



## **Cesarean Section and Urinary Tract Infection Correlation with Bronchiolitis in Lebanese Hospitalized Children between One Month and Two Years Old**

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### **Authors' contributions**

*This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** Bronchiolitis of infancy is a clinically diagnosed respiratory condition presenting with breathing difficulties, cough, poor feeding, and irritability and, in the very young, apnea.

**Objective:** To determine the effect of cesarean section and UTI on bronchiolitis in children aged 2 months to 2 years.

**Design:** Retrospective population-based data linkage cohort study of 202 cases in Rafic Hariri University Hospital (RHUH) and Makassed University Hospital (MUH).

**Methods:** We reviewed retrospectively and studied prospectively the charts of the bronchiolitis hospitalized children between one month and two years in RHUH and MUH between 2011 and 2012 and continued prospectively until 2013. We studied: age, date of admission, type of delivery,

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gestational age, presence of UTI, screening and investigations done, related congenital diseases. The UTI is considered only when urine culture is positive. The type of delivery also mentioned.

**Results:** Our study showed that 48% of bronchiolitis patients were born by cesarean section delivery compared with spontaneous vaginal delivery, these children had increased risk of admissions for bronchiolitis with (OR 2.71; CI 95%) and 10.16% of all patients had UTI.

**Conclusion:** Physicians and expectant parents need to be made aware of this additional risk of elective cesarean sections and associated infant morbidity to aid in deciding the most appropriate mode of delivery. In infants and children with bronchiolitis continue to have a clinically important rate of UTIs.

*Keywords: Respiratory Syncytial Virus (RSV); Urinary Tract Infection (UTI); Rafic Hariri University Hospital (RHUH); Makassed University Hospital (MUH).*

## 1. INTRODUCTION

Several studies showed a correlation between cesarean section and UTI with Bronchiolitis [1,2]. Our target was to study if this correlation is applicable in Lebanon specifically at RHUH and MUH hospitalized children from one month till two years old between 2011 and 2013.

Bronchiolitis is a lower respiratory tract infection that primarily affects the small airways (bronchioles). It is a common cause of illness and hospitalization in infants and young children. It is an illness in children under two years of age characterized by wheezing and airway obstruction due to primary infection or reinfection with a viral or bacterial pathogen, resulting in inflammation of the small airways/bronchioles.

Bronchiolitis is typically caused by a viral infection. The proportion of disease caused by specific viruses varies depending upon the season and the year. Respiratory syncytial virus (RSV) is the most common cause, followed by rhinovirus; less common causes include parainfluenza virus, human metapneumovirus, influenza virus, adenovirus, corona virus, and human bocavirus. With molecular diagnostics, coviral infection may occur in approximately one-third of young children hospitalized with bronchiolitis.

Bronchiolitis often is preceded by a one- to three-days history of upper respiratory tract symptoms, such as nasal congestion and/or discharge and mild cough. It typically presents with fever (usually  $\leq 38.3^{\circ}\text{C}$ ), cough, and mild respiratory distress. Physical examination reveals tachypnea and intercostal and subcostal retractions, often with expiratory wheezing. The chest may appear hyper expanded with increased anteroposterior (AP) diameter and may be hyper resonant to percussion. Findings on auscultation include any combination of expiratory wheeze, prolonged

expiratory phase, and both coarse and fine crackles. Mild hypoxemia (oxygen saturation  $< 95$  percent) commonly is detected by pulse oximetry, even without clinical signs of desaturation.

The rate of cesarean section delivery is increasing in the world. There have been numerous reports associating cesarean section delivery with poor outcomes, including birth trauma in infants [3,4], respiratory morbidity of the newborn [1], respiratory distress syndrome [2,5], and admissions to advanced care nursery and transient tachypnea of the newborn [6,7].

A study from Perth's Telethon Institute for Child Health Research has found that 11% of babies born by cesarean section delivery are more likely to be admitted to hospital with the serious respiratory infection, bronchiolitis, in the first year of life.

So we studied each patient with type of delivery if normal or cesarean section. Furthermore, compared with normal vaginal delivery, children delivered by cesarean section have a 20–60% increased risk of asthma in childhood [8,9], and a threefold increased risk in adulthood [10], although it is not known if these associations were found with elective or emergency cesarean section deliveries.

In another analysis using population-based record linked data, it noted an increased risk of hospitalization for acute lower respiratory infection under 24 months of age in non-Aboriginal children who were delivered by elective cesarean section (OR 1.34; 95% CI 1.22 to 1.48) [11].

The results of this study were 16% of children were delivered by elective cesarean section. In adjusted analysis, compared with spontaneous

vaginal delivery, these children had increased risk of admissions for bronchiolitis at age < 12 months and 12–23 months independent of other fetal and maternal factors.

Another study has found that 6.5% of babies with bronchiolitis have urinary tract infection.

In a prospective cohort study of 156 previously healthy febrile infants with bronchiolitis, none and 1.9% had bacteremia or urinary tract infection (UTI) respectively, in comparison with 2.7% and 13.6% of 261 febrile controls [12]. This study concluded that previously healthy febrile infants aged 24 months or younger with bronchiolitis are unlikely to have bacteremia or UTI.

A cross-sectional study found that 6.5% of febrile infants up to 60 days old with bronchiolitis had a UTI and none had bacteremia or meningitis in comparison with 10% (UTI), 2.3% (Bacteremia) and 0.8% (Meningitis) in febrile non-bronchiolitic infants in the same age range [3].

Several studies showed a correlation between cesarean section and UTI with bronchiolitis.

### 1.1 Objectives

Our objective is to determine cesarean section and UTI correlation with bronchiolitis in infants and young children.

## 2. METHODOLOGY

### 2.1 Study Population and Description

We conducted a retrospective study in two hospitals RHUH and MGH, where we studied charts of infants between one month and two years of age in the period from January, 2011 till December, 2012. Then we studied prospectively the new cases of hospitalized bronchiolitis from January, 2013 till December, 2013.

We didn't enroll immediately any patient with:

- Structural problems: Bronchoscopy
- URTD: Polysomnography
- Previous Premature
- Esophageal disease: Barium swallows, pH probes, scopes
- Primary ciliary dyskinesia: Nasal ciliary motility, exhaled NO, EM, saccharine test
- TB: Mantoux, induced sputum/ gastric lavage/ BAL= culture & PCR
- Bronchiectasis

- Cystic fibrosis
- Systemic immune deficiency: IgG subtypes, lymphocytes & neutrophil function and HIV
- Cardiovascular disease: Echocardiography confirmation.

Our inclusion criteria's are:

All hospitalized children between one month and two years old with bronchiolitis in RHUH and MUH known as previously healthy or with recurrent bronchiolitis.

In this study we had not taken the signed consent of the parents of each individual, and our study protocol was approved by the IRBs committees of both Hospitals.

Physicians who evaluated the patients in the MUH and RHUH performed a standard history and physical examination on all enrolled patients.

Data presented in each chart included: patient name, age, gestational age, gender, previous medical history, previous surgical history, history of food or drugs allergies, history of vaccination, home medication, family history, previous hospitalization chart if present, number of hospitalization days, and recent history of respiratory signs or symptoms.

Physical examination data included: Vital signs; oxygen saturation, temperature, respiratory rate, blood pressure; and the presence of cough, rhinorrhea, rales or flaring, retractions, wheezing, and any specific infection source. Maximum temperature was defined as the highest rectal temperature recorded either at home or in the hospital.

After the history and physical examination, a standardized laboratory evaluation was performed including CBCD and platelets count in all patients, urine analysis and urine culture in some patients if done. Chest radiographs (CXRs) were performed at the discretion of the examining physicians if indicated. All CXRs if done were interpreted by a professional radiologist.

Therapeutic decisions, including those regarding IV hydration, and other medications were at the discretion of the responsible physician and not determined by study protocol. The charts also include status on discharge, discharge medications and follow up.

To guide our work and to prevent errors we designed a study chart. This chart includes information collected from patient's files that were hospitalized. The chart first had included the hospital's name in which the child has been hospitalized, the name of the patient, his case number and the phone number in case we have some information to know about.

Data was collected from cases diagnosed as bronchiolitis. We documented hospitalization days. The age was added to the chart, those below one month and those above two years were not enrolled in the study.

We added the gestational age of each child to exclude premature. We mentioned the type of delivery either normal vaginal delivery or cesarean section with indication. In the history of present illness, the important symptoms that were been included are cough, fever, difficulty of breathing, vomiting, poor feeding, apnea, runny nose. In the physical exam, the important clinical findings were expiratory wheezes, grunting, nasal flaring, subcostal, suprasternal, intercostal and xiphoid retractions, abdominal respiration and tachypnea.

Vitals signs upon admission were documented: Temperature, blood pressure, pulse, respiratory rate, and oxygen saturation. Past medical history was also mentioned.

We added if urine analysis for each individual has been done or not. Not all children had a urine culture. For those where urine culture has been done, we noted if it is positive or negative. For the positive one, we indicated the microorganism.

In our chart, we added the results of chest radiograph if it was been done. Then we filled a discharge description which included the status of the patient on discharge.

Because diagnosis of bronchiolitis is mainly a clinical diagnosis and the results of chest radiograph do not affect our diagnosis so, what interested us are the clinical manifestations. The white blood cell count also does not affect the diagnosis but could affect the management and the prognosis.

## 2.2 Statistical Analysis

Data were analyzed using Statistical Package of Social Sciences (SPSS) version 16.0 program using whole numbers, frequencies, means.

## 3. RESULTS

Overall 202 children diagnosed as bronchiolitis and admitted to both RHUH and MUH between 2011 and 2013, 101 patients (50%) had fever at presentation and 101 patients (50%) were afebrile. 88 had difficulty of breathing which are 56.4% and 114 had not which are 43.6%.

From 202 bronchiolitis patients, 52 children (26%) had associated vomiting and 150 had not (74%). 94 patients (46.5%) of studied individuals had poor feeding and 108 (53.5%) had not. Starting with respiratory symptoms, overall 202 of studied individuals, 15 patients (7.4%) had apnea, 186 (92.6) had not.

Concerning cough in studied individuals, 186 patients had cough and 16 had not. About coryza, 63 patients had it and 139 had not. Overall 202 children diagnosed as bronchiolitis, 90 patients had expiratory wheezing on physical exam (44.5%) and 112 had not (55.5).

Concerning intercostal retractions, overall 202 patients studied 58 patients (28.7%) had intercostal retractions. 36 children had subcostal retractions (17.8%). 10 children had suprasternal retractions (4.9%). Total patients with different retractions are 104 (51.5%).

Overall 202 children hospitalized for bronchiolitis, the urine analysis and culture was done for 118 patients (58.41%) but urine analysis was not taken into consideration to diagnose UTI.

From 118 patients studied, 106 patients had negative urine culture and 12 patients results revealed positive urine culture (10.16%).

From whose urine culture was positive (12) 10 patients had *E. coli* urinary tract infection, one had *Pseudomonas*, one patient had *Proteus*.

Overall 202 children diagnosed as bronchiolitis and admitted to both RHUH and MUH between 2011 and 2013, 107 babies born by normal vaginal delivery (53%), 95 babies born delivered by cesarean section (47%) with Odds ratio 2.71 with lower 95 (OR) = 2.02 and upper 95 (OR) = 3/65 with its Confidence Interval 95%.

## 4. DISCUSSION

We have found evidence of an association between elective caesarean delivery and hospitalizations for bronchiolitis in infants, a finding which to our knowledge has not been

previously reported in Lebanese infants and children. In this era of increasing rates of elective caesarean deliveries across world, this association between a potentially modifiable factor and significant infant morbidity is of public health importance.

There have been reported associations between caesarean delivery and subsequent asthma in childhood and adulthood [1]. There are also numerous reports linking early viral infections and subsequent asthma in children [1,2].

The association we report here follows on from these previous findings and biologically plausible explanations are now needed. The essential difference between elective caesarean and other modes of delivery is the absence of labor. The act of labor promotes the production of various cytokines and activates the infant's and mother's immune system. Therefore the cytokine environment differs in a newborn delivered by elective caesarean section, as shown by the lower levels of interleukin (IL) 6 and IL-10 in their cord blood than in those who had a normal vaginal delivery. The anti inflammatory cytokine IL-10 may be particularly important in this regard as production of this cytokine in neonates has been linked with resistance to the development of bronchiolitis.

Moreover, elective caesarean delivery has been associated with increased risk for early allergic sensitization, and the expression of allergy-trophic Th2-polarised immunity in young children has in turn been associated with increased susceptibility to symptomatic viral illness requiring hospitalization in infancy.

Hospital diagnosis coding is homogeneous throughout RHUH and MUH, thereby reducing any bias in our study. Additionally, we have been able to distinguish between caesarean and spontaneous vaginal deliveries.

Cesarean delivery is a major abdominal surgical operation and can present a greater risk of maternal morbidity compared with spontaneous vaginal delivery.

Our study showed that from overall 202 children diagnosed as bronchiolitis and admitted to both RHUH and MUH between 2011 and 2013, 107 patients were delivered by normal vaginal delivery (53%), 95 patients were delivered by cesarean section (47%) with (OR 2.71; CI 95%).

In another analysis using population-based record linked data, it noted an increased risk of hospitalization for acute lower respiratory infection under 24 months of age in non-Aboriginal children who were delivered by elective cesarean section (OR 1.34; 95% CI 1.22 to 1.48) [11].

Early viral illness, in particular bronchiolitis caused by Respiratory Syncytial Virus, has been shown to be associated with increased risk of asthma in children, [12,13] and the risk of persistent wheeze in children increases with increasing number and severity of viral infection episodes [14,15].

If elective cesarean section delivery heightens the risk of acute lower respiratory infection, specifically bronchiolitis, it may explain the relationship noted between cesarean section delivery and subsequent bronchiolitis and then asthma.

Previously, they investigated risk factors of children hospitalized at least once for acute lower respiratory infection. In the current analysis they used number of hospitalizations as a continuous measure of severity. They examined the relationship with elective cesarean section delivery, independent of obstetric factors, by investigating the associations with hospitalization frequency for both bronchiolitis and pneumonia in children aged < 12 months and at age 12–23 months.

In this prospective and retrospective, bicenter study at MUH and RHUH, we found that young infants with bronchiolitis had clinically important rates of UTIs (10.1%).

A cross-sectional study found that 6.5% of febrile infants up to 60 days old with bronchiolitis had a UTI and none had bacteremia or meningitis in comparison with 10% (UTI), 2.3% (bacteremia) and 0.8% (meningitis) in febrile non-bronchiolitic infants in the same age range.

Another study done in 2004 by Group of the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics which objective was the objective of this study was to determine the risk of SBI in young febrile infants who are infected with RSV compared with those without RSV infections. They enrolled 1248 patients, including 269 (22%) with RSV infections. The overall SBI status could be determined in 1169 (94%) of the 1248

patients and the rate of SBIs was 11.4%. The rate of UTI in the RSV-positive infants was 5.4% compared with 10.1% in the RSV-negative infants (risk difference: 4.7%).

Our study showed from 118 patients studied, 106 patients had negative urine culture and 12 patients had positive urine culture (10.1%).

From whose urine culture was positive (which were 12) nine patients had *E. coli* urinary tract infection, one had *Pseudomonas*, one patient had *Proteus* and one patient had other microorganism.

Thus, it seems that one cannot necessarily obviate urine and blood testing in these infants on the basis of RSV status alone.

No one has sought to develop and/or evaluate protocols and decision rules to identify infants with bronchiolitis who are at risk for UTI.

Some investigators have demonstrated that the presence of a clinically recognizable viral syndrome reduces the likelihood of a bacterial infection. Other investigators have shown that the presence of a viral infection may in fact predispose patients to subsequent bacterial infection.

Our study examined children who were younger than two years and had bronchiolitis and reported a 10.1% rate of UTI.

Although these rates are similar to other studies that examined UTI in young febrile infants, the rate of UTI in the patients with bronchiolitis infection in our study was higher than that reported in previous studies of these infants.

This may be explained by the retrospective nature of most of the previous studies and the lack of urine culture results on all enrolled patients in those studies.

In the current study, we applied conservative criteria to define UTI, requiring a positive urine culture. However, this was not performed routinely in all patients in the current study.

There was importance of our study because our study was prospective and retrospective and all evaluations and data collection were standardized.

## 5. LIMITATIONS AND PERSPECTIVES

The specific type of RSV testing was also not standardized across institutions.

Although the rapid RSV immunoassay is highly sensitive and specific, was not performed to all patients.

A second limitation is that the comparison of enrolled patients and missed patients revealed a slightly higher rate of UTI in the enrolled patients, which may suggest a small selection enrollment bias.

## 6. CONCLUSION

1. Physicians and expectant parents need to be made aware of this additional risk of elective cesarean sections and associated infant morbidity to aid in deciding the most appropriate mode of delivery.
2. Qualitative studies are now needed to understand women's and physicians' views regarding elective caesarean delivery, and laboratory studies should be undertaken to test the hypothesis that elective cesarean delivery results in altered development of antiviral immunity in infants.
3. In infants and children with bronchiolitis continue to have a clinically important rate of UTIs.
4. Therefore, urine testing cannot be omitted by the presence of bronchiolitis infection in these infants and young children.
5. Additional study of an even larger cohort is needed to assess the risk of UTI and the correlation with cesarean section in bronchiolitis infants and children.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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