



## ORIGINAL ARTICLE

## Lower lymphocyte response in severe cases of acute bronchiolitis due to respiratory syncytial virus<sup>☆</sup>

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## KEYWORDS

Bronchiolitis;  
Respiratory syncytial  
virus;  
Lymphocytosis;  
Severity

## Abstract

**Introduction:** Acute bronchiolitis (AB) of the infant has a serious outcome in 6–16% of the hospital admitted cases. Its pathogenesis and evolution is related to the response of the T lymphocytes. The objective of the present study is to determine if the lower systemic lymphocytic response is related to a worse outcome of AB in hospitalised infants.

**Patients and method:** Retrospective observational-analytical study of cases-controls nested in a cohort of patients admitted due to RSV-AB between the period from October 2010 to March 2015. Those with a full blood count in the first 48 h of respiratory distress were included. Infants with underlying disease, bacterial superinfection, and premature infants <32 weeks of gestation were excluded. The main dichotomous variable was PICU admission. Other variables were: gender, age, post-menstrual age, gestational and post-natal tobacco exposure, admission month, type of lactation, and days of onset of respiratory distress. Lymphocyte counts were categorised by quartiles. Bivariate analysis was performed with the main variable and then by logistic regression to analyse confounding factors.

**Results:** The study included 252 infants, of whom 6.6% (17) required PICU admission. The difference in mean  $\pm$  SD of lymphocytes for patients admitted to and not admitted to PICU was  $4044 \pm 1755$  and  $5035 \pm 1786$ , respectively (Student-t test,  $P < 0.05$ ). An association was found between PICU admission and lymphocyte count  $<3700/\text{ml}$  (Chi-squared,  $P = 0.019$ ; OR: 3.2) and it was found to be maintained in the logistic regression, regardless of age and all other studied factors (Wald 4.191  $P = 0.041$ , OR: 3.8).

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**Conclusions:** A relationship was found between lymphocytosis <3700/ml in the first days of respiratory distress and a worse outcome in previously healthy infants <12 months and gestational age greater than 32 weeks with RSV-AB.

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## PALABRAS CLAVE

Bronquiolitis;  
Virus respiratorio  
sincitial;  
Linfocitosis;  
Gravedad

## Menor respuesta linfocitaria en casos graves de bronquiolitis aguda por virus respiratorio sincitial

### Resumen

**Introducción:** La bronquiolitis aguda (BA) del lactante tiene una evolución grave entre el 6 y el 16% de los casos ingresados. Su patogenia y evolución está relacionada con la respuesta de los linfocitos T. El objetivo del presente estudio es comprobar si la menor respuesta linfocitaria sistémica está relacionada con una peor evolución de la BA en lactantes ingresados.

**Pacientes y método:** Estudio observacional-analítico retrospectivo de casos-controles anidados en una cohorte de ingresados por BA-VRS en el periodo de octubre del 2010 a marzo del 2015. Se incluyó a aquellos con hemograma en las primeras 48 h de dificultad respiratoria. Se excluyó a los lactantes con patología de base, sobreinfección bacteriana y prematuros ≤ 32 semanas de gestación. La variable principal dicotómica fue ingreso UCIP. Otras variables fueron: sexo, edad, edad posmenstrual, exposición gestacional y posnatal al tabaco, mes de ingreso, tipo de lactancia y días de evolución del distrés respiratorio. Las cifras de linfocitos fueron categorizadas por cuartiles. Se realizó un análisis bivariante con la variable principal y posteriormente regresión logística para analizar factores de confusión.

**Resultados:** El estudio incluyó a 252 lactantes. El 6,6% (17) precisó UCIP. La diferencia de media ± DE de linfocitos para pacientes ingresados y no ingresados en UCIP fue de  $4.044 \pm 1.755$  y  $5.035 \pm 1.786$ , respectivamente (*t* de Student,  $p < 0,05$ ). Se encontró asociación entre ingreso UCIP y la cifra de linfocitos < 3.700/ml (Chi cuadrado  $p = 0,019$ ; OR: 3,2), que se mantuvo en la regresión logística con independencia de la edad y del resto de factores estudiados (Wald 4,191  $p = 0,041$ ; OR: 3,8).

**Conclusiones:** Existe relación entre la linfocitosis < 3.700/ml en los primeros días de la dificultad respiratoria y una peor evolución en lactantes < 12 meses previamente sanos y edad gestacional mayor de 32 semanas con BA-VRS.

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## Introduction

Acute bronchiolitis (AB) has a more severe course in infants, with 6–16% of those admitted to hospital requiring supportive care in paediatric intensive care units (PICUs).<sup>1–3</sup> Various studies have sought to identify factors associated with a severe course of disease,<sup>2,4–8</sup> but when it comes to previously healthy children with no predisposing factors, the current evidence has not clearly established which infants may be at higher risk.<sup>9</sup> There is widespread agreement that preterm and young infants are most likely to require higher levels of care<sup>2</sup> (and that respiratory syncytial virus (RSV) is the most frequent and virulent aetiological agent involved in cases in infants).<sup>5,10,11</sup> There is also evidence of an association between the month of birth and the severity of AB.<sup>12,13</sup> It is unclear whether the presence of viral coinfection increases the severity of disease, although there is a growing consensus that bacterial superinfection increases the length of stay and the need for supportive care.<sup>2,14,15</sup>

Infants are at high risk of severe complications of viral respiratory tract infections. It is known that the pathogenesis of AB is associated with the activity of T-helper (Th) lymphocytes, which are recruited at the level

of the respiratory epithelium by different cytokines and chemokines secreted in response to infection, and specifically with an increased CD8<sup>+</sup>/CD4<sup>+</sup> T cell ratio, which is higher the more severe the disease.<sup>16</sup> In this regard, some authors have suggested the possibility that systemic lymphocyte counts, which are highly correlated with the increase in the levels of interferon gamma (INFγ) in the acute phase of infection, may be associated with a more severe course of AB, reflecting a skewing towards a Th2-dominated response of an allergic/inflammatory nature.<sup>17,18</sup>

The aim of our study was to determine whether the systemic lymphocyte response in RSV infection was associated with poorer outcomes in a series of infants admitted with AB in the absence of comorbidity.

## Patients and methods

We conducted an observational and analytical case-control study in a cohort of children admitted with a diagnosis of AB between October 1, 2010 and March 31, 2015. We were able to conduct this study because AB is a frequent disease whose management is standardised, so that the electronic health

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