Research Article

Treatment of Infants Admitted With Acute Bronchiolitis and its Comparison with Modern Treatment Methods in the Only University Hospital in Rafsanjan

Zahra Kamiab[1] , **Nahid Masoodpoor**[2*] , **Zeinab Hassani Kabotarkhani**[3]

[1]Department of Family Medicine, School of Medicine; Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
[2]Department of Pediatrics, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
[3]School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

Abstract

Background: Various treatment approaches are used in different centers to treat infant bronchiolitis, some of which are not indicated and are not based on strong scientific evidence. W aimed to evaluate the treatment of admitted infants with acute bronchiolitis in the only medical hospital in Rafsanjan and compare it with modern treatment methods.

Methods: This descriptive study was conducted on 100 infants admitted to Ali-Ibn Abi Talib hospital in Rafsanjan, southern Iran. Demographic information and risk factors, including age, birth weight, history of exposure to cigarette smoke, and other factors affecting this disease, and all therapeutic measures were collected in a researcher-made checklist. The data were analyzed using SPSS software, version 20, and the treatment was compared to the latest clinical guidelines of the American Academy of Pediatrics (AAP) and England National Institute for Health and Care Excellence (NICE), and Cochrane meta-analyses.

Results: 79%, 37%, 41%, and 3% of the children received antibiotics, corticosteroids, bronchodilators, and epinephrine, respectively. The most important risk factors were smoking in parents (91%), malnutrition (60%), low birth weight (71%), male sex (62%), and being born in autumn (60%).

Conclusion: According to the results of this study, there is a large gap between treatment approaches and up-to-date and valid international guidelines. Therefore, compiling local treatment and care instructions for these patients to be used in medical centers would be useful.

Keywords: Acute bronchiolitis, Infants, Drug therapy, Guidelines; Rafsanjan

***Correspondence to**
Nahid Masoodpoor,
Email: dr-masoodpoor@
yahoo.com

Open Access
Scan to access more
free content

Background

Lower respiration infection is one of the most common causes of hospital admission in children under the age of two, and acute bronchiolitis is found in about 18% of children under the age of 12 months (1). According to the World Health Organization (WHO), about 150 million people around the world are affected by this disease annually, especially in the winter, of which 95% occur in developing countries (2). The main cause of this disease is the respiratory syncytial virus (RSV) in 75% of the cases, but other viruses such as the influenza virus, par influenza, mycoplasma, and some adenoviruses can also be involved in its development (3, 4). During the acute stage of bronchiolitis, the infected virus gives an inflammatory response that leads to edema and infiltration of inflammatory cells into the lower airways (5). In general, the first wheezing attack in children aged 2 to 24 months and lack of cause for wheezing along with symptoms such as fever, coughing, apnea, subcostal retractions, tachypnea, heart rate increase, and oxygen saturation decrease are considered as bronchiolitis (6). Bronchiolitis is a self-limiting disease and does not require admission in healthy infants (7). Based on the results of previous studies, usually about 7%-13% of the children require admission, and the mean length of stay in the hospital is about 1 day (range: 0-3) (8, 9), and the odds of being admitted in groups with known risk factors is high. These risk factors include chronic lung disease, chronic heart failure, immunodeficiency, low birth weight, early birth, nervous system abnormalities and other birth disorders, birth in the winter, malnutrition, exposure to cigarette smoke or tobacco, lack of breastfeeding, multifetal pregnancy, cerebral palsy, Down syndrome and cystic fibrosis (10, 11). RSV infection usually resolves within two weeks, while immunocompromised hosts can retain and spread the virus for several months. Although a relatively short, self-limiting infection, RSV bronchiolitis causes chronic respiratory complications in some children, especially in the form of recurrent episodes of wheezing that often lead to the diagnosis of

asthma in the first decade of life (12).

A review of the studies revealed that different centers use different therapeutic approaches, such as the use of corticosteroids, bronchodilators, racemic epinephrine, antibiotics, ribavirin, hypertonic saline, and physical therapeutic techniques (13) for control of the disease. Oxygen therapy is indicated in children with low hemoglobin saturation (14). There is insufficient evidence to support the routine use of bronchodilators in bronchiolitis (15). Racemic epinephrine may be more appropriate than salbutamol or a placebo in an emergency, but there is little evidence of its use in the admitted population (16). Secondary bacterial infection is also uncommon in bronchiolitis, so the use of antibiotics is unnecessary unless the severe clinical condition requires intensive care unit (ICU) admission (17). Inhalation or systemic corticosteroids are also not recommended in many studies (18, 19). According to numerous evidence since 1950, supportive therapies have been most effective, and the prescription of some of these treatments is not indicated and is not based on strong scientific evidence, or their use has been accompanied by an increase in the length of hospital stay without reducing the chance of readmission (9).

Objectives

We aimed to evaluate the most common risk factors for acute bronchiolitis in infants and to evaluate the treatment used and compared it with different modern therapeutic approaches used in children with acute bronchiolitis admitted to a university hospital.

Methods

This descriptive study was conducted in the only teaching hospital in Rafsanjan city. All infants who were diagnosed with acute bronchiolitis and admitted to the pediatric ward of Ali-Ibn Abi Talib Hospital in Rafsanjan in the second half of 2016 (n = 100) were included by census method. It should be noted that Rafsanjan city is located in the north of Kerman province and has a rural and urban population of 270 000 and this hospital is the only public hospital in this area, and patients of this city refer to it. The diagnosis of acute bronchiolitis was based on specialized physicians' diagnosis based on the symptoms of coughing, runny nose, wheezing, and a clinical examination based on the hearing of the wheezing in the entire lungs and the rejection of other differential diagnoses (20).

Patients' information was collected in a researcher-made checklist after obtaining their consent and ensuring the confidentiality of their information. After receiving the Ethics Committee Code (IR.RUMS.REC.1394.216), a written informed consent form was taken before entering the study. The checklist information includes age, sex, gestational age, birth weight, nutrition, birth season, birth rank, history of exposure to cigarette or tobacco smoke, history of chronic lung and heart disease, and other diseases affecting the course of the disease and the weight growth status of infant, as well as all necessary therapeutic actions were performed on the patient and admission time.

Given the high cost of diagnostic procedures for diseases such as chronic lung disease, chronic heart failure, immunodeficiency, abnormal nervous system and other congenital malformations, cerebral palsy, Down syndrome, and cystic fibrosis, diagnosis of the mentioned cases was made only on the basis of interview, self-declaration of parents and, if possible, clinical examination. The risk factor for malnutrition was also investigated by the researcher by examining growth charts related to infants.

The inclusion criteria were living in Rafsanjan city and surrounding villages, the age range of infants and children up to 24 months, having informed consent to participate in the study. The exclusion criteria were an incomplete checklist, infant death during the study, and transferring the patient to another center for any reason. The data were analyzed using SPSS software, version 20. After ensuring the accuracy of data entry, they were analyzed using descriptive statistics.

Results

We studied 100 admitted infants, 62 (62%) of whom were boys, and 38 (38%) were girls. The mean ± SD age of the infants was 107 ± 10.60 days (range: 10 to 605 days). 70% of the children were exclusively breastfed. Also, infection was most prevalent in children under three months (34%), and infection was more common in boys (62%), infants born in autumn (60%), malnourished infants (60%), infants with history of exposure to cigarette smoke (91%), and infants with low birth weight (71%). Heart failure, cerebral palsy, Down syndrome, cystic fibrosis, and immunodeficiency were not seen in any of the patients, and a history of chronic lung disease was reported in only 4% of the patients. In the present study, the most common age groups in infants were less than 50 days (34%) followed by 50-100 days (24%). Also, 22% of the infants were preterm (Table 1).

With respect to treatment, we found that in addition to supportive treatments such as liquid therapy (93%) and oxygen therapy (37%), 79% of the infants received antibiotics, 37% received corticosteroids, 41% received bronchodilators, and 3% received epinephrine (Table 2).

Discussion

The main objective of this study was to evaluate the treatment of children with acute bronchiolitis. Besides supportive therapies, such as liquid therapy and oxygen therapy, 79% of the infants received antibiotics, 37% received corticosteroids, 41% received bronchodilators, and 3% received epinephrine. Since 1950, all effective

Table 1. Demographic Variables and Risk Factors in Infants With Acute Bronchiolitis

Variable	No. (%)
Age (days)	
1-50	34 (34)
100-51	24 (24)
150-101	13 (13)
200-151	16 (16)
≥ 200	13 (13)
Birth rank	
1	29 (29)
2	34 (34)
3	25 (25)
4	7 (7)
≥5	5 (7)
Birth season	
Spring	4 (4)
Summer	13 (13)
Autumn	60 (60)
Winter	23 (23)
Gestational age	
Term	78 (78)
Preterm	22 (22)
Gender	
Girls	38 (38)
Boys	62 (62)
Malnutrition	
Yes	60 (60)
No	40 (40)
Nutrition	
Breastfeed	70 (70)
Others	30 (30)
Exposure to smoke	
Yes	91 (91)
No	9 (9)
Low birth weight	
Yes	71 (71)
No	29 (29)
History of chronic lung disease	
Yes	4 (4)
No	96 (96)
heart failure / cerebral palsy/ down syndrome/ cystic fibrosis/ immunodeficiency	
Yes	0 (0)
No	100 (100)

Table 2. Frequency of Therapeutic Interventions and Admission Time in Admitted Infants With Acute Bronchiolitis

Variable	No. (%)
Antibiotic therapy	79 (79)
Epinephrine	3 (3)
Corticosteroids	37 (37)
Serum Therapy	93 (93)
Oxygen therapy	37 (37)
Bronchodilators	41 (41)
Fumigation	27 (27)
Admission time (days)	
1-3 days	59 (59)
4-6 days	34 (34)
7-8 days	7 (7)

therapies for acute bronchiolitis have been largely supportive (9). In fact, the most important innovation in the treatment of acute bronchiolitis was a non-invasive supportive treatment of oxygen supply through the nasal cannula, which was safe, feasible, and cost-effective. Additionally, based on the latest clinical guidelines provided by the American Academy of Pediatrics (AAP) (21) and the National Institute of Health Care (NICE) (22), when the oxygen saturation is less than 90% (AAP) or 92% (NICE) of the reference level, nasogastric or intravenous prescription of oxygen supplementation and oral fluid therapy are recommended.

The important point is that both the AAP and NICE guidelines agree on avoiding the use of antibiotics, hypertonic saline, montelukast, ipratropium bromide, unstable albuterol, salbutamol, adrenaline, and prescription of systemic and inhaled corticosteroids and anti-viruses. Moreover, in examining the Cochrane meta-analyses, the prescription of antibiotics did not affect the disease (23), and the use of bronchodilators in the treatment of acute bronchiolitis had no effect on oxygen saturation and did not reduce hospital admissions or shorten the admission time in infants (24). It should be noted that the main reference for pediatric medicine also states that antibiotics should not be used in patients with bronchiolitis, except for cases susceptible to bacterial infection. Reviewing the literature on the prediction of effective treatments in the future can help prevent the onset of acute bronchiolitis because of the mass production of an RSV vaccine, which is under further clinical studies (25). Another ideal strategy in the treatment of acute bronchiolitis in the future is the use of antiviral drugs (26) or an herbal mucolytic drug, which is able to destroy the terminal bronchioles. Moreover, many studies have been reported on the use of DNAase, and their results are still being discussed (27, 28).

In contrast to these guidelines, which have a high level of evidence, several studies have shown wide variation

in the diagnosis and treatment of acute bronchiolitis. Studies in the United States, Canada, and the Netherlands have shown that there are many different treatments that may be more related to physicians' preferences than the severity of the disease. In fact, this variable pattern indicates a lack of consensus or lack of knowledge among physicians about best practices (29-31). As shown in the results of the present study in the evaluation of treatment, other than supportive therapies such as fluid therapy (93%) and oxygen therapy (37%), children were treated with considerable amounts of antibiotics, corticosteroids, bronchodilators, and a small percentage of epinephrine. Therefore, there is a large gap between the methods and treatment approaches of this center with up-to-date and valid international guidelines.

The main risk factors associated with the incidence of acute bronchiolitis in the present study included smoking by parents (91%), malnutrition (60%), the peak age of incidence of diseases under three months, and male sex. In addition, 22% of the infants were preterm, and 30% were fed with milk other than breast milk. Hubble and Osborne explained the clinical aspects of acute bronchiolitis in the British Medical Journal for the first time in 1941. They introduced the disease as a disease associated with influenza in children aged less than 2 years. They also reported that its incidence was associated with social components affecting health, such as belonging to poor classes, malnutrition, living in limited space, and close exposure to infections (32).

In a study conducted on 304 infants with acute bronchiolitis, a history of preterm birth significantly led to poor treatment outcomes and increased need for mechanical ventilation ($P = 0.002$), more ICU admissions, and increased admission time ($P = 0.021$ and $P < 0.0001$) in infants (33). Also, in a study on 1814 children, non-breastfed children were at a higher risk of admission because of acute bronchiolitis (HR: 1.57; 95% CI: 1.00-2.48) (34). The direct effect of smoking by parents on the development of asthma and acute bronchiolitis in children was reported in a meta-analysis (35). In a study published in Mexico in 2018, the odds ratio of acute bronchiolitis in children exposed to smoking was also more than that of other children (OR, 3.5; 95% CI, 1.99-6.18; $P = 0.0001$) (36).

Conclusion

In this study, the large gap between treatment methods and approaches with up-to-date and valid international guidelines and the lack of native guidelines, as well as the high prevalence of risk factors such as exposure to cigarette smoke and malnutrition, required better education of mothers in areas such as child nutrition, education, the provision of smoking cessation facilities for parents, and the promotion of breastfeeding. Also, compiling local treatment and care instructions for these patients to be used in medical centers would be useful.

References

1. Hasegawa K, Tsugawa Y, Brown DF, Mansbach JM, Camargo CA Jr. Trends in bronchiolitis hospitalizations in the United States, 2000-2009. Pediatrics. 2013;132(1):28-36. doi: 10.1542/peds.2012-3877.

2. Rudan I, Boschi-Pinto C, Biloglav Z, Mulholland K, Campbell H. Epidemiology and etiology of childhood pneumonia. Bull World Health Organ. 2008;86(5):408-16. doi: 10.2471/blt.07.048769.

3. Tregoning JS, Schwarze J. Respiratory viral infections in infants: causes, clinical symptoms, virology, and immunology. Clin Microbiol Rev. 2010;23(1):74-98. doi: 10.1128/cmr.00032-09.

4. Schiller O, Levy I, Pollak U, Kadmon G, Nahum E, Schonfeld T. Central apnoeas in infants with bronchiolitis admitted to the paediatric intensive care unit. Acta Paediatr. 2011;100(2):216-9. doi: 10.1111/j.1651-2227.2010.02004.x.

5. Simoes EA. Respiratory syncytial virus infection. Lancet. 1999;354(9181):847-52. doi: 10.1016/s0140-6736(99)80040-3.

6. Faghihlou E, Rezaei F, Salemi V, Nasseri M, Mamishi S, Mahmoodi M, et al. A study of human respiratory syncytial virus genotypes in children less than 5 years of age with acute respiratory symptoms in 2007 and 2009. J Ilam Univ Med Sci. 2010;18(3):69-78. [Persian].

7. Thiyagarajan P, Bala Gopal M, Ghosh SK, Sarkar M. To study the efficacy of non-invasive ventilation in severe bronchiolitis. IntJ Pediatr Res. 2017;4(2):108-114. doi: 10.17511/ijpr.2017.i02.03.

8. Murray J, Bottle A, Sharland M, Modi N, Aylin P, Majeed A, et al. Risk factors for hospital admission with RSV bronchiolitis in England: a population-based birth cohort study. PLoS One. 2014;9(2):e89186. doi: 10.1371/journal.pone.0089186.

9. Castro-Rodriguez JA, Rodriguez-Martinez CE, Sossa-Briceño MP. Principal findings of systematic reviews for the management of acute bronchiolitis in children. Paediatr Respir Rev. 2015;16(4):267-75. doi: 10.1016/j.prrv.2014.11.004.

10. Teshome G, Gattu R, Brown R. Acute bronchiolitis. Pediatr Clin North Am. 2013;60(5):1019-34. doi: 10.1016/j.pcl.2013.06.005.

11. 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(9725):1545-55. doi: 10.1016/s0140-6736(10)60206-1.

12. Wright M, Mullett CJ, Piedimonte G. Pharmacological management of acute bronchiolitis. Ther Clin Risk Manag. 2008;4(5):895-903. doi: 10.2147/tcrm.s1556.

13. Huntzinger A. AAP Publishes recommendations for the diagnosis and management of bronchiolitis. Am Fam Physician. 2007;75(2):265-7.

14. Zorc JJ, Hall CB. Bronchiolitis: recent evidence on diagnosis and management. Pediatrics. 2010;125(2):342-9. doi: 10.1542/peds.2009-2092.

15. Gadomski AM, Brower M. Bronchodilators for bronchiolitis. Cochrane Database Syst Rev. 2010(12):CD001266. doi: 10.1002/14651858.CD001266.pub2.

16. Hartling L, Bialy LM, Vandermeer B, Tjosvold L, Johnson DW, Plint AC, et al. Epinephrine for bronchiolitis. Cochrane Database Syst Rev. 2011(6):CD003123. doi: 10.1002/14651858.CD003123.pub3.

17. Tahan F, Ozcan A, Koc N. Clarithromycin in the treatment of RSV bronchiolitis: a double-blind, randomised, placebo-controlled trial. Eur Respir J. 2007;29(1):91-7. doi: 10.1183/09031936.00029206.

18. Patel H, Platt R, Lozano JM, Wang EE. Glucocorticoids for acute viral bronchiolitis in infants and young children. Cochrane Database Syst Rev. 2004(3):CD004878. doi: 10.1002/14651858.cd004878.

19. Ermers MJ, Rovers MM, van Woensel JB, Kimpen JL, Bont LJ. The effect of high dose inhaled corticosteroids on wheeze in infants after respiratory syncytial virus infection: randomised double blind placebo controlled trial. BMJ. 2009;338:b897. doi: 10.1136/bmj.b897.

20. Ralston SL, Lieberthal AS, Meissner HC, Alverson BK, Baley JE, Gadomski AM, et al. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. Pediatrics. 2014;134(5):e1474-502. doi: 10.1542/peds.2014-2742.

21. National Institute for Health and Care Excellence (NICE). Bronchiolitis in Children. London: NICE; 2015.

22. Farley R, Spurling GK, Eriksson L, Del Mar CB. Antibiotics for bronchiolitis in children under two years of age. Cochrane Database Syst Rev. 2014(10):CD005189. doi: 10.1002/14651858.CD005189.pub4.

23. Gadomski AM, Scribani MB. Bronchodilators for bronchiolitis. Cochrane Database Syst Rev. 2014;2014(6):CD001266. doi: 10.1002/14651858.CD001266.pub4.

24. Marcdante K, Kliegman R. Nelson Essentials of Pediatrics. 8th ed. Elsevier; 2018. p. 402.

25. Chiu C. Novel immunological insights in accelerating RSV vaccine development. Vaccine. 2017;35(3):459-60. doi: 10.1016/j.vaccine.2016.11.069.

26. Simões EA, DeVincenzo JP, Boeckh M, Bont L, Crowe JE Jr, Griffiths P, et al. Challenges and opportunities in developing respiratory syncytial virus therapeutics. J Infect Dis. 2015;211 Suppl 1:S1-S20. doi: 10.1093/infdis/jiu828.

27. Nenna R, Tromba V, Berardi R, De Angelis D, Papoff P, Sabbatino G, et al. Recombinant human deoxyribonuclease treatment in hospital management of infants with moderate-severe bronchiolitis. Eur J Inflamm. 2009;7(3):169-74. doi: 10.1177/1721727x0900700307.

28. Enriquez A, Chu IW, Mellis C, Lin WY. Nebulised deoxyribonuclease for viral bronchiolitis in children younger than 24 months. Cochrane Database Syst Rev. 2012;11(11):CD008395. doi: 10.1002/14651858.CD008395.pub2.

29. Willson DF, Horn SD, Hendley JO, Smout R, Gassaway J. Effect of practice variation on resource utilization in infants hospitalized for viral lower respiratory illness. Pediatrics. 2001;108(4):851-5. doi: 10.1542/peds.108.4.851.

30. Wang EE, Law BJ, Boucher FD, Stephens D, Robinson JL, Dobson S, et al. Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) study of admission and management variation in patients hospitalized with respiratory syncytial viral lower respiratory tract infection. J Pediatr. 1996;129(3):390-5. doi: 10.1016/s0022-3476(96)70071-9.

31. Brand PL, Vaessen-Verberne AA. Differences in management of bronchiolitis between hospitals in The Netherlands. Dutch Paediatric Respiratory Society. Eur J Pediatr. 2000;159(5):343-7. doi: 10.1007/s004310051284.

32. Hubble D, Osborn GR. Acute bronchiolitis in children. Br Med J. 1941;1(4177):107-26.1. doi: 10.1136/bmj.1.4177.107.

33. Horn SD, Smout RJ. Effect of prematurity on respiratory syncytial virus hospital resource use and outcomes. J Pediatr. 2003;143(5 Suppl):S133-41. doi: 10.1067/s0022-3476(03)00509-2.

34. Lanari M, Prinelli F, Adorni F, Di Santo S, Faldella G, Silvestri M, et al. Maternal milk protects infants against bronchiolitis during the first year of life. Results from an Italian cohort of newborns. Early Hum Dev. 2013;89 Suppl 1:S51-7. doi: 10.1016/s0378-3782(13)70016-1.

35. Jones LL, Hashim A, McKeever T, Cook DG, Britton J, Leonardi-Bee J. Parental and household smoking and the increased risk of bronchitis, bronchiolitis and other lower respiratory infections in infancy: systematic review and meta-analysis. Respir Res. 2011;12(1):5. doi: 10.1186/1465-9921-12-5.

36. Robledo-Aceves M, Moreno-Peregrina MJ, Velarde-Rivera F, Ascencio-Esparza E, Preciado-Figueroa FM, Caniza MA, et al. Risk factors for severe bronchiolitis caused by respiratory virus infections among Mexican children in an emergency department. Medicine (Baltimore). 2018;97(9):e0057. doi: 10.1097/md.0000000000010057.