Predicting the Severity of Bronchiolitis in a Resource-poor Setting

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Abstract

Introduction: Bronchiolitis is the leading acute viral infection in infants. Early diagnosis and determination of severity of bronchiolitis in children is crucial for rapid initiation of treatment. This may be difficult to achieve in a resource-poor setting, where laboratory support and facilities for hospitalization are limited. Objectives: To determine the clinical predictors for severe bronchiolitis in children below 24 months of age in a resource-poor setting. Study
Design: Prospective descriptive study. Place and duration of study: Paediatric emergency department of a tertiary hospital over a period of one year. Patients and Methods: Children below 24 months age presenting with bronchiolitis. Children were classified as having severe or moderate bronchiolitis, depending upon the improvement seen in respiratory rate 48-72 hours after admission. Nasopharyngeal aspirates and serum samples obtained from the cases were used to detect the viral etiology. The clinical characteristics in the two groups were compared using Chi square/ student's t-test where applicable, and were correlated with the disease severity. The sensitivity, specificity, and relative risk for the various clinical parameters in detecting severity of bronchiolitis were obtained by statistical analysis. Results: Bronchiolitis accounted for 1.7% of the pediatric admissions. Respiratory rate ≥ 68/m, and the use of accessory muscles of respiration were found to be major clinical determinants for severe bronchiolitis. Influenza virus (H3N2) followed by respiratory syncytial virus were the dominant viral pathogens. Conclusion: Respiratory rate and the use of accessory muscles of respiration can predict the severity of bronchiolitis in the absence of advanced diagnostic facilities in developing countries.

INTRODUCTION

Bronchiolitis is a common acute viral infection of infancy clinically characterized by cough, fever, tachypnoea, wheeze, hyperinflation, and chest retraction. [1] Though, a self-limiting condition requiring mainly supportive treatment, admission may be required for close monitoring, hydration, oxygen or bronchodilator therapy. In countries where facilities for high-dependency and intensive care are scarce, and/or are located far from the point of initial assessment, clinical examination can be of special benefit in predicting the severity of bronchiolitis.

Several studies have been conducted in the western hemisphere [2,3,4,5,6] and a few in Africa [7,8] as well, but none in South East Asia, to determine the predictors of severity of bronchiolitis. Previous studies have used a combination of clinical criteria and intensive monitoring like oximetry and blood gas analysis to ascertain the disease severity. Therefore, we designed a study based solely on clinical parameters that could predict the severity of acute bronchiolitis in settings where facilities for radiography, pulse oximetry, blood gas analysis, and hospitalization are not routinely available.

PATIENTS AND METHODS

This study was conducted prospectively, in the paediatric emergency department of Guru Teg Bahadur Hospital, a tertiary hospital located in Delhi over a period of one year. All children between 2-24 months age, admitted with a clinical diagnosis of bronchiolitis, were included in the study. Clinically, bronchiolitis was defined as the first episode of acute wheezing, tachypnoea, and concomitant signs of viral respiratory illness in a child below 2 years of age. [9] Tachypnoea was defined as per the WHO recommendations, i.e., respiratory rate ≥ 40/min in children ≥ 12 months and respiratory rate ≥ 50/min in children aged 2 months till 12 months. [10] All children included in the study were hospitalized. Children who had already received bronchodilators/steroids prior to admission in our hospital, and those with chronic lung disease were excluded.

A detailed history was obtained and physical examination performed for all children at admission. Respiratory rate and heart rate were measured at admission and again after 10 minutes, while the child was breathing room air without any recent disturbance/feeding/crying. All enrolled cases received standard treatment that included intravenous fluids and humidified oxygen. Participants were re-assessed clinically after 48-72 hours of hospitalization and classified as having moderate or severe bronchiolitis based solely on the improvement in the respiratory rate. Children were classified as having moderate disease if (i) the tachypnoea subsided within 48-72h of hospitalization, or, (ii) there was a decrease in respiratory rate by at least 25% within first 48-72 h of hospitalization. The rest were labeled as having severe bronchiolitis.

VIRAL ISOLATION AND SEROLOGY

Secretions from the nasopharynx were taken on the day of admission with a mucus collector attached to wall suction. Specimens were stored at 4°C and processed for viral isolation within 4 hours. Viral cultures were done using rhesus monkey kidney, LLC-MK2, HEP-2, and HELA cell cultures. Fluorescent antibody technique (FAT) was used for virus identification in tissue cultures. Serology for respiratory syncytial virus (RSV), parainfluenza virus, influenza A and B and adenovirus was estimated. Serological testing included haemagglutination inhibition for influenza A and B and microneutralization for respiratory syncytial virus (RSV), parainfluenza virus, influenza A and B and adenovirus. A fourfold rise in antibody titers was considered as evidence of infection.

ETHICAL CLEARANCE AND CONSENT

Prior approval by the Institutional ethics' committee and informed written consent from the primary caretakers of all children enrolled in the study were obtained.

STATISTICAL ANALYSIS

The two groups were compared with respect to their historical and physical characteristics, at enrolment. Chi-square was used for categorical variables and t-test for quantitative variables. Univariate analysis was performed to identify the factors (personal, demographic, environmental, or clinical) predicting the severity of bronchiolitis. A multivariate logistic regression model was used to identify the most important factor determining the severity of bronchiolitis (dependent variable). Statistical analysis was done using SPSS software.

RESULTS

Bronchiolitis constituted 1.7% (166 children out of 9500) of all hospital admissions in the pediatrics department. Of these, 100 children (mean age 5.1 ± 4.3 months) fulfilled the inclusion criteria and consented for the study. Viral etiology could be established in 67 cases; Influenza A (H3N2): 35, respiratory syncytial virus: 25, parainfluenza type-1: 10, and adenovirus in 1 child. Four cases had dual infection with influenza A and parainfluenza type-1. Table 1 compares the personal, socio-demographic, environmental, and, clinical parameters in the two groups.

Figure 1

Table 1: Characteristics of the Children with Bronchiolitis in the Two Groups

Parameter	Moderate/Severe (n=49)*	Mild (n=51)	P value
Mean age (months)	4.8 ± 3.7	5.5 ± 4.9	0.42
Age			
≤ 3 months	24 (49.0%)	23 (45.1%)	0.43
4-6 months	17 (34.7%)	16 (31.4%)	
> 6 months	8 (16.3%)	12 (23.5%)	
General appearance* **			
Well appearing	2 (4.1%)	8 (15.7%)	**0.04**
Ill non-toxic	27 (55.1%)	32 (62.7%)	
Ill Toxic	20 (40.8%)	11 (21.6%)	
Duration of prodromal symptoms	3.5 ± 2.9	3.8 ± 2.3	0.57
Family history of atopy/asthma	12 (24.5%)	14 (27.5%)	0.76
Personal history of atopy	3 (6.1%)	2 (3.9%)	0.68
Family history of smoking	25 (51%)	27 (52.9%)	0.84
Use of kerosene oil for cooking/lighting	19 (38.8%)	21 (41.2%)	0.69
Living in urban settlement	43 (87.8%)	42 (82.3%)	0.44
Improper drainage	32 (65.4%)	35 (68.6%)	0.72
Inadequate ventilation	29 (59.2%)	33 (64.7%)	0.57
Overcrowding	20 (40.8%)	13 (25.5%)	0.10
Heart rate (bpm)**	137.7 ± 16.8	128 ± 15.4	**0.003**
Respiratory rate (/min)*	74.7 ± 10.5	60.0 ± 11.6	**0.0000**
Respiratory rate at admission ≥ 68/min	31 (63.3%)	9 (17.6%)	**0.0000**
Marked accessory muscle use at admission	42 (85.7%)	26 (51.0%)	**0.0002**
• **Presence of intercostal retraction**	13 (26.5%)	9 (17.6%)	**0.006**
• **Presence of subcostal retraction**	24 (48.9%)	13 (25.5%)	**0.016**
Diffuse wheezing	24 (48.9%)	11 (21.6%)	**0.004**
Crepitations present	11 (22.4%)	4 (7.8%)	**0.04**
Presence of grunting	15 (30.6%)	7 (13.7%)	**0.04**

**Two children had cyanosis at admission, both required admission to ICU and died.*

On a univariate analysis, respiratory rate at admission, use of accessory muscles of respiration, presence of diffuse wheeze, crepitations in chest, and grunting, were found to be associated with severe bronchiolitis. Amongst them, respiratory rate at admission was found to be the most important predictor of severe bronchiolitis on logistic regression model using F test at a 0.05 level of significance. A discriminant analysis was then performed and a cut off respiratory rate of ≥ 68/min at presentation was found to

have the maximum risk for severe bronchiolitis (sensitivity: 78.3%, specificity: 75.9%, positive predictive value: 77%, negative predictive value: 80.4%). Presence of accessory muscle use had a sensitivity of 85.7% and specificity of 49% in predicting severe bronchiolitis. All the five factors when combined could predict 80% of cases of severe bronchiolitis correctly, whereas respiratory rate ≥68/min at admission could correctly diagnose severe bronchiolitis in 77% of cases.

DISCUSSION

We found respiratory rate ≥ 68/min and the use of accessory muscles of respiration at presentation to be the most important predictors for severe bronchiolitis. Other clinical criteria found helpful in predicting severe bronchiolitis included the presence of diffuse wheeze, presence of grunting, crepitations in chest, and ill appearance of the infant. Age, exclusive breast-feeding, family history of atopy/asthma, overcrowding, improper drainage and ventilation, exposure to effluents like kerosene, and the presence of animals in home did not affect the severity of bronchiolitis.

As seen in our study, tachypnoea has been previously found to be the best indicator of severity of acute bronchiolitis. [12][13] Voets et al., [3] found children with respiratory rate ≥ 45 per minute to have a relative risk of 4.57 for severe bronchiolitis. Cherian and Simoes [14] demonstrated that respiratory rate more than 45 per minute and age below 6 months had a sensitivity of 94% and specificity of 88% in determining severe bronchiolitis. In contrast, Mulholland et al., [15] did not find the respiratory rate at presentation to predict the severity of bronchiolitis but found clinical signs like cyanosis and crepitations in chest to predict disease severity. We found the presence of crepitations to be associated with severe bronchiolitis but found no relationship between the presence of cyanosis and disease severity. This could be due to the limited number of cases detected with cyanosis, only 2, in our study. This may also be partly explained by the racial pigmentation and the presence of anemia in our study population due to which cyanosis may have been missed. Foy et al., [4] found children below 2 years to be most susceptible to bronchiolitis but did not find the severity of bronchiolitis to be related to the age or sex of the child. Parott et al., [5] found males to have significantly greater chances of being affected by severe disease and hospitalization. Family history of atopy or asthma was seen in 26% of our cases but did not affect the severity of asthma, contrary to that reported by Erikson et al., [6] . Previously breast-feeding has been found to confer protection from severe bronchiolitis. [16] However, we did not find any relationship between exclusive breast-feeding and severe disease. This may have been due to a small number of babies on exclusive breast-milk in our study population.

We did not include pulse oximetry or arterial blood gas estimations for correlating with the severity of bronchiolitis, for the want of advanced diagnostic and intensive care facilities at peripheral health care centers in developing countries. Though hypoxemia has previously been found to be associated with occurence of apnea, duration of viral shedding and tachypnoea in bronchiolitis, [17] it may be an unreliable parameter to ascertain severity of bronchiolitis when used alone. [18][19] Mallory et al., [20] found that reliance on pulse oximetry may have been responsible for almost 250% increase in hospitalization rates for bronchiolitis in the past 2 years in the United States, despite this the mortality rates have remained constant. [21] In a recent multi-centric study from United States of America, a safe discharge was predicted in children<2 years with bronchiolitis by a respiratory rate below 40 breaths per minute and oxygen saturation>94% at admission. [22] Radiographic findings in bronchiolitis are often nonspecific, leading to indiscriminate use of antibiotics and wastage of time and resources. [11]

Though, a balanced approach involving a rational combination of clinical signs, laboratory, and radiographic investigations, may provide the best estimate of the severity of bronchiolitis, but tachypnoea coupled with the use of accessory muscles can serve as rapid, simple, and reliable parameters for predicting the severity of bronchiolitis, in a resource-poor setting.

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