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Assessment of clinical predictors of hypoxemia in patients of acute lower respiratory infections in children: A hospital-based study

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Abstract
Aim: The aim of this study was to study clinical predictors of hypoxemia in patients of acute lower respiratory infections in children.
Material & Methods: The observational prospective study was conducted in the General Pediatric Ward and Pediatric Intensive Care Unit of a tertiary care hospital. This was a hospital-based study completed for 1 year. The sample size taken for this study was 100. All children admitted with acute lower respiratory tract infections between the age group of 2 month to 5 years of age and diagnosed with pneumonia or bronchiolitis were included in the study.
Results: A total of 100 cases were enrolled in the study, out of which 70 were male and 30 were female. Out of the 100 cases enrolled, 48 were below the age of 12 months and 52 were above 12 months of age. The mean age was 16.4 months. The most common and significant symptoms were rapid breathing and difficulty breathing. The least common symptom was noisy breathing and pain in the abdomen. Tachypnea (88%), pallor (86%) and nasal flaring (80%), crepitations (added sounds), and subcostal retractions had better sensitivity for detecting hypoxemia. However, these signs had low specificity for hypoxemia. Head nodding (95%), intercostal retractions (82%), and cyanosis (85%) were highly specific for predicting hypoxemia. Males 68 out of 70 were significantly more hypoxemic than females 27 out of 30. Most cases have moderate hypoxemia which includes 80%. 35 cases out of the total 100 were diagnosed to have bronchiolitis, whereas 65 cases had pneumonia.
Conclusion: It was observed that a combination of clinical signs and symptoms can be used to predict hypoxemia when facilities of pulse oximetry and arterial blood gas analysis are not available, especially in low-resource settings.

Keywords: Bronchiolitis, clinical predictors, hypoxemia, pneumonia

Introduction
Acute lower respiratory tract infections are a major cause of morbidity and mortality among children in developing countries, accounting for about 30% of mortality in children under 5 years of age [1, 2]. Most of these deaths occur at home before children enter the healthcare system [3]. Acute respiratory infections (ARIs) contribute to 15–30% of all under-five deaths in India and most of these are preventable [4]. According to National Family Health Survey-4, the prevalence of ARI is 3.7% with a maximum rate of acute respiratory tract infection in children at 4.7% [5]. Oxygen therapy improves the outcome of children with moderate or severe acute lower respiratory tract infection and, in those with hypoxaemia, the severity of hypoxia correlates with outcome [6]. Hypoxaemia is the most serious manifestation of severe pneumonia in children. The case fatality rate of pneumonia is inversely related to the arterial haemoglobin oxygen saturation (SaO2). The duration and severity of hypoxemia are important and its early recognition and appropriate treatment improve the outcome of these children [7]. Although the most reliable way to detect hypoxemia is arterial blood gas analysis (ABG), by which direct determination of arterial SpO2 is done, machines to make these measurements are expensive and need constant maintenance and are not widely available in developing countries, thus making clinical predictors of hypoxemia important in the initiation of oxygen therapy. Pulse oximetry is the most reliable, non-invasive, accurate method of measuring arterial hemoglobin oxygen saturation (SpO2) in pneumonia [8] and

also in other illnesses in children [9, 10], but it is also not extensively available so the study was planned with the objectives to calculate the sensitivity, specificity, positive predictive value, and negative predictive value of clinical parameters in predicting hypoxemia – cyanosis, level of consciousness, tachypnea, retractions, head nodding, wheeze, and crepitations and to correlate the degree of hypoxemia. Therefore, to help health-care professionals decide that children are hypoxemic and might benefit from oxygen it is important to accurately identify by the abuse of clinical signs alone. The diagnosis is clinical and is made on the basis of symptoms and signs such as fever, cough, rapid breathing, grunting, wheeze, crepitations without performing any investigations, and due to the unavailability of pulse oximetry at peripheral level**,** it is important to study which clinical predictors of hypoxemia we can reliably sort out for initiation of oxygen therapy. The duration and severity of hypoxemia is important and its early recognition and appropriate treatment improve the outcome of these children.

The aim of this study was to study clinical predictors of hypoxemia in patients of acute lower respiratory infections in children

Materials and Methods

The observational prospective study was conducted in the General Pediatric Ward and Pediatric Intensive Care Unit of a tertiary care hospital. This was a hospital-based study completed for 1 year. The sample size taken for this study was 100. All children admitted with acute lower respiratory tract infections between the age group of 2 month to 5 years of age and diagnosed with pneumonia or bronchiolitis were included in the study. Any child suffering from chronic respiratory illness, congenital heart disease, severe dehydration, severe anemia, and congestive cardiac failure or shock were excluded from the study. The case children had an arterial haemoglobin SaO2 of < 90%, measured by pulse oximeter. This SaO2 is generally considered to reflect severe hypoxaemia.

Diagnosis of acute lower respiratory tract infection is purely clinical on the basis of the presence of symptoms such as fever, cough, rapid breathing, noisy breathing, difficulty in breathing, refusal to feed, and convulsions and signs such as tachypnea, cyanosis, wheezing, grunting, use of accessory muscles of respiration, and presence of added sounds on auscultation or abnormal sounds [11].

Hypoxemia has been defined as per Pediatric Advanced Life Support guidelines as SpO2 less than 94% and classified as [12]

- Mild: 94–90%
- Moderate: 85–90%
- Severe: <85%

After due approval from the Ethical Committee, any child presenting with difficulty in breathing and coughing as per the ARI control program and diagnosed with Pneumonia or bronchiolitis and after obtaining consent from parents were included in the study. He/she was subjected to detailed history and clinical examination for the presence of the above signs and symptoms. Arterial saturation of all patients was recorded using a portable pulse oximeter and ABG was done. The degree of hypoxemia between ABG and SpO2 was correlated. After obtaining a detailed history, and examination, vital parameters were recorded such as the general condition of the child/infant, heart rate, respiratory rate, saturation (SpO2), temperature, level of consciousness, pallor, cyanosis, and head nodding and other significant clinical findings such as tachypnea, retractions, adventitious sounds such as crepitations, wheeze, and rhonchi were also taken into account. Tachypnea which is considered to be a compensatory mechanism to maintain minute ventilation [13] was defined as per the WHO age-specific cutoff values [11]. ABG was recorded in all patients as it is the gold standard to diagnose hypoxemia to correlate the degree of hypoxemia as per the ABG with the clinical predictors mentioned above.

Statistical analysis

Analyses were performed using SPSS for Windows, SAS for Windows, and Epi-Info software packages. Analysis of the result was done in the form of sensitivity, specificity, positive predictive value, and negative predictive value. p-value of <0.05% was considered to be statistically significant and the Chi-square test, t-test, and ANOVA will be used whenever required for data analysis.

Results

Table 1: Demographic details

Gender	N%
Male	70 (70)
Female	30 (30)
Age groups	
Below 12 months	48 (48)
Above 12 months	52 (52)
Symptoms	
Rapid breathing	35 (35)
Difficulty breathing	30 (30)
Fever	9 (9)
Nasal discharge	8 (8)
Cough	7 (7)
Noisy breathing	5 (5)
Pain abdomen	5 (5)
Diagnosis	
Bronchioloitis	35 (35)
Pneumonia	65 (65)

A total of 100 cases were enrolled in the study, out of which 70 were male and 30 were female. Out of the 100 cases enrolled, 48 were below the age of 12 months and 52 were above 12 months of age. The mean age was 16.4 months. The most common and significant symptoms were rapid breathing and difficulty breathing. The least common symptom was noisy breathing and pain in the abdomen. 35 cases out of the total 100 were diagnosed to have bronchiolitis, whereas 65 cases had pneumonia.

Table 2: Sensitivity and specificity of hypoxemic signs

Signs	Sensitivity	Specificity
Pallor	86	36
Cyanosis	40	85
Level of consciousness	32	76
Tachypnea	88	28
Nasal flaring	80	40
Supraclavicular	76	34
Intercostal	55	82
Subcostal	70	20
Wheeze	28	90
Crepitations	80	18
Head nodding	15	95

Tachypnea (88%), pallor (86%) and nasal flaring (80%), crepitations (added sounds), and subcostal retractions had better sensitivity for detecting hypoxemia. However, these signs had low specificity for hypoxemia. Head nodding (95%), intercostal retractions (82%), and cyanosis (85%) were highly specific for predicting hypoxemia.

Table 3: Staging of hypoxemia and its gender-wise distribution

Hypoxemia	Male (%)	Female (%)	p-value
Mild (40)	28 (70)	12 (30)	
Moderate (40)	32 (80)	8 (20)	
Severe (15)	8 (53.34)	7 (46.66)	.0003
No (5)	2 (40)	3 (60)	
Total	70	30	

Males 68 out of 70 were significantly more hypoxemic than females 27 out of 30. Most cases have moderate hypoxemia which includes 80%.

Discussion

Globally, pneumonia is a leading cause of death among children <5 years old, accounting for >90% of acute lower respiratory infection-related deaths [14]. Hypoxaemia is a major complication of pneumonia, associated with an increase in the risk of death with increasing severity of hypoxaemia [15]. Definitions of hypoxaemia have not been uniform (being often based on the practicality of limited oxygen supplies) [16]. Investigators have defined hypoxaemia from <96.6% to <90% oxygen saturation at sea level and <85% to <88% at higher altitudes [17]. For simplicity, a couple of on-going international multicenter clinical trials for pneumonia therapy are using cut-offs of <90% at sea level and <88% at higher altitude to define hypoxaemia.[18] WHO defined hypoxemia as an SaO2 < 90% by pulse oximetry [19]. Hypoxaemia is a common and serious complication in severely ill children [19]. Most severely ill children with hypoxaemia present with clinical signs of pneumonia [19, 20]. Hypoxaemia is one of the major risks of death from pneumonia, and much work has been carried out looking at clinical signs of hypoxemia in patients with pneumonia [21, 22].

A total of 100 cases were enrolled in the study, out of which 70 were male and 30 were female. Out of the 100 cases enrolled, 48 were below the age of 12 months and 52 were above 12 months of age. The mean age was 16.4 months. The most common and significant symptoms were rapid breathing and difficulty breathing. The least common symptom was noisy breathing and pain in the abdomen. In contrast, Motwani *et al*. [23], in their study of 204 cases, observed hypoxemia to be more common in females as compared to males. Basnet *et al*. [24], in their study on 150 children under 5 years, assessed the accuracy of clinical signs to differentiate lower and upper respiratory tract infections and observed that rapid breathing and fast breathing were significantly associated with hypoxemia. Redd *et al*. [25] in their study on 950 children ascertained that the most common symptoms were cough (99%) and difficulty in breathing (17%), running nose was observed to be the next most common symptom in their study which was not similar to our study as the most common symptom was rapid and difficulty in breathing.

Tachypnea (88%), pallor (86%) and nasal flaring (80%), crepitations (added sounds), and subcostal retractions had better sensitivity for detecting hypoxemia. However, these signs had low specificity for hypoxemia. Head nodding (95%), intercostal retractions (82%), and cyanosis (85%) were highly specific for predicting hypoxemia. Children with pneumonia often presented with hypoxaemia and remained hypoxaemic for longer compared to those without pneumonia. Children with pneumonia present with inflammation in the lung parenchyma and often experience increased oxygen demand and inadequate oxygen supply due to the reduction of diffusion of oxygen at the level of the blood gas barrier at alveolar region of respiratory zone of lung leading to hypoxaemia. A number of physical signs were highly significantly associated with hypoxaemia, but the sensitivity of each sign alone was low. Cyanosis has long been known to be associated with hypoxaemia [26, 27], but the difficulty of its detection, especially in children with dark pigmentation of the skin, makes it an insensitive marker. In our study, the respiratory rate was a poor predictor of hypoxaemia, as found in other studies [28, 29].

Conclusion

It was observed that a combination of clinical signs and symptoms can be used to predict hypoxemia when facilities of pulse oximetry and arterial blood gas analysis are not available, especially in low-resource settings. Tachypnea, pallor and nasal flaring, crepitations, and subcostal retractions are highly sensitive, whereas head nodding, intercostal retractions, and cyanosis were highly specific clinical signs for predicting hypoxemia. However, ABG analysis remains the gold standard to predict hypoxemia. Early detection can lead to prompt intervention by instituting oxygen therapy, thus reducing mortality and morbidity due to acute lower respiratory tract infections.

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