

RESUMO

DURAÇÃO DE VÔMITO MAIOR OU IGUAL A 2,5 DIAS: FATOR INDEPENDENTEMENTE ASSOCIADO COM PIOR EVOLUÇÃO EM CRIANÇAS COM BRONQUIOLITE: Introdução: Bronquiolite é a principal causa de internamento em lactentes. É uma doença de curso variado. O grupo de crianças que evolui com deterioração clínica encontra-se mal definido na literatura. Objetivo: Identificar fatores presentes na admissão que são associados com pior evolução em crianças hospitalizadas com bronquiolite. Metodologia do Estudo: Estudo de coorte prospectivo conduzido em enfermaria pediátrica nas Obras Sociais Irmã Dulce, Salvador, Brasil, realizado de maio de 2015 a julho de 2016. Critérios de inclusão: Idade <2 anos, diagnóstico de bronquiolite na admissão hospitalar e assinatura do termo de consentimento livre e esclarecido (TCLE). Dados clínicos, exame físico na admissão e desfechos foram registrados. Um modelo de regressão logística multivariada ajustado para idade foi utilizado para avaliar associação entre necessidade de tratamento em Unidade de Terapia Intensiva (UTI) e duração de internamento hospitalar (DIH) ≥ 5 dias (variáveis de desfecho) e fatores detectados durante admissão (variáveis preditoras). Resultados: O grupo de estudo compreendeu 172 pacientes. Destes, 5 (2.9%;IC 95%:1.1%-6.3%) foram transferidos para UTI e 69 (40.1%;IC 95%:33.0%-47.6%) tiveram DIH ≥ 5 dias. A mediana da idade foi 5.2 meses (IQR:3.6-8.2) e a mediana da duração de vômitos foi de 1 dia (IQR:1-3); prematuridade <30 semanas (3.5%), <37 semanas (14.5%) foram reportados, além de desnutrição grave (4.7%) e presença de estertores crepitantes na ausculta pulmonar (27.9%). Desnutrição grave (OR 21.53;IC95% 1.43–323.66), prematuridade <30 semanas (OR 13.85;IC95% 1.23–155.89) e duração de vômitos (OR 1.92;95%CI1.16–3.17) foram independentemente associados com transferência para UTI. Prematuridade <37 semanas (OR 3.89; IC95% 1.55–9.79) e presença de estertores crepitantes na ausculta

pulmonar durante admissão (OR 3.11;95%CI 1.45–6.70) foram independentemente associados com DIH ≥ 5 dias. A área abaixo da curva ROC entre duração de vômito como fator preditor de transferência para UTI foi 0.92(IC95% 0.81–1.04) com ponto de corte na melhor performance 2.5 dias (sensibilidade 100%; especificidade 79%). Conclusão: Crianças admitidas com bronquiolite e relatando vômitos por ≥ 2.5 dias devem receber atenção máxima.

Palavras-chaves: 1. Bronquiolite; 2. Fatores de risco; 3. Desfecho; 4. UTI

ABSTRACT

OBJECTIVE: To identify factors present upon admission that are associated with worsening evolution among children hospitalized with bronchiolitis.

METHODS: This prospective cohort was conducted at the pediatric ward of the Children's Hospital, Salvador, Brazil, from May 2015 to July 2016. Inclusion criteria comprised age <2 years, admission to hospital due to bronchiolitis, and written informed consent. Clinical data, physical findings upon admission and outcome were registered. Multi-variable logistic regression analysis in a model adjusted for age was used to assess association between Intensive Care Unit (ICU) treatment/length of hospital stay (LOS) ≥ 5 days (outcome variables) and factors detected upon admission (predictor variables).

RESULTS: The study group comprised 172 patients, out of which 5 (2.9%;95%CI:1.1%-6.3%) were transferred to ICU and 69 (40.1%;95%CI:33.0%-47.6%) whose LOS ≥ 5 days. Overall, the median age was 5.2 months (IQR:3.6-8.2) and the median duration of vomiting was 1 day (IQR:1-3); prematurity <30 weeks (3.5%), <37 weeks (14.5%) were reported and severe malnutrition (4.7%) and crackles (27.9%) were found. Severe malnutrition (OR 21.53;95%CI 1.43–323.66), prematurity <30 weeks (OR 13.85;95%CI 1.23–155.89) and duration of vomiting (OR 1.92;95%CI1.16–3.17) were independently associated with ICU transfer. Prematurity <37 weeks (OR 3.89;95%CI 1.55–9.79) and crackles (OR 3.11;95%CI 1.45–6.70) were independently associated with LOS ≥ 5 days. The area under the ROC curve for duration of vomiting to predict transfer to the ICU was 0.92(95%CI 0.81–1.04) the cutoff for best performance being 2.5 days (sensitivity 100%; specificity 79%).

CONCLUSION: Children admitted with bronchiolitis reporting vomiting ≥ 2.5 days should receive maximal attention.

Key-words: 1. Bronchiolitis; 2. Risk factors; 3. Outcome; 4. ICU

Figure 1. ROC curve for duration of vomiting to predict transfer to ICU.

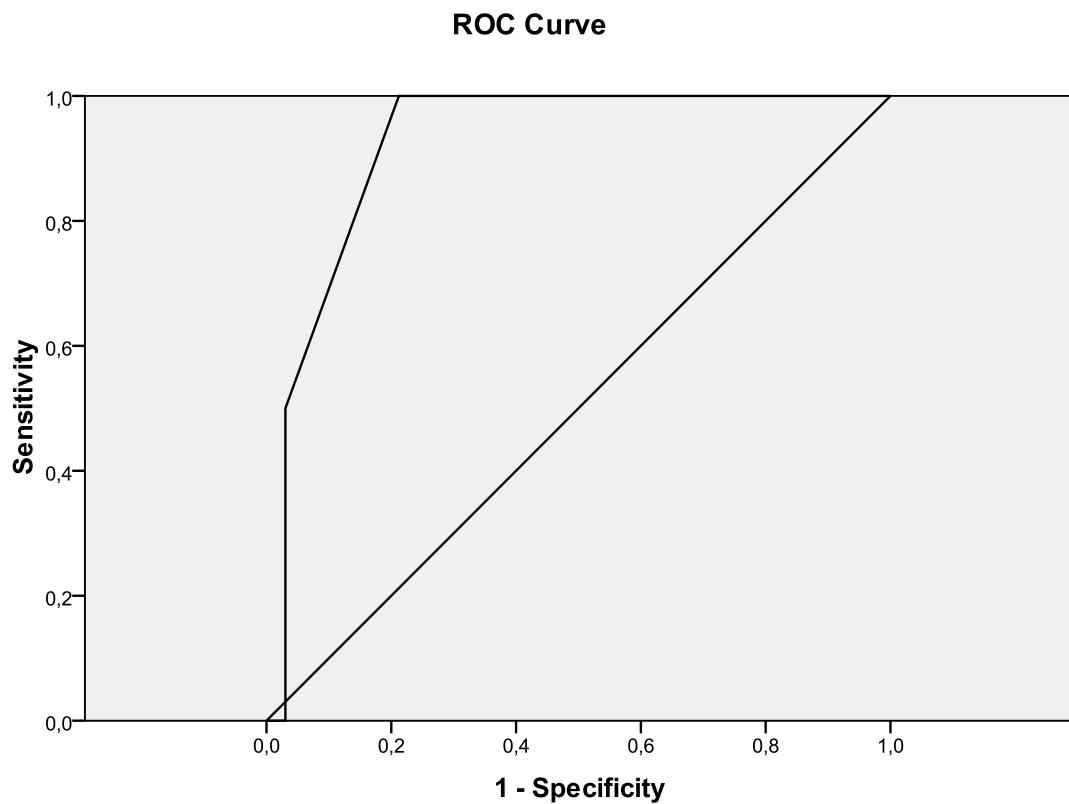


Table 1. Baseline characteristics of 172 children hospitalized with bronchiolitis

| Characteristics | n (%) | Median (p25-p75) |
|-------------------------------------|-----------------------------|--------------------------|
| Age (months) | | 5.2 (3.6 – 8.2) |
| < 2 month | 15 (8.7) | |
| 2 – 11 month | 138 (80.2) | |
| ≥ 12 months | 19 (11.1) | |
| Male gender | 109 (63.4) | |
| Race | | |
| Mixed | 87 (50.6) | |
| Black | 57 (33.1) | |
| White | 28 (16.3) | |
| History | | |
| Duration of disease ≤ 7 days | 133/171 (77.8) ^a | |
| Duration of disease ≤ 5 days | 89/171 (52.0) ^a | |
| Difficulty breathing | 163/171 (95.3) ^a | 2.0 (1 – 4) ^c |
| Cough | 160/171 (93.6) ^a | 5.0 (3 - 7) ^c |
| Fever | 97/171 (56.7) ^a | 2.0 (1 – 3) ^c |
| Wheezing | 70/171 (40.9) ^a | 2.0 (1 – 4) ^c |
| Vomiting | 35/171 (20.5) ^a | 1.0 (1 – 3) ^c |
| Co-morbidities | 10 (5.8) | |
| Congenital heart disease | 4 (2.3) ^b | |
| Chronic lung disease | 2 (1.2) ^b | |
| Down's syndrome | 1 (0.6) | |
| Diabetes mellitus type 1 | 1 (0.6) | |
| Chronic liver disease | 1 (0.6) | |
| Sickle cell disease | 1 (0.6) | |
| HIV – infected mother | 1 (0.6) | |
| Hydronephrosis | 1 (0.6) ^b | |
| Obstetric history | | |
| Prematurity < 30 weeks | 6 (3.5) | |
| Prematurity 30 – 36 weeks | 19 (11.0) | |
| Delivery | | |
| Vaginal | 109/171 (63.8) ^a | |
| C – section | 62/171 (36.2) ^a | |
| Smoking mother during pregnancy | 20 (11.6) | |
| Mother with asthma during pregnancy | 7 (4.1) | |
| Mechanical ventilator | 8 (4.7) | |
| Season of birth | | |
| Summer | 59 (34.3) | |
| Spring | 38 (22.1) | |
| Fall | 38 (22.1) | |
| Winter | 37 (21.5) | |

| | |
|---------------------------------------|-----------------------------|
| Infant history | |
| Atopic dermatitis | 2 (1.2) |
| Previous bronchiolitis | 2 (1.2) |
| Palivizumab use | 1 (0.6) |
| Environmental factor | |
| Smokers at home | 42 (24.4) |
| Mold at home | 65 (37.8) |
| Breastfeeding | |
| Currently exclusive | 43 (25) |
| Currently non-exclusive | 73/167 (43.7) ^a |
| Mother's history of atopy | |
| Asthma | 22 (12.8) |
| Rhinitis | 20 (11.6) |
| Bronchitis | 4 (2.3) |
| Eczema | 1 (0.6) |
| Physical examination | |
| Fever ($\geq 37.4^{\circ}\text{C}$) | 7/145 (4.8) ^a |
| Tachypnea ≥ 70 breaths/min | 7/168 (4.2) ^a |
| Tachycardia ≥ 200 beats/min | 0 |
| RDAI score ^d | |
| 0 – 5 points | 138/170 (81.2) ^a |
| 6 – 10 points | 32/170 (18.8) ^a |
| Nutritional status | |
| Well-nourished | 142 (82.6) |
| Malnutrition | 13 (7.6) |
| Severe malnutrition | 8 (4.7) |
| Overweight | 7 (4.1) |
| Obesity | 2 (1.2) |
| Sensorial status | |
| Normal | 168 (97.7) |
| Irritable | 3 (1.7) |
| Lethargic | 1 (0.6) |
| Chest retraction | 84 (48.8) |
| Prolonged expiratory phase | 26/170 (15.3) ^a |
| Hypersonant chest | 2/167 (1.2) ^a |
| Stridor | 4/171 (2.3) ^a |
| Reduced vesicular murmur | 5 (2.9) |
| Rhonchi | 77 (44.8) |
| Expiratory wheezing | 69/171 (40.4) ^a |
| Inspiratory wheezing | 15/170 (8.8) ^a |
| Crackles | 48 (27.9) |
| Regular cardiac rhythm | 172 (100) |

| | |
|---------------------|-----------|
| Normal heart sounds | 172 (100) |
| Cardiac murmurs | 2 (1.2) |
| Enlarged liver | 4 (2.3) |
| Enlarged spleen | 1 (2.3) |
| Abdominal bloating | 4 (2.3) |
| Cyanosis | 0 |

^a The denominator was not 172 because there was missing information.

^b One patient presented cardiac disease and chronic lung disease concomitantly and another patient presented chronic lung disease and hydronephrosis concomitantly.

^c Duration in days

^d Respiratory Distress Assessment Instrument score

Table 2. Comparison of baseline characteristics between patients who were or were not transferred to ICU and between patients who did or did not stay ≥ 5 days in the hospital

| Characteristics | Intensive Care Unit treatment | | | Length of hospital stay ≥ 5 days | | |
|--|-------------------------------|-----------------------------|-------|---------------------------------------|------------------|-----|
| | Yes n = 5 | No n = 167 | p | Yes n = 69 | No n = 103 | p |
| Age (months) ^a | 7.1 (4.1 – 6.8) | 5.1 (1 – 23) | 0.5 | 5.0 (1.1 – 23.0) | 5.3 (1.0 – 22.2) | 0.3 |
| Male gender | 4 (80.0) | 105 (62.9) | 0.7 | 44 (63.8) | 65 (63.1) | 0.9 |
| Mixed or Black race | 5 (100) | 139 (83.2) | 1.0 | 57 (82.6) | 87 (84.5) | 0.7 |
| History | | | | | | |
| Duration of disease ≤ 7 days | 4 (80.0) | 129/166 (77.7) ^b | 1.0 | 49/68 (72.1) ^b | 84 (81.6) | 0.1 |
| Duration of disease ≤ 5 days | 2 (40.0) | 87/166 (52.4) ^b | 0.7 | 34/68 (50) ^b | 55 (53.4) | 0.7 |
| Difficulty breathing | 5 (100) | 158/166 (95.2) ^b | 1.0 | 65/68 (95.6) ^b | 98 (96.1) | 0.1 |
| Duration of difficulty breathing (days) ^a | 1 (1-8.5) | 2 (1-4) | 0.4 | 2 (1-4) | 2 (1-4) | 0.9 |
| Cough | 5 (100) | 155/166 (93.4) ^b | 1.0 | 61/68 (89.7) ^b | 99 (96.1) | 0.1 |
| Duration of cough (days) ^a | 3 (2 – 6.5) | 5 (3 - 7) | 0.3 | 5 (3-7) | 5 (3-7) | 0.8 |
| Fever | 2 (40.0) | 95/166 (57.2) ^b | 0.7 | 37/68 (54.4) ^b | 60 (58.3) | 0.6 |
| Duration of fever (days) ^a | 2 (1 – 3) | 2 (1 – 3) | 0.9 | 2 (1-3) | 2 (1-3) | 0.9 |
| Wheezing | 1 (20.0) | 69/166 (41.6) ^b | 0.7 | 33/68 (48.5) ^b | 37 (35.9) | 0.1 |
| Duration of wheezing (days) ^a | 4 (4-4) | 2 (1 – 3.5) | 0.3 | 2 (1,5 – 4) | 2 (1 – 3) | 0.1 |
| Vomiting | 2 (40.0) | 33/166 (19.9) ^b | 0.3 | 15/68 (22.1) ^b | 20 (19.4) | 0.7 |
| Duration of vomiting (days) ^a | 4 (3 – 5)↑ | 1 (1 – 2) | 0.026 | 1 (1-3) | 1 (1-2) | 0.8 |
| Co-morbidities | | | | | | |
| Congenital heart disease | 0 | 4 (2.4) | 1.0 | 3 (4.3) | 1 (1.0) | 0.3 |
| Chronic lung disease | 0 | 2 (1.2) | 1.0 | 2 (2.9) | 0 | 0.2 |
| Down's syndrome | 0 | 1 (0.6) | 1.0 | 1 (1.4) | 0 | 0.4 |

| Obstetric history | | | | | | |
|---------------------------------------|----------------------|------------------------------|------|----------------------------|-----------------------------|-------|
| Prematurity < 30 weeks | 2 (40.0)↑ | 4 (2.4) | 0.01 | 6 (8.7)↑ | 0 | 0.004 |
| Prematurity 30 – 36 weeks | 0/3 (0) ^c | 19 / 163 (11.7) ^c | 1.0 | 11/63 (17.5) ^c | 8 (7.8) ^c | 0.06 |
| C - section delivery | 1 (20) | 61/166 (36.7) ^b | 0.7 | 24 (34.9) | 38 (37.3) | 0.7 |
| Smoking mother during pregnancy | 0 | 20 (12.0) | 1.0 | 7 (10.1) | 13 (12.6) | 0.6 |
| Mother with asthma during pregnancy | 0 | 7 (4.2) | 1.0 | 1 (1.4) | 6 (5.8) | 0.2 |
| Neonatal mechanical ventilator | 0 | 8 (4.8) | 1.0 | 5 (7.2) | 3 (2.9) | 0.3 |
| Season of birth | | | | | | |
| Spring | 0 | 38 (22.8) | 0.6 | 12 (17.4) | 26 (25.2) | 0.2 |
| Summer | 1 (20.0) | 58 (34.7) | 0.7 | 26 (37.7) | 33 (32.0) | 0.4 |
| Fall | 2 (40.0) | 36 (21.6) | 0.3 | 13 (18.8) | 25 (24.3) | 0.4 |
| Winter | 2 (40.0) | 35 (21.0) | 0.3 | 18 (26.1) | 19 (18.4) | 0.2 |
| Infant history | | | | | | |
| Atopic dermatitis | 0 | 2 (1.2) | 1.0 | 1 (1.4) | 1 (1.0) | 1.0 |
| Environmental factor | | | | | | |
| Smokers at home | 0 | 42 (25.1) | 0.3 | 14 (20.3) | 28 (27.2) | 0.3 |
| Breastfeeding | | | | | | |
| Currently exclusive | 1 (20) | 42 (25.1) | 1.0 | 14 (20.3) | 29 (28.2) | 0.2 |
| Currently non-exclusive | 1 (20) | 72/162 (44.4) ^b | 0.4 | 22 /68 (32.4) ^b | 51/99 (51.5) ^b ↑ | 0.01 |
| Mother's history of atopy | 1 (20) | 46 (27.5) | 1.0 | 18 (26.1) | 29 (28.2) | 0.8 |
| Physical examination | | | | | | |
| Malnutrition | 0 | 13/161 (8.1) ^b | 1.0 | 7/61 (11.5) ^b | 6 (5.8) | 0.2 |
| Severe malnutrition | 2 (40.0)↑ | 6 (3.6) | 0.02 | 8 (11.6)↑ | 0 | 0.001 |
| Fever ($\geq 37.4^{\circ}\text{C}$) | 0 | 7/140 (5.0) ^b | 1.0 | 4/58 (6.9) ^b | 3/87 (3.4) ^b | 0.4 |
| Tachypnea ≥ 70 breaths/min | 0 | 5/163 (3.1) ^b | 1.0 | 1/67 (1.5) ^b | 4/101 (4.0) ^b | 0.6 |

| | | | | | | |
|---------------------------------------|----------|-----------------------------|-----|---------------------------|----------------------------|------|
| RDAI ^d score 6 – 10 points | 1 (20.0) | 31/165 (18.8) ^b | 1.0 | 16/68 (23.5) ^b | 16/102 (15.7) ^b | 0.2 |
| Chest retraction | 3 (60.0) | 8 (48.5) | 0.7 | 40 (58.0) | 44 (42.7) | 0.05 |
| Prolonged expiratory phase | 4 (80.0) | 140/165 (84.8) ^b | 0.6 | 9/68 (13.2) ^b | 17/102 (16.7) ^b | 0.5 |
| Rhonchi | 4 (80.0) | 91 (54.5) | 0.4 | 27 (39.1) | 50 (48.5) | 0.2 |
| Expiratory wheezing | 1 (20.0) | 68/166 (41.0) ^b | 0.6 | 30.0 (44.1) | 39 (37.9) | 0.4 |
| Inspiratory wheezing | 1 (20.0) | 14/165 (8.5) ^b | 0.4 | 8/68 (11.8) ^b | 7/102 (6.2) ^b | 0.3 |
| Crackles | 2 (40.0) | 46 (27.5) | 0.6 | 26 (37.7)↑ | 22 (21.4) | 0.02 |

Results as n (%) otherwise when not informed.

^a Results as median (interquartile range).

^b Different denominator due to missing information.

^c Excluded premature < 30 weeks.

^d Respiratory Distress Assessment Instrument score.

Table 3. Multivariable logistic regression analysis of risk factors for Intensive Care Unit treatment in children hospitalized with bronchiolitis.

| Factors | ICU | | OR | 95%CI | <i>P</i> |
|--|-----------------|---------------|--------------|----------------------|-------------|
| | Yes n = 5 | No n = 167 | | | |
| Age (months) ^a | 7.1 (4.1 – 6.8) | 5.1 (1 – 23) | 1.05 | 0.79 – 1.39 | 0.7 |
| Severe malnutrition | 2 (40%) | 6 (3.6%) | 21.53 | 1.43 – 323.66 | 0.03 |
| Prematurity < 30 weeks | 2 (40%) | 4 (2.4%) | 13.85 | 1.23 – 155.89 | 0.03 |
| Duration of vomiting (days)^a | 4 (3-5) | 1 (1-2) | 1.92 | 1.16 – 3.17 | 0.01 |

^a Median (IQR)

ICU, Intensive Care Unit; OR, odds ratio; CI, confidence interval

Table 4. Multivariable logistic regression analysis of risk factors for length of hospital stay ≥ 5 days in children hospitalized with bronchiolitis.

| Factors | LOS ≥ 5 days | | OR | 95%CI | <i>P</i> |
|--|----------------------------|----------------------------|-------------|--------------------|--------------|
| | Yes n = 69 | No n = 103 | | | |
| Age (months) ^a | 5.0 (1.1 – 23.0) | 5.3 (1.0 – 22.2) | 0.92 | 0.85 – 1.01 | 0.07 |
| Severe malnutrition | 8 (11.6%) | 0 (0%) | 3030.55 | 0.0 – 2.227E+20 | 0.7 |
| Prematurity (< 37 weeks)^b | 17 (24.6%) | 8 (7.8%) | 3.89 | 1.55 – 9.79 | 0.004 |
| Ongoing non-exclusive breastfeeding | 22/68 (32.3%) ^c | 51/99 (51.5%) ^c | 0.56 | 0.28 – 1.15 | 0.1 |
| Crackles | 26 (37.7%) | 22 (21.4%) | 3.11 | 1.45 – 6.70 | 0.004 |

^a Median (IQR); LOS, length of hospital stay; OR, odds ratio; CI, confidence interval

^b Prematurity was included as 2 levels: < 30 weeks and 30 – 36 weeks of gestational age.

^c The total denominator was not 172 because there was missing information.