Viral Aetiology of Bronchiolitis in Hospitalised Children in a Tertiary Center in Tehran

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ABSTRACT

One of the causes of infants' hospitalizations is bronchiolitis, while different viral agents could be causative agents. As there is little information regarding the common agents of bronchiolitis in Iranian infants, we designed this study to determine which agents were responsible for hospitalization due to bronchiolitis among infants in an Iranian tertiary center. Two hundred and three infants with bronchiolitis who were hospitalized in Bahrani hospital were enrolled. Data regarding age, sex, duration of hospitalization, exposure to smoking, previous antibiotic usage and fever were collected for all enrolled cases. Throat sample by means of soap was collected and rapid test with immunochromatography (IC) test was performed. Rapid test was positive in 59 (29%) cases and three cases had concomitant infection with two viruses. The most common viral agent was RSV (Respiratory Syncytial Virus). Mean age was significantly lower in cases with RSV or RSV+ adenovirus infectious in comparison with other two groups (adenovirus or influenza only), while mean duration of hospitalization was significantly longer in RSV/RSV+ adenovirus group. RSV is the most common viral etiology of bronchiolitis in Iranian infants less than one year old, which is related with younger age and longer duration of hospitalization.

Keywords: bronchiolitis, infants, Iran.

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INTRODUCTION

Bronchiolitis is one of the causes of emergency department visits and hospitalization for infants under the age of two (1, 2). One in nine infants develops bronchiolitis in the first year of life, which will result in hospitalization and increased mortality (3, 4). Clinical presentation depends on age, sex, immune response, previous history of bronchiolitis, environmental factors, and immune system response to infection (5). Inflammation, edema, airways epithelial cells necrosis, secretion of mucus, and bronchospasm are manifestations of bronchiolitis (6). Clinical manifestations mimic common cold, including runny nose, mild fever, and cough (7). The most common etiologic agent is the respiratory syncytial virus (RSV), which is severe and likely to involve the lower respiratory tract (8). Other agents, including parainfluenza virus, rhinovirus, adenovirus and influenza A and B, are less common than RSV (9). As there is little information regarding common agents of bronchiolitis in Iranian infants, we designed this study to determine which agents were responsible for hospitalization due to bronchiolitis among infants in an Iranian tertiary center. □

MATERIAL AND METHODS

This cross sectional study was conducted in Bahrami children hospital (affiliated to Tehran University of Medical Sciences) between January 2015 and March 2017.

Inclusion criteria were age less than one year and final diagnosis of bronchiolitis, and exclusion criteria were diagnosis of asthma, sinusitis, otitis, reflux disease, pneumonia and congenital airway anomalies.

All parents were asked to fill informed consent forms before study entrance. The study was approved by the local ethics committee.

Data regarding age, sex, duration of hospitalization, exposure to smoking, previous antibiotic usage and fever were collected for all enrolled cases.

Throat sample by means of soap was collected and a rapid test based on immunochromatography (IC) was performed.

Data analysis was conducted with SPSS software version 22 (IBM, Chicago, IL, USA).

Data were presented as Mean $\pm$ SD for continuous variables or frequencies for categorical variables. Chi square test with Fisher's exact test were used for comparison of categorical variables. Independent sample t test was used to compare continuous variables. P value 0.05 was considered as significant. □

RESULTS

Two hundred and three cases were enrolled. Mean age was 5.6 ± 3.1 months, 115 (56.7%) were males and 88 (43.3%) females (male to female ratio 1.3). Fever was present in 173 (85.2%) of all subjects and 22 (10.8%) had smoking exposure at home. Seventy two cases (35.5%) received antibiotics before hospitalization. The rapid test was positive in 59 (29%) cases and three cases had concomitant infection with two viruses. Frequencies of virus infections are summarized in Table 1.

No (frequency)	Positive rapid test
39 (66%)	RSV
11 (18.6%)	Adenovirus
3 (5%)	RSV + adenovirus
6 (10%)	Influenza

TABLE 1. Frequency of infection with different viruses

Age, frequency of fever, and duration of hospitalization were significantly different between rapid test positive and negative groups (Table 2).

	Positive test	Negative test	P value
Age (months)	0.002	6 ± 3.1	4.5 ± 2.9
Sex			
Female	26 (44.1%)	62 (43.1%)	0.89
Male	33 (55.9%)	82 (56.9%)	
Exposure to cigarette	0.42	14 (9.7%)	8 (13.6%)
Fever	55 (93.2%)	0.04	118 (81.9%)
History of antibiotic usage	22 (37.3%)	0.72	50 (34.7%)
Duration of hospitalization	5.5 ± 1.5	0.001	3.2 ± 1.1

TABLE 2. Sex distribution in both groups

Mean age was significantly lower in cases with RSV or RSV+ adenovirus infectious in comparison with other two groups, while mean duration of hospitalization was significantly longer in RSV/RSV+ adenovirus group (Table 3).

	RSV/RSV+adenovirus N= 42	Adenovirus N=14	Influenza N=6	P value
Age (months)	0.002	6.8±3.3	6.2±2.9	3.6±2.4
Sex				
Female	18 (42.9%)	8 (57.1%)	2 (33.3%)	
Male	24 (57.1%)	6 (42.9%)	4 (66.7%)	
Exposure to cigarette	7 (16.7%)	1 (7.1%)	2 (33.3%)	NS
Fever	40 (95.2%)	5 (85.7%)	6 (100%)	NS
Time of hospitalization				NS
Spring	1 (2.4%)	5 (35.7%)	0	
Summer	1 (2.4%)	2 (14.3%)	0	
Autumn	12 (28.6%)	2 (14.3%)	2 (33.3%)	
Winter	28 (66.7%)	5 (35.7%)	6 (66.7%)	
History of antibiotic usage	28 (59.6%)	4 (28.6%)	2 (33.3%)	NS
Duration of hospitalization	5.9±1.6	4.8±1.3	4.3±0.8	0.01

TABLE 3. Age distribution in both groups

Bronchiolitis is one of the main causes of hospitalization and infant mortality, and factors such as young age of the mother, low birth weight, live birth order, low 5-min Apgar score were associated with bronchiolitis (10). The most common virus responsible for infant bronchiolitis is RSV infection (10). It was reported that 50-80% of bronchiolitis related hospitalizations were due to RSV(10).

The results of the current study showed that the most frequent etiologic agents of bronchiolitis in enrolled infants were RSV and adenovirus. Frequency of fever and duration of hospitalization were significantly higher in cases with positive rapid test. In this study, 19% of all hospitalizations were due to RSV, which is in agreement with the report of Milani, who detected a RSV infection in 19% of children with acute respiratory infection who were hospitalized in six pediatric hospitals (11). In the study of Uduman *et al.*, 90% RSV of positive patients were infants (12). In their retrospective analysis, Janahi *et al.* found that at least one virus was responsible of bronchitis in 85% of enrolled cases, and RSV, followed by rhinovirus (RV) were the most common etiologic agents (13). This finding is in agreement with previous studies, which showed that RSV was the most common etiologic agent of bronchiolitis in children (14-16).

Our results showed that most RSV infections occurred in winter and autumn. The peak outbreak of RSV infection is in winter and RSV is responsible for most hospitalizations in winter and spring (17). Rivera-Sepulveda *et al* found that most RSV related hospitalizations occurred in September through December (18). In temperate

countries, RSV mostly peaks during late fall and winter, while in tropical and semi-tropical regions, RSV occurs throughout the year, especially in rainy season (19-21). Our results also showed that the mean age of patients with RSV/RSV+ adenovirus infection was significantly lower than other two groups, while the mean duration of hospitalization stay was significantly longer in RSV/RSV+ adenovirus group. In Janahi *et al.*'s study, the duration of hospitalization was longer for cases with RSV infection (13). Other authors found that there was significant association between RSV genomic load and longer duration of hospitalization (22). In Garcia *et al.*'s study, the mean age of infants with RSV infection was 6.3 months and that of non-RSV group eight months, whereas the median duration of hospitalization was three days in the RSV group and two days in the non-RSV group (9). Similarly to previous studies, male subjects were more likely to have bronchiolitis than female ones, the male to female ratio being 1.3 in our study, while in Janahi *et al.*'s study it was almost 2, which was in agreement with Gupta *et al.*'s findings (23). This could be due to narrower peripheral airways in male infants than female ones.

Bronchiolitis is one of the most common causes of hospitalization in infants under the age of two, which may be often triggered by bacteria, fungi and virus infection (13). It is a self limiting disease, and the rate of bronchiolitis related hospitalization has been increasing lately (13). Childhood respiratory infection could be a predisposing factor of chronic respiratory diseases.

RSV is the most frequent viral agent that accounts for 50-90% of all cases (13). In a study conducted in Sweden, infants with bronchiolitis were followed up to ages 7 and 13, and asthma was found in 30% of all subjects at age 7 and in 37% at age 13 (24).

So, proper management of bronchiolitis at younger age will be helpful in controlling future disease development.

The limitation of this study includes the fact that it was conducted in a tertiary hospital. Thus, larger multicentric studies are recommended. □

CONCLUSION

RSV is the most common viral etiology of bronchiolitis in Iranian infants less than one year old, which is related to younger age and longer duration of hospitalization. □

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REFERENCES

1. Stensballe LG, Simonsen JB, Thomsen SF, Larsen A-MH, Lysdal SH, Aaby P, et al. The causal direction in the association between respiratory syncytial virus hospitalization and asthma. *Journal of Allergy and Clinical Immunology* 2009;1:131-137.
2. Hall CB, Weinberg GA, Iwane MK, Blumkin AK, Edwards KM, Staat MA, et al. The burden of respiratory syncytial virus infection in young children. *New England Journal of Medicine* 2009;6:588-598.
3. Viswanathan M, King VJ, Bordley C, Honeycutt AA, Wittenborn J, Jackman AM, et al. Management of bronchiolitis in infants and children. *Evidence report/technology assessment (Summary)* 2003;69:1.
4. Joseph M, Witt M, Sharieff GQ. Evidence-based assessment and management of acute bronchiolitis in the emergency department. *Pediatric Emergency Medicine Practice* 2011;3:1-20.
5. Piedimonte G, Perez MK. Respiratory syncytial virus infection and bronchiolitis. *Pediatrics in review* 2014;12:519..
6. Mahyar A, Ayazi P, Ahmadi NK, Nikoo STP, Hamzehloo S, Taremiha A, et al. Zinc sulphate for acute bronchiolitis: A double-blind placebo-controlled trial. *Infez Med* 2016;4:331-336.
7. Fernandes RM, Hartling L. Glucocorticoids for acute viral bronchiolitis in infants and young children. *JAMA* 2014;1:87-88.
8. Shay DK, Holman RC, Newman RD, Liu LL, Stout JW, Anderson LJ. Bronchiolitis-associated hospitalizations among US children, 1980-1996. *JAMA* 1999;15:1440-1446.
9. García CG, Bhore R, Soriano-Fallas A, Trost M, Chason R, Ramilo O, et al. Risk factors in children hospitalized with RSV bronchiolitis versus non-RSV bronchiolitis. *Pediatrics* 2010;6:e1453-e1460.
10. Holman RC, Shay DK, Curns AT, Lingappa JR, Anderson LJ. Risk factors for bronchiolitis-associated deaths among infants in the United States. *The Pediatric Infectious Disease Journal* 2003;6:483-489.
11. Milani M. Respiratory syncytial virus infection among young children with acute respiratory infection. *Acta Medica Iranica* 2003;4:269-272.
12. Glezen WP, Taber LH, Frank AL, Kasel JA. Risk of primary infection and reinfection with respiratory syncytial virus. *American journal of diseases of children* 1986;6:543-546.
13. Janahi I, Abdulkayoum A, Almshwesh F, Alkuwari M, Al Hammadi A, Alameri M. Viral aetiology of bronchiolitis in hospitalised children in Qatar. *BMC Infect Dis* 2017;1:2017-2225.
14. Halasa N, Williams J, Faouri S, Shehabi A, Vermund SH, Wang L, et al. Natural history and epidemiology of respiratory syncytial virus infection in the Middle East: Hospital surveillance for children under age two in Jordan. *Vaccine* 2015;47:6479-6487.
15. Mansbach JM, Piedra PA, Teach SJ, Sullivan AF, Forgey T, Clark S, et al. Prospective multicenter study of viral etiology and hospital length of stay in children with severe bronchiolitis. *Archives of pediatrics & adolescent medicine* 2012;8:700-706.
16. Skjerven HO, Megremis S, Papadopoulos NG, Mowinkel P, Carlsen K-H, Lødrup Carlsen KC. Virus type and genomic load in acute bronchiolitis: severity and treatment response with inhaled adrenaline. *The Journal of infectious diseases* 2015;6:915-921.
17. Moler FW, Ohmit SE. Severity Of Illness Models For Respiratory Syncytial Virus-Associated Hospitalization. *American journal of respiratory and critical care medicine* 1999;4:123.
18. Rivera-Sepulveda A, Garcia-Rivera EJ. Epidemiology of bronchiolitis: a description of emergency department visits and hospitalizations in Puerto Rico, 2010-2014. *Tropical medicine and health* 2017;1:24.
19. Weber MW, Mulholland EK, Greenwood BM. Respiratory syncytial virus infection in tropical and developing countries. *Tropical medicine & international health* 1998;4:268-280.
20. Molinari-Such M, García I, García L, Puig G, Pedraza L, Marín J, et al. Respiratory syncytial virus-related bronchiolitis in Puerto Rico. *Puerto Rico health sciences journal* 2009;2:137-140.)
21. Rodríguez DA, Rodríguez-Martínez CE, Cárdenas AC, Quilaguy IE, Mayorga LY, Falla LM, et al. Predictors of severity and mortality in children hospitalized with respiratory syncytial virus infection in a tropical region. *Pediatric pulmonology* 2014;3:269-276.
22. Hasegawa K, Jartti T, Mansbach JM, Laham FR, Jewell AM, Espinola JA, et al. Respiratory syncytial virus genomic load and disease severity among children hospitalized with bronchiolitis: multicenter cohort studies in the United States and Finland. *The Journal of infectious diseases* 2014;10:1550-1559.
23. Gupta R, Helms PJ, Jolliffe IT, Douglas AS. Seasonal variation in sudden infant death syndrome and bronchiolitis—a common mechanism? *American journal of respiratory and critical care medicine* 1996;2:431-435.
24. Sigurs N, Gustafsson PM, Bjarnason R, Lundberg F, Schmidt S, Sigurbergsson F, et al. Severe respiratory syncytial virus bronchiolitis in infancy and asthma and allergy at age 13. *American journal of respiratory and critical care medicine* 2005;2:137-141.