

# The use of C-reactive protein in predicting bacterial co-Infection in children with bronchiolitis

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## Abstract

**Aim:** The aim of the study was to evaluate the use of C-reactive protein (CRP) in predicting bacterial co-infection in patients hospitalized for bronchiolitis and to correlate the results with the use of antibiotics.

**Patients and Methods:** This is a prospective study that included patients diagnosed with bronchiolitis admitted to a tertiary care medical centre during the study period. A tracheal aspirate culture was taken from all patients with bronchiolitis. Blood was drawn to test C-reactive protein level, white cell count, transaminases level, and blood sugar level

**Results:** Fifty patients were enrolled in the study and were divided into two groups. Group 1 included patients with positive tracheal aspirate culture and Group 2 included those with negative culture. All patients with a CRP level  $\geq 2$  mg/dL have had bacterial co-infection. White cell count, transaminases and blood sugar levels were not predictive for bacterial co-infection

**Conclusion:** Bacterial co-infection is frequent in infants with moderate to severe bronchiolitis and requires admission. Our data showed that a CRP level greater than 1.1 mg/dL raised suspicion for bacterial co-infection. Thus, a tracheal aspirate should be investigated microbiologically in all hospitalized patients in order to avoid unnecessary antimicrobial therapy

## Introduction

Acute bronchiolitis is one of the most common respiratory disease in children younger than 2 years of age. It results in narrowing or obstruction of the lower respiratory tract<sup>1</sup> and occurs in association with viral infections, most commonly the respiratory syncytial virus (RSV), in around 75% of the cases. By the age of 2 years, nearly all children are infected at-least once by RSV bronchiolitis. Usually, it is seasonal and peak prevalence is in the winter months, when such viruses are widespread, re-infection during a single season is possible<sup>2</sup>. Preterm and male children are most commonly effected and it is the leading cause for more than 125,000 hospitalizations and 250 deaths yearly in the United States<sup>3</sup>. Premature infants and infants with chronic lung diseases are more prone to acute bronchiolitis related morbidity and mortality<sup>4</sup>. Acute bronchiolitis is characterized by inflammation, oedema and necrosis of epithelial cells lining small airways with consequent obstruction. The clinical symptoms include cough, tachypnea, rhinorrhea, congestion, wheezing and low grade fever<sup>5</sup>. In more severe cases, patients also develop respiratory distress requiring hospitalization<sup>5</sup>. Bacterial co-infection is clinically well documented in viral respiratory diseases. One possible mechanism is that viral infections facilitate bacterial colonization, adherence and translocation through the epithelial barrier,

paving the way for bacterial disease<sup>6</sup>. Diagnosis of bronchiolitis is based on patient's clinical history and examination. Age less than 24 months a history of prematurity, underlying cardiopulmonary disease or immunodeficiency are the common risk factors for the disease. Coming to the complementary diagnostic tests, CRP level measurement is considered to be of more efficacious use<sup>5</sup>.

C reactive protein is an acute phase protein synthesized by the liver in response to stimuli causing tissue damage. CRP production is also elicited by IL-1, IL-6, TNF- $\alpha$  and TGF. A number of conditions stimulate CRP synthesis like pulmonary infarction, inflammation and neoplasia, though bacterial infections are the most common stimuli leading to marked elevation in CRP levels within few hours<sup>7,8</sup>.

Although antimicrobial therapy is not recommended for treatment of patients with bronchiolitis unless there is concern about complications such as secondary bacterial pneumonia, the reported rate of use of antibiotics varies from 28% to 62% across hospitals in America<sup>9</sup>

The aim of this study was to evaluate CRP as a predictor of such complications in patients hospitalized for bronchiolitis and to co-relate the results with the use of antibiotics.

### **Materials and Methods**

All children's diagnosed with acute bronchiolitis under the age of 2 years, admitted to a tertiary care medical centre were studied during the study period. The study was approved by the institutional ethical committee and a written informed consent was taken prior commencing the study. The diagnosis of bronchiolitis was based on clinical background, defined as the evidence of new onset of lower respiratory tract symptoms of strongly suspected viral infection cause in children less than 2 years of age

The sex, age, weight and height of the patient as well as duration of hospitalization were recorded. Blood was drawn upon admission and sent for analysis. Automated blood count, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), blood sugar (BS) and C-reactive protein (CRP) were performed. CRP was determined by immunophelometry. A CRP level > 0.3 mg/dL was considered positive.

Specimens of tracheal aspirate were obtained by passage of a 10F suction catheter into the trachea, while avoiding oropharyngeal contamination. The suction catheter was attached to a sterile mucus trap.

A plain chest radiograph was performed for all patients to exclude a concomitant bacterial pneumonia. The chest radiograph was checked by the radiologist who was blinded to the study. Antibiotics, steroids, bronchodilators and oxygen supplement were added according to the clinical results of the patient and tracheal aspirate culture

Patients were divided into two groups according to the results of the tracheal aspirate culture:

Group 1 included patients with positive tracheal aspirate culture

Group 2 included those with negative culture.

### **Inclusion criteria:**

Children below the age of two years who were admitted with acute bronchiolitis,  
Guardians / Care takers of the children who signed the written informed consent

**Exclusion criteria:**

Evidence of pneumonia on chest radiograph upon admission

Patients with evidence of other associated infections (Acute otitis media, acute gastroenteritis)

Patients with underlying chronic lung disease

Prior use of antibiotics 2 weeks before admission

Patients with systemic disease

Previous exposure to mechanical ventilation

Malnutrition

Immunocompromised patients

Presence of two morphotypes from trachea aspirate culture

**Statistical Analysis**

Statistical analysis was performed with the use of Sigma stat software (SPSS Inc) version 13.0. For comparison of categorical data, chi-square and Fisher exact tests were used. Results were analyzed by repeated measures Analysis of Variance (repeated measures ANOVA). A p value < 0.05 was considered as significant

**Results**

A total of 50 patients were enrolled in the study. Amongst them, 28 were males and 22 were females. There were 30 patients with positive tracheal aspirate, i.e., group 1 and the rest 20 had negative tracheal aspirate belonging to group 2.

The mean age of the patients was similar in both groups (107±80 days in group 1 versus 128±114 days in group 2) as well as the growth parameters. The most common organisms cultured were Haemophilus influenzae (n=8), Moraxella catarrhalis (n=6), Escherichia coli n=4, Staphylococcus aureus (n=4), Streptococcus pneumoniae (n=4), Klebsiella pneumonia (n=2), and Pseudomonas aeruginosa (n=2).

The mean CRP level was 1.41± 2.65 mg/dL in group 1 versus 0.71± 1.21 mg/dL in group 2, but the difference was not significant. The tracheal aspirate culture was positive in 84.6% of patients in group 1 compared to 16% in group 2 when the CRP level was ≥1.1 mg/dL (p<0.05)

Six patients have had bacterial co-infection when the CRP level was ≥ 2 mg/dL (Table 1). Table 2 summarizes the results of laboratory studies in both groups.

A chest radiograph was obtained for all patients who are admitted with the diagnosis of bronchiolitis. Antimicrobial therapy was initiated in 86.2% of patients in group 1 compared to 50% in group 2 (p<0.006).

The use of bronchodilators and steroids was similar in both groups. The duration of hospitalization of patients was  $6.98 \pm 2.12$  days in group 1 compared to  $5.17 \pm 0.12$  days in group 2 and it was not significant

**Table 1 Results of tracheal aspirate culture in correlation with the CRP level**

CRP level (mg/dl)	Group 1 (N=30)	Group 2 (N=20)	P Value
<1.1	18 (48.6%)	19 (51.4%)	NS
>1.1	11 (84.6%)	2 (15.3%)	0.05
<2	23 (53.4%)	20 (46.5%)	NS
>2	6 (100%)	0	-

NS= not significant. A p value <0.05 was considered as significant

**Table 2 Results of laboratory studies in both groups**

	Group 1 (N=30)	Group 2 (N=20)	P value
WBC (cells/mm <sup>3</sup> )	12.27± (4.31)	13.21 ±(7.91)	0.61
CRP (mg/dl)	1.28 ± (2.78)	0.37 ±(0.39)	0.11
SGPT (IU/l)	29.07 ±(18.16)	37.90 ±(17.89)	0.13
SGOT (IU/l)	40.17 ±(12.81)	47.11 ±(20.7)	0.12
Blood sugar(mg/dl)	117.18±(36.32)	102.17±(18.71)	0.17

Values are given as mean ± SD. A p value <0.05 was considered as significant

### Discussion:

Acute bronchiolitis is a lower respiratory tract infection which is highly prevalent in children who are less than 2 years of age. It is a viral infection with respiratory syncytial virus (RSV). This virus is considered to be frequently implicated in the disease. Other agents less frequently associated includes parainfluenza virus and some adenoviruses<sup>5,10</sup>. Diagnosis is usually based on history and physical examination along with clinical symptoms. Laboratory or radiological studies are not routinely used for diagnosis<sup>11</sup>. In the present study, the diagnosis was based on clinical background and the chest radiograph was performed in all the patients to exclude the pneumonia.

The reported prevalence of bacterial co-infection with acute bronchiolitis varies between 33% and 44% according to several studies<sup>12-14</sup>. Three prospective studies showed that CRP has better predictive value than other acute phase reactants. Interestingly, in all three of them mean CRP was significantly higher in children with serious bacterial infections compared with children with benign infections and when taken in conjunction with other acute phase reactants, gave good probability of serious bacterial infections<sup>15-17</sup>.

Kneyber et al found that 33% of children in whose admission, endotracheal aspirates were performed had a bacterial culture. In our study, we found a higher percentage of the positive culture(60%), most commonly Hemophilus influenza, Moraxella Catarrhalis and E.coli<sup>18</sup>

Dultweiler et al studied retrospectively 127 infants admitted to ICU for RSV bronchiolitis and found that 44% of those ventilated and endotracheally sampled had concomitant bacterial pneumonia<sup>19</sup>

The highest CRP values was found to have significant co-relation with indirect markers of bronchiolitis severity. 48 patients who were hospitalized for acute bronchiolitis were analyzed for CRP, IL-6, procalcitonin and leukocyte counts and it was concluded that the severity of bronchiolitis did not have significant influence on any of these values<sup>20</sup>.

In the present study, patients with positive and negative tracheal aspirates, had similar CRP values. However, we noticed a high probability of bacterial co-infection, when the CRP level was greater than 1.1mg/dL, compared to 100% as the CRP level exceeds 2mg/dL.

Bronchiolitis was commonly seen in male children who were on breastfeeding and living in crowded areas. There was no difference between the two groups in regard to age, sex, weight and height.

Most children with viral infections shows low WBC and CRP values. High WBC, CRP levels or both were seen in children with respiratory adenovirus infections.

Hepatitis is commonly associated with RSV positive bronchiolitis with prevalence of 49%. RSV disease in ventilated children was more severe, if transaminase levels were elevated. We determined the transaminase level, owing to the hypothesis that hepatitis could occur in patients with bronchiolitis regardless of the etiology. Eight patients had elevated SGOT and SGPT levels, but the percentage of occurrence did not differ between both the groups<sup>21</sup>

Hyperglycemia is more frequent in children with bronchiolitis, however in the present study, hyperglycemia was not frequent in patients with bronchiolitis or those with bacterial co-infection, due to the fact that we did not standardize the timing of blood glucose analysis

Bronchiolitis is primarily treated by supportive therapy by concentration on major effects of the conditions like inadequate feeding, respiratory distress and apnea. Few studies also have evaluated the beneficial role of using steroids<sup>22</sup>. The American Academy of Pediatrics (AAP) recommends that both the bronchodilators and steroids should not be routinely used in the management of bronchiolitis<sup>1</sup>. Antibacterial medications should only be used in children with bronchiolitis who have specific indication of bacterial infection co-existence. The occurrence of bacterial co infection was higher in patients with high CRP level, the level of CRP would help the clinician treat patients for whom antimicrobial therapy is needed<sup>23</sup>.

## Conclusion

In infants with bronchiolitis who are moderate to severe enough to require admission, a bacterial co-infection is frequent. Our data showed that a CRP level greater than 1.1 mg/dL raises the suspicion of bacterial co-infection. Thus, a tracheal aspirate should be investigated microbiologically in all hospitalized patients in order to avoid unnecessary antimicrobial therapy

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