Can Clinical Symptoms or Signs Accurately Predict Hypoxemia in Children with Acute Lower Respiratory Tract Infections?

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Objectives: *To determine clinical predictors of hypoxemia in children with acute lower respiratory tract infection (ALRI).* ***Design:*** *Cross-sectional study.* ***Setting:*** *Emergency department of All India Institute of Medical Sciences, a tertiary care hospital.* ***Subjects:*** *109 under five children, with ALRI.* ***Methods:*** *Clinical symptoms and signs were recorded. Oxygen saturation was determined by a pulse oximeter. Hypoxemia was defined as oxygen saturation less than 90%. The ability of various clinical symptoms and signs to predict the presence of hypoxemia was evaluated.* ***Results:*** *Twenty-eight (25.7%) children were hypoxemic. No symptoms were statistically associated with hypoxemia. Tachypnea, suprasternal indrawing, intercostal indrawing, lower chest indrawing, cyanosis, crepitations, and rhonchi were statistically significantly associated with hypoxemia. A simple model using the presence of rapid breathing (≥80/min in children £ 3m, ≥70/min in >3 –12m and ≥60/min in >12m) or lower chest indrawing had a sensitivity of 78.5% and specificity of 66.7% for detecting hypoxemia. No individual clinical symptom/sign or a combination had both sufficient sensitivity and specificity to identify hypoxemia.* ***Conclusion:*** *None of the clinical features either alone or in combination have desirable sensitivity and specificity to predict hypoxemia in children with acute lower respiratory tract infection.*

Key words: *Acute lower respiratory tract infections, hypoxemia, pulse oximetry.*

ACUTE lower respiratory tract infections (ALRI) are the leading cause of morbidity and mortality among children in developing countries, causing about one-third of all deaths in childhood(l). Hypoxemia is an important risk factor for mortality in children with ALRI(2). Pulse oximetry is a simple technique to determine the oxygen saturations. However, detection of hypoxemia by use of pulse oximetry is not feasible in most situations in developing countries. In addition, the availability of supplementary oxygen is poor. It is, therefore, important to accurately identify hypoxemic children by use of clinical signs alone. Various symptoms and signs have been evaluated for their ability to predict hypoxemia(2-7).

We determined the prevalence of hypoxemia in children with ALRI presenting to emergency service of a tertiary care hospital and tried to identify the clinical signs predictive of hypoxemia.

Methods

This study was carried out from August 1999 to October 1999 in the Emergency

department of All India Institute of Medical Sciences, New Delhi (altitude: 239 m above the sea level). Children less than 5 years of age, presenting with an acute history of cough and rapid respiration or difficulty in breathing were included in the study, according to the WHO criteria for ALRI(8). Children with asthma, congenital heart disease, severe anemia, peripheral circulatory failure, children needing ventilatory support, and severe dehydration were excluded.

A history was obtained from the mother about the presence and duration of various symptoms: cough, fever, and difficulty in breathing, rapid breathing, diarrhea, irritability, convulsions, feeding pattern, and inability to drink / feed.

The child was examined and the following signs were recorded: appearance, weight, heart rate, respiratory rate (counted for 60 seconds when the child was quite and at rest), cyanosis, chest retraction, grunting, nasal flaring, head nodding, pallor, crepitations or rhonchi on auscultation and the state of consciousness. One of the authors collected the data, after they were trained by the senior author to identify the above-mentioned clinical signs. The findings were randomly crosschecked during the study.

A portable oximeter (Ohmeda Biox 3700e pulse oximeter [BOC Health Care]) was used to measure oxygen saturation with an appropriately sized sensor on the finger or the toe. The reading was taken in a blinded manner by another author, while the child was breathing room air. Hypoxemia was defined as oxygen saturation less than 90%.

The statistical analysis was performed with software package 'STATA 7.0' (STATA Corp., TX, USA). The study sample was divided into two groups: Group 1-children having oxygen saturation <90%, Group 2-children having oxygen saturation ³90%. Baseline characteristics were compared. Frequency of different symptoms / signs in both groups was calculated. Sensitivity, specificity and likelihood ratios were calculated for different symptoms and signs. Chi-square and *t*-test were applied as indicated. Ninety-five percent confidence intervals were calculated for sensitivity, specificity and the likelihood ratios(9). Different combinations of signs found to be significant in the univariate analysis were evaluated for their ability to predict hypoxemia.

Results

One hundred and nine children were evaluated in the study. Twenty-eight (25.7%) children were found to have hypoxemia (Group 1); the median (95% confidence interval) oxygen saturation was 87% (86-88%). The median (95% confidence interval) oxygen saturation in Group 2 was 95% (94-98%). The mean (S.D.) age of participants in Group 1 (hypoxemic) and Group 2 (non-hypoxemic) was 25.9 (17.9) months and 23.3 (16.9) months respectively. The distribution of patients in three age groups £ 3m, >3-12m, >12m) in the two groups were similar; there were 1, 9, 18 hypoxemic children and 3, 25, 53 children non-hypoxemic children in these age groups, respectively. The sex distribution was comparable (Group l-17 boys, Group2 -58 boys). The mean (SD) weight of children in these two groups was 11 (4.5) kg and 10.1 (4.1) kg respectively. None of these differences between the two groups were statistically significant.

None of the symptoms evaluated were found to have a statistically significant association with hypoxemia.

The mean respiratory rate in Group 1 was 62.8/min compared with 52.1/min in Group 2

(P = 0.0096). *Table I* lists the sensitivity, specificity and likelihood ratio of different signs used to predict hypoxemia. Different respiratory rate cutoff in different age groups (£3 m, >3-12 m, >12 m) were evaluated for association with hypoxemia (*Table I*). A respiratory rate cutoff of ³70/min in children £3 m, ³60/min in >3m-12m, ³50/min in >12m age group had a sensitivity of 82.1% and specificity of 51.8% for detecting hypoxemia. Increasing the cutoff further by 10/min in each age category led to decline in the sensitivity to 53.6% while the specificity improved to 77.8%. Presence of suprasternal indrawing, intercostal indrawing, lower chest indrawing, cyanosis, crepitations, and rhonchi were also significantly associated with hypoxemia.

Nasal flare was present in 8 children in Group 1 and 15 in Group 2, head nodding was seen in 0 and 2 children and restlessness in 2 and 9 respectively in the two groups. Figures were comparable between two groups.

Various combinations of clinical signs were evaluated for predicting hypoxemia (*Table II*). Presence of crepitations or chest indrawing or respiratory rate ³60/min in children £3 m, ³50/min in >3-l2 m and ³40/min in >12 m had 96.4% sensitivity for predicting hypoxemia, while the specificity was only 12.3%. A simple model using presence of either lower chest indrawing or presence of respiratory rate ³80/min in children £3 m, ³70/min in >3-12 m and ³60/min in >12 m had maximum specificity (66.7%) amongst various combinations evaluated; however, the sensitivity was lower at 78.5%.

Discussion

We have evaluated various symptoms and signs for their ability to identify hypoxemia in children with symptoms of acute respiratory tract infection. None of symptoms and signs evaluated was both sufficiently sensitive and specific. Use of combination *e.g.*, presence of either tachypnea or lower chest indrawing only slightly improved the predictive ability.

We have used likelihood ratios in addition to sensitivity and specificity to evaluate the utility of different clinical markers to predict hypoxemia. These ratios do not change with the pretest probabilities of the disease (*i.e.* prevalence). This would permit better evaluation of the utility of various clinical signs to predict hypoxemia. As per obtained 95% confidence intervals of likelihood ratios the presence or absence of most clinical signs or symptoms will have limited impact on the pretest odds.

Various symptoms and signs have been evaluated to identify the clinical markers of hypoxemia in earlier studies(2-7). It is evident from this review that there are no symptoms or signs which are both sufficiently sensitive and specific to identify hypoxemia. Various models using combinations of symptoms / signs have also not been able to improve the predictive ability(2,5,7,8). In addition, there is lack of agreement amongst different studies. Different values are obtained when these models are applied to different datasets. This difference may be due to lack of agreement between different observers(10) or may reflect the inability of clinical signs to accurately predict hypoxemia. These studies have been conducted in different altitudes. While three studies included children under 5 years of age (3,5,6), others had included younger children (2,4,7). Some of the studies done earlier (2,3,5,6) have also included young infants while others (4,7) have not. Signs of systemic infection in young infants are non-specific; this may be the reason for their exclusion in some studies. We had included children less than 3 months of age; there were only 4 such children.

TABLE I–*Sensitivity and Specificity of Different Clinical Markers to Predict Hypoxemia*

Parameter	Children with signs (%)	Hypoxemic children (n=28)	Non-Hypoxemic Children (n=81)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	Positive Likelihood ratio (95%CI)	Negative Likelihood ratio (95%CI)	P value
Respiratory rate £3 m : ³60/min >3-12 m : ³50/min ³12 m : ≥40/min	87 (79.8)	25	62	89.3 (71.8, 98.9)	23.5 (14.8, 34.2)	1.17 (0.98, 1.39)	0.46 (0.15, 1.43)	0.148
Respiratory rate £3 m : ³70/min >3-12 m: ³60/min ³12 m : ≥50/min	62 (56.9)	23	39	82.1 (63.1, 93.9)	51.8 (40.5, 63.1)	1.71 (1.28, 2.27)	0.34 (0.15, 0.78)	0.002
Respiratory rate £3 m : ³80/min >3-12 m: ³70/min ³12 m : ≥60/min	33 (30.3)	15	18	53.6 (33.8, 72.4)	77.8 (67.2, 86.3)	2.41 (1.41, 4.11)	0.60 (0.39, 0.90)	0.002
Suprasternal indrawing	14 (12.8)	8	6	28.6 (13.2, 48.7)	92.6 (84.6, 97.2)	3.86 (1.47, 10.15)	0.77 (0.61, 0.98)	0.004
Intercostal indrawing	19 (17.4)	9	10	32.1 (15.9, 52.3)	87.7 (78.5, 93.9)	2.6 (1.18, 5.74)	0.77 (0.59, 1.01)	0.017
Lower chest indrawing	21 (19.3)	10	11	35.7 (18.6, 55.9)	86.4 (77,93)	2.63 (1.25, 5.52)	0.74 (0.56, 0.99)	0.01
Grunt	10 (9.2)	4	6	14.2 (4, 32.7)	92.5 (84.4, 97.2)	1.9 (0.58, 6.26)	0.93 (0.79, 1.09)	0.286
Cyanosis	7 (6.4)	4	3	14.2 (4, 32.7)	96.2 (89.4, 99.2)	3.81 (0.91, 15.98)	0.89 (0.76, 1.04)	0.05
Crepitations	45 (41.3)	19	26	67.8 (47.6, 84.1)	67.9 (56.6, 77.8)	2.11 (1.41, 3.17)	0.47 (0.27, 0.83)	0.001
Rhonchi	31 (28.4)	17	14	60.7 (40.5, 78.5)	82.7 (72.7, 90.2)	3.51 (2, 6.16)	0.47 (0.3, 0.76)	<0.001

TABLE II–*Utility of Different Combinations to Predict Hypoxemia*

Presence of	Hypoxemic children	Non-Hypoxemic Children	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	Positive Likelihood ratio (95% CI)	Negative Likelihood ratio (95% CI)
Respiratory rate £3 m : ³60/min >3-12 m : ³50/min ³12 m : ³40/min or lower chest indrawing or crepitations	27	71	96.4 (81.6, 99.9)	12.3 (6.1, 21.5)	1.1 (0.99, 1.23)	0.29 (0.04, 2.16)
Respiratory rate £3 m : ³70/min >3-12 m : ³60/min ³12 m : ³50/min or lower chest indrawing	24	46	85.7 (67.3, 95.9)	43.2 (32.2, 54.7)	1.51 (1.18, 1.92)	0.33 (0.13, 0.85)
Respiratory rate £3 m : ³80/min >3-12 m : ³70/min ³12 m : ³60/min or lower chest indrawing	22	57	78.5 (59, 91.7)	66.7 (55.3, 76.8)	1.53 (1.17, 1.99)	0.44 (0.21, 0.92)
Respiratory rate £3 m : ³80/min >3-12 m : ³70/min ³12 m : ³60/min or crepitations or rhonchi	25	39	89.3 (71.8, 97.7)	51.9 (40.5, 63.1)	1.85 (1.43, 2.4)	0.21 (0.07, 0.61)

Key Messages

- Clinical symptoms and signs alone or in combination do not have sufficient sensitivity and specificity to predict hypoxemia in children with acute lower respiratory tract infection. Therefore, pulse oximetry is desirable for identification of hypoxemia.
- However, in the absence of pulse oximetry, a simple clinical model such as presence of rapid breathing (³80/min in children £3m, ³70/min in >3 -12m and ³60/min in >12m) or lower chest indrawing may be used for detection of hypoxemia in children with pneumonia.

While there is no clear evidence available, oxygen supplementation may have more efficacy in the subgroup with lower saturations. However, our study does not permit subgroup analysis to determine the ability of clinical symptoms and signs to detect lower oxygen saturations, for example less than 85%.

Except for cyanosis, none of the clinical symptoms /signs in children with lower respiratory tract infections can be explained by hypoxemia alone, *e.g.*, tachypnea may also be due to acidosis, fever, central nervous system causes in addition to hypoxemia. Lower chest indrawing or grunt or symptoms like poor feeding / inability to feed are better explained by severity of pneumonia. A severe pneumonia is more likely to be associated with hypoxemia; therefore, some of the markers of severe pneumonia may also be significantly associated with hypoxemia. It is unlikely that any of these markers of severity of pneumonia will have both good sensitivity and specificity to identify hypoxemic children. In addition, there is lack of agreement among observers for clinical signs of respiratory disorders(10).

The study was conducted in a tertiary care center and there may be a referral bias. The study was conducted predominantly in one season that may have led to particular illness pattern bias. We did not validate the pulse oximetry findings with arterial blood gas results as we thought it unnecessary in light of evidence supporting accuracy of pulse oximetry. Wide confidence intervals for various parameters suggest that the sample size of the study was small. At the upper limits of the confidence intervals for sensitivity and specificity, various symptoms and signs will appear quite useful. For more accurate estimations, a larger study will be required.

Clinical symptoms and signs alone or in combination do not have sufficient sensitivity and specificity to predict hypoxia in children with acute lower respiratory tract infection. Efforts should me made to provide low cost pulse oximeters in resource poor settings.

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