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Original Article

Clinical Predictors of Hypoxemia in Children with Acute Lower Respiratory Illness at a Tertiary Care Hospital in Bangladesh

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Abstract

Background: *Acute lower respiratory infections (ALRI) remain the major cause of morbidity and mortality among children under five years of age. Hypoxaemia is a serious complication of ALRI and represents an important risk factor for mortality. Early identification and prompt management of hypoxaemia can significantly improve outcomes in affected children. As arterial blood gas analysis is not accessible in all primary healthcare settings in developing countries, it is important to identify clinical signs that can predict hypoxemia.* ***Objectives:*** *To identify the clinical predictors of hypoxaemia in children with ALRI admitted to the Paediatrics ward of Chittagong Medical College Hospital (CMCH), Chattogram, Bangladesh.* ***Materials & Methods:*** *This hospital-based cross-sectional study included 100 children aged 2 to 60 months with ALRI admitted to the Paediatrics ward of CMCH. Demographic information, including age, sex, and place of residence, as well as presenting symptoms, were recorded for each patient. Symptoms such as cough, breathing difficulty, feeding difficulty, sleep disturbance, lethargy and clinical signs such as central cyanosis, nasal flaring, restlessness, head nodding, fast breathing, chest in drawing, grunting, crepitations, and rhonchi were recorded. Oxygen saturation in these children was measured using ABG analysis to identify hypoxaemia. Continuous variables were reported as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. The frequency of various symptoms and signs in both groups was calculated and analyzed using the Chi-square (χ^2) test. Sensitivity, specificity, positive predictive value, and negative predictive value were determined for each symptom and sign. Statistical significance was defined as $p<0.05$, with a 95% confidence interval.* ***Results:*** *Out of 100 children, 46% had hypoxaemia as per ABG criteria (pO2 <60 mmHg). In hypoxaemic group 23 (50%) patients had feeding difficulty, 13 (28.5%) patients had cyanosis, 11 (23.9%) patients had head nodding, and 16 (34.8%) patients had grunting which has statistical significance. So, feeding difficulty, cyanosis, head nodding and grunting were single or independent significant predictors of hypoxaemia. Certain symptom combinations, especially nasal flaring with grunting, and cyanosis with nasal flaring were strongly linked to hypoxaemia with high specificity and predictive value. Restlessness with cyanosis and feeding difficulty with nasal flaring and cyanosis showed 100% specificity and positive predictive value, making these combinations reliable indicators of hypoxaemia.* ***Conclusion:*** *Feeding difficulty, cyanosis, head nodding and grunting were independent predictors of hypoxaemia in this study. Establishing clinical guidelines and ensuring effective oxygen delivery systems can significantly enhance treatment quality, ultimately reducing both morbidity and mortality.*

Keywords: *Acute Lower Respiratory Illness, Hypoxemia, Clinical Predictors*

Introduction: Acute respiratory infections (ARIs) are a major cause of childhood morbidity and mortality in the developing countries[1]. These infections involve both the upper and lower respiratory tracts. Acute lower respiratory infections (ALRIs) are mainly represented by pneumonia, but may also include bronchiolitis, tracheobronchitis, and croup[2]. Current global estimates suggest that 120–156 million ALRI cases occur each year, resulting in about 1.4 million deaths, with over 95% of these deaths occurring in low- and middle-income nations[3,4].

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In Bangladesh, several well-known risk factors for pneumonia-such as malnutrition, low birth weight, indoor air pollution, overcrowding, and lack of exclusive breastfeeding are frequently present[5].

ALRI is a major cause of mortality among children in Bangladesh, with approximately 30–50% of children under the age of two (2) affected annually[6]. A variety of infectious agents are responsible for ALRI, with Streptococcus pneumoniae being the most commonly detected bacterial pathogen and Respiratory Syncytial Virus (RSV) the most frequent viral cause[7]. Numerous studies have reported RSV as a leading reason for hospitalization in cases of community-acquired pneumonia (CAP), with prevalence rates ranging from 15.1% to 67.0%[8]. With the exception of a limited number of regions, seasonal peaks of RSV and influenza in Asia, Africa, and South America consistently coincide with the rainy season[9].

Hypoxaemia, a condition characterized by reduced oxygen levels in the blood, frequently complicates severe childhood illnesses and may signal an increased risk of death[10]. It commonly arises from cardiac and pulmonary disorders, particularly ALRI such as pneumonia and bronchiolitis[11]. Pulse oximetry is considered the preferred method for assessing the need for and the effectiveness of oxygen therapy, and in developed countries it is routinely used as part of standard clinical care; however, it can only measure oxygen saturation[12]. The most accurate assessment is obtained through arterial blood gas (ABG) analysis, which measures the partial pressure of oxygen (PaO_2) to identify hypoxaemia, along with carbon dioxide (CO_2) levels, blood pH, and major blood electrolytes. Despite its advantages, ABG analysis has notable limitations: blood gas analyzers are costly and require expensive reagents, making them difficult to afford in resource-limited healthcare settings[13].

In low-resource settings, physicians must depend on observable clinical symptoms and signs to diagnose hypoxaemia in children with ALRI. Over the past two decades, numerous studies have assessed the accuracy of these clinical indicators in identifying hypoxaemia. The most commonly evaluated signs include fast breathing, respiratory distress, poor feeding or drinking, cyanosis, grunting, lethargy, nasal flaring, head nodding, indrawing of chest, and abnormal breath sounds such as rhonchi and crackles (crepitations) detected through auscultation[11,14-16]. The purpose of this study is to determine the key clinical predictors of hypoxaemia in children with acute lower respiratory illness, enabling earlier detection and prompt management, particularly in hospitals with limited resources.

Materials and Methods

This hospital-based cross-sectional study was conducted from March 2018 to February 2019 in the Department of Paediatrics at Chittagong Medical College and Hospital (CMCH), Chittagong, Bangladesh. Ethical clearance was obtained from the Institutional Ethical Review Board of Chittagong Medical College (Ref: CMC/PG/2018/441). Using purposive sampling, 100 children aged 2 months to 5 years, of either sex, admitted to the Paediatrics ward with a diagnosis of acute lower respiratory infection (ALRI) were enrolled. Children with bronchopulmonary dysplasia, cystic fibrosis, congenital heart disease, congestive cardiac failure (CCF), severe dehydration, severe anemia, congenital cystic malformations, or neuromuscular disorders were excluded from the study.

In this study, ALRI included bronchiolitis, bronchopneumonia, bronchial asthma, and kerosene poisoning. Written informed consent was obtained from the guardians or attendants of all participants before clinical evaluation. The respiratory rate was measured over a full minute, and a comprehensive respiratory examination was conducted to assess for central cyanosis, head nodding, grunting, nasal flaring, chest indrawing, fast breathing, crepitations, and rhonchi. Chest X-rays were also performed and interpreted independently by a radiologist. The final diagnosis was based on the patient's history, clinical findings, and radiological results. Fast breathing was defined according to the IMCI 2016 guidelines as a respiratory rate of ≥50 breaths per minute for children aged 2–12 months, and ≥40 breaths per minute for those aged 12–60 months[17]. Chest indrawing was identified as the inward movement of the lower chest during inspiration, while central cyanosis was recorded when a bluish discoloration of the tongue or oral mucosa was observed[13]. Head nodding, typically indicative of severe respiratory distress, was defined as rhythmic head movement in sync with breathing[18]. The presence of wheezing and crepitations was also documented, and nasal flaring was defined as visible movement of the ala nasi[19].

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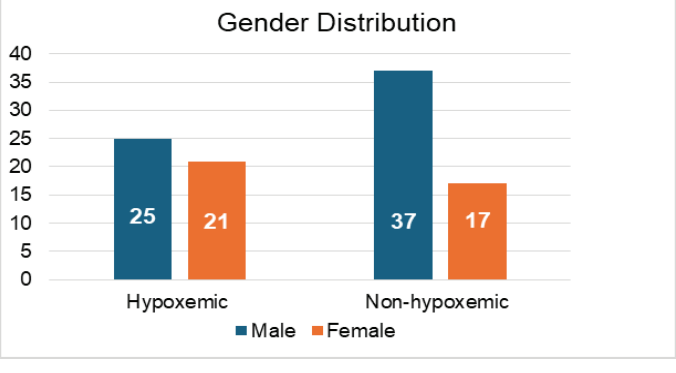
Blood samples were collected for arterial blood gas (ABG) analysis. Before arterial puncture, the Modified Allen test was performed when applicable to evaluate the adequacy of collateral circulation between the radial and ulnar arteries. Arterial blood was drawn under strict aseptic conditions, with successful sampling confirmed by the bright red color and high-pressure flow of the blood. The samples were analyzed within 30 minutes of collection. Measurements of pH, pCO_2, and pO_2 were performed using electrochemical methods with the RADIOMETER ABL80 FLEX analyzer at Delta Health Care in Chattogram. Based on the ABG results, children were classified into two groups: the hypoxemic group, with a PaO_2 below 60 mmHg, and the non-hypoxemic group, with a PaO_2 of 60 mmHg or higher.

Data was processed and statistically analyzed using SPSS version 23. Continuous variables were presented as mean ± standard deviation (SD), while categorical variables were presented as frequencies and corresponding percentages. The frequencies of different symptoms and signs in both groups were calculated and compared using the Chi-square (χ^2) test. A p-value of <0.05 was considered statistically significant, with results reported at a 95% confidence interval.

Results

In this study, 100 patients diagnosed with ALRI were enrolled and subsequently categorized into two groups based on their arterial blood gas (ABG) results. Among them, 46 patients (46%) were found to be hypoxaemic (PaO_2 < 60 mmHg), while the remaining 54 patients (54%) were classified as non-hypoxaemic ($PaO_2 \geq 60$ mmHg). The distribution of gender among non-hypoxemic and hypoxemic children is presented in figure 1. Among the 54 non-hypoxemic patients, 37 cases were male and 17 were female. In contrast, among the 46 hypoxemic patients, 25 cases were male and 21 were female.



Distribution of symptoms and signs in hypoxemic and non-hypoxemic groups are presented in table I. Table shows that in hypoxaemic group 23 (50%) patients had feeding difficulty, 13 (28.5%) patients had cyanosis, 11 (23.9%) patients had head nodding, and 16 (34.8%) patients had grunting. The percentage distribution of these symptoms and signs were significantly higher in hypoxaemic groups of patients. So, feeding difficulty, cyanosis, head nodding and grunting were independent significant predictors of hypoxaemia. Odds ratio was more significant for cyanosis, grunting and lethargy ($p<0.05$).

Distribution of symptoms and signs according to sensitivity and specificity are presented in table II. Among these symptoms and signs sensitivity was high in breathing difficulty (71.7%), nasal flaring (71.7%) and crepitations (82.6%) with a low specificity. On the other hand, specificity was high in feeding difficulty (77.8%), sleep disturbance (83.3%), lethargy (98.2), cyanosis (94.4%), head nodding (90.7%) and grunting (92.6%). Positive predictive value was more in lethargy (83.3%), cyanosis (81.3%) and grunting (80%). Negative predictive value was more in feeding difficulty (64.6%), nasal flaring (65.8%) and grunting (62.5%).

Table I: Distribution of symptoms and signs in hypoxemic and non-hypoxemic groups of patients

Symptoms and signs	Total	Hypoxemic (n=46)	Non-hypoxemic (n=56)	Odds ratio	p-value
Breathing difficulty	71	33 (71.7%)	38 (70.4%)	1.07	0.880
Feeding difficulty	35	23 (50.0%)	12 (22.2%)	3.50	**0.004**
Sleep disturbance	12	3 (6.5%)	9 (16.7%)	0.34	0.120
Lethargy	6	5 (10.9%)	1 (1.9%)	6.46	0.580
Cyanosis	16	13 (28.5%)	3 (5.6%)	6.69	**0.002**
Nasal flaring	62	33 (71.7%)	29 (53.7%)	2.19	0.064
Restlessness	19	6 (13.0%)	13 (24.1%)	0.47	0.161
Head nodding	16	11 (23.9%)	5 (9.3%)	3.08	**0.046**
Grunting	20	16 (34.8%)	4 (7.4%)	6.67	**0.001**
Crepitations	82	38 (82.6%)	44 (81.5%)	1.08	0.884
Rhonchi	24	9 (19.6%)	15 (27.8%)	0.63	0.338

*p-values were derived from $\chi 2$ test

Table II: Distribution of symptoms and signs according to sensitivity and specificity

Symptoms and signs	Sensitivity %	Specificity %	PPV %	NPV %
Breathing difficulty	71.7	29.6	46.5	55.2
Feeding difficulty	50.0	77.8	65.7	64.6
Sleep disturbance	6.5	83.3	25.0	51.1
Lethargy	10.9	98.2	83.3	56.4
Cyanosis	28.3	94.4	81.3	60.7
Nasal flaring	71.7	46.3	53.2	65.8
Restlessness	13.1	75.9	31.6	50.6

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Head nodding	23.9	90.7	68.8	58.3
Grunting	34.8	92.6	80.0	62.5
Crepitations	82.6	18.5	46.3	55.6
Rhonchi	16.6	72.2	37.5	51.3

PPV: Positive predictive value;

NPV: Negative predictive value

Distribution of combination of symptoms and signs in hypoxemic and non-hypoxemic group of patients are presented in table III. Among combination of symptoms and signs nasal flaring with grunting 12 (26.1%), cyanosis with nasal flaring 11 (23.9%), feeding difficulty with head nodding with cyanosis 12 (26.1%) and feeding difficulty with nasal flaring with cyanosis 5 (10.9%). Grunting with nasal flaring (p=0.001), cyanosis with nasal flaring (p=0.001), feeding difficulty with head nodding and cyanosis (p=0.011) and feeding difficulty with nasal flaring and cyanosis (p=0.001) were found to be significantly associated with hypoxemia. Odds ratio was more significant in nasal flaring with grunting (9.18) and cyanosis with nasal flaring (16.1%).

The diagnostic accuracy of various combinations of symptoms and signs for predicting hypoxaemia in children with ALRI is summarized in Table IV. Among the combination of symptoms and signs nasal flaring with grunting (26.1%) and feeding difficulty with head nodding with cyanosis (26.1%). Combinations of different symptoms and signs increased the specificity with subsequent decrease in sensitivity. The specificity of head nodding with cyanosis (98.2%), nasal flaring with grunting (96.3%), cyanosis with nasal flaring (98.2%), restlessness with cyanosis (100%), feeding difficulty with head nodding with cyanosis (92.6%) and feeding difficulty with nasal flaring with cyanosis (100%). Positive predictive value was more in restlessness with cyanosis (100%) and feeding difficulty with nasal flaring with cyanosis (100%). Negative predictive value was more in nasal flaring with grunting (60.1%) and cyanosis with nasal flaring (60%).

Table III: Distribution of combination of symptoms and signs in non-hypoxemic and hypoxemic group of patients.

Symptoms and signs	Hypoxemic (n=46)	Non- hypoxemic (n=56)	Odds ratio	p-value
Head nodding + cyanosis	3 (6.5%)	1 (1.9%)	3.69	0.235
Nasal flaring + grunting	12 (26.1%)	2 (3.7%)	9.18	**0.001**
Cyanosis + nasal flaring	11 (23.9%)	1 (1.9%)	16.1	**0.001**
Restlessness +cyanosis	4 (4.3%)	0 (0%)	0.49	0.122
Feeding difficulty+Head nodding +cyanosis	12 (26.1%)	4 (7.4%)	4.11	**0.011**
Feeding difficulty +Nasal flaring +cyanosis	5 (10.9%)	0 (0%)	4.26	**0.001**

*p-values were derived from $\chi 2$ test

Table IV: Diagnostic accuracy of combinations of symptoms and signs in predicting hypoxaemia among children with ALRI

Symptoms and signs	Sensitivity %	Specificity %	PPV %	NPV %
Head nodding + cyanosis	6.52	98.2	45	55
Nasal flaring + grunting	26.1	96.3	85.7	60.1
Cyanosis + nasal flaring	23.9	98.2	91.7	60.0
Restlessness +cyanosis	4.53	100	100	55.1
Feeding difficulty+ Head nodding +cyanosis	26.1	92.6	75.0	59.5
Feeding difficulty + Nasal flaring +cyanosis	10.9	100	100	56.8

PPV: Positive predictive value;
NPV: Negative predictive value

Discussion

The high prevalence of hypoxaemia among children experiencing respiratory distress represents a major public health concern and adversely affects child health outcomes. Clinical signs and symptoms of respiratory distress can serve as important indicators of hypoxaemia[20]. This study aimed to identify the key clinical predictors of hypoxaemia in children diagnosed with acute lower respiratory infection (ALRI). Overall, a male predominance was observed in both groups, which is consistent with findings from a previous study[21]. A range of symptoms and signs have been assessed in previous studies to determine the clinical predictors of hypoxemia[15,16,22-24]. We evaluated five symptoms and nine clinical signs for their ability to detect hypoxaemia in children presenting with ALRI. Among these, feeding difficulties, cyanosis, grunting respirations, and head nodding were identified as independent predictors of hypoxaemia in hospitalized children aged 2 months to 5 years.

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Consistent with our results, numerous previous studies have reported cyanosis and grunting respirations as independent predictors of hypoxaemia in children under five with severe pneumonia[16,22,25]. Grunting is an inspiratory sound produced when a child breathes against a partially closed glottis, serving as a form of self-generated positive pressure ventilation to compensate for ventilation-perfusion mismatch, often caused by lung consolidation or increased dead space[26]. This mechanism leads to the accumulation of deoxygenated haemoglobin, and when levels exceed 5 g/dL, cyanosis becomes clinically evident. Cyanosis is widely recognized as a critical sign for initiating oxygen therapy in children with pneumonia[11,18].

It is important to note that, apart from cyanosis, no single clinical symptom or sign in children with ALRI can be attributed solely to hypoxaemia. For instance, fast breathing may result not only from low oxygen levels but also from other conditions such as metabolic acidosis, fever, or central nervous system disorders. Signs like chest wall retractions, grunting respirations, or symptoms such as poor feeding are more reflective of the overall severity of pneumonia. Since severe pneumonia is more commonly associated with hypoxaemia, certain markers of disease severity may also show a significant correlation with hypoxaemia. However, there remains a lack of inter-observer agreement regarding the identification and interpretation of clinical signs of respiratory disorders, which can limit the reliability of clinical assessment alone[27].

A previous study reported that head nodding is an under-recognized, ALRI-specific clinical predictor of mortality in hypoxaemic young children[23]. In that study, 8 children presented with head nodding at admission, of whom 6 were severely hypoxaemic. In our study, 16 children exhibited head nodding upon admission, and 11 of these were found to be hypoxaemic. Unlike cyanosis, which can be influenced by factors such as skin pigmentation, anemia, and variability between observers, head nodding is a more consistently recognizable sign that can be observed easily without undressing the child. Furthermore, it can be easily taught to primary healthcare workers with limited training[15].

Head nodding is an age-dependent clinical sign that is specific to ALRI and is most useful in young children without co-morbidities[16]. This is supported by a recent study in which many children also had co-existing conditions such as diarrhea and malnutrition[28]. In that study, metabolic acidosis did not significantly affect outcomes in patients with or without head nodding, suggesting that the presence of co-morbidities may influence this relationship. Consequently, the observation of head nodding should alert primary healthcare workers to prioritize these patients for immediate oxygen therapy or timely referral to an appropriate healthcare facility. Poor feeding is commonly associated with severe systemic illnesses, particularly in infants and neonates, often caused by gram-negative organisms[29], and its presence is an important indicator for hospital admission and urgent treatment. Consistent with our findings, a study from Nepal reported that inability to feed, along with cyanosis and grunting respirations, was strongly correlated with hypoxaemia in children with severe pneumonia[30].

Zhang et al.[31] reported substantial variability in the sensitivity and specificity of different symptoms and signs across the studies included in their meta-analysis. In our study, parental or caregiver-reported breathing difficulty and crepitations on lung auscultation showed relatively high sensitivity for detecting hypoxaemia. However, both indicators demonstrated low specificity. In contrast, feeding difficulty, lethargy, sleep disturbance reported by caregivers and cyanosis, head nodding and grunting respiration on observation had high specificity but low sensitivity. In general, a test with high sensitivity is valuable for ruling out a condition when the result is negative. This indicates that the absence of these symptoms and signs may help exclude a diagnosis of hypoxaemia. However, symptoms and signs that are highly sensitive but have low specificity can lead to a large number of false-positive diagnoses of hypoxaemia.

On the other hand, symptoms and signs with high specificity but low sensitivity could be helpful to confirm a diagnosis of the hypoxaemia in their presence. Apart from the uncertainty in confirming a diagnosis, the absence of the above-mentioned symptoms and signs may also fail to identify hypoxaemia in many children who in fact have this condition, due to low sensitivity. In the present study, various combinations of clinical signs were significantly associated with hypoxaemia, demonstrating high specificity but low sensitivity. These findings are partially consistent with the study by Kushwah et al[19]. This suggests that, in resource-

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limited settings, such combinations of signs may be reasonably used to identify children with pneumonia who are likely to be hypoxaemic.

Hypoxaemia can have serious consequences if untreated, while oxygen therapy has minimal side effects. In well-resourced settings, highly sensitive tests are preferred. However, in resource-limited countries like Bangladesh, oxygen is costly and often only available in urban centers. Therefore, guidelines with high specificity are essential to avoid overwhelming referral systems and conserving limited oxygen supplies. Our data indicates that relying on only a few physical signs may either miss hypoxaemia or lead to unnecessary oxygen use. In this study, certain combinations of signs showed high specificity and may help guide oxygen use when resources are scarce.

Conclusion

Hypoxaemia is a frequent and manageable complication seen in children with respiratory as well as non-respiratory infections, particularly in developing countries. Feeding difficulty, cyanosis, head nodding and grunting were independent predictors of hypoxaemia in this study. Combinations of symptoms such as cyanosis with nasal flaring, feeding & breathing difficulty, crepitation and head nodding also indicated hypoxaemia in children with ALRI. Establishing clinical guidelines and ensuring effective oxygen delivery systems can significantly enhance treatment quality, ultimately reducing both morbidity and mortality.

Conflict of Interest: The authors declare that they have no conflicts of interest related to the publication of this paper.

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