

Study of Incidence of Pulmonary Bacterial Co-Infection in Children with Acute Bronchiolitis

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Abstract

Background: Bronchiolitis is a viral lower respiratory tract infection in infants typically under a year of age clinically diagnosed with symptoms of upper respiratory tract infection progressing into lower respiratory tract illness with respiratory distress and crackles, wheeze, and crepitation. The aim of this study was to estimate the incidence of pulmonary bacterial co-infection in children with acute bronchiolitis and assess the severity of bronchiolitis. **Methods:** This is a cross-sectional that included 100 children suffering from acute bronchiolitis to determine the incidence of bacterial co-infection in them that required admission to hospital for acute bronchiolitis. The cases were collected from pediatric department, Benha University Hospitals. **Results:** In our study, the incidence of hospital admission in the study participants was 82% of them, 46 (46%) patients were admitted to PICU, 36 (36%) patients were admitted to ward, and 18 (18%) patients were not admitted to hospital. We found that the isolated pathogenic bacterial co-infection in the study participants was 13%. The culture outcomes in the study participants showed that 6% patients were positive for Klebsiella, 5% patients were positive for Streptococcus, 2% patients were positive for both, and 87% patients were negative. **Conclusion:** Nearly 13% of the pediatric inpatients with RSV bronchopulmonary infection showed bacterial co-infection. The most common bacterial respiratory pathogens associated with RSV bronchopulmonary infection in children were 6% positive for Klebsiella, 5% positive for Streptococcus, 2% were positive for both, and 87% were negative.

Key words: pulmonary bacterial co-infection - children - acute bronchiolitis

Introduction:

Bronchiolitis is a viral lower respiratory tract infection in infants typically under a year of age clinically diagnosed with symptoms of upper respiratory tract infection progressing onto lower respiratory tract illness with respiratory distress and crackles, wheeze, and crepitation. Most cases are self-limiting and respond to symptomatic care while some would require hospitalization (1).

Respiratory syncytial virus (RSV) is the most common pathogenic agent responsible for respiratory infections in children up to the age of 2 years and causes a wide range of clinical manifestations, including upper respiratory tract infections (URTIs) and lower respiratory tract infections (LRTIs) (2).

More than 60% of all children are infected by RSV within 1 year after birth and nearly all children are infected by RSV at least once within 2 years after birth (Public Health England. Respiratory syncytial virus (RSV), Centers for Disease Control and Prevention 2021).

In children below the age of 1 year, RSV represents the second cause of death globally after malaria, the first cause of death among respiratory infections, and the first cause of hospitalization (3 & 4).

In 2015, the estimated global impact of RSV infections in children below the age of 5 years was approximately 33 million LRTI episodes (uncertainty range: 21.6–50.3 million), 3.2 million hospitalizations (uncertainty range: 2.7–3.8 million), and 120,000 deaths (uncertainty range: 94,000–149,000) (5).

Many advocates against the routine use of antibiotics in bronchiolitis because of the reported low incidence of concurrent or secondary bacterial infections in patients with RSV. However, these studies focused on extrapulmonary bacterial co-infection, such as bacteremia and urinary tract infection (6).

Some retrospective studies investigated the occurrence of bacterial co-infection in children with severe RSV infection requiring PICU admission and found the incidence of pulmonary bacterial co-infection to vary between 17.5 and 44%. In these studies, the diagnostic yields of bacterial co-infection were obtained by broncho-tracheal lavage. However, the incidence of bacterial co-infection with RSV bronchopulmonary infection in pediatric inpatients not requiring PICU admission and the prevalence of antimicrobial-resistant pathogenic bacteria isolated from these patients are unclear (7).

The aim of this study was to estimate the incidence of pulmonary bacterial co-infection

in children with acute bronchiolitis and assess the severity of bronchiolitis.

Patients and Methods

Type of the study:

This study was a cross sectional study.

Patients:

This study was conducted on 100 pediatric inpatients aged between 2 months & 36 months having acute bronchiolitis from pediatric department, Benha university hospitals during the period from - August 2021 and March 2022. Fifty six (56%) patients were males and 44 (44%) patients were females.

Administrative design:

The study was approved by the local ethics committee on research involving human subjects of Benha faculty of medicine (.

Ethical considerations:

On admission, an informed consent was obtained from the child's parents before being enrolled in the study.

All patients were subjected to the following: -

- A full medical history was taken.

- A full clinical examination was done to assess severity and complications
- Chest X-ray for exclusion of pneumonia
- CBC was done for WBCs count and anemia
- CRP was done as marker for bacterial infection
- sputum bacterial culture was performed to detect bacterial infection.

To obtain good-quality sputum samples from children, we typically use a tongue depressor with a light to depress the tongue and induce the cough reflex, then pick out aspirate sputum with a 1-ml disposable syringe.

The samples of sputum were cultured in sheep blood agar medium and horse blood chocolate agar medium and MacConkey's agar.

Inclusion criteria

Pediatric patients having acute bronchiolitis

Patients aged Between 2 months & 36 months

Both sexes

Exclusion criteria:

Underlying conditions such as chronic lung disease e.g., cystic fibrosis, Bronchopulmonary disease or congenital

anomalies, Chronic systemic illness e.g., liver disease or kidney disease were also evaluated to be excluded. Also children under 2 months or older than 2½ years are excluded.

Results:

The age of the study participants ranged from 2 to 15 months with a mean of 5.15 ± 3.07 months. Of the study participants, 56 (56%) patients were males and 44 (44%) patients were females **Table 1**.

The incidence of bacterial co-infection in the study participants was 13%.

The culture outcomes in the study participants showed that 6 (6%) patients were positive for Klebsiella, 5 (5%) patients were positive for

Streptococcus, 2 (2%) patients were positive for both, and 87 (87%) patients were negative **Table 2 & figure 1**.

The incidence of hospital admission in the study participants was 82% of them, 46 (46%) patients were admitted to PICU, 36 (36%) patients were admitted to ward, and 18 (18%) patients were not admitted to hospital.

The length of stay for patients admitted to hospital ranged from 3 to 10 days with a mean value of 4.8 ± 2.3 days.

Regarding incidence of complications in the study participants, 2 (2%) patients had bronchopneumonia, 11 (11%) patients had pneumonia, and 87 (87%) had no complications **Table 3**.

Table 2: Baseline characteristics in the study participants

Study participants (n =100)		
Age (months)	Mean ± SD	5.18 ± 3.07
	Range	2 - 15
Gender	Male	56 (56%)
	Female	44 (44%)

Table 2: Incidence of bacterial co-infection in the study participants

Study participants (n =100)	
Positive for Klebsiella	6 (6%)
Positive for Streptococcus	5 (5%)
Positive for Streptococcus and Klebsiella	2 (2%)
Negative	87 (87%)

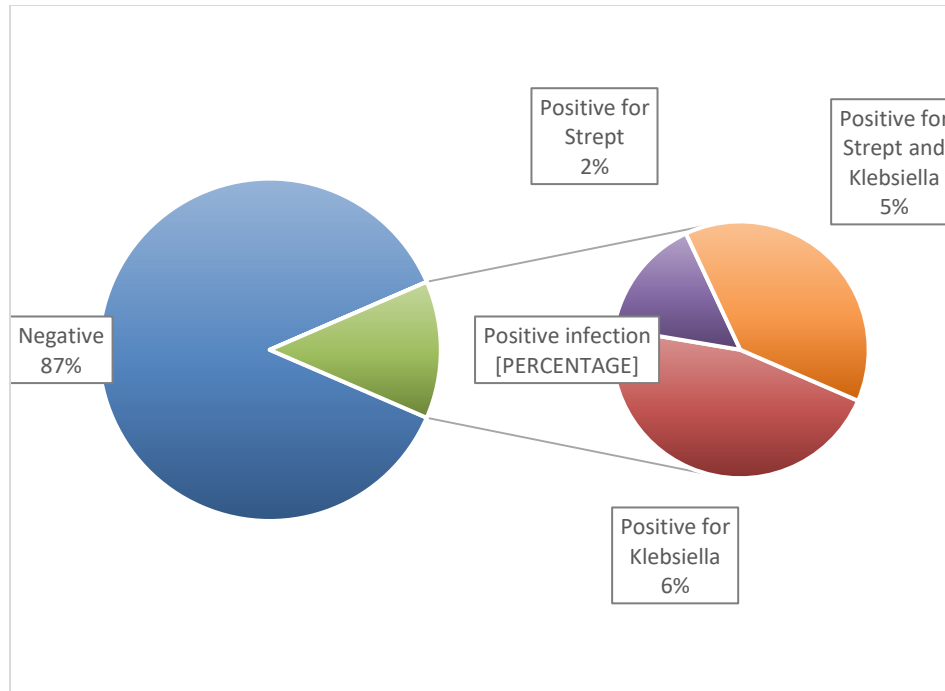


Figure 1: Incidence of bacterial co-infection in the study participants

Table 3: Incidence of hospital admission, length of stay, and complications in the study participants

Study participants (n =100)		
Hospital admission	PICU	46 (46%)
	Ward	36 (36%)
	No	18 (18%)
Length of hospital stay (days)	Mean ± SD	4.8 ± 2.3
	Range	3 - 10
Complications	Bronchopneumonia	2 (2%)
	pneumonia	11 (11%)
	No	87 (87%)

Discussion

In our study, the age of the study participants ranged from 2 to 15 months with a mean of 5.15 ± 3.07 months. Of the study participants, 56% patients were males and 44% patients were females.

The healthy URT is colonized by a community of mucosal dwelling

microorganisms (the microbiota), including both commensals and potential pathogens kept under control by the host immune system. There is a growing body of evidence demonstrating that viral respiratory infections can stimulate a substantial increase in bacterial load (8).

In our study, the incidence of hospital admission in the study participants was 82% of them, 46 (46%) patients were admitted to PICU, 36 (36%) patients were admitted to ward, and 18 (18%) patients were not admitted to hospital.

Regarding incidence of complications in the study participants, 2 (2%) patients had bronchopneumonia, 11 (11%) patients had pneumonia, and 87 (87%) had no complications.

This may be due to that the antibiotics may have converted some of the co-infection patients into the low bacterial growth group, or even prevented bacterial growth altogether.

Interestingly, we compared demographic and clinical characteristics of our patients including Hemoglobin, Platelets, CRP levels and white blood cell counts to confirm the complications in the study participants.

Further exploration of our observations is warranted, including the clinical relevance of the cultured micro-organisms. We find that the isolated pathogenic bacterial co-infection in the study participants was 13%. The culture outcomes in the study participants showed that 6% patients were positive for *Klebsiella*, 5% patients were

positive for *Streptococcus*, 2% patients were positive for both, and 87% patients were negative.

Similarly, the retrospective study (9) (82 PICU admissions with 65 (79%) ventilated) found that nine (33%) of the children on whom admission endotracheal aspirates were performed had a positive bacterial culture. 20% only of their patients were cultured, Ten of the 38 infants (26.3%) had positive microbiological cultures upon PICU admission, only one of which blood cultures 3.7% was positive (non-typable *Hemophilus influenzae* and *Streptococcus mitis*, which was considered not be a contamination). 33.3% of infants had a positive culture from endotracheal aspirates, which yielded *Staphylococcus aureus* in five infants, nontypable *H. influenzae* in two, coagulase-negative staphylococci in one, and both *S. aureus* and nontypable *H. influenzae* in one.

. Although (10; 9) showed that the presence of *S. aureus* represent upper airway colonization, the micro-organism is also associated with pneumonia in infancy and young childhood. Coagulase-negative staphylococci are known to cause respiratory tract disease in neonates. Nontypable *H. influenzae* may also be associated with LRTD in certain infants. This study has a limitation

that the microbiological investigations not were performed in all patients in this study.

There are studies that have detected high bacterial presence in approximately 40% of LRT samples from paediatric RSV infections such as Duttweiler, Nadal and Frey which carried on 127 patients with median age 1.7 months, range newborn to 5.8 years. They found the risk of bacterial pneumonia in intubated infants was 43.9% and corresponded roughly with numbers found in non-ICU RSV patients (32% and 59%) (11).

They isolate bacteria from tracheal aspirates and blood specimens as follow: *Haemophilus influenzae* in 17 patients, *Moraxella catarrhalis* in 12 patients, *Streptococcus pneumoniae* in 11 patients, *Streptococcus pyogenes* in 1 and *Staphylococcus aureus* in 8 patients (11).

The numbers for their bacterial co-infections may be a conservative estimate as: (1) for methodological reasons, a diagnosis of bacterial pneumonia was only made in intubated patients; and (2) there were infants already on antibiotics when cultures were taken, thus preventing possible bacterial infections from being diagnosed; (3) diagnosis of bacterial pneumonia was only

attempted in cases where a tracheal aspirate was available for microbiological investigation; (4) pneumonia in the non-ICU RSV patients was diagnosed on clinical signs and radiological findings only.

Thorburn and his colleagues study a group of 181 children of median age 1.6 months were admitted to the PICU. 43% of them had other co-morbidities (congenital heart disease n = 37, chronic lung disease n = 8, immunodeficiencies n = 4, abnormality of large airways n = 5, congenital heart disease and abnormality of large airways n = 8, congenital heart disease and chronic lung disease n = 4, neuromuscular disease n = 7). Co-morbidity did not increase the risk of positive bacterial cultures. 42% of children admitted with severe RSV infection harbored bacterial pathogens in their lower airways. These critically run a serious risk of developing bacterial pneumonia (12).

They also found that *Pseudomonas aeruginosa* was the most common of the abnormal bacteria. *Streptococcus pneumoniae* was isolated from relatively few patients as a result of prior antibiotic use.

Limitations of (12) study: Many of the children with RSV had received antibiotics

for only one day or less (often a single dose close to intubation). All those patients with positive bacteriology in their endotracheal secretions had the same organisms isolated on admission surveillance swabs, indicating primary endogenous infection. This reinforces the view that potential pathogens are carried first in the nasopharynx and then there is migration down the trachea into the lower airways. The organisms isolated on admission were generally normal community organisms because most of the patients were in good health before RSV infection and PICU admission.

Randolph et al. (13) retrospectively examined 165 previously healthy infants admitted to the intensive care unit over a 12-year period with laboratory confirmed RSV infection, 38% of whom required mechanical ventilation. They found that 38% of the 63 intubated infants had “probable” or “possible” bacterial pneumonia. The limitations of this study are that not all patients had cultures sent. In addition, the lack of clear diagnostic criteria in the literature for identifying bacterial pneumonia in patients with RSV lower respiratory infection may have resulted in over- or under-diagnosis of probable pneumonia.

Usually, the bacteria co-detected with respiratory viruses are opportunistic pathogens, such as *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae* and *Moraxella catarrhalis* (9; 12; 7; 13).

Wiegers et al., studied 167 patients with mean age was 2.9 months, 37.7% of them had a bacterial co-infection and 40.1% low bacterial growth. Co-infections occurred within 48 h from intubation in 82.5% co-infections. *H.influenza* (40.0%), *S.pneumoniae* (27.1%), *M.catarrhalis* (22.4%), and *S.aureus* (7.1%) were the most common pathogens. This corroborates with data from bronchiolitis studies in Liverpool and Zurich (15; 12; 11).

Several limitations applied to the study done in 2019 (15), firstly, the majority of the patient’s received antibiotics prior to sampling. They may have overestimated the role of bacterial co-infections in children with bronchiolitis as we recruited children based on the clinical discharge diagnosis of the attending PICU consultant. Secondly, not every patient who was admitted to the PICU had a culture and cultures were performed based on clinically suspicion.

Six hundred and twenty inpatients with RSV pneumonia, were studied (16) with median age 1.33 months; 59% males; 32.4% co-infected with bacteria. The three most common bacteria are *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Haemophilus influenzae*.

There are several limitations in (15) study that all the cases with RSV infection were detected by using the rapid antigen test; most probably, severe cases would be tested for the possibility of RSV infection, while milder cases might be missed. they did not include patients with a history of allergies or suspected aspiration pneumonia, so they could not provide data on the clinical manifestations of these groups. Finally, the etiologic diagnosis of lower respiratory tract infection in children remains challenging.

Conclusion:

Nearly 13% of the pediatric inpatients with RSV bronchopulmonary infection showed bacterial co-infection. The most common bacterial respiratory pathogens associated with RSV bronchopulmonary infection in children were 6% positive for *Klebsiella*, 5% positive for *Streptococcus*, 2% were positive for both, and 87% were negative.

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