



## SCIENTIFIC LETTER

## Admission to intensive care due to severe bronchiolitis in Colombia: How are we with respect to the rest of Latin America? ☆



### Ingreso en cuidados intensivos debido a bronquiolitis grave en Colombia: ¿dónde nos encontramos en relación con el resto de Latinoamérica?

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Sir,

Bronchiolitis (BR) is the most common cause of admission to the Pediatric Intensive Care Unit (PICU).<sup>1</sup> Although no specific recommendations referred to critically ill children are available, the main clinical practice guides advocate supportive treatment and consider most diagnostic and

pharmacological interventions to be futile.<sup>2,3</sup> In developing countries such as Colombia, the epidemiological information on patients with BR admitted to intensive care is limited. The present study was carried out to compare the characteristics, interventions and clinical outcomes of infants with BR admitted to three Colombian PICUs pertaining to a Latin American collaborative network, and to compare their care outcomes in the Latin American context. For this purpose we compared our data against those of another 23 Units in the region (5 countries), based on the Latin American Pediatric Network (Red Pediátrica de Latinoamérica [LARed]) of which we form part.<sup>4</sup>

During the period between 1 January and 31 December 2018, a total of 886 children with BR were entered in the registry. To the effects of our analysis, we excluded 132 infants with diagnoses at discharge different from BR or with previous bronchopulmonary disease conditions. The final study sample thus consisted of 754 patients.

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**Table 1** Comparison of the demographic characteristics, risk factors and severity at the time of admission.

Variable	Global LA Red		Colombia (COL)		Rest of LA (LA)		P-value <sup>b</sup>	
Number of cases, n (%)	754		357 (47.3%)		397 (52.7%)			
Age (months), med IQR	3.8	5.4	3.8	6.2	3.7	4.7	.360	
Weight (kg), med IQR	6.1	3.1	6.0	3.2	6.3	3.0	.050	
Gender, n %							.117	
Female 1	271	35.9%	118	33.1%	153	38.5%		
Male 2	483	64.1%	239	66.9%	244	61.5%		
Comorbidities, n %	166 22.0%		65 18.2%		101 25.4%		.017	
Respiratory comorbidities	48 6.4%		25 7.0%		23 5.8%		.497	
Other comorbidities (non-respiratory)	152 20.2%		56 15.7%		96 24.2%		.004	
Heart disease	25 16.4%		10 16.7%		15 13.9% <sup>a</sup>			
Prematurity	93 61.2%		41 68.3%		52 48.1%			
Malnutrition	6 3.9%		3 5.0%		3 2.8%			
Genetic disorders	15 9.9%		4 6.7%		11 10.2%		.540 <sup>c</sup>	
Neurological deficits	14 9.2%		4 6.7%		10 9.3%			
Others	19 12.5%		5 8.3%		14 13.0%			
Severity scores, n <sup>a</sup> med IQR								
Mortality risk PIM3%	702	0.36% 0.39%	350	0.41% 0.54%	352	0.25% 0.33%	.000	
M-WCAS	631	4.5 2	304	6 2	327	4 1.5	.000	
SaO <sub>2</sub> /FiO <sub>2</sub>	213	139 101	140	100 79	73	202 88	.000	
FiO <sub>2</sub>	213	70 50	140	100 43	73	47 20	.000	
Type of admission, n %								
Intensive care	432 57.3%		312 87.4%		120 30.2%			
Intermediate care	322 42.7%		45 12.6%		277 69.8%		.000	

COL: Colombian Units; FiO<sub>2</sub>: fraction of inspired oxygen; LA: Latin American Units; med IQR: median and interquartile range; n %: absolute number and percentage in column; PIM3%: mortality risk according to the Pediatric Index of Mortality 3 scale; M-WCAS: respiratory severity according to the modified Woods-Downes scale; SaO<sub>2</sub>: arterial oxygen saturation.

<sup>a</sup> Number of patients with measured data required for the calculation.

<sup>b</sup> Comparison between Colombia and the rest of Latin America. Pearson chi-squared test for categorical variables or nonparametric Wilcoxon test for the comparison of continuous variables; *P* < .05 is regarded as significant.

<sup>c</sup> Statistical power <80% for detecting significant differences.

Table 1 shows the demographic characteristics and data referred to non-respiratory comorbidities, and offers a comparative analysis of Colombian Units (COL) and Latin American Units (LA). Of note is the absence of comorbidities in most cases, and the COL group showed fewer non-respiratory comorbidities (15.7 vs. 24.2%; *P* = .004), with no statistically significant differences according to the type of comorbidity – though the capacity to detect relative differences of >25% was low.

On assessing severity, we recorded a low median probability of mortality based on the PIM3 (Pediatric Index of Mortality 3) score (0.36%; interquartile range [IQR] 0.39) and moderate breathing difficulty according to the modified Woods-Downes Clinical Asthma Score (M-WCAS) (M-WCAS 4.5; IQR 2) – though these scores were comparatively higher in the COL group. In those cases where oxygenation could be evaluated (use of defined FiO<sub>2</sub> systems), impairment was seen to be greater in the COL group: median SaO<sub>2</sub>/FiO<sub>2</sub> 100; IQR 79) versus median SaO<sub>2</sub>/FiO<sub>2</sub> 202; IQR 88) in the LA group (*P* < .0001).

Upon admission to the PICU, the patient transfer respiratory support measures were seen to be diverse. A total of 51.4% of the patients were admitted to the Unit with respiratory support based on conventional oxygen therapy; 37.9% were admitted with high-flow nasal cannulas (HFNCs); 2.4%

were admitted with continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) support; and 7.0% were admitted with invasive mechanical ventilation (IMV). On individually comparing each type of therapy, the COL group only showed a significantly lesser use of conventional nasal cannulas (10.6 vs. 54.7%; *P* = .0004). With regard to the rest of the systems, although relative differences of >25% were observed, the low statistical power was unable to confirm significance.

A high incidence of respiratory syncytial virus (RSV) was observed, with some significant differences between regions. In effect, a higher frequency of RSV and metapneumovirus was recorded in the LA group, while negative viral panels and parainfluenza virus were more common in the COL group. Antibiotic use was high (56.3%), despite a low declared suspicion of bacterial infection in 70 cases (9.3%) and even lesser confirmation based on culture or serological testing. High frequency of use and great variability were also observed on analyzing the use of adjuvant drug therapies: while the COL group used significantly more antibiotics (66.7 vs. 46.9%; *P* < .0001), adrenaline (14.3 vs. 2.0%; *P* = .0007) and hypertonic therapies (27.5 vs. 10.8%; *P* < .000), the LA group used more antiviral agents (0.3 vs. 2.5%; *P* = .01), corticosteroids (3.4 vs. 17.9%; *P* < .0001) and bronchodilators (9.0 vs. 68.8%; *P* < .0001).

**Table 2** Comparison of outcomes.

Outcomes	Global LARed		Colombia (COL)		Rest of LA (LA)		P-value <sup>a</sup>
<i>Days of stay, med IQR</i>	5.4	5.5	6.8	5.9	4.6	4.1	.000
<i>Days of IMV, med IQR</i>	6.4	5.3	6.6	5.2	5.5	4.7	.062
<b>Mortality</b>							
Expected, n 95%CI	6.9	4.5–9.3	1.9	1.5–2.3	5.0	2.6–7.4	
Observed, n %	1 (0.13%)		0 (0.0%)		1 (0.25%)		
SMR, n 95%CI	0.1	0.2–0.1	0	–	0.2	0.1–0.4	
<b>Complications</b>							
Associated to IMV	43	5.7%	23	6.4%	20	5.1%	.411
Associated to NIMV	9	1.2%	3	0.8%	6	1.5%	.393
Infections associated to healthcare	15	0.02	6	1.7%	9	2.3%	.555
Rescue therapies <sup>b</sup>	107	14.2%	88	24.6%	19	4.8%	.000
<b>Nueva morbidity<sup>c</sup> (N = 523)</b>							
Change <3 on FSS	508	97.1%	172	92.5%	336	99.7%	.000
Change ≥3 on FSS	15	2.9%	14	7.5%	1	0.3%	

COL: Colombian Units; LA: Latin American Units; med IQR: median and interquartile range; n %: absolute number and proportion; 95%CI: 95% confidence interval; SMR: standardized mortality ratio, calculated as observed mortality with respect to expected mortality; FSS: Functional Status Scale; IMV: invasive mechanical ventilation; NIMV: noninvasive mechanical ventilation (including high-flow nasal cannula).

<sup>a</sup> Comparison between Colombia and the rest of Latin America. Chi-squared test for categorical variables and Fisher exact test for groups with fewer than 5 data per cell, or Pearson test for more data; nonparametric Wilcoxon test for the comparison of medians;  $P < .05$  is regarded as significant.

<sup>b</sup> Rescue therapies include: neuromuscular relaxants, high-frequency ventilation, prone decubitus.

<sup>c</sup> New morbidity defined as an increase in the FSS general score of  $\geq 3$ .

A significant difference was observed in relation to the frequency of IMV as initial support and maximum support in both the COL group (initial: 52.7%; maximum: 56.9%) and the LA group (initial: 9.07%; maximum: 19.4%). Variability was also recorded in relation to the other respiratory support systems, though no statistically significant differences were observed.

Overall, mortality (absolute and standardized according to the PIM3) was low. The COL group was characterized by longer stay in the PICU, a greater use of rescue therapies (neuromuscular relaxants, prone decubitus, high-frequency ventilation) and greater residual morbidity defined as an increase of  $\geq 3$  points on the Functional Status Score (FSS) at discharge (Table 2).

Our results indicate that both the epidemiological profile and the type of therapies and clinical outcomes of infants admitted to Colombian PICUs due to BR differ from those of their Latin American peers. The data show the variability of practices to be a frequent phenomenon in Colombia.

Of note is the observation that the patients in the COL group were in more serious condition at the time of admission. This could be explained by the geographical setting (over 1500 m above sea level), where altitude could have an important influence upon hypoxemia.<sup>5</sup>

Although the suspicion (and confirmation) of bacterial coinfection was low, we recorded a high use of antibiotics, which would go against the recommendations of the clinical practice guides referred to children with BR.<sup>6</sup> The indication of antibiotics in patients admitted to the PICU remains the subject of debate among pediatric intensivists. The antibiotic indication rate in our series was below that reported by

some large series in other parts of the world, where the proportion of antibiotic prescription in infants admitted to the PICU ranges in practically all cases above 50% as reported by Shein et al.<sup>7</sup>

One recently described phenomenon is the variability of clinical, diagnostic and therapeutic practices in children with BR.<sup>8,9</sup> Our findings evidence that this situation is common in Latin America. The great variability and high frequency of use of coadjuvant therapies (nebulizers, antibiotics, corticosteroids) seen in all the Latin American regions analyzed is a matter of concern. There is a dissociation between the general treatment recommendations warranted by the scientific evidence and actual clinical practice. For many healthcare professionals, supportive treatment might not be enough, and concern about “not doing anything” and “letting the situation evolve with monitoring alone” can result in an overuse of futile and sometimes deleterious therapies.<sup>10</sup>

The Colombian PICUs were characterized by a greater use of IMV and a lesser use of noninvasive therapies such as HFNC and BiPAP, compared with the LA group. The use of rescue therapies (e.g., prone decubitus and high-flow ventilation) in the patients subjected to IMV was higher in the COL group. This may be explained by the greater severity of the patients at the time of admission or may serve to alert us to the possible overuse (over-indication) of such invasive and rescue measures – particularly considering that a less invasive strategy affords similar outcomes in children with BR.<sup>9</sup>

In conclusion, significant differences were observed in the epidemiological profile and care outcomes in Colombia, with greater patient severity at the time of admission and

the use of more invasive respiratory support measures, a longer PICU stay, and higher residual morbidity. This situation warrants the implementation of collaborative initiatives to reduce such variability, improve the quality of care and optimize resource utilization.

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## Appendix 1.

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