Clinical predictors of hypoxemia in Indian children with acute respiratory tract infection presenting to pediatric emergency department

Yashwant Kumar Rao, Tanu Midha, Pankaj Kumar, Virendra Nath Tripathi, Om Prakash Rai
Kanpur, India

Background: **In developing countries, facilities for measuring arterial oxygen saturation are not available in most settings, which make it difficult for health providers to detect hypoxemia in children with acute respiratory tract infection (ARI). Most health providers rely on symptoms and signs to identify hypoxemia and start oxygen therapy. Therefore, this study was conducted to determine the clinical predictors of hypoxemia in children with ARI.**

Methods: **It was a cross-sectional study carried out at the Pediatric Emergency Department of GSVM Medical College, Kanpur, India in children in the age group between 2 months and 5 years, presenting with ARI. All children with ARI attending the pediatric emergency department from April 2007 to September 2008 were included in the study. Clinical signs and symptoms including fever, cough, nasal flaring, inability to feed/drink, cyanosis, chest wall retraction, wheezing, grunting, tachypnea and crepitations were noted and oxygen saturation (SpO_2) was measured. Hypoxemia was defined as SpO_2 <90%.**

Results: **Of the 261 children included in the study, 62 (23.8%) had hypoxemia. Chest wall retraction (sensitivity=90%), crepitations (sensitivity=87%), nasal flaring (sensitivity=84%), tachypnea (sensitivity=81%) and inability to feed (sensitivity=81%) were observed to be the most sensitive indicators of hypoxemia while the best predictors were cyanosis [positive predictive value (PPV)=88%] and nasal flaring (PPV=53%).**

Conclusions: **Chest wall retraction was found to be the most sensitive indicator, and cyanosis was the most specific indicator for hypoxemia. Of all the clinical signs and symptoms of hypoxemia, none had all the attributes of being a good predictor. A new hypoxemia score has been designed using a combination of clinical signs and symptoms to predict the need for supplemental oxygen therapy.**

World J Pediatr 2012;8(3):247-251

Key words: **acute respiratory tract infections; hypoxemia; hypoxemia score; pulse oximetry**

Author Affiliations: Department of Pediatrics, GSVM Medical College, Kanpur, India (Rao YK, Kumar P, Tripathi VN); Department of Community Medicine, GSVM Medical College, Kanpur, India (Midha T); Department of Pulmonary Medicine, GSVM Medical College, Kanpur, India (Rai OP)

Corresponding Author: Yashwant Kumar Rao, L-20, GSVM Medical College, Kanpur-208002, India (Email: ykraoneo@yahoo.co.in)

doi: 10.1007/s12519-012-0365-1

Introduction

Acute respiratory tract infections (ARI) cause more than two million deaths worldwide in children less than five years of age.[1] They are one of the major causes of preventable morbidity and mortality in under-five children, especially in developing countries.[2] The deaths are mainly due to hypoxemia, which is a manifestation of severe respiratory distress.[3] The arterial oxygen saturation (SpO_2), measured using a pulse oximeter, has been shown to predict the outcome in children with acute respiratory tract infection and the mortality is directly related to fall in oxygen saturation in the arterial blood.[4] Several studies have revealed that the outcome in ARI is improved by delivery of oxygen to hypoxemic children.[3,5] In developing countries like India, facilities for measuring arterial oxygen saturation are not available in most primary health care settings and even in some secondary and tertiary health care settings. This poses a challenge for health care providers to detect possible hypoxemia in acutely ill children and start oxygen therapy. Most clinicians rely on clinical symptoms and signs to identify hypoxemia. Therefore, in order to predict the presence of hypoxemia in children with ARI, it is of utmost importance to find a minimum set of signs and symptoms that can be used

by the health care provider to institute oxygen therapy timely in sick children.

Various signs and symptoms have been studied by many authors to predict hypoxemia in children with ARI.[5,6] The present study was designed with the aim to determine the prevalence of hypoxemia in children presenting with ARI and to identify the clinical signs and symptoms that could predict hypoxemia in children with ARI seen in a pediatric emergency department.

Methods

The study was conducted at the Pediatric Emergency Department of GSVM Medical College, Kanpur. The city of Kanpur is situated in the state of Uttar Pradesh in North India at an altitude of 126 meters above the sea level.

This was a cross-sectional study, comprising all children with signs and symptoms suggestive of an ARI aged between 2 months and 5 years, who attended the Pediatric Emergency Department from April 2007 through September 2008. The study was approved by the ethical committee of the institute. ARI was defined as acute onset of respiratory symptom(s) including cough, rhinorrhea, fast/difficult breathing, chest wall retraction and wheeze of less than 14 days.[7] ARI includes all infections of the respiratory tract, both upper respiratory infection (URI) and lower respiratory infection (LRI). URI was defined as a child presenting with fever, cough and nasal or ear discharge. By definition, any acute respiratory infection involving the area above the vocal cords was classified as URI.[8] LRI was defined as any infection that affects the airways below the epiglottis and includes acute laryngitis, tracheitis, bronchitis, bronchiolitis, and lung infections such as pneumonia, tuberculosis and empyema.[9] Only acute cases of LRI were included in our study. Patients with history of chronic respiratory problems, bronchial asthma, congenital heart disease, congenital malformations and tuberculosis were excluded from the study.

After admission of the child in the pediatric emergency department, a detailed history was taken, followed by a physical examination including weight and presence or absence of various clinical symptoms and signs such as fever, cough, tachypnea, inability to feed, nasal flaring, wheezing, grunting, cyanosis, crepitations on auscultation, and chest wall retraction. Clinical observations were made and recorded by the Junior Resident doctor. Informed verbal consent was obtained from the parents.

Respiratory rate was counted by observational method for complete one minute. Each upward movement of the abdominal and chest wall, on visual observation, was counted as one breath.

The "syndrome of pneumonia" was defined as a history of cough or difficulty in breathing along with an elevated respiratory rate for age (if age was between 2 months and 11 months, ≥50 breaths/min; if age was between 1 year and 5 years, ≥40 breaths/min), and no signs of severe pneumonia syndrome. Severe pneumonia syndrome was defined as a history of cough or difficulty in breathing along with lower chest wall indrawing or nasal flaring and no signs of very severe pneumonia syndrome. Very severe pneumonia syndrome was defined as cough or difficulty in breathing along with any one of the following signs: cyanosis, inability to drink or breastfeed, convulsions, lethargy or unconsciousness.[10] Bronchiolitis was defined as a clinical syndrome characterized by acute onset of respiratory symptoms like fast breathing along with wheezing and/or crackles in a child, 3 months to 2 years of age, with a prodromal upper respiratory catarrh.[8] Tracheobronchitis was defined as a child presenting with barking cough, hoarse voice and high-pitched inspiratory stridor, that followed a prodrome of mild fever, rhinorrhoea and sore throat. Breath sounds are normal with no added sounds, except transmission of stridor.[8]

Tachypnea was defined as an elevated respiratory rate for age, that is ≥50 breaths/min in a child with age between 2 months and 11 months; ≥40 breaths/min in a child with age between 1 year and 5 years.[10] Chest wall retraction was defined as an inward movement of the lower chest wall on breathing in, when the child was lying flat in his mother's lap or on the examination table and the child was quiet, calm and breathing normally. Cyanosis was recorded as presence of bluish discoloration of the tongue, buccal mucosa, ear lobes, palpebral conjunctiva, tip of the nose and finger tips.[7] SpO_2 was recorded at the finger or toe with a pulse oximeter (Nellcor Puritan Bennet NPB-40) using a pediatric sensor of the appropriate size. The measurement of oxygen saturation was recorded after stabilization of the reading for at least one minute. Hypoxemia was defined as SpO_2 <90%.[7]

Data were analyzed using Microsoft Excel 2007. Results were presented as sensitivity, specificity, positive predictive value (PPV) or negative predictive value (NPV).

Results

In the present study, 261 children with ARI aged between 2 months and 5 years were studied. Of these children, 55.9% presented with pneumonia and 34.5%

with bronchiolitis (Table 1). SpO_2 ranged from 72% to 100%. Hypoxemia was found in 62 children (23.8%), who were further classified according to the diagnostic categories of ARI (Table 2). In the children with very severe pneumonia, 77.8% were hypoxemic, followed by severe pneumonia (32.4%), non-severe pneumonia (9.5%), and bronochiolitis (8.9%).

Table 1. Distribution of acute respiratory tract infection (ARI) patients according to diagnosis

Type of ARI	*n*	Percentage (%)
Upper respiratory infection	11	4.2
Pneumonia	146	55.9
Bronchiolitis	90	34.5
Tracheobronchitis	14	5.4
Total	261	100.0

Table 2. Prevalence of hypoxemia (SpO_2<90%) in acute respiratory tract infection patients with respect to diagnosis

Diagnosis	*n*	Hypoxemic patients SpO_2 <90% (%)
Upper respiratory infection	11	0 (0.0)
Non-severe pneumonia	42	4 (9.5)
Severe pneumonia	68	22 (32.4)
Very severe pneumonia	36	28 (77.8)
Bronchiolitis	90	8 (8.9)
Tracheobronchitis	14	0 (0.0)
Total	261	62 (23.8)

The sensitivity, specificity and predictive value of individual clinical signs for hypoxemia are shown in Table 3. Chest wall retraction was the most sensitive indicator of hypoxemia (sensitivity=90%), followed by crepitations (sensitivity=87%), nasal flaring (sensitivity=84%), tachypnea (sensitivity=81%), and inability to feed (sensitivity=81%), while the best predictors were cyanosis (PPV=88%) and nasal flaring (PPV=53%).

Based on our findings of PPV for individual symptoms and signs predictive of hypoxemia, we developed a hypoxemia score assigning weightage to each of the symptoms and signs depending on its PPV. A sign with PPV between 75% and 100% like cyanosis was assigned a score value of 4. Signs with PPV between 50% and 74% like nasal flaring, grunting and chest wall retraction were assigned a score value of 3 each. Signs and symptoms with PPV between 25% and 49% like inability to feed, fever, tachypnea, crepitations and wheezing were assigned a score value of 2 each. A symptom like cough with PPV less than 24% was assigned a score value of 1.

Summing up the individual score values of all the symptoms and signs present in a child, every child was given a hypoxemia score. Then this score was analyzed for sensitivity, specificity and PPV at different ranges (Table 4).

Among the 62 cases presenting with hypoxemia, mortality occurred in 11 (17.7%). Of 11 children who

Table 3. Predictive value of clinical signs for hypoxemia (SpO_2<90%) in children with acute respiratory tract infection

Clinical features	Hypoxemic patients (*n*=62)	Non-hypoxemic patients (*n*=188)*	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Complaints						
Fever	42	92	68	51	31	83
Cough	40	130	65	31	24	72
Inability to feed	50	68	81	64	42	90
Respiratory signs						
Nasal flaring	42	46	84	76	53	93
Cyanosis	16	2	32	99	88	80
Grunting	28	28	45	85	50	82
Tachypnea	50	68	81	64	42	90
Crepitations	54	68	87	64	45	94
Wheezing	28	50	45	73	36	80
Chest wall retraction	56	57	90	70	50	96

*: 11 cases of URI were excluded from the analysis because of incomplete data.

Table 4. Predictive value of hypoxemia score for hypoxemia (SpO_2<90%) in children with acute respiratory tract infection

Score	Hypoxemic patients (*n*=62)	Non-hypoxemic patients (*n*=188)*	Sensitivity (%)	Specificity (%)	Positive predictive value (%)
18 to 24	35	4	56	98	90
12 to 17	13	7	21	96	65
6 to 11	12	53	19	72	18
0 to 5	2	124	3	35	2

*: 11 cases of URI were excluded from the analysis because of incomplete data.

died of hypoxemia, 7 (63.6%) had a hypoxemia score in the range of 18-24 and 4 (36.4%) had a hypoxemia score in the range of 12-17.

Discussion

In the present study, a high prevalence of hypoxemia (23.8%) was observed in children with ARI, who were less than 5 years old. Another study also reported that 25.7% of children under five years of age with ARI were hypoxemic.[11]

In a review[12] of published and unpublished studies on acute lower respiratory tract infection, the median prevalence of hypoxemia in World Health Organization (WHO) defined pneumonia requiring hospitalization (severe and very severe classifications) was 13%, but the prevalence varied widely. The prevalence of hypoxemia varied in different settings and different cut-off values were used for SpO_2. Duke et al[6] observed that 73% of patients with ARI had hypoxemia (defined as SpO_2<88%). A higher prevalence was reported because of a lower cut-off value. Usen et al[13] reported that 5.9% of the children with ARI were hypoxemic. In outdoor settings, 6%-9% of the children were found to be hypoxemic, whereas in emergency wards the prevalence of hypoxemia ranged from 31%-43% to a maximum of 47% in hospitalized children, which may be due to the selection bias that likely exist between different health care facilities. Hypoxemia is more likely to occur in an emergency department of referral hospital than in a primary care setting.[13]

The study was carried out in Kanpur city, which lies in the state of Uttar Pradesh, where the immunization coverage is substantially low, even for vaccines that are provided free of cost: *Bacille Calmette Guerin* (61%), 3 doses of *Diptheria Pertussis Tetanus* (30%) and measles (37.7%).[14] *H. Influenzae* and *Pneumococcus* vaccines are not provided free of cost by the Government of India under the Universal Immunization Program and are unaffordable for the general population. Also, the illiteracy rate is very high in this region, and the majority of the people are unaware of these vaccines. Therefore, the immunization coverage with these vaccines is almost negligible. This may be one of the reasons for the high prevalence of hypoxemia in our study.

Even though hypoxemia is a major risk factor for death in children with ARI in developing countries, oxygen is not part of the first line treatment. Because oxygen is not readily available in developing countries, it tends to be given to the most seriously ill children, whose outcome is poor. Oxygen might be useful if given earlier in the course of the disease. Clinical signs are not clear cut, however, studies have shown that presence of cyanosis and grunting together with a raised respiratory rate can significantly increase the detection of hypoxemia.[15]

Certain clinical signs and symptoms in patients with ARI are predictive of hypoxemia, indicating that detection of hypoxemia using these may play a very important role in the clinical management of patients with ARI.[16,17] In developing countries where facilities for measurement of SpO_2 are not easily available at all centers, these clinical criteria are very important. WHO has published recommendations for hospital management of pneumonia in developing countries, suggesting that with limited availability of oxygen, only children with cyanosis or inability to drink should be given oxygen. Our findings strongly support the current WHO recommendations surrounding triage for the detection of hypoxemia.[5]

Besides chest wall retraction, nasal flaring, tachypnea, inability to feed and crepitations were other clinical signs that were sensitive in the identification of hypoxemia but none of these signs could independently do so. The signs with high sensitivity had poor specificity and vice versa. Reliance on a single clinical sign may not be optimal. Ayieko et al[18] observed that the sensitivity is low for most signs, so combinations need to be used, including respiratory rate >60 breaths per minute, inability to feed, and altered mental status.

Because a combination of clinical signs and symptoms will be better predictive of hypoxemia, a hypoxemia score has been designed to assess the need for supplemental oxygen therapy. A high score was found to have a high positive predictive value for hypoxemia in the present study. It was also observed that the mortality was high in children with a high hypoxemia score. Various studies in children with acute lower respiratory infection (ALRI) have shown that hypoxemia is a strong risk factor for mortality and the use of supplemental oxygen reduces mortality from ALRI.[3,12] The presence of hypoxemia is predictive of short-term mortality, indicating that the detection and treatment of hypoxemia may be a crucial part of the clinical management of severely ill children in a hospital. Conversely, the absence of hypoxemia predicts a low risk of death, even in the presence of radiographic pneumonia. Supplemental oxygen is essential for survival in hypoxemic children and also prevents morbidity that may occur from prolonged hypoxemia.[19,20] Oxygen supplementation in children with respiratory distress has no serious adverse effects, therefore even children with a low hypoxemia score can be given supplemental oxygen but in case of scarce resources preference should be given to those with a high hypoxemia score.

Certain limitations of the study must be acknowledged. Data regarding radiographic findings were not included in the present study. Since India is a resource poor country, radiographic investigation was not done in all the patients; it was only done when clinical diagnosis was doubtful. Accurate data regarding duration of illness prior to admission could not be obtained because of a high level of illiteracy; hence this was not included in the study. In our study, the correlation of the hypoxemia score with SpO_2 was not analyzed. Further studies may be carried out to evaluate the hypoxemia score at different levels of SpO_2.

In conclusion, most of the ARI children in the present study were diagnosed with pneumonia. The prevalence of hypoxemia was highest in children with very severe pneumonia. No single sign had adequate sensitivity and specificity as a reliable predictor of hypoxemia. A new hypoxemia score has been developed by combination of clinical signs and symptoms to decide whether children are in need of supplemental oxygen.

Funding: None.
Ethical approval: This study was approved by the ethics committee of GSVM Medical College, Kanpur, India.
Competing interest: None.
Contributors: Rao YK and Midha T contributed to concept and design, data analysis and interpretation, manuscript preparation and revision, and final approval. Kumar P contributed to concept and design, collection of data, manuscript preparation and revision, and final approval. Tripathi VN and Rai OP contributed to concept and design, manuscript preparation and revision, and final approval.

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Received April 7, 2011
Accepted after revision October 10, 2011