Clinical predictors of acute radiological pneumonia and hypoxaemia at high altitude

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Abstract

Fast breathing has been recommended as a predictor of childhood pneumonia. Children living at high altitude, however, may breathe faster in response to the lower oxygen partial pressure, which may change the accuracy of prediction of a high respiratory rate. To assess the usefulness of clinical manifestations in the diagnosis of radiological pneumonia or hypoxaemia, or both, at high altitude (2640 m above sea level), 200 children aged 7 days to 36 months presenting to an urban emergency room with cough lasting less than seven days were studied. Parents were interviewed and the children evaluated using standard forms. The results of chest radiographs and pulse oximetry obtained after clinical examination were interpreted blind. Radiological pneumonia and haemoglobin oxygen saturation <88% were used as 'gold standards'. One hundred and thirty (65%) and 125 (63%) children had radiological pneumonia and hypoxaemia respectively. Crepitations and decreased breath sounds were statistically associated with pneumonia, and rapid breathing as perceived by the child's mother, chest retractions, nasal flaring, and crepitations with hypoxaemia. The best single predictor of the presence of pneumonia is a high respiratory rate, although the results are not as good as those reported by other studies. A respiratory rate ≥50/minute had good sensitivity (76%) and specificity (71%) for hypoxaemia in infants. Hypoxaemia had a good sensitivity and specificity for pneumonia mainly in infants (83% and 73%, respectively). Logistic regression analysis showed that decreased or increased respiratory sounds and crepitations were associated with pneumonia, and that hypoxaemia is the best predictor when auscultatory findings are excluded. These results suggest that some clinical predictors appear to be less accurate in Bogota than in places at lower altitude, and that pulse oximetry can be used for predicting pneumonia.

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About four million children younger than 5 years of age die of pneumonia each year, mainly in developing countries, where mortality from acute respiratory infections is up to 26 times higher than that in developed countries.[1] The technical advisory group on acute respiratory infections of the World Health Organisation (WHO) proposed in 1984 a system for the management of acute respiratory infections.[2] One important component of this strategy is the classification of acute respiratory infection according to its severity based on simple clinical findings. This classification can be used by primary health workers for making decisions about the use of antibiotics and referral to hospital, among others. Briefly, children between 2 months and 5 years of age with cough and chest indrawing, or other danger signs, are considered to have very severe disease or severe pneumonia, and are referred to a medical facility for further evaluation and treatment. Children with fast breathing (respiratory rate ≥50/minute for children between 2 and 11 months and ≥40/minute for those between 12 months and 5 years) and without danger signs are classified as having pneumonia and treated as outpatients with antimicrobial drugs. Finally, children with cough and without fast breathing, chest indrawing, or danger signs are classified as not having pneumonia, but only a cough or cold, and receive treatment for fever and wheezing if they are present.[3] This strategy, whose effectiveness has been documented through several field studies,[4] has been adopted by the Ministry of Health in Colombia.[5]

These guidelines are based on several studies, conducted at low altitude, which have shown that fast breathing is an adequate predictor of pneumonia.[6-8] Additional studies, however, have produced different and in some instances contradictory results.[9,10] The only published study conducted at high altitude found that the respiratory rate was not a good parameter for predicting radiological pneumonia, and that the presence of hypoxaemia detected by pulse oximetry was a better predictor than the physical findings.[11] One potential explanation for these results could be the higher respiratory rate observed in normal children living at high altitudes in response to the lower oxygen partial pressure.[11]

Pulse oximetry is a non-invasive and accurate method of measuring the saturation of haemoglobin with oxygen (Sa_{O_2}).[12,13] Two published studies conducted at high altitude used this system to assess the relation between individual clinical signs and hypoxaemia in children with pneumonia, and found that a low Sa_{O_2} can predict the presence of pneumonia more accurately than the physical examination,[11] and that a mother's report of cyanosis ('blueness') was the best single predictor of hypoxaemia in young infants.[14] Other workers have recognised the limitations of clinical signs for identifying hypoxaemia in children with pneumonia.[15]

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The goal of this study was to determine how helpful signs and symptoms were in predicting radiological pneumonia or hypoxaemia detected by pulse oximetry, and the usefulness of hypoxaemia in the diagnosis of radiological pneumonia. The patients studied were a group of children under 3 years of age with symptoms of acute respiratory infection living at high altitude (Bogota, Colombia; 2640 m above sea level).

Patients and methods

Two hundred and one children with symptoms of acute respiratory infection who attended the emergency room or the outpatient department of the Clinica Infantil Colsubsidio (a tertiary care centre that also provides primary care) between March 1991 and March 1992, and whose evaluation included a chest radiograph (ordered independently by the treating paediatrician) were enrolled in the study. Patients were eligible if they had presented with cough lasting up to seven days. Children were excluded if they had cardiovascular, pulmonary, or neurological congenital defects, if they were born before term (requiring admission to hospital as newborn infants), had chronic diseases (including bronchial asthma, cancer, metabolic disorders, and immunosuppression), or had had previous episodes of wheezing.

After obtaining verbal informed consent from the caretaker (usually the mother), all children were evaluated by one of three of the authors (NM, MLM, BD). Data on symptoms and clinical signs of acute respiratory infection were obtained using a standardised questionnaire which included information such as the presence of rapid breathing as perceived by the mother, fever or hypothermia, loss of appetite, drowsiness, refusal to eat or drink, abdominal distention or seizures. The presence of nasal flaring, retractions, or grunting was established with the child's chest naked, and the respiratory rate was determined by counting the respiratory movements for one minute. Concomitant axillary temperature and the status of the child (quiet or fussy/crying) were recorded. Finally, the results from a medical chest examination, including the presence of abnormal respiratory sounds (wheezes, crepitations, rhonchi, reduced breath sounds) were also obtained.

The 'gold standards' used in the study were the presence of pneumonia confirmed radiographically or of hypoxaemia detected using pulse oximetry. Immediately after the physical examination, the Sao_2 was measured three times using a Nellcor N10 oximeter with an adhesive sensor attached to the child's index finger. A previous study in 189 healthy children living in Bogota found that 95% of them had a Sao_2 value $\geqslant$88%; therefore, we defined hypoxaemia as a mean Sao_2 less than 88%.[16] In all instances a chest radiograph with anteroposterior and lateral projections was obtained within two hours of the clinical evaluation. All films were interpreted by the same radiologist, who has extensive experience in paediatric radiology and who was blind to the clinical findings of each subject. As the radiological pattern does not allow the determination of the aetiological agent in patients with acute respiratory infection,[17 18] and because most episodes of pneumonia in developing countries are produced by bacterial agents,[19] the presence of any kind of infiltrate (alveolar or interstitial) in the chest radiograph of this group of symptomatic children was considered as pneumonia. To determine whether the diagnostic characteristics of the clinical predictors evaluated changed in accordance with the radiological pattern, however, a second analysis was performed, considering pneumonia only in those patients with alveolar infiltrates.

Sensitivities (the proportion of children with positive findings among those with confirmed radiological pneumonia or hypoxaemia) and specificities (the proportion of children without positive findings among those without radiological pneumonia or hypoxaemia) were calculated for each symptom and sign. To determine the best cut off point for continuous variables (that is, respiratory rate), sensitivities and specificities were obtained for each cut off value and these results were used to construct receiver operator characteristic curves.[20] Children who were crying during the physical examination were excluded from the respiratory rate evaluation, but were included for the assessment of all other clinical manifestations. The use of pulse oximetry for predicting pneumonia was evaluated by obtaining the sensitivity and specificity of hypoxaemia for predicting radiological results. Similar analyses were performed for the group of infants and for children older than 12 months. χ^2 Analysis was used to assess the statistical association of each sign with radiological pneumonia or hypoxaemia.[21] Finally, the independent association of each clinical finding with pneumonia or hypoxaemia was evaluated using logistic regression analysis.[22]

Results

One child had to be excluded due to intense vascular collapse secondary to septic shock that produced no readings during the pulse oximetry assessment, and 28 (14%) more who were crying during the physical examination were excluded from the respiratory rate assessment. Table 1 summarises the main baseline findings of the 200 subjects finally included in the study. The mean (SD) duration of cough before the evaluation was 3·6 (2·0) days. In 179 patients (89·5%) the paediatrician on duty

Table 1 Baseline characteristics of the 200 subjects included in the study

	No (%)
Age (months)	
<12	62 (31)
13–24	83 (42)
>24	55 (28)
Male sex	102 (51)
Previous antipyretic drugs	158 (79)
Previous antibiotic drugs	40 (20)
Radiological pneumonia	130 (65)
Hypoxaemia	125 (63)

Table 2 Sensitivity and specificity of several symptoms reported by the mother in the diagnosis of radiological pneumonia or hypoxaemia (Sao_2 <88%)

	Pneumonia		*Hypoxaemia*	
Symptom	*Sensitivity*	*Specificity*	*Sensitivity*	*Specificity*
Rapid breathing	81	20	89	30
Breathing difficulty	51	50	56	58
Chest retractions	44	35	46	45
Grunting	61	45	63	47
Fever	92	17	88	9
Loss of appetite	88	13	90	16
Refusal of solid food	79	25	79	24
Refusal of liquids	45	56	49	63
Refusal of breast feeding	32	58	35	60
Difficult to wake up	11	87	12	89
Abdominal distention	25	85	25	83
Cold to the touch	37	76	36	73
Seizures	2	91	4	95

Table 3 Sensitivity and specificity of several physical signs in the diagnosis of radiological pneumonia or hypoxaemia (Sao_2 <88%)

	Pneumonia		*Hypoxaemia*	
Sign	*Sensitivity*	*Specificity*	*Sensitivity*	*Specificity*
Any chest retraction	81	36	83	40
Subcostal retractions	72	36	76	43
Intercostal retractions	72	48	79	55
Supraclavicular retractions	15	91	18	95
Grunting	41	66	45	72
Nasal flaring	56	53	63	65
Wheezing	15	76	21	86
Rhonchi	82	7	86	15
Crepitations	80	55	79	53
Decreased breath sounds	21	97	19	81
Abdominal distention	15	83	19	90
Seizures	8	99	0	97

made a positive admission diagnosis for acute lower respiratory tract infection. No deaths occurred in these children.

Table 2 shows the sensitivity and specificity of symptoms obtained from the mother for the diagnosis of pneumonia or hypoxaemia. As far as the diagnosis of pneumonia is concerned, none of the manifestations evaluated has simultaneously adequate sensitivity and specificity, although some showed high sensitivity. Similar results were observed for predicting hypoxaemia. The analyses in accordance with age and with different definitions of radiological pneumonia did not modify these results. Table 3 gives the sensitivities and specificities of the physical findings. Both the presence of crepitations and of decreased breath sounds had a good discriminative capacity for the diagnosis of pneumonia ($p<0\cdot00001$), the former with adequate sensitivity and fair specificity and the second with poor sensitivity but a high specificity. These findings did not change when the analysis was repeated in accordance with age and the radiological definition of pneumonia. In the diagnosis of hypoxaemia, the presence of retractions, nasal flaring, crepitations, or decreased breath were associated with a low Sao_2 reading ($p<0\cdot001$), but showed poor sensitivity or specificity, or both. Table 4 presents the sensitivity and specificity of several respiratory rate cut off points for the diagnosis of pneumonia and hypoxaemia according to age. In infants the lowest rate of false diagnoses for radiological pneumonia and hypoxaemia were observed with a respiratory rate ⩾50/minute, whereas for older children the best cut off point for the two disorders was ⩾40/minute. The results obtained for the diagnosis of hypoxaemia were slightly better than those observed for radiological pneumonia in the two age groups.

The presence of a low Sao_2 was an adequate predictor of pneumonia in infants, with a sensitivity of 83% and a specificity of 73%. The usefulness of hypoxaemia for older children was less adequate, however (sensitivity 70%, specificity 43%). The figures for the two age groups combined were 73% and 57%, respectively. The results of the analysis using different Sao_2 cut off points were similar to those obtained with the threshold of 88%.

To assess the statistical association between the studied clinical predictors and the diagnosis of pneumonia or hypoxaemia, several multivariate models were fitted using logistic regression analysis, in which various combinations of symptoms and signs were used as independent variables and the presence of pneumonia or hypoxaemia were the dependent variables. With respect to the diagnosis of pneumonia, the first model, in which all independent variables were used, showed that only some auscultatory findings (decreased breath sounds, increased transmission of respiratory sounds, and crepitations) were independently associated with pneumonia (likelihood ratios of 6·3, 3·9, and 3·7 respectively). A second model using the forward stepwise method (which allows the assessment of the contribution of each independent variable when added one by one to the model)[22] selected the same set of variables included in the first model. Finally, as not all cases of acute respiratory infection are evaluated by medical staff, a third model assessed only some clinical manifestations that can be evaluated by workers with limited training. When all auscultatory signs were excluded, the presence of hypoxaemia or fever had an independent association with the radiological pneumonia (likelihood ratios 3·3 and 3·0 respectively). The inclusion of the respiratory rate in all these models did not improve their predictive value. The same strategies were used to evaluate the association of all independent variables with hypoxaemia. All three models selected several clinical signs that can be obtained by non-medical but well trained staff (chest retractions, nasal flaring, and grunting). Neither the inclusion of the respiratory rate nor of symptoms as perceived by the mother

Table 4 Sensitivity and specificity of several respiratory rate cut off points for the diagnosis of radiological pneumonia or hypoxaemia according to age

	Pneumonia		*Hypoxaemia*	
Respiratory rate (breaths/minute)	*Sensitivity*	*Specificity*	*Sensitivity*	*Specificity*
0–11 Months				
⩾20	100	0	100	0
⩾30	100	0	100	0
⩾40	90	27	96	38
⩾50	70	58	76	71
⩾60	35	77	40	86
⩾70	20	100	16	100
12–36 Months				
⩾20	100	0	100	0
⩾30	90	4	95	16
⩾40	68	52	73	61
⩾50	37	67	39	71
⩾60	9	93	12	100
⩾70	4	100	4	100

improved the predictive capacity of these models.

Discussion

Our results, obtained in a group of patients with acute respiratory infection living at 2640 m above sea level, show that the usefulness of symptoms and signs for predicting pneumonia is intermediate between that reported at lower[6–8] and at higher[11] altitudes. None of the symptoms obtained from the mothers in our group was adequate for the diagnosis of radiological pneumonia, findings that differ from those reported by Cherian *et al*[7] and by Mulholland *et al*,[8] who found that the presence of rapid breathing had sensitivities and specificities of about 90% and 91% respectively. Several systemic manifestations, such as a history of fever or of decreased appetite, have appropriate sensitivity; however, their value as predictors is limited due to their low specificity.

None of the physical signs assessed in our subjects had adequate sensitivity and specificity simultaneously; however, the presence of crepitations or decreased breath sounds showed a statistical association with radiological pneumonia. On the other hand, our findings confirm that the best single predictor of the presence of radiological pneumonia is a high respiratory rate, although its sensitivity and specificity are not as good as those reported by other workers at lower altitudes. In the group of infants, a respiratory rate $\geqslant$50/minute had a sensitivity of 70% and a specificity of 58%, lower than the figures reported by Cherian *et al* (89% and 92% respectively).[7] Similar results were observed in the group of children between 12 and 36 months of age, in whom a respiratory rate $\geqslant$40/minute had a sensitivity of 68% and a specificity of 52% (82% and 88% in the study of Cherian *et al* respectively). These findings reduce the value of a high respiratory rate as an isolated sign for identifying children with pneumonia at high altitude. The sensitivity and specificity of tachypnoea in our group, however, are higher than those reported by Reuland *et al* in Peru at 3750 m above the sea level.[11] These workers found that none of the respiratory rate cut off points evaluated had adequate sensitivity and specificity for predicting radiological pneumonia.

There are at least two potential explanations for the differences between our findings and those of other studies. Firstly, the higher respiratory rates observed in normal children living at high levels above the sea, in response to the lower oxygen partial pressure, might reduce the diagnostic accuracy of tachypnoea at high altitudes. In fact, 41% of healthy infants evaluated in Peru had a respiratory rate above 50/minute.[11] As far as we know, there are no studies about the normal respiratory rate in children living in Bogota to confirm this association. Secondly, some of the reported studies have used different criteria to confirm the presence of pneumonia. In fact, the studies that have reported better results have used clinical findings to confirm the diagnosis.[6 7] Several studies conducted in developed countries have used chest radiographs as the gold standard. Leventhal studied 136 children with fever or respiratory symptoms who attended the emergency room of one US university hospital, 26 (19%) of whom had radiological pneumonia.[23] The presence of tachypnoea (not defined in the paper) had the highest sensitivity (81%) and a specificity of 60%. Zukin *et al* found that the presence of fever had the highest sensitivity (94%) but a low specificity (36%) in a similar study that included 125 children (18 cases of radiological pneumonia).[24] Grossman and Caplan found that no single symptom, sign, or laboratory test had a good sensitivity and specificity for predicting radiological pneumonia in 155 American children, and that the general impression obtained by the doctor was more useful than any other sign (sensitivity 80%, specificity 68%).[25] Finally, Steinhoff *et al* found that no isolated sign could predict the presence of radiological pneumonia in children under 5 years of age living in Baltimore (M C Steinhoff *et al*, unpublished results). The use of chest radiographs at sea level in Swaziland and the Philippines by Mulholland *et al* resulted in sensitivities and specificities that are higher than those found here, but that are not as good as those reported by studies without radiological diagnosis.[8]

Most cases of pneumonia in developing countries are produced by bacterial agents.[19] This, alone with the difficulties in establishing an aetiological diagnosis based on radiological findings,[17 18] led us to define pneumonia as the evidence of radiological abnormalities in the lung in children with clinical manifestations of acute respiratory infection. To determine whether the inclusion of patients with interstitial infiltrates (considered less likely to correspond to a bacterial pneumonia) could change the sensitivity or specificity of some clinical findings, a second analysis excluding patients with only interstitial infiltrates was performed. The results obtained were almost identical to those observed when all radiological abnormalities were considered as pneumonia, which suggests that the outcome definition had no influence on the findings.

The results obtained in our population for diagnosing hypoxaemia were similar to those for radiological pneumonia. None of the symptoms described by the children's mothers was a good predictor, although rapid breathing had a good sensitivity (89%) but low specificity (30%). The presence of chest retractions, nasal flaring, or crepitations had a statistical associated with a low Sa_{O_2} and adequate sensitivities but low specificities. These results did not change when the analysis was repeated stratifying by age. The respiratory rate was also the best single predictor of hypoxaemia, mainly for infants, among whom a figure $\geqslant$50/minute had the best sensitivity and specificity. These results, similar to those found by Reuland in Peru,[11] are encouraging but imply false positive and false negative rates that are relatively high. One potential explanation for this limitation of the respiratory rate to predict a low SaO_2 could be the relatively poor response to hypoxaemia described in subjects living at high altitude,[26] which can also contribute to the poor utility of this sign to predict radiological pneumonia, as mentioned previously.

One of the most encouraging results in this study is that the presence of hypoxaemia seems to be a better predictor of pneumonia than any clinical manifestation (sensitivity 83%, specificity 73%). These findings are similar to those reported by Reuland in Peru.[11] Although this technique for measuring the blood oxygen saturation is still uncommon in our setting, this may be due to its relatively recent introduction into clinical practice. Given its advantages (high sensitivity, non-invasiveness, validity, and reliability), it is possible that its use in the diagnosis of hypoxaemia and pneumonia will become more popular in the future. On the other hand, the use of pulse oximetry in our study has shown that most patients with pneumonia in Bogota have hypoxaemia, and therefore oxygen is required for treatment in our city and probably in other places at a similar altitude.

Finally, we consider that some caution is required before using our results in different settings. Our study population was obtained from children attending an urban tertiary care centre, and who were considered by their paediatricians to be sick enough to require a chest radiograph. Therefore, they probably represent relatively severe cases of acute respiratory infection. This could help to explain the relatively high rates of radiological pneumonia and hypoxaemia. Although our findings are applicable in similar environments, places with a lower prevalence of pneumonia or hypoxaemia could have different results. The positive predictive value (the probability of radiological pneumonia or hypoxaemia in a child with positive clinical findings) will be lower in places with a lower prevalence of these two disorders.

In conclusion, our findings suggest that no single clinical manifestation can predict accurately the presence of pneumonia in Bogota, and that the best single predictor of pneumonia or hypoxaemia, or both, is a high respiratory rate. Our results are not as good as those reported by other studies, however, and confirm previous findings which suggest that the classification systems developed at lower altitudes may have limited performance at high altitude. On the other hand, the presence of hypoxaemia detected by non-invasive methods such as pulse oximetry may be useful for detecting pneumonia, and perhaps for aiding in the decision of ordering chest radiographs for patients with acute respiratory infection. Therefore, the contribution of pulse oximetry to the management of patients with acute respiratory infection deserves further research.

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