses are observed more frequently throughout winter months and infection becomes easier due to the increase in the time spent by children in closed areas (14). Following winter months, acute bronchiolitis peaks at the beginning of spring. This increase in the number of cases is in parallel to the RSV season (18).

In our study, no significant difference was found between the subjects who did and did not have a family history of atopy in terms of clinical course and hospitalization duration. There are studies in the literature showing that the clinical course of bronchiolitis was more severe in subjects who had a history of atopy, and subjects with a family history of eczema among atopy findings had a more severe clinical picture compared with controls, but the clinical picture was not different among subjects with a family history of asthma and allergic rhinitis (14, 19). In a study conducted with subjects who did and did not have bronchiolitis, no significant difference was found between the two groups in terms of family history of allergic rhinitis, eczema, and asthma (14).

In our study, multiple viral agents were found in one-third of the subjects in whom a respiratory panel was obtained. In addition, RSV was observed in one-third of the subjects and rhinovirus was found to be the most common agent. In clinical assessments, it was found that the need for HFCN was higher in RSV-positive subjects. RSV positivity ranges between 30% and 80% in patients diagnosed as having acute bronchiolitis, and RSV ranks first in many studies (11, 20, 21). In a study conducted in our country, it was observed that one-third of the subjects were RSV positive (22). In a study conducted by Ramagopal et al. (23), the subjects who were diagnosed as having bronchiolitis were divided into two groups as RSV and non-RSV, and no difference was found in terms of prematurity, physical examination findings, acute-phase reactants, and supportive oxygen treatment, whereas the hospitalization

duration was found to be significantly longer in RSV-positive subjects. In addition, recent studies showed that the number of subjects in whom rhinovirus was found was close to the number of subjects in whom RSV was found among children who presented with bronchiolitis and wheezing (24–26). In a study conducted by Janahi et al. (7), multiple viral agents were found in 33% of the subjects. In a study conducted by Kanık et al. (27), a single viral agent was found in 55.3% of the subjects, and no difference was found in hospitalization duration between the subjects with single and multiple viral agents. In our study, viral agents were evaluated in single and multiple groups, and similar agents were observed between the two groups.

In our study, it was observed that white blood cell count, CRP, MPV, neutrophil/lymphocyte ratio (NLR), and WBC/MPV values were not efficient in predicting the need for hospitalization in the ICU and need for HFCN in patients with a diagnosis of acute bronchiolitis. It has been stated that WBC and CRP values are not significant for making a diagnosis of acute bronchiolitis, and additional investigations are not necessary in outpatients (1). However, some studies showed that the CRP values were higher in patients with acute bronchiolitis compared with healthy individuals (28). Although the hospitalization duration was found to be longer in patients with increased CRP and WBC values, there are some studies showing that the WBC count was within the normal range by age in patients with acute bronchiolitis (1, 11, 29). In studies that investigated the relationship between bronchiolitis and MPV, the MPV value was found to be higher in healthy children and no difference was found between subjects who had mild, moderate, and severe bronchiolitis. It was thought that it would be more appropriate to make comparisons using follow-up MPV values in addition to instantaneous measurements of MPV values (6, 30).

In recent years, the effects of the ratios of some values in the complete blood count to each other on specifying clinical severity and predicting hospitalization process, have been investigated. As the values in the complete blood count are more easily accessible compared with other values, they are investigated in terms of efficiency of use (31). For example, NLR and the WBC/MPV ratio were found to be higher in subjects who had a diagnosis of bronchiolitis compared with healthy individuals, and neutrophil and NLR values were found to be significantly higher in subjects with severe bronchiolitis compared with subjects with mild bronchiolitis in a study involving 34 healthy children and 77 subjects with bronchiolitis. With this result, it was advocated that NLR values might have prognostic importance (28). No studies have reported the limits for these ratios; it has only been

shown that they may be higher compared with healthy individuals or with clinical severity. The fact that the number of subjects in our study was higher compared with the present literature suggested that the relationship between NLR and acute bronchiolitis should be re-evaluated with large sample sizes.

In our study, no difference was found between the subjects who received treatment methods other than hydration and oxygen therapies in terms of the need for HFCN and need for hospitalization in the ICU. The hospitalization duration was found to be significantly longer in the group that received nebulized salbutamol and intravenous steroid treatment. The AAP stated that hydration and oxygen treatment was efficient treatment for acute bronchiolitis, and many meta-analyses have shown that nebulized salbutamol and intravenous corticosteroids were not efficient in acute bronchiolitis (1, 32, 33). In addition, it has been reported that the adverse effects (tachycardia, arrhythmia) of these medical therapies used complicate clinical monitoring (1). However, some authors recommend that systemic steroid should be tried in treatment management if the picture of acute bronchiolitis cannot be differentiated from an acute asthma attack (34). In particular, hydration has been reported to be the first-line treatment to compensate dehydration occurring as a result of fever and underfeeding in children with acute bronchiolitis (35). In a study conducted by Mussman et al. (36), bronchodilator treatment and respiratory scores were compared, and no significant difference was found between the groups. Considering that clinically related factors were found to be similar between the two groups and three treatment choices of physicians were not made according to clinical severity (some patients did not receive nebulized salbutamol, though they continuously needed oxygen, and patients who received nebulized salbutamol despite never needing oxygen), the fact that need for HFCN and hospitalization in the ICU was similar in the two groups in our study supported the assumption that the approach of oxygen plus hydration therapy was sufficient in these patients as indicated in the AAP guidelines. In addition, it was thought that the process of treatment decrement prolonged hospitalization duration in the subjects in whom nebulized salbutamol and intravenous steroid treatment were initiated.

As our study was conducted by patient records, risk factors for acute bronchiolitis such as breastfeeding duration, socioeconomic level and exposure to cigarette smoking in the family, could not be evaluated due to insufficient specification. In addition, acute bronchiolitis clinical severity scores at the time of admission and at the time of discharge could not be obtained from the

patient records. Although it was found that the parameters and ratios evaluated in complete blood counts and acute-phase reactants were not efficient in predicting the need for HFCN and hospitalization in the ICU, these values were not compared with those of healthy children as done in other studies.

In conclusion, clinically related factors were evaluated in patients with acute bronchiolitis in our study and it was observed that LBW, preterm birth, a personal or family history of atopy, presence of fever, and increased acute-phase reactants were not correlated with hospitalization duration, HFCN, and hospitalization in the ICU. In addition, it was found that the hospitalization duration was longer in subjects younger than one year or in subjects with congenital heart disease, and the need for HFCN was higher in the subjects with RSV positivity, congenital heart disease or an oxygen saturation below 93% at the time of presentation. Also, it was observed that there was no difference between subjects who did and did not receive nebulized salbutamol and/or intravenous steroid in terms of the need for HFCN and hospitalization in the ICU, and the hospitalization duration was significantly longer in subjects who received these additional therapies. In light of this information, it was thought that the AAP recommendations were sufficient in general treatment approaches, and increased rate of application of these recommendations in our clinic was appropriate.

Ethics Committee Approval: Tepecik Training and Research Hospital-10.04.2019, decision No: 2019/6–13.

Informed Consent: The data were obtained from patient records, therefore informed consent was not obtained.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - Ö.Ü., B.K.D., A.K.; Design - Ö.Ü., B.K.D., K.E.; Supervision - Ö.Ü., M.H.; Funding - Ö.Ü., M.Y., H.Ö.H., Y.D.; Materials - Ö.Ü., A.K., K.E.; Data Collection and/or Processing - Ö.Ü., M.Y., H.Ö.H., Y.D.; Analysis and/or Interpretation - Ö.Ü., A.K., K.E.; Literature Review - Ö.Ü., M.Y., H.Ö.H., Y.D.; Writing - Ö.Ü., M.Y., A.K., K.E., B.K.D.; Critical Review - A.K., K.E., B.K.D., M.H.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Etik Kurul Onayı: Tepecik Eğitim ve Araştırma Hastanesi-10.04.2019, karar No:2019/6–13.

Hasta Onamı: Veriler hasta kayıtlarından elde edildi, bu nedenle hasta onamı alınmadı.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir - Ö.Ü., B.K.D., A.K.; Tasarım - Ö.Ü., B.K.D., K.E.; Denetleme - Ö.Ü., M.H.; Kaynaklar - Ö.Ü., M.Y., H.Ö.H., Y.D.; Malzemeler - Ö.Ü., A.K., K.E.; Veri Toplanması ve/veya İşlemesi - Ö.Ü., M.Y., H.Ö.H., Y.D.; Analiz ve/veya Yorum - Ö.Ü., A.K., K.E.; Literatür Taraması - Ö.Ü., M.Y., H.Ö.H., Y.D.; Yazıyı Yazan - Ö.Ü., M.Y., A.K., K.E., B.K.D.; Eleştirel İnceleme - A.K., K.E., B.K.D., M.H.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Mali Destek: Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

References

- Ralston SL, Lieberthal AS, Meissner HC, et al. Clinical Practice Guideline: The Diagnosis, Management, and Prevention of Bronchiolitis. *Pediatrics* 2014; 134: 1474–502. [CrossRef]
- Fitzgerald DA, Kilham HA. Bronchiolitis: assessment and evidence-based management. *Med J Aust* 2004; 180: 399–404. [CrossRef]
- Meissner HC. Viral Bronchiolitis in Children. *N Engl J Med* 2016; 374: 62–72. [CrossRef]
- Mansbach JM. Clinical features can help predict which infants with bronchiolitis will need hospital admission. *J Pediatr* 2012; 160: 174–5. [CrossRef]
- Florin TA, Plint AC, Zorc JJ. Viral bronchiolitis. *Lancet* 2017; 389: 211–24. [CrossRef]
- Ergül AB, Altuner Torun Y, Uytun S, Aslaner H, Paç Kısaaslan A, Şerbetçi MC. Reduction in mean platelet volume in children with acute bronchiolitis. *Türk Pediatri Ars* 2016; 51: 40–5. [CrossRef]
- Janahi I, Abdulkayoum A, Almeshwesh F, Alkuwari M, Hammadi A, Alameri M. Viral aetiology of bronchiolitis in hospitalised children in Qatar. *BMC Infect Dis* 2017; 17: 139. [CrossRef]
- Skjerven HO, Hunderi JO, Brüggmann-Pieper SK, et al. Racemic adrenaline and inhalation strategies in acute bronchiolitis. *N Engl J Med* 2013; 368: 2286–93. [CrossRef]
- Fernandes RM, Bialy LM, Vandermeer B, et al. Glucocorticoids for acute viral bronchiolitis in infants and young children. *Cochrane Database Syst Rev* 2013; 2013: CD004878. [CrossRef]
- Yalçın E, Karadağ B, Uzuner N, ve ark. Türk Toraks Derneği Akut Bronşiyolit Tanı ve Tedavi Uzlaşı Raporu. *Turkish Thoracic J* 2009; 10: 3–7.
- Özköse R. Akut bronşiyolit ön tanısı ile yatarak tedavi gören hastaların retrospektif olarak incelenmesi. *Uzmanlık Tezi. T.C. Sağlık Bakanlığı Haydarpaşa Numune Eğitim ve Araştırma Hastanesi*. 2008.
- Benigno V, Cusimano RA, Colanino G, Basile A, Varia F, Grutta S. Is appearance of bronchiolitis affected by environmental and genetic factors? [Article in Italian]. *Pediatr Med Chir* 1991; 13: 155–7.
- Turan S, Nalbantoğlu B, Çelik Güzel E, Nalbantoğlu A, Hatipoğlu S. Evaluation of Socioeconomic Status of Bebebs With Acute Bronchiolitis. *Child J* 2013; 13: 29–35.
- Nenna R, Cutrera R, Frassanito A, et al. Modifiable risk factors associated with bronchiolitis. *Ther Adv Respir Dis* 2017; 11: 393–401. [CrossRef]
- Karakoç F, Dağlı E. Bronşiyolit Tanı ve Tedavisi. *Çocuk Göğüs Hastalıkları* 2007; 133–7.
- Albernaz Ep, Menezes AM, Cesar JA, Victora CG, Barros FC, Halpern R. Risk factors associated with hospitalization for bronchiolitis in the post-neonatal period. [Article in Portuguese]. *Rev Saude Publica* 2003; 37: 485–93. [CrossRef]
- Bar-Oz B, Netzer D, Arad I. Rehospitalization of very-low-birth-weight infants after discharge from neonatal intensive care units. [Article in Hebrew]. *Harefuah* 1995; 128: 687–9, 743.
- Okutan Ö, Çelik, C. Akut bronşiyolitlerde güncel bilgiler. *Sted/ Sürekli Tıp Eğitimi Derg* 2005; 14: 5–7.
- Yoon PW, Black RE, Moulton LH, Becker S. The effect of malnutrition on the risk of diarrheal and respiratory mortality in children <2 y of age in Cebu, Philippines. *Am J Clin Nutr* 1997; 65: 1070–7. [CrossRef]
- McMillan JA, Tristram DA, Weiner LB, Higgins AP, Sandstrom C, Brandon R. Prediction of the duration of hospitalization in patients with respiratory syncytial virus infection: use of clinical parameters. *Pediatrics* 1988; 81: 22–6.
- Wennergren G, Hansson S, Engström I, et al. Characteristics and prognosis of hospital treated obstructive bronchitis in children ages less than two years. *Acta Paediatr* 1992; 81: 40–5. [CrossRef]
- Ertem E, Tanaç R, Çoker M. Akut bronşiyolit ve respiratuar sinsisyal virüs. *T Klin Pediatri* 1996; 5: 602.
- Ramagopal G, Brow E, Mannu A, Vasudevan J, Umadevi L. Demographic, Clinical and Hematological Profile of Children with Bronchiolitis: A Comparative Study between Respiratory Syncytial Virus [RSV] and [Non RSV] Groups. *J Clin Diagn Res* 2016; 10: SC05–8. [CrossRef]
- Nicolai A, Frassanito A, Nenna R, et al. Risk Factors for Virus-induced Acute Respiratory Tract Infections in Children Younger Than 3 Years and Recurrent Wheezing at 36 Months Follow-Up After Discharge. *Pediatr Infect Dis J* 2017; 36: 179–83. [CrossRef]
- Midulla F, Nicolai A, Ferrara M, et al. Recurrent wheezing 36 months after bronchiolitis is associated with rhinovirus infections and blood eosinophilia. *Acta Paediatr* 2014; 103: 1094–9. [CrossRef]
- Wu JJ, Jin Y, Lin N, et al. Detection of human bocavirus in children with acute respiratory tract infections in Lanzhou and Nanjing, China. *Biomed Environ Sci* 2014; 27: 841–8.

27. Kanık A, Eliaçık K, Koyun B, et al. Viral Etiology of Acute Bronchiolitis in Hospitalized Infants and the Effect on Clinical Course. *J Pediatr Inf* 2016; 10: 93–8. [\[CrossRef\]](#)
28. Çelik Güzel E, Fidan Ç, Güzel S, Paketçi C, Çelikkol ÜA. Bronşiolitli çocuklarda hastalık aktivitesinin değerlendirilmesinde nötrofil/lenfosit oranı yeni bir biyobelirteç olabilir mi? *Namık Kemal Tıp Dergisi* 2019; 7: 13–8.
29. Payne CB. Bronchiolitis, *Pediatric Respiratory Disease: Diagnosis and treatment*. WB Saunders Company, Philadelphia 1993.p.205–18.
30. Thorburn K, Fulton C, King C, Ramaneswaran D, Alammara A, McNamara PS. Transaminase levels reflect disease severity in children ventilated for respiratory syncytial virus (RSV) bronchiolitis. *Sci Rep* 2018; 8: 1803. [\[CrossRef\]](#)
31. Kartal O, Kartal AT. Value of neutrophil to lymphocyte and platelet to lymphocyte ratios in pneumonia. *Bratisl Lek Listy* 2017; 118: 513–6. [\[CrossRef\]](#)
32. Garrison MM, Christakis DA, Harvey E, Cummings P, Davis RL. Systemic corticosteroids in infant bronchiolitis: A meta-analysis. *Pediatrics* 2000; 105: E44. [\[CrossRef\]](#)
33. Ricci V, Delgado Nunes V, Murphy MS, Cunningham S; Guideline Development Group and Technical Team. Bronchiolitis in children: summary of NICE guidance. *BMJ* 2015; 350: h2305. [\[CrossRef\]](#)
34. Bülow SM, Nir M, Levin E, et al. Prednisolone treatment of respiratory syncytial virus infection: a randomized controlled trial of 147 infants. *Pediatrics* 1999; 104: e77.
35. Yıldırım Ş, Kaymaz N, Topaloğlu N, et al. Do we really ponder about necessity of intravenous hydration in acute bronchiolitis? *Colombia Médica* 2016; 47: 21–4. [\[CrossRef\]](#)
36. Mussman GM, Sahay RD, Destino L, Lossius M, Shadman KA, Walley SC. Respiratory Scores as a Tool to Reduce Bronchodilator Use in Children Hospitalized With Acute Viral Bronchiolitis. *Hosp Pediatr* 2017; 7: 279–86. [\[CrossRef\]](#)