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A study of clinical predictors of Hypoxemia in children with Acute Respiratory Illness

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Abstract:
Background:*In developing countries, acute lower respiratory illness (ALRI) contributes to significant mortality in children below the age of 5 years and hypoxemia is the major contributing factor for mortality in these children. Early detection of hypoxemia and treatment improves outcome in these children. As pulse oximeter is not available in all health care facilities in developing countries, clinical signs which predict hypoxemia should be identified*. ***Objectives:****To determine the clinical predictors of hypoxemia in children aged 2 months to 5 years with acute respiratory illness.* ***Methods:*** *A hospital based study was conducted at pediatric ward of Sri Ramachandra Medical College and Research Institute, Chennai for a period of one year. Children of age group 2 months - 5 years, who were admitted with signs and symptoms suggestive of an acute respiratory illness, were included in the study.* ***Results:*** *Of the 75 children included in the study, 26.7%(20) children were found to be hypoxemic (Spo2<90%). All 20 children (100%) in the hypoxemic group had very severe pneumonia. 65% of children in the age group 13-60months were found to be hypoxemic. History of rapid breathing, Tachypnea, restlessness, inability to feed, cyanosis, suprasternal indrawing, intercostal retractions, subcostal retractions, crepitations and wheeze were significantly associated with hypoxemia. Tachypnea (PPV 90%) and crepitations (PPV 80%) were the best predictors of hypoxemia.* ***Conclusion:*** *None of the individual symptoms and signs could be used as sole criteria for predicting hypoxemia, however the most sensitive indicators of hypoxemia were restlessness and sub costal retractions while the best predictors were tachypnea and crepitations. This study validates the WHO criteria of giving oxygen to children with very severe pneumonia*
Keywords – *Acute respiratory illness, hypoxemia, pulse oximeter, saturation*

I. Introduction

Acute Respiratory tract infections (ARI) are among the major causes of preventable morbidity and mortality worldwide, with most of the deaths occurring in under five children in developing countries[1]. Hypoxemia is the most serious manifestation of severe respiratory illness in children and a strong risk factor for mortality. The case fatality rate is inversely related to oxygen saturation of arterial blood. The hemoglobin oxygen saturation (SpO_2) measured using a pulse oximeter has been shown to predict outcome in ARI and delivery of oxygen to hypoxemic children may improve the outcome. It is therefore important to identify a minimum set of clinical signs that can reliably predict presence of hypoxemia in children with ARI that can be used by health care provider to institute oxygen therapy.

II. Objectives

To determine the clinical predictors of hypoxemia in children aged 2 months to 5 years with acute respiratory illness

III. Materials And Methods

A hospital based study was conducted at pediatric ward of Sri Ramachandra Medical College and Research Institute, Chennai for a period of one year. Children of age group 2 months - 5 years, who were admitted with signs and symptoms suggestive of an acute respiratory illness, were included in the study.
ARI was defined as an acute onset of respiratory symptoms such as cough, rhinorrhea, fast/difficult breathing and chest wall indrawing of less than 14 days duration.Patients with history of chronic respiratory symptoms,

bronchial asthma, congenital heart disease, congenital malformations, and those needed cardiopulmonary resuscitation at admission were excluded from the study.

Within half an hour of arrival to pediatric ward a standardised history was obtained from the mother about the presence and duration of various symptoms: cough, fever, rapid breathing, irritability, convulsions, feeding pattern.

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), Tachypnea is defined as respiratory rate >60/min in children less than 2 months of age , >50/min in children 2-12 months of age, >40/min in children >12 months of age. cyanosis, chest retraction, grunting, nasal flaring, head nodding, inability to feed, crepitations or rhonchi on auscultation and state of consciousness. Impaired consciousness was recorded if the child was abnormally sleepy or difficult to wake, not responsive to verbal or painful stimulus. Children were classified as having No pneumonia, pneumonia, severe pneumonia and very severe pneumonia according to the WHO criteria.

Oxygen saturation (SpO_2) was measured at finger or toe with a pulse oximeter (Nellcor™ N-550, USA) using an appropriate sized pediatric sensor. The oximetry measurement was recorded after stabilization of the reading for one minute. Hypoxemia was defined as SpO_2 <90 %. Chest X-ray was obtained in patients wherever applicable. Chest X-ray was read by a radiologist who was unaware about the clinical condition of the child.

Radiological pneumonia is defined as presence of any kind of infiltrate (alveolar or interstitial) in the chest X-ray. Bronchiolitis is defined radiologically as diffuse hyperinflation with flattening of diaphragm, widening of intercostal space. Collapse is defined radiologically as Tracheal displacement towards the side of the collapse, Mediastinal shift towards the side of the collapse, elevation of the hemidiaphragm, reduced vessel count on the side of the collapse, herniation of the opposite lung across the midline.

Analysis was done using SPSS for window (version 10.0) and Epi-info6 software packages. Each clinical finding was analised for association with hypoxemia using 2 x 2 table (Chi-square test). Sensitivity, specificity, positive (PPV) or negative predictive values (NPV) were calculated.

IV. Results

In the present study, out of 75 children, 26.7% (20) children were found to be hypoxemic. Saturation ranges from 86%-89% in the hypoxemic group and about 96%- 100% in the non hypoxemic group (table 1). Majority of the children in both hypoxemic (60%) and non hypoxemic groups (69%) were males (table 2). Among the 75 children, 62.7% (47) of children were in the age group of >12 months. Only 4% of children were less than 3months of age and mean age is 24.37months (table 3). In the hypoxemic group, 65% (13) of children were in the age group of 13- 60 months and in the non hypoxemic group 61.9% (34) of children were in the age group of 13-60 months (table 4). Nutritional status of the children was assessed by IAP (Indian Academy of Pediatrics) classification of malnutrition. Of the 29 children who had malnutrition, 30% (6) of children were in the hypoxemic group. There is no statistical difference between the two groups (P>0.05) (table 5). All 20 children in the hypoxemic group had very severe pneumonia. About 41.8% (23) children in the non hypoxemic group had pneumonia (table 6). Tachypnea, restlessness, inability to feed, cyanosis, suprasternal indrawing, intercostal retractions, subcostal retractions, crepitations and wheeze were significantly associated with hypoxemia. Tachypnea (PPV 90%) and crepitations (PPV 80%) were the best predictors of hypoxemia (table 7&8).

Table 1: Oxygen Saturation by Pulse Oximetry

Saturation	Number	Mean	Standard Deviation
<90%	20 26.7%	88.45%	1.0
>90%	55 73.3%	97.47%	1.07

Table 2: Distribution of Children according to Sex and Saturation

Saturation	Sex		Total
	Male	Female	
<90%	12 60%	8 40%	20 100%
>90%	38 69%	17 31%	55 100%

Table 3: **Distribution of Children by Age in Months**

Age (in months)	Number	Percentage
<3	3	4%
3-12	25	33.3%
>12	47	62.7%
TOTAL	75	100%

Table 4: Distribution of Children According to Age in Months and Saturation

Saturation	Age (in months)			Total
	< 3	3- 12	13 – 60	
<90%	1 5%	6 30%	13 65%	20 100%
>90%	2 3.6%	19 34.5%	34 61.9%	55 100%

Table 5: Nutritional Status of Children and Saturation

Saturation	Normal Nutrition	Malnutrition	Total
<90%	14 70%	6 30%	20 100%
>90%	32 58.2%	23 41.8%	55 100%

Table 6: Distribution of Pneumonia according to Saturation

	CLASSIFICATION				Total
	Very Severe Pneumonia	Severe pneumonia	Pneumonia	No Pneumonia	
<90%	20 100%	0	0	0	20 100%
>90%	1 1.8%	18 32.7%	23 41.8%	13 23.7%	55 100%

Table 7: Predictive Value of Clinical Symptoms for Hypoxemia (Spo_2 <90%) In Children with ARI

Variables	Hypoxemic children (n=20)	Non hypoxemic children (n=55)	P value	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
H/o rapid Breathing	19	12	<.001	61.2%	97.7%	95%	78%
H/o fever	12	27	>0.05	30.7%	77.7%	60%	50.9%
H/o nasal Discharge	10	28	>0.05	26.3%	72.9%	50%	49.1%
H/o feeding Difficulty	1	1	>0.05	50%	73.9%	5%	98.2%
H/o sleep Disturbances	2	1	>0.05	66.6%	75%	10%	98.2%
H/o drowsy	2	1	>0.05	66.6%	75%	10%	98.2%
H/o difficulty breathing	2	1	>0.05	66.6%	75%	10%	98.2%

Table 8: Predictive Value of Clinicial Signs For Hypoxemia (Spo_2 <90%) In Children With ARI

Variables	Hypoxemic children (n=20)	Non hypoxemic children (n=55)	P value	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Nasal Flaring	11	17	>0.05	39.2%	80.8%	55%	69%
Restlessnes	4	1	<0.05	80%	77.1%	20%	98%
Inability to feed	4	2	<0.05	66.6%	76.8%	20%	96.3%
cyanosis	4	2	<0.05	66.6%	76.8%	20%	96.3%
Supra Sternal Indrawing	7	4	<0.01	63.6%	79%	35%	92.7%
Inter Costal Retractions	10	8	0.01	55%	82.4%	50%	85.4%
Subcostal Retractions	11	4	<0.01	73.3%	85%	55%	92.7%
Crepitations	16	17	<0.01	48.4%	90.4%	80%	69%
Wheeze	13	19	<0.05	40.6%	83.7%	65%	65.4%
Tachypnea	18	20	<0.01	47.3%	94.5%	90%	63.6%

V. Discussion

In our study, 26.7% children had hypoxemia (saturation <90%) and saturation ranged from 86-89% in the hypoxemic group. Kabra, found that 25.7% children were hypoxemic and oxygen saturation ranged from 86-88% in the hypoxemic group[1]. Hypoxemia was defined as arterial saturation <90% recorded by pulse oximetry. A cut off point of 90% was chosen because saturations below this regarded by most clinicians as indicating clinically significant hypoxemia. An arterial oxygen saturation of 90% generally corresponds to an arterial oxygen tension of 60-70mmHg, although this relation is affected by factors such as temperature, pH, altitude, and age. Below an arterial oxygen tension of 60-70 mmHg, the haemoglobin dissociation curve falls steeply such that further decreases in arterial oxygen tension are associated with greater decreases in arterial oxygen saturation[2]. Studies reporting the prevalence of hypoxemia measured by pulse oximeter showed wide variations and are not comparable because the cut off values used to define hypoxemia; study population, setting, and the altitude in which they were conducted differ[3,4,5].

In the present study, majority of the children in hypoxemic group were males. This finding was similar to that of Kabra[1], while other studies reported insignificant difference between males and females with regard to prevalence of hypoxemia[6,7].

In our analysis, we found that 65% of children in the age group of 13-60 months were found to be hypoxemic. This finding was similar to that seen in the study by Kabra[1], which had 64.2% children of the age group 13-60 months in the hypoxemic category. Sudha, found that infancy group were more vulnerable to hypoxemia[6]. Other studies on hypoxemia in children with ARI have not assessed the role of age as a risk factor[8]. In the present study, there were only 7 children in the infancy group under hypoxemic category.

In the present study nutritional status of children did not achieve a statistical significance between hypoxemic and non hypoxemic group. West and colleagues followed up 83 hypoxemic (SpO_2<90%) and 107 non-hypoxemic Gambian Children aged under 5 who survived a severe ALRI episode. They concluded that survival depends more on nutritional status than on having been hypoxemic[9].

WHO categorizes child as very severe pneumonia, when the child had central cyanosis, inability to drink and further instructs that these children to be admitted in hospital and given oxygen[10]. In the present study, all 20 children in the hypoxemic group had very severe pneumonia. This validates the WHO criteria of giving oxygen to children with very severe pneumonia. Sudha., in their study found that 80% children with very severe pneumonia were hypoxemic[6]. In a systemic review of published literature Lozano also reports that the frequency of hypoxemia (pooled prevalence) is determined by the severity of the illness while outpatient children and those with a clinical diagnosis of upper acute respiratory illness (ARI) had a low risk of hypoxemia (pooled estimate 6-9%), the prevalence increased among the hospitalised children (47%) and those with radiologically confirmed pneumonia[5].

H/O rapid breathing was significantly associated with hypoxemia in resemblance to studies done by Reuland and sudha [6,11]. H/O nasal discharge, H/O feeding difficulty, H/O sleep disturbances, H/O drowsy and H/O difficulty in breathing were not significantly associated with hypoxemia(P value >0.05).Kabra observed that none of the clinical symptoms were significantly associated with hypoxemia[1]. H/o feeding difficulty attained a highly significant values in relation to hypoxemia in the studies done by usen and weber[2,12]. Onyango and sudha observed high significance of hypoxemia with history of difficulty in breathing[3,6].

Clinical symptoms are subjective as given by the observer and may not always be reliable. Among the clinical symptoms, H/O rapid breathing was the best predictor of hypoxemia and also had sensitivity of 61.2% in predicting hypoxic children. Earlier studies also demonstrated h/o rapid breathing as good predictor of hypoxemia[6,11].

The clinical signs significantly associated with hypoxemia in the study were tachypnea, restlessness, inability to feed, cyanosis, chest indrawing and crepitations. In the present study, nasal flaring was not significantly associated with hypoxemia, which is similar to that observed in kabra study[1].In other studies nasal flaring had significant association with hypoxemia[2,12] .Restlessness was significantly (p value 0.05) associated with hypoxemia. Weber, in his study reported that restlessness was inversely related to hypoxemia[13]. Inability to feed was significantly (p value <0.05) associated with hypoxemia. Several studies described inability to feed was significantly associated with hypoxemia[2,3,5] Cyanosis was significantly (p value <0.05) associated with hypoxemia, which is found to be akin with many studies[1,2,5,6]. In the current study, chest indrawing was significantly associated with hypoxemia. Presence of Chest indrawing categorizes a child as having severe pneumonia requiring hospital admission. This sign was also significantly associated with hypoxemia in the studies done by sudha and kabra. Crepitations and wheeze were significantly associated with hypoxemia in divergence to other studies[1,6,12].

In the current study, we had no children with grunting. Restlessness had 80% sensitivity and 77% specificity in predicting hypoxemia. Weber found that restlessness was inversely related to hypoxemia[12] and was not associated with hypoxemia in a study done by usen[2].

WHO currently advocates giving oxygen to children with ARI who are unable to drink as a result of their illness[4]. Our study showed that inability to feed had 66% sensitivity and 76.8% specificity in predicting hypoxia in children with acute respiratory illness. Studies from Gambia[2], Peru[5] , and Kenya[3] found that inability to feed has been significantly associated with hypoxemia. The specificity of this sign was good in Gambia[2] and lower in Peru[5] & Kenya[3] . However sensitivity of this sign varied widely between 16% and 68%.

In the present study, cyanosis had 66.6% sensitivity and 76.8% specificity in predicting hypoxia. Cyanosis is invariably associated with hypoxemia[10,14] but the difficulty of its detection, especially in dark skinned children, makes it an insensitive marker[3,11]. In our study most of the cyanosed individuals were below the age of 1 year. In the reviewed studies, it was not recognised in older children (>1yr of age) in Kenya[3] and the maximum sensitivity was 42% in Papua New Guinea[15]. Singhi study showed cyanosis had 3% sensitivity and 100% specificity in predicting hypoxia[13]. In their study none of the cyanosed children were under the age of 1 year. Kabra found that cyanosis had 14.2% sensitivity and 96.2% specificity in predicting hypoxemia[1].

Chest wall in drawing (retractions) is contemplated as vital sign of severe ALRI. Earlier studies have reported wide range of results[3,11,14,15]. It was highly sensitive (88% -90%) in predicting hypoxemia in many studies[6,13,16] where as it was stated to be more specific in a study done by kabra[1]. In the current study, this sign had better specificity (85%) than sensitivity (73.3%) in predicting hypoxemia.

Tachypnea in the existing study was defined using cut-off values based on age according to WHO guidelines[10]. Tachypnea predicted hypoxemia with a sensitivity of 47.3% and specificity of 94.5% in the current study. Reuland (altitude 3750m) and Onyango (altitude 1670 m) described an increased occurence of rapid breathing in children with hypoxemia [3,11,]. In a study from Gambia, the risk of hypoxemia doubled in children with a respiratory rate of 70/min and augmented by about 3% for each increase of one breath in respiratory rate[2]. Singhi found that the presence of tachypnea had 65% sensitivity and 80% specificity in predicting hypoxemia[13]. Similarly, in the Kabra study, increasing the respiratory cut off by 10/minute lead to a decline in sensitivity from 82.1% to 53.6% and increment in specificity from 51.8% to 77.8%[1]. An elevated respiratory rate in a sick child with pneumonia could result from metabolic acidosis secondary to dehydration from fever, panting and inability to drink as well as decreased peripheral perfusion. This would limit the usefulness of increasing respiratory rate as a sole criteria in assessing the degree of hypoxia[17].

In our analysis, auscultatory findings of either wheeze or crepitations had sensitivity of 40.6%, 48.4 % and specificity of 83.7%, 90.4% respectively. At high altitude presence of either rhonchi or crepitations had 96% sensitivity and 47% specificity to predict hypoxia[11]. Kabra found that the presence of crepitations (sensitivity 67.8% , specificity 67.9%) and wheeze (sensitivity 60.7%, specificity 82.7%) in predicting hypoxia in children[1]. In the existing study, 45.3% children had radiologically defined pneumonia and radiological findings were not significantly associated with hypoxemia and this is contrary to the study done by Lozano where radiological pneumonia had 65% sensitivity and significant association with hypoxemia[8].

Oxygen therapy not only improves the survival, but it may also be preventing substantial morbidity that may occur from prolonged hypoxemia in children who survive[18,19,20]. Supplemental oxygen given to children with chest indrawing who have not yet progressed to hypoxemia may offer several advantages. It may prevent exhaustion from rapid respiratory efforts by improving arterial oxygenation and by decreasing acidosis. However this aspect needs further studies. Our data suggest that using only a few physical signs, hypoxemia will be missed in certain children or oxygen will be wasted in children who do not really need it. In resource poor countries where oxygen has to be brought in cylinders, pulse oximeters might be a cost effective and objective option to assess hypoxemia, it will allow precise identification of children in need of oxygen. In the present study, there is no independent clinical sign which is highly predictive of hypoxemia. A combination model

using clinical signs predictive of hypoxemia was not done in the study. This study validates the WHO criteria of giving oxygen to children with very severe pneumonia.

In the present study, the study population is small and was conducted in a tertiary referral care centre which involved limited population with severe disease. In our study there are no children with severe malnutrition, since children with severe malnutrition can have respiratory distress due to co- existing diseases. This aspect also needs further studies.

VI. Conclusion

- None of the individual symptoms and signs could be used as sole criteria for predicting hypoxemia, however the most sensitive indicators of hypoxemia were restlessness and sub costal retractions while the best predictor was tachypnea and crepitations.
- This study validates the WHO criteria of giving oxygen to children with very severe pneumonia**.**

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