Parental severity assessment predicts supportive care in infant bronchiolitis

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ABSTRACT

Aims

In infants with acute bronchiolitis, the precision of parental disease severity assessment is unclear. We aimed to determine if parental assessment at the time of hospitalisation predicted the use of supportive care, and subsequently determine the likelihood that the infant with acute bronchiolitis would receive supportive care.

Methods

From the Bronchiolitis ALL south-east Norway study, we included all 267, 0-12 month old, infants with acute bronchiolitis whose parents at the time of hospitalisation completed a 3-item visual analogue scale (VAS) concerning Activity, Feeding and Illness. Respiratory rate, oxygen saturation (SpO₂) and use of supportive care were recorded daily. By multivariate logistic regression analyses we included significant predictors available at hospital admission to predict the use of supportive care.

Results

The parental Activity, Feeding and Illness VAS scores significantly predicted supportive care with odds ratios of 1.23, 1.26 and 1.36, respectively. The prediction algorithm included parental Activity and Illness scores, SpO₂, gender and age, with an area under the curve of 0.76 (95% CI 0.69, 0.81). A positive likelihood ratio of 2.1 gave the highest combined sensitivity of 81% and specificity of 61%.

Conclusion

Parental assessment at hospital admission moderately predicted supportive care treatment in infants with acute bronchiolitis.

Key notes

- The clinical relevance of parental disease perception of acute bronchiolitis in their infant is poorly documented.
- In this study comprising 267 infants from the Bronchiolitis ALL South-east Norway study, we found that parental assessment by a 3-item visual analogue scale at the time of hospital admission moderately predicted the use of supportive care in infants with acute bronchiolitis.
- Parental disease assessment using a visual analogue scale may improve clinical decision-making.

Key Words: Acute bronchiolitis, Disease severity, Infants, Parental assessment, Predicting supportive care.

INTRODUCTION

Acute bronchiolitis is the leading cause of hospital admissions in infants, particularly during winter epidemics (1,2). At present, general severity scores (3-5) and more specific bronchiolitis severity scores (6-9), combining objective and subjective parameters such as heart rate, respiratory rate, peripheral capillary oxygen saturation (SpO₂), chest retractions and wheezing, have been developed to predict disease severity, need of hospital admission and need of supportive care (10-13). However, it is largely unclear if factors available at the time of hospitalisation may predict progression of disease and need for supportive care, and the ability of the available paediatric dyspnoea scores to provide an accurate reflection of disease severity is questioned (14).

The decision to admit an infant to hospital is based on a number of factors, including the experience of the attending physicians (11), risk of complications and need for supportive care (2,15-17). Parental empowerment and collaboration with healthcare providers is increasingly emphasized in clinical decision- making (18,19). However, there are few studies determining the accuracy and predictive ability of parental evaluation of disease severity of their child.

The visual analogue scale (VAS) is a widely recognised assessment tool (20) that may reduce confounding effects of variations in individual interpretation (21). The VAS has been found useful in assessment of asthmatic symptom perception in children (22), whereas we are unaware of studies reporting the usefulness of VAS to assess severity of acute bronchiolitis.

The primary aim of the present study was to determine if parental assessment of their infant with acute bronchiolitis at hospital admission predicted the use of supportive care during hospitalisation. Secondly, based upon predictors available at the time of hospital

admission, we aimed to determine the individual likelihood that the infant with acute bronchiolitis would receive supportive care.

SUBJECTS AND METHODS

Study Design

This observational sub-study of the Bronchiolitis ALL south-east Norway study comprised all 267 infants whose parents completed a three-item VAS assessment during study enrolment.

Briefly this multi-centre, randomised, factorially designed clinical trial enrolled 404 infants with acute bronchiolitis younger than 12 months of age at the time of admission to one of eight hospitals in south-east Norway in 2010 and 2011 (23). Inclusion criteria included clinical signs of bronchiolitis (24) and a clinical score (9) of at least four on a scale from 0-10, 10 indicating most severe disease (Table S1). The exclusion criteria were severe underlying disease, more than one previous episode of wheeze, more than four weeks persisting lower airway symptoms, and use of inhaled or systemic steroids in the last four weeks.

The study assessments at enrolment included a structured parental interview, parental assessment by a three-item VAS score, clinical score performed by the attending physician and SpO₂ measurement. The use of oxygen supplement, nasogastric tube feeding and ventilatory support were recorded daily.

Parents of all infants provided signed informed consent prior to enrolment. The trial was approved by the Regional Committees for Medical and Health Research Ethics and by the Norwegian Medicine Agency. The Bronchiolitis All south-east Norway study was registered at Clinicaltrial.gov number, NCT00817466, EudraCT number, 2009-012667-34 and was registered in the Norwegian Biobank Registry. The study was audited by the Norwegian Medicines Agency in 2011.

Subjects

The included 267 infants with mean age of 128 days, had a mean ($\pm$ standard deviation (SD)) length of hospital stay of 82 ($\pm$ 68) hours. Apart from higher maternal educational

attainment ($p=0.026$) and a higher percentage of Caucasian mothers ($p=0.048$) among the included infants, they were largely similar to infants who were not included due to missing parental assessments (Table S2).

Methods

Baseline and clinical characteristics recorded at enrolment included SpO₂, heart rate, and respiratory rate.

The parental assessment consisted of a three-item smiley VAS on a 10-centimeter single horizontal line where 10 indicates most severe, as outlined in Figure S1 and online supplementary methods. The three categories concerned the activity level hereafter termed Activity, the interest in food, hereafter termed Feeding and finally the question “How ill is the child?” hereafter termed Illness.

Disease severity was further assessed at enrolment (23) by the attending physician applying a clinical score (9) previously used to assess the effects of racemic adrenalin in infants with acute bronchiolitis. The score is outlined in table S1.

The use of supportive care was recorded three times daily and included nasogastric-tube feeding, oxygen supplement and ventilatory support by continuous positive airways pressure or intubation.

Outcomes

The main outcome was the use of any supportive care, while secondary outcomes were each of the supportive care modalities, assessed separately.

Statistical analyses

Continuous data are presented as mean values with SD, minimum and maximum or 95 per cent confidence intervals (95% CI), when appropriate. Categorical data are given as numbers and percentages. Associations and prediction results are presented as odds ratios

(OR), with 95% CI and sensitivity, specificity, predictive values and likelihood ratios are given as percentage with 95% CI.

Each parental VAS score was categorised into quartiles, and we compared the use of supportive care in the upper versus lowest quartile, using Pearson chi-square.

To evaluate the diagnostic accuracy of parental assessments, we performed receiver operating characteristic (ROC) analyses for each of the VAS items for each of the main and secondary outcomes. For each ROC curve, the optimal cut-off and the sensitivity, specificity, positive and negative predicted values were calculated. We then determined the risk of receiving supportive care by using bivariate logistic regression analyses, including all three parental VAS items, respiratory rate and SpO₂, adjusting for age and gender.

To develop an algorithm for predicting the use of supportive care based upon information available at enrolment, we used the Hosmer stepdown procedure (25) of multivariate logistic regression analyses. The final model including predictors with a significance level of $p < 0.25$ in bivariate analyses, based upon the following variables; gender, age given in days at enrolment, all VAS items, SpO₂, respiratory rate. Analyses were repeated substituting respiratory rate with the physician assessed clinical score. The resulting final prediction algorithm was used to estimate the probability of receiving supportive care in a child with acute bronchiolitis. The area under the curve (AUC) as well as sensitivity, specificity, positive and negative predicted values of the algorithm were determined by ROC curves. To provide estimates for individual probability of receiving supportive care, we determined the probability curve of the predication algorithm based upon the multi-variate regression analyses.

The significance level was set to 0.05 (5%). Analyses were conducted in SAS version 9.4 (SAS Institute Inc., North Carolina, USA), IBM SPSS version 22.0 (IBM, New York, USA.) and R 3.3.0 (The R Foundation, Vienna, Austria).

RESULTS

The baseline and clinical characteristics at inclusion are shown in table 1. The VAS assessments were mostly completed by mothers (n=220), and the rest by 42 fathers, two specified and three unspecified care providers.

The VAS scores were highest for Feeding with a mean (SD) of 5.9 (2.0), followed by Feeding of 5.1 (3.3) and Activity of 4.8 (2.8), respectively.

Any supportive care was provided for 50.2% of the infants, more often among the 106 girls (58.4%) than among the 161 boys. None of the infants were intubated, whereas 40.4% received oxygen supplement, 27.3% received nasogastric tube feeding and 7.9% received ventilatory support by continuous positive airways pressure. Infants who received supportive care were of similar age to infants who did not, but had significantly longer hospital stay with a mean (SD) of 115 ($\pm$ 73) hours compared to 49 ($\pm$ 40) hours in infants not receiving supportive care.

For 10.5 % of the infants, the scores were classified into the upper, most severe, quartile for all three VAS items, while this was the case for two VAS items in 9.7% of the infants. The background characteristics were similar among children categorised into the lowest versus highest quartile of each VAS item, with a few exceptions. As shown in Table S3, infants who were scored most severe in the VAS items Activity and Feeding had mothers with higher education and were older than infants scored less severe, whereas infants scored most severe by the VAS item Illness more often had non-Caucasian parents.

Infants scored in the upper quartile for all three parental VAS items received any supportive care, oxygen supplement and nasogastric tube feeding significantly more often than infants scored in the lower quartiles, as shown in Figure 1. Similarly, infants scored in the highest compared to lower quartiles for Activity and Feeding more often received ventilatory support as shown in Figure S2.

All three parental VAS items, SpO₂ and respiratory rate were significantly associated with the use of supportive care, with Feeding having the highest OR (1.36) for receiving any supportive care (Table 2). The ability of each of the three VAS items to predict the use of supportive care ranged from an AUC of 0.60 to 0.71 (Table S4). The optimal cut-off values are shown by the respective ROC curves in figure S3. The parental VAS item Illness was most strongly associated with supportive care, providing positive and negative likelihood ratios of 2.1 and 0.55, respectively using the optimal cut-of value of 6.2 with a sensitivity of 61% and specificity of 71% (Table S5).

The prediction algorithm for supportive care was based upon the final logistic regression model including the VAS items Feeding and Illness, SpO₂, age and gender. The VAS item Activity was a significant predictor in the bivariate analysis, but did not reach statistical significance in the multivariate analysis. Additional analyses substituting respiratory rate with the clinical score did not improve of the prediction algorithm (data not shown).

The values of the prediction described in figure 2 algorithm ranged from minimum -2.9 to maximum 2.7, with 2.7 corresponding to a 94% probability of receiving supportive care. The discriminant ability given by the AUC of the prediction algorithm was 0.76 (95% CI:0.69-0.81) ($p<0.001$). The highest combined sensitivity of 81% (73%,87%) and specificity of 61% (52%, 69%) was found with a cut off value of ≥ -0.18 , giving positive and negative predictive values of 68% (60%, 75%) and 76% (66%, 84%), respectively. The probability of a child hospitalised with acute bronchiolitis receiving supportive care in our cohort was determined by plotting the algorithm value into the predictive probability curve, as shown in Figure 2.

DISCUSSION

In this study in infants with acute bronchiolitis, parental assessment of disease severity at time of hospital admission was significantly associated with use of supportive care. The VAS item Illness was the strongest single predictor of supportive care, while the overall prediction algorithm included two of the three VAS items, SpO₂, age and gender. The AUC of 0.76 in our prediction model based upon factors available at the time of hospital admission indicated a moderate to good ability to predict the use of supportive care.

Our findings that parental disease severity assessment at the time of hospital admission predicted supportive care for acute bronchiolitis, has to our knowledge not previously been reported. Although an AUC of 0.60-0.71 for the three individual VAS items indicated modest prediction, all three VAS items were significantly associated with receiving any, or at least one of the supportive care modalities commonly used in acute bronchiolitis management. These findings are supported by a systematic review (18) identifying the importance of parental concern in severity perception of infectious disease in children, as well as by a report by Walsh et al showing that a history of poor feeding was associated with increased length of stay in 182 infants with acute bronchiolitis (11). Our finding that Illness was most closely associated with each supportive care modality as well as any supportive care, may indicate that an overall assessment, rather than assessment of specific functions better captures parental concern. Although parents generally perceive their child as more ill than do healthcare providers (26,27) and rarely underestimate disease severity (28), our results indicate that parental VAS assessment of their infant illness may increase the likelihood of predicting the need for supportive care.

In line with our findings that two of the three parental VAS items together with SpO₂, age and gender significantly predicted supportive care, Corneli et al (12) demonstrated that SpO₂ of 97% or less predicted an increased length of hospital stay, without identifying other significant predictors (12). As in our study, respiratory rate significantly predicted the need for

hospitalisation of infants with acute bronchiolitis (13), while we, in contrast the study by Marlais et al, were unable to show heart rate to be a significant predictor of severity outcomes. Young age is a known risk factor of hospital admission (13), need for intensive care (10) and length of stay. In addition, our study found younger age as a predictor of supportive care. Although boys dominated hospital admissions for acute bronchiolitis in our, as well as in other studies (2,13), female sex increased the likelihood of receiving supportive care, all other factors being equal. To our knowledge, this has not previously been reported.

The AUC of 0.76 in our supportive care prediction algorithm is comparable to the AUC of 0.81 reported by Marlais et al (14) predicting the need of hospital admission, but lower than the AUC of 0.86 of the Pediatric Risk of Admission score (4). In contrast to our prediction algorithm applied to moderately to severe acute bronchiolitis in patients already admitted to hospital, the latter two algorithms assessed predicted if the risk of being admitted to hospital, suggesting a group of infants with less severe disease. Nevertheless, similar to our model, the prediction model by Marlais et al including age, respiratory rate, heart rate, SpO₂, while they also included duration of symptoms (14) where we included parental severity assessment. Variations in predictive precision of these algorithms are likely to be explained by different factors influencing the risk of being hospitalised versus the risk of receiving supportive care, as well as the latter probably representing a group of infants with more homogenous disease severity. An AUC exceeding 0.75 may be considered clinically useful (29), suggesting that our prediction model including parental assessment may be useful for predicting if an infant will need supportive care during hospitalisation. Although values of less than -0.18 increases the likelihood that the infant will not need supportive care, such prediction is only modest owing to the specificity of 61% using the optimal cut-off value of -0.18.

Along with our previous study; the Bronchiolitis ALL study South-east Norway, documenting that inhaled racemic adrenaline was not superior to saline inhalations in reducing length of

hospital stay or use of supportive care (23), no available treatment is found to shorten the course of the bronchiolitis or hasten the resolution of symptoms. This leaves supportive care as the only useful therapy (2) and the main medical reason for the need to stay in hospital. The use of supportive care was therefore chosen as the marker of disease severity, received by 50% in the present study. The clinical decision-making of hospitalisation and hospital discharge depend on subjective perceptions as well as objective factors and may be influenced by the experience of the attending physicians (11,17), the risk for complications (2,16), time of the day, distance to the child's home, parental anxiety, as well as need for supportive care (2,15). At present, no score clearly outperforms others in predicting the outcome of acute bronchiolitis in terms of severity (14). The clinical score performed by doctors, a proxy for objective judgement, did not reach the final prediction model, whereas a significant model included the parental assessment together with other objective severity markers. This suggests that the use of standardised parental assessment tools together with objective measures, may improve the accuracy of predicting therapeutic needs of infants with acute bronchiolitis.

Strengths and limitations of this study

In the present large, prospective study, supportive care was recorded daily throughout the hospital stay. The missing parental assessments in 137 infants who were not included in the present study probably reflect hectic activity and priority issues in the paediatric wards during winter epidemics of viral lower respiratory tract infections. However, as baseline characteristics among these infants were similar to those of the included infants, the lack of parental assessments are unlikely to have a major impact on the interpretation of the results. The parents were asked to assess their infant's disease severity as soon as possible, and independently of the clinical score by the physician. The doctor's clinical decision of hospital admission and further management had thus most probably not a significant impact upon the parental assessments. However, as almost all children were referred to hospital by general

practitioners, they may have influenced the parental perception of their infant's condition. The applicability of the parental VAS- scores outside a hospital setting is therefore unclear.

CONCLUSION

Parental disease assessment using a three-item VAS at the time of admission to hospital predicted the use of supportive care in infants with acute bronchiolitis. A prediction algorithm including two of the three VAS items, SpO₂, age and gender, had a moderate to good ability to predict the use of supportive care for acute bronchiolitis. Standardised parental disease assessment at the time of hospital admission could be considered to improve the likelihood of predicting the need for supportive care, and thereby need for hospitalisation of infants with acute bronchiolitis.

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The study was performed within ORAACLE (the Oslo Research Group of Asthma and Allergy in Childhood; the Lung and Environment).

ABBREVIATIONS

SpO ₂	peripheral capillary oxygen saturation
VAS	Visual analogue scale
SD	Standard deviation
CI	Confidence interval
OR	Odds ratio
ROC	Receiver operating characteristic
AUC	Area under the curve

Conflict of interest:

The authors have no conflicts of interest to disclose.

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Table 1. Characteristics of the 267 infants with parental VAS scores hospitalized with acute bronchiolitis shown by those who received and did not receive supportive care.

	Supportive care (n=134)	No supportive care (n=133)	p-value
Male sex (%)	72/134 (54)	89/133 (67)	0.028
Age (mean (range)) in days	118 (14, 364)	137 (7, 347)	0.07
Weight (mean (range)) in grams	6187 (3070, 11655)	6931 (2925, 11400)	0.001
Length (mean (range)) in centimetres	61.6 (48, 80)	64.4 (50, 80)	0.019
Infant medical history (%)			
Reported atopic eczema	7/124 (5.6)	22/129 (17.1)	0.004
Reported allergies	2/125 1.6	2/127 1.6	0.99
Parental socio-demography			
Mother Caucasian (%)	107/130 82.3	116/131 88.5	0.13
Father Caucasian (%)	110/130 84.6	111/131 84.7	0.76
Maternal education ^a (mean (SD))	3.9 (0.9)	4.0 (0.9)	0.75
Paternal education ^a (mean (SD))	3.8 (1.0)	3.8 (0.9)	0.56
Parental smoking (%)	15/106 14.2	18/121 14.9	0.99
Parental medical history	3.8 (1.0)	3.8 (0.9)	0.56
Maternal Asthma	18/111 (16.2)	19/109 (17.6)	0.79
Paternal Asthma	14/111 (12.6)	13/108 (12.0)	0.90
Maternal rhinitis/ rhinoconjunctivitis	20/119 (16.8)	22/125 (17.6)	0.87
Paternal rhinitis/ rhinoconjunctivitis	28/119 (23.5)	20/125 (16.0)	0.14
Clinical characteristics at hospitalisation			
SpO ₂ (SD) ^b	95 (3)	97 (3)	<0.001
Respiratory rate- breaths/min (SD)	55 (11)	52 (12)	0.044
Heart rate- beats/min (SD)	156 (18)	151 (18)	0.024

^aEducation was categorised from 1 (no school completed) to 5 (higher education, more than three years).

^b SpO₂ denotes peripheral capillary oxygen saturation by pulse oximetry.

Table 2 The table reports the Odds Ratio for infants 0-12 months of age admitted to hospital with acute bronchiolitis receiving supportive care based upon parental disease severity assessment by three visual analogue scale (VAS) items; Activity, Feeding, Illness, respiratory rate and peripheral capillary oxygen saturation (SpO₂) at the time of hospital admission.

	Oxygen supplement OR (95% CI)	Nasogastric tube feeding OR (95% CI)	Ventilatory support OR (95% CI)	Any supportive treatment OR (95% CI)
VAS Activity	1.22 (1.11, 1.35)	1.30 (1.16, 1.45)	1.23 (1.02, 1.49)	1.26 (1.15, 1.39)
VAS Feeding	1.14 (1.05, 1.23)	1.32 (1.19, 1.46)	1.28 (1.07, 1.52)	1.23 (1.13, 1.34)
VAS Illness	1.34 (1.17, 1.55)	1.40 (1.20, 1.64)	1.35 (1.04, 1.75)	1.36 (1.18, 1.56)
Respiratory rate	1.01 (0.99, 1.04)	1.03 (1.01, 1.06)	1.0 (0.96, 1.05)	1.02 (1.0, 1.05)
SpO ₂	0.77 (0.69, 0.85)	0.87 (0.80, 0.96)	0.73 (0.63, 0.84)	0.78 (0.70, 0.86)

Bivariate Odds Ratios (OR) are adjusted for age and gender. Each VAS item was scored from 0-10, 10 being most severe, while a lower SpO₂ denoted more severe disease. An OR of SpO₂ of 0.77 should therefore be interpreted as a 23% increase risk of receiving supportive care for each percent reduction in SpO₂.

Figure Legends:

Figure 1 Associations between parental Visual Analogue Scale (VAS) score at inclusion and need of supportive care during hospital stay in 267 infants with parental VAS score.

Presented with the 95% upper Confidence Interval. The level of significance is presented comparing upper to lower quartile.

Each of the three VAS items; Activity, Feeding and Illness are presented in figure S2.

Figure 2 Predicted probability curve for receiving supportive care, based upon the parental visual analogue scale (VAS) items; Feeding and Illness, SpO₂, age and gender.

Once the algorithm value is calculated using the algorithm;

$17.9 + 0.16 \times \text{VAS Feeding} + 0.19 \times \text{VAS Illness} - 0.21 \times \text{SpO}_2 + \text{Gender (male=1, female =2)} \times 0.62 - \text{Age (days)} \times 0.004$, the individual probability of receiving supportive care is estimated from the probability curve.

Example 1 (circle): Using median VAS of the lower quartile, male gender and mean age.

VAS Feeding: 0.6, VAS Illness: 3.4, SpO₂ (%): 94, Male: value 1, Age (days): 128, gives an algorithm value of -0.99 with a predicted probability of receiving supportive care of 27%.

Example 2 (square): Using median VAS of the upper quartile, female gender and young age.

VAS Feeding: 9.4, VAS Illness: 8.2, SpO₂ (%): 94, Female: value 2, Age (days): 30, gives an algorithm value of 2.34 with a predicted probability of receiving supportive care of 91%.

Figure 1

Figure 2