Bronchiolitis in Abha, Southwest Saudi Arabia: Viral etiology and predictors for hospital admission

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Summary

Background: **Bronchiolitis is the most common lower respiratory tract infection in children less than 24 months of age and the most frequent cause of hospitalization in infants under 6 months of age.**

Objectives: **To determine the viral etiology and predictors for hospital admission of children with bronchiolitis in Abha city, southwest Saudi Arabia.**

Methods and materials: **Children five years old or younger diagnosed with bronchiolitis were enrolled in the study as a study-group of admitted cases (n=51) and a control-group of non-admitted cases (n=115). Clinical features and risk factors of bronchiolitis were recorded at the time of presentation and the clinical course was monitored during the hospital stay. Nasopharyngeal aspirates (NPA) for respiratory virus isolation were obtained from each of the admitted cases at the time of hospital admission.**

Results: **Prematurity, chronic lung diseases, atopic dermatitis, pure formula feeding, passive smoking and age = one year were significant predictors of admission. Respiratory syncytial virus (RSV) was isolated in 40 % of the admitted cases. Eighty percent of brochiolitis due to RSV were in children less than six months of age. Adenovirus was isolated in 22% of cases. Other viruses isolated were: Influenza virus A (11%), influenza virus B (7%), Parainfluenza viruses (18%), parainfluenza virus type 1 (4%), parainfluenza virus type 2 (2%) and parainfluenza virus type 3 (13 %).**

Conclusions: **Respiratory syncytial virus was the most frequent cause of admitted-cases of bronchiolitis, followed by adenovirus, parainfluenza virus and influenza virus, respectively. Prematurity, history of atopy, chronic lung disease, passive smoking, age = one year and lack of pure breast-feeding were significant predictors for admission of bronchiolitis cases.**

Key-words: ***Bronchiolitis, Respiratory syncytial virus, Hospitalization, Breast feeding.***

Résumé

Introduction: Bronchiolite est une infection de l'appareil respiratoire inférieur le plus ordinaire chez des enfants âgés de moins de 12 mois et la cause la plus fréquente d'hospitalisation des enfants âgés de moins de 6 mois.

Objectifs: Déterminer l'étiologie virale et les causes d'admission dans l'hôpital des enfants atteints de la bronchiolite dans la ville d'Abha au sud ouest d'Arabie saoudite.

Méthode et matériels: Des enfants âgés de cinq ans ou moins dignostiqués atteints de la bronchialite ont été inscrits pour cette étude comme groupe d'étude des cas admis (n = 51) et un groupe témoin de cas non-admis (n = 115). Des traits cliniques et facteurs de risques de la bronchilite ont été notés pendant la présentation et on avait également surveillé le traitement clinique au cours du séjour dans l'hopital filtre à vide de Nasopharyngite (NPA) pour l'isolement du virus respiratoire a été obtenu de chaque cas admis pendant l'admission dans l'hôpital.

Résultat: Prématurité, maladie chronique du poumon dermatite atopique, lait en poudre pur, tabagisme passif, et âge <- un an étaient des conditions importantes d'admission virus respiratoire syncytial (VRS) était isolé en 40% des cas admis quatre vingt pourcent de brochiolite attribuable au VSR étaient chez des enfants âgés de moins de six mois Adenovivus était isolé en 22% des cas. D'autres virus isolés étaient: virus de la grippe B (7%), virus parainfluenza (18%), virus parainfluenza type 1 (4%), virus parainfluenza type 2 (2%) et virus parainfluenza type 3 (13%).

Conclusion: Virus respiratoire syncytial et la cause la plus fréquente des cas admis de la bronchiolite suivi par virusadeno, virus parainfluenza et virus influenza respectivement prématurité, histoire d'atopie. La maladie chronique du poumon, tabagisme passif, âge ≤ un an et manque d'allaitement maternel pur étaient des prédicateurs pour l'admission de cas de bronchiolite.

Introduction

Bronchiolitis is primarily a clinical diagnosis. Typically, infants present with cough, breathing difficulty associated with coryza, tachypnoea and wheezing.[1-2] Less commonly, young infants, especially those born prematurely, may present with apnoea before developing the characteristic cough, tachypnoea and the use of the accessory muscles of respiration.[2, 3]

Bronchiolitis is the most common lower respiratory tract infection in children less than 24 months of age and the most frequent cause of hospitalization in infants under 6 months of age.[4,5] It is caused by viral infection of the lower respiratory tract, principally by respiratory syncytial virus (RSV), which gives rise to a widespread small-airway narrowing due to airway oedema, resulting in air trapping.[4-6] It is a self-limiting condition, but may be life-threatening causing significant morbidity in small infants and patients with chronic diseases and often leads to long-term respiratory symptoms.[7] Many outbreaks of viral respiratory tract illness associated with increased rates of hospitalization and death have been reported in the literature.[8-10]

An understanding of the conditions which control the evolution of acute viral bronchiolitis can help in predicting the resources that should be made available for adequate

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treatment. Recently, several strategies for prophylaxis and treatment of RSV infections have been developed.[11,12] Passive immunization using RSV immunoglobulin and monoclonal antibodies for prevention of RSV diseases in premature infants, have provided effective forms of prophylactic intervention for high-risk groups.[11,12]

RSV activity in the United States is monitored by the National Respiratory and Enteric Virus Surveillance System, a voluntary laboratory-based system started in 1990. Currently, there is no similar epidemiological system operating in the developing countries.[13] Although several studies on bronchiolitis have been reported from the developed countries, [9,14,15] literature search revealed no reports on bronchiolitis in Saudi Arabia. This study is aimed at determining the significant predictors for hospitalization of children with bronchiolitis and the viral etiology of admitted cases in southwestern Saudi Arabia.

Materials and methods

Study setting

Abha, capital city of Assir province in south-western Saudi Arabia (population 1 200 000, elevation: 3133 metres above sea level). Agriculture is the main occupation in the Abha region because of the abundance of water. Industrial activity in the region includes: construction materials and timber processing, maintenance workshops and other secondary industries. As an urban population, people enjoy many modern facilities but retain the basic dietary and social habits of rural communities. Health services are provided primarily by primary health care centers.

This study was carried out at Assir Central Hospital - Abha (ACH), pediatric emergency room and pediatric ward from October 1997 to September 2001.

Study population

Children five-years old or younger were enrolled in this study. Each child was considered eligible if he or she met the age criterion, had symptoms and signs of respiratory tract infection and was diagnosed clinically as having bronchiolitis and if informed consent was obtained from parents or legal guardians for study participation.

Study design

This was a case-control study. A random sample of children suffering from bronchiolitis who were admitted into the pediatric ward at ACH, from September 1997 to October 2001 (n=51), made up the study group. One hundred and fifteen children who were diagnosed clinically as having bronchiolitis in the emergency room but did not need admission at the time of diagnosis were selected as the control group. Both groups were age and sex matched.

Methods:

I. Clinical features, including bronchiolitis clinical score[17], were recorded at the time of presentation. Oxygen-saturation was measured by pulse oximetry (Biox 3740, Ohmeda, USA). Subsequently, the clinical course was monitored during the hospital-stay including: the paediatric intensive care unit admission, the need for mechanical ventilation, associated complications, duration of hospital-stay and mortality. Bronchiolitis clinical score was calculated for each child based on the following; i) accessory muscle findings: no retraction (0 point), intercostals retraction (1 point), intercostals & suprasternal retractions (2 points) and nasal flaring (3 points). ii) Wheeze findings: no wheeze and well (0 point), end-expiratory wheeze (1 point), pan-expiratory ± inspiratory wheeze (2 points) and wheeze audible without stethoscope (3 points).

II. Information was obtained from parents on: whether the child was ever breastfed, the age at which infant formula was first given, and the age at which breast-milk was last known to be given. Children were classified into one of the following categories: never breastfed, breastfed but also formula-fed before the sixth month of age (mixed, early formula), breast-fed but also formula fed after the age of six-month (mixed, late formula) or exclusively breastfed (never formula-fed).

III. Nasopharyngeal aspirate (NPA) was obtained from each hospitalized child at the time of hospital admission for respiratory virus diagnosis.[18] Clinical specimens – (NPAs) were collected by vacuum suction through a plastic catheter with a specimen trap. Approximately 3 ml of transport medium (phosphate-buffered saline solution with 0.5% gelatin) was suctioned through the catheter into the trapped-specimen and transported within 1 to 2 hours on wet ice to the laboratory. NPAs were placed in tubes with 2 ml of the same transport-medium. For virology study, all the clinical specimens were analyzed for verification of the presence of respiratory viruses at the Virology laboratory of the Department of Microbiology, College of Medicine, Abha, Saudi Arabia. Enzyme-linked immunoabsorbant assay (ELISA) and indirect immunofluorescence assay (IFA) - for antigen detection of influenza viruses A and B, parainfluenza viruses 1, 2 and 3, RSV and Adenoviruses, using the monoclonal antibodies from the Respiratory Viruses Panel I Viral Screening & Identification Kit (Chemicon International Inc.®, Temecula, California), were performed.

Statistical analysis

The comparison of proportions was performed with the Chi-square test for categorical variables and the Wilcoxon rank sum test for continuous variables. The Mann-Whitney test was used for the comparison of the averages. Analyses were performed with the Epi Info Software program, Version 6.03.

Odds ratios (OR) and 95% confidence intervals (CI) were calculated. To estimate which risk factors were independently related to hospital admission, the risk factors were included in multivariate forward stepwise logistic regression analysis. Odd ratios and 95% CI were also calculated for significant risk factors in this model.

Results

Table 1 shows the socio-biological characteristics of the

Table 1 Socio-biological characteristics of infants with bronchiolitis (Control and study group)

Characteristics	Control group N = 115	Study group N = 51	p value
Male: Female ratio	65:50	27:24	0.09
Age (months)	8.8 ± 3.9	7.6 ± 3.5	0.12
More than one sibling	79 (69%)	38 (74%)	0.68
Low monthly income	30 (26%)	13 (25%)	0.57

Table 2 Clinical characteristics of infants with bronchiolitis (Control and study groups)

Characteristics	Control group N = 115	Study group N = 51	p value
Weight (Kg)	11.9 ± 6.8	12.6 ± 5.5	0.34
Pure breast feeding	43(37%)	4 (7%)	0.01
Passive smoking	15 (13%)	19 (37%)	0.01
Child atopy	12 (10%)	18 (35%)	0.02
Infants ≤ one year	57 (49.5%)	33 (65%)	0.01
Oxygen saturation (%)	90.0 ± 1.24	86.4 ± 4.7	0.001
Bronchiolitis clinical score	2.2 ± 0.80	4.5 ± 1.5	0.01

Table 3 Predictors of hospitalization for infants with bronchiolitis

Predictors	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Prematurity	4.97 (3.81 - 5.16)*	3.44 (2.27 - 4.33)*
Congenital heart defects	1.21 (1.10 - 2.32)*	1.11 (0.85 - 1.95)
Chronic lung diseases	4.53 (2.42 - 5.46)*	3.12 (2. 19 - 3. 78)*
Atopic child	5.14 (4. 96 - 6.89)*	4. 75 (3.98 - 5.16)*
Atopic father	1. 35 (1.01 - 2.19)*	0.84 (0.65 - 1.23)
Atopic mother	1.74 (1.03 - 2. 69)*	0.97 (0.84 - 1. 72)
Atopic parents	2.28 (2.07 - 3.62)*	1.02 (0.96 - 1.81)
Breast feeding		
Exclusive breast milk	0.75 (0.46 - 1.24)	0.43 (0.22 - 1.13)
Mixed breast and formula milk	6.45 (4.31 - 8.33)*	4. 15(3.68 - 5. 24)*
Never breast milk	8.05 (6.37 - 5.14)*	2.51(2.11 - 3.73)*
History of exposure to smoking	4.18 (3.47 - 5.14)*	2.51(2.11 - 3.73)*
Age (one year or less)	9.52 (7.86 - 10.74)*	3.44 (2.27 - 4.33)*

** Statistical significance at 0.05 level*

Table 4 Types of viruses, age and sex distribution of infants admitted with bronchiolitis

Type of virus*	< 6mon.	6 - 12 months	12 - 24 months	Total no (%)
RSV	15 (75%)	2(25%)	1 (6%)	18 (40%)
Influenza virus A	0	1(13%)	4(23%)	5(11%)
Influenza virus B	1(5%)	0	2 (12%)	3 (7%)
Adenovirus	4 (20%)	2 (25%)	4 (24%)	10 (22%)
Parainfluenza virus 1	0	0	2 (12%)	2 (4%)
Parainfluenza virus 2	0	0	1 (6%)	1(2%)
Parainfluenza virus 3	0	3 (37%)	3 (50%)	6 (14%)
Total	20(100%)	8(100%)	17(100%)	45(100%)

** Respiratory viruses were isolated in 45 cases*

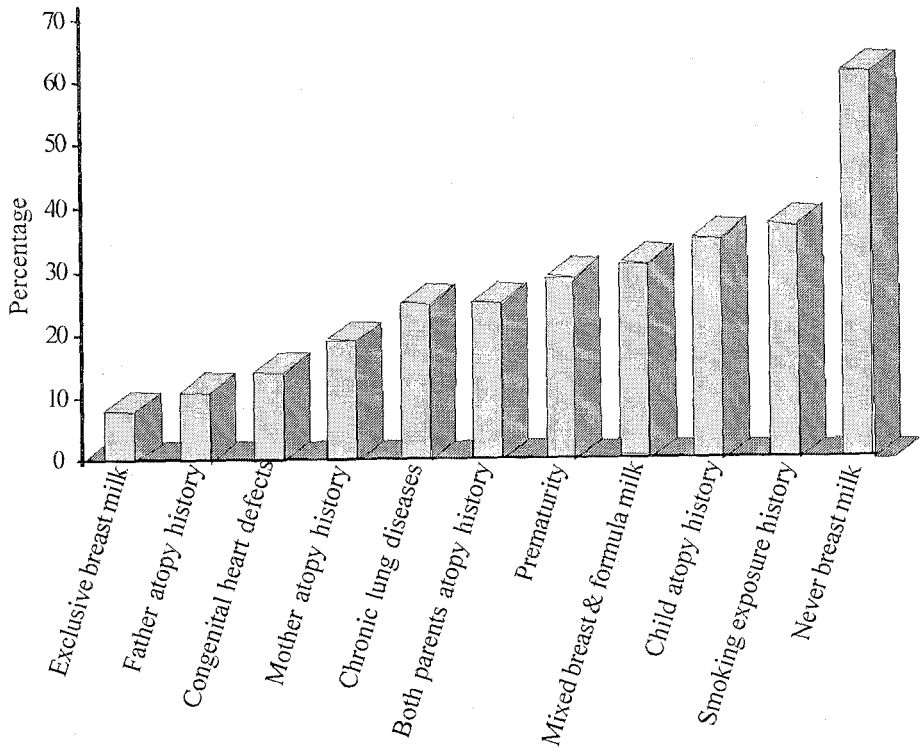

Fig. 1 ***Predictor factors of hospitalization in children with bronchiolitis***

study and control groups of children with bronchiolitis. There was no significant sex difference between the two groups (p=0.07). With regards to age, there was no significant difference between the mean age of both groups (p=0.57). However, infants less than one-year old constituted a significantly higher proportion of the study group(65%) than that of the control group (49.5%) (p=0.01). Both groups were comparable regarding the number of siblings (p=0.68) and family's monthly-income (p=0.57).

Table 2 shows the clinical characteristics of the study and control groups. The study group had significantly lower proportion of purely breast-fed infants (p=0.01), and higher proportion of passive smoking (p=0.01), and the history of child's atopy (p=0.02). The mean bronchiolitis score was significantly higher for the study group than that for the control group (p=0.01), while the mean oxygen saturation was significantly lower (p = 0.01).

Figure 1 shows the frequency of different predictors of hospitalization in children with bronchiolitis.

Applying logistic regression analysis to hospitalization with bronchiolitis as a dependent variable and the other variables as independent variable, it was found that: prematurity (OR=3.44,95%CI:2.27-4.33), chronic lung disease (OR=3.12,95%CI:2.19-3.78), atopic child (OR=4.75,95%CI:3.98-5.16), artificial feeding (OR=6.19,95%CI:5.60-7.39), exposure to smoking (OR=2.51,95%CI:2.11-3.73) and age of one year or less (OR=3.44,95%CI:2.27-4.33)- were all significant predictors of hospitalization.(Table 3).

Table 4 shows the distribution of the forty-five hospital-admitted cases of bronchiolitis according to the viral etiology and age. RSV was isolated in 40% of cases and ranked first as an etiological factor for of bronchiolitis, followed by adenoviruses (22%), and parainfluenza virus type 3 (14%). Other causative agents were: Influenza A(11%), Influenza B(7%), Parainfluenza type 1(4%) and Parainfluenza type 2 (2%). About one-half (n=20, 44%) of all viruses were isolated from infants aged 6 months and under. RSV caused 75% of these infections, followed by adenovirus (20%). On the other hand, more than one-third (38%) of the viruses were isolated from children aged 12-24 months with adenovirus making up 24% of these viruses.

Regarding the clinical course and the hospital stay, eight infants needed admission to the Paediatric Intensive Care Unit (PICU) seven (88%) of whom were under six months of age, with one being 10 months old. RSV was isolated in 50% of these infants and 62% of these infants were exclusively on artificial milk. Four of these infants (50%) needed mechanical ventilation and three of them (75%) were less than three months of age.

Fourteen infants (27%) who where admitted with bronchiolitis, developed complications. Six of them developed gastroenteritis, 5 developed aspiration pneumonitis and 3 developed sepsis. One infant with aspiration pneumonitis, sepsis and pneumothorax died. Most of the children (82%) were discharged from the hospital within five days of admission (95% CI: 80.92-83.47). Nine infants (18%) stayed more than seven days and five of them (56%) were infected with RSV and the remaining were infected by adenovirus. None of them was exclusively on breast milk.

Discussion

Breastfeeding has been associated with lower rates of a variety of infant's illnesses[22] including: wheezing, lower respiratory tract illnesses, pneumonia, upper respiratory tract

illnesses, otitis media, gastroenteritis, meningitis, and necrotizing enterocolitis.[19,20,21] It is widely believed that breastfeeding is causally associated with these lower rates, either because breast milk contains elements which might provide both specific and nonspecific protection against illness or because it is more hygienic, particularly in areas with poor sanitation.[9,20,21]

In the present study, multivariate analysis showed that pure formula feeding was a significant predictor of hospitalization for viral bronchiolitis (Adjusted odd ratio = 6.19; 95% CI:5.60-7.39). This was followed by mixed breast and formula feeding (Adjusted odd ratio = 4.15; 95% CI:3.68-5.24). Meanwhile, infants who were exclusively breast fed in the first six months of life had a mild course of the disease, less complications, lower rate of admission to a PICU and shorter hospital stay.

In our study, multivariate analysis showed that bronchiolitis was significantly associated with a history of atopy in the infants and/or in both parents. A close link between RSV-induced bronchiolitis and atopy has been identified in another study.[22]

Other predictors of hospitalization for viral bronchiolitis which showed significant association between bronchiolitis and hospital admission rate are: Age one-year or younger, history of prematurity, chronic lung diseases and passive smoking. Although Lanari et al.[23] and Simoes[24] reported similar findings regarding the bronchiolitis and hospital admission's association with the young age, prematurity and passive smoking, no such association with chronic lung diseases were reported in previous studies. However, one explanation for the new finding in this study may be that most of the premature infants have hyaline membrane diseases at birth and some of these infants will continue to have chronic lung diseases (bronchopulmonary dysplasia) and they are more prone to develop lower respiratory tract infections and more severe clinical course compared to healthy infants. Alterations in airway wall properties in infants with history of chronic respiratory disorders have been demonstrated in a study reported by Frey's group[25].

The incidence of low oxygen saturation (<85%) was higher in infants admitted with bronchiolitis than the control group ($p < 0.05$; adjusted OR = 0.43 95% CI = 0.27-0.56). In larger-scale pediatric studies which included infants with bronchiolitis, Rosen et al.[26] and Rubin et al.[27] reported similar results with base line $SaO2 < 85\%$ pointing to the need for hospitalization.

It has been reported that low socioeconomic conditions constitute a recognized risk factor for RSV bronchiolitis in developed countries.[23,24] Although our results showed no significant difference between the two groups regarding the number of siblings or the monthly-income of the family the socio-economic factors such as over-crowding, educational status, heath service availability and utilization and environment of the place of residence were not investigated. Our data showed that RSV was the most common causative agent for respiratory tract infection in children who were admitted into hospital with bronchiolitis. Similar observation has been reported in other studies[28]. The RSV was recognized as the single most frequent pathogen in the lower respiratory tract infections in infants and young children in the developed countries while little is known about the situation in the developing countries [28]

Nacimento et al.[9] reported that viral respiratory tract infections are common in young children and decreases in frequency and severity with age. Regarding the details of viral etiology, it was found that children less than 6 months of age and, in particular, infants less than three months of age, were more affected with RSV followed by adenovirus. The high prevalence of RSV in children up to six months of age reflects the low antibody response which tends to increase with age, and the limited protection provided by maternal antibodies.[29] In this study, we found that infants younger than 6 months of age had more clinical symptoms and signs and some of them had admission into PICU, while some needed mechanical ventilation. One of these patients died from severe complications. This group of infants had longer hospital-stay compared to children older than six months of age. Our results were similar to a study in Brazil[28] which showed that adenovirus was the most common viral pathogen in children less than two years of age and parainfluenza type 3 was the third most common viral pathogen in infants under six months of age who were hospitalized for bronchiolitis.

Children with a history of congenital heart defects, prematurity, or chronic lung diseases had more severe disease, more need for oxygen and longer hospital-stay than healthy children with similar diagnosis. It has been shown that severe RSV infections may occur in previously healthy infants and young children but premature infants and children with cardiac, pulmonary, or immune system disturbances are at the greatest risk[16,30,31].

Conclusions: Respiratory syncytial virus (RSV) was the most important and the most frequent cause of bronchiolitis in our study, followed by adenovirus, parainfluenza virus and influenza virus. History of prematurity, atopy and chronic lung diseases, as well as the lack of breast-feeding were risk factors in patients with bronchiolitis. Severe clinical course, including: PICU admission, mechanical ventilation and complications were more pronounced in infants younger than six months of age, in infants affected by RSV and in infants who had never been breast fed.

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