



## Short communication

## Respiratory syncytial virus in Brazilian infants – Ten years, two cohorts

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## ABSTRACT

**Background:** Each year, a considerable amount of children will experience at least one episode of acute viral bronchiolitis (AVB) during their first year of life. About 10% of them will be hospitalized, with significant physical and economic burdens.

**Objectives:** To compare two cohorts of infants with AVB, from same region, in a ten-year interval, regarding epidemiologic factors and viral etiology.

**Study design:** Cohorts: 142 (2004) and 172 (2014) infants at ages zero to 12 months; clinical diagnosis of AVB; medical care in hospital and genetic screening of nasopharyngeal secretion for respiratory viruses.

**Results:** The comparative analysis showed a difference in the percentage of respiratory syncytial virus (RSV) positive patients [2004 (33.1%); 2014 (70.3%)] ( $p < 0.01$ ). No differences were noted regarding gender, breastfeeding, tobacco exposure, crowding and maternal education. There was a difference as to the month of incidence (seasonality) of AVB (higher in April 2014). There was a higher age at attendance in the first cohort, and lower birth weight and gestational age ratios in the second cohort ( $p < 0.05$ ). There were no differences in hospitalization time, need of mechanical ventilation and number of deaths, however a difference regarding comorbidities was noted (higher in 2004) ( $p < 0.001$ ).

**Conclusion:** None of the analyzed variables had an impact on severity features. Virology and immunology must be considered in this kind of situation, by studying genetic variants and the maturation of the immune system in AVB by RSV or other viruses.

## 1. Background

Acute Viral Bronchiolitis (AVB) is the most common cause of hospitalization among infants during the first 12 months of life [1]. A variety of viral etiologies are known to cause AVB, particularly the respiratory syncytial virus (RSV) [2]. The RSV virus has two subtypes, A and B, which occur in different frequencies and combinations each year [3,4]. About 10% of the AVB cases demand hospitalization; mortality rates are 1% or less, mainly in cases with associated co-morbidities [5]. An effective vaccine is not available; current treatment is only supportive; preventive measures are limited to very expensive monoclonal antibodies [6]. AVB seems to be correlated with seasonality, gender, gestational birth age, birth weight, breastfeeding, tobacco exposure,

crowding, maternal education and viral etiology [7–10]. In this study, epidemiologic risk factors, clinical features and viral identification in nasopharyngeal secretion by polymerase chain reaction (PCR) were evaluated and compared in two cohorts (2004 [11] and 2014) with 314 infants with AVB.

## 2. Study design

Descriptive study with a comparison of two cohorts; sample was composed of infants under 12 months of age (for effect of comparison between two cohorts) with AVB and that demanded hospitalization. Patients were attended in a metropolitan region, in public and private hospitals, in a seasonal AVB period for the region (April to September).

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**Table 1**  
Epidemiological and clinical data in 2004 and 2014 cohorts of infants with acute viral bronchiolitis.

Feature	Group	2004 (n = 142)	2014 (n = 172)	Total (n = 314)	p-value	Odds ratio	95%CI
Seasonality	April	27	53	80	<b>0.007*</b>	<b>0.528</b>	<b>0.298 to 0.922</b>
	May	39	55	94			
	June	35	35	70			
	July	16	19	35			
	August	19	9	28			
	September	6	1	7			
Sex	Female	56	70	116	0.908*	0.949	0.587 to 1.531
	Male	86	102	188			
Birth weight	< 3000 g	23	71	94	<b>&lt; 0.001#</b>	<b>0.276</b>	<b>0.153 to 0.485</b>
	> 3000 g	119	101	220			
Age at attendance	Months	4.47 ± 2.99	3.76 ± 2.85	4.08 ± 2.94	<b>0.019<sup>‡</sup></b>		
		3.5 (1–11)	3 (0–11)	3 (0–11)			
Gestational age	< 37 weeks	14	40	54	<b>0.002#</b>	<b>0.361</b>	<b>0.187 to 0.695</b>
	≥ 37 weeks	128	132	260			
Breastfeeding	< 1 month	50	50	100	0.397#	1.304	0.787 to 2.161
	≥ 1 month	92	120	212			
Tobacco exposure	Yes	53	49	102	0.116#	1.483	0.922 to 2.384
	No	89	122	211			
Number people at home	< 5	94	98	192	0.13#	1.457	0.897 to 2.379
	≥ 5	48	73	121			
Maternal education	< 5 years	33	39	72	1#	1.009	0.573 to 1.77
	≥ 5 years	109	130	239			
Previous co-morbidities	Yes	35	14	49	<b>&lt; 0.001#</b>	<b>3.653</b>	<b>1.813 to 0.723</b>
	No	107	157	264			
Time of hospitalization	< 5 days	82	104	186	0.646#	0.894	0.555 to 1.471
	≥ 5 days	60	68	128			
Mechanical ventilation	Yes	22	33	55	0.456#	0.773	0.406 to 1.45
	No	120	139	259			
Death	Yes	0	3	3	0.254#	–	–
	No	142	169	311			

Values with positive association are presented in bold. The odds ratio values were based on 2004 cohort. The conditional maximum-likelihood estimate was based on Fisher's Exact test.

\*  $\chi^2$  Test.

# Fisher Test.

<sup>‡</sup> Mann-Whitney Test; 95%CI, 95% confidence interval.

**Table 2**  
Viral identification in nasopharyngeal secretion for RSV, respiratory syncytial virus (RSV) in 2004 and 2014 cohorts of Brazilian Infants with acute viral bronchiolitis.

Identification	2004	2014	Total	p-value	Odds ratio	95%CI
RSV positive	47	121	168	<b>&lt; 0.01#</b>	<b>4.769</b>	<b>2.892 to 7.968</b>
RSV negative	95	51	146		Reference	–
RSV group A	32	8	40	<b>&lt; 0.01*</b>	0.5945	0.221 to 1.434
RSV group B	13	89	102		<b>16.05</b>	<b>0.047 to 34.24</b>
RSV ND group	121	51	172		Reference	–

ND, non-determined. The odds ratio values were based on 2014 cohort. The conditional maximum-likelihood estimate was based on Fisher's Exact test.

\*  $\chi^2$  test.

# Fisher test; 95%CI, confidence interval.

**Table 3**  
Viral identification in nasopharyngeal secretion/frequency of respiratory viruses in 2004 cohort of infants with acute viral bronchiolitis (n = 142).

Viral identification	Frequency (%)
None	88 (62%)
RSV group non determined	26 (18.3%)
RSV group A	13 (9.2%)
RSV group B	7 (4.9%)
Metapneumovirus	7 (4.9%)
RSV group A + metapneumovirus	1 (0.7%)
Total	142 (100%)

RSV, respiratory syncytial virus.

Diagnosis was based on clinical data, which defines AVB as being the first episode of acute respiratory distress with wheezing, preceded by upper airway symptoms such as rhinorrhea and cough, with or without fever [1,5]. The criterion for severe bronchiolitis was oxygen saturation

lower than 92%, which demanded oxygen therapy [1]. Exclusion criteria were previous episodes of wheezing. A total of 314 patients were selected (2004: 142; 2014: 172). The studies were approved by the Ethical Committee from University of Campinas [#076/2003 (2004) and #00869612.7.0000.5404 (2014)]. In both cohorts' nasopharyngeal secretions were collected during the first 24 h after hospital admission. In the first cohort, by a washing technique with saline solution followed by aspiration. In the second cohort, collection was done by an aspiration technique without saline solution. Only the described technique for each cohort was accepted. The collected samples were analyzed to viral etiology by Polymerase Chain Reaction (PCR). In the first Cohort, PCR Rt kit (ABI PRISM Big Dye Terminator Cycle Sequencing Ready Reaction kit, Applied Biosystems TM, Foster City, USA) screened RSV and Metapneumovirus [11]; in the second cohort, Seeplex RV15 ACE detection kit (Seegene, Concord, CA) screened 13 types of RNA viruses and two of DNA viruses: RSV subtypes A and B; rhinovirus A/B/C; parainfluenza virus 1, 2, 3, and 4; adenovirus; coronavirus 229E/NL63 and OC43; influenza A virus and influenza B virus; bocavirus 1/2/3/4; metapneumovirus; and enterovirus. Epidemiologic data [gender, age at attendance, seasonality, gestational age, birth weight, breastfeeding, tobacco exposure, crowding (more than 5 people at home) and maternal education] were analyzed. Clinical data such as previous co-morbidities (lung disease, heart disease, immunodeficiency, undernourishment, Down Syndrome), time of hospitalization, need of mechanical ventilation and death were analyzed and compared in both cohorts. Statistical analysis was performed using the Mann-Whitney,  $\chi^2$  and Fisher Exact tests in the Statistical Package for the Social Sciences software, version 24 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.). Adopted value of significance was 5%.

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