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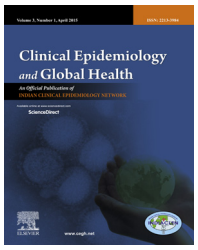

Original Article

Malnutrition and anaemia associated with hypoxia among hospitalized children with community-acquired pneumonia in North India

Tarishi Nemani, Shally Awasthi *

Department of Pediatrics, King George's Medical University, Lucknow, Uttar Pradesh, India

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ABSTRACT

Objectives: To assess the prevalence and explore the risk factors for hypoxia (SpO_2 levels <92%) in ambient air in children hospitalized with community-acquired pneumonia (CAP).
Methods: This was an observational study, conducted in a tertiary care teaching hospital in north India. Included were children aged 1 month to 5 years having pneumonia with lower chest indrawing (LCI) or severe pneumonia. Excluded were those on oxygen supplementation at time of hospitalization, patients in shock, those with cyanotic congenital heart disease and where parental consent was not obtained. World Health Organization criteria were used for assessing the severity of CAP. Anaemia and moderate malnutrition were defined as haemoglobin <10 g/dl and weight/height <−2 SD, respectively. Peripheral oxygen saturation was measured using a single, portable, battery-powered pulse oximeter at the time of admission and a cut-off of <92% was used to define hypoxia. Haemoglobin was measured by cyanmethemoglobin method.
Results: From July 2013 to June 2014, 165 patients with CAP were admitted, of which 135 patients were eligible for inclusion, and of them, 74.8% (n = 101) had pneumonia with LCI and 25.2% (n = 34) had severe pneumonia. Hypoxia was found in 40% (n = 54/135) of the patients, and of them, 37% (n = 20/54) had pneumonia with LCI and 63% (n = 34/54) had severe pneumonia. Hypoxia was associated with severity of pneumonia (p value <0.001). In the unconditional logistic model, adjusted risk of hypoxia with malnutrition was 12.1 ((95% CI) 5.0–29.4, p value <0.001) and with anaemia was 4.5 ((95% CI) 1.8–11.2, p value 0.001).
Conclusion: Since a substantial proportion of CAP had hypoxia at hospitalization, prompt detection at admission is essential especially in children with anaemia and malnutrition. Moreover, primary prevention of malnutrition and anaemia in children less than 5 years would contribute significantly in reducing prevalence of hypoxia and thus CAP-related mortality.

* *Corresponding author.*
E-mail address: shally07@gmail.com (S. Awasthi).
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1. Introduction

World Health Organization in November 2015 estimated that 0.92 million children under the age of 5 years die of pneumonia, accounting for 15% of total number of deaths in this age group worldwide. In India, during the year 2011, pneumonia was responsible for about 18% of all deaths of children under 5 years of age.[1]

In patients with pneumonia, hypoxia is a predictor of severe disease and has been shown to be a risk factor for death.[2,3] There is no doubt that detection of hypoxia presents a challenge in resource-limited health facilities. Many studies have demonstrated a low predictive value of clinical signs of hypoxia.[4–7] Hence, there is a need to objectively monitor hypoxia among children presenting to health care facilities. There is also lack of information in the medical literature on risk factors of hypoxia in children with community-acquired pneumonia (CAP). Therefore, the aim of our study was to explore the risk factor of hypoxia in patients of CAP and to assess the prevalence of hypoxia, which we defined as SpO_2 levels <92% in ambient air[8] in children hospitalized with CAP. Having knowledge of these risk factors and their optimum management, we would be able to reduce morbidity and mortality due to severe hypoxia in patients of CAP.

2. Materials and methods

This prospective, observational study was conducted for 1 year (July 2013–June 2014) at the Department of Paediatrics, King George's Medical University, Lucknow (26°55′ N, 80°59′ E), a tertiary care, referral teaching hospital at an altitude of 252 m.

The study was conducted after approval from the institutional ethics committee. Included were children aged 1 month to 5 years with CAP after obtaining written informed parental consent. Excluded were patients on oxygen supplementation at the time of hospitalization, patients in shock, defined as blood pressure below 5th percentile for age and sex, or if not recordable, capillary refill time >3 s, known cases of congenital cyanotic heart disease and cases where consent was not obtained from parents. WHO criteria were used for assessing the severity of CAP defined as no pneumonia, pneumonia with lower chest indrawing (LCI) and severe pneumonia.[9] WHO criteria were also used for assessing anaemia[10] and malnutrition[11] in children. Primary outcome measure was hypoxia defined as $SpO_2 < 92\%$ in ambient air.[8]

Any patient with history of fever, cough and difficulty in breathing was screened by an emergency team doctor on duty. As a part of screening, respiratory rate was counted and simultaneously nasal flaring, LCI and cyanosis were ascertained. Respiratory rate was counted for 1 min twice. Haemodynamic stability was assessed by measuring blood pressure and capillary refill time. All patients of pneumonia with LCI and severe pneumonia were admitted. A pulse oximeter was used to measure SpO_2 at the time the patient was admitted by a resident doctor on duty, who was trained in using pulse oximeter by T.N. SpO_2 was recorded using a single, portable, battery-powered pulse oximeter (Finger Pulse Oximeter Model No. SHO 3002, Harsons, India) with the sensor device placed over the finger (index or middle) or the big toe. The emitting and receiving diodes were carefully opposed. Once a stable plethysmograph waveform was obtained, the saturation reading was watched over at least 30 s and a value was recorded. Hypoxia was defined as $SpO_2 < 92\%$ in ambient air.[8] All patients of pneumonia with LCI not having hypoxia were discharged within 24 h on oral antibiotics.

Venous blood (3 ml) of patients enrolled was withdrawn with full aseptic precautions for routine investigations, and determining C-reactive protein and serum albumin. Haemoglobin was measured by cyanmethemoglobin method. Serum C-reactive protein levels were detected by the Vitros 250 Chemistry System by ELISA method (Ortho-Clinical Diagnostics, Inc., Johnson & Johnson Co., USA). Digital chest radiograph posterior–anterior view was done. All X-rays were read by one clinician. Chest X-ray findings were grouped in categories such as endpoint consolidation, non-endpoint infiltrate and pleural effusion according to WHO criteria.[12]

Data were collected in preformed questionnaires on demographic variables including age, sex, number of siblings, birth order, vaccination status, any co-morbidity, parent education and socio-economic status and household. Height (in cm) was measured by stadiometer for children ≥2 years of age and length by infantometer for younger children; weight was measured in kg; mid arm circumference (in cm) was obtained by measuring tape. Clinical variables included respiratory rate, heart rate, difficulty in breathing, wheeze, fever, cough, inability to feed, chest indrawing, cyanosis, blood pressure and capillary refill time.

Sample size for the study was determined by raosoft online sample size calculator.[13] Assuming that 50% of the participants will be having hypoxia (as this will give the largest sample size), then to estimate this with a 10% precision and 95% confidence level, we required to recruit a minimum of 96 cases. Data were entered in MS Excel and SPSS software version 15 was used. Univariate analysis was done to assess the distribution of baseline variables by computing frequency, percentages and mean with standard deviation. Thereafter, chi-square test was used for analyzing difference in proportion for different categories. The Student *t* test was used to analyze difference between two groups for continuous variables. The data were confirmed as significant if p value obtained was <0.05. The odd's ratio with 95% confidence limit was also calculated to assess the association of various risk factors with hypoxia. We also calculated and reported the sensitivity and specificity of clinical features for predicting hypoxia. Unconditioned logistic regression was done to find predictors of hypoxia from among those that had univariate association with it using a two-tailed distribution.

3. Results

The study was conducted from July 2013 to June 2014. Total number of cases of CAP reporting to our facility was 165, out of which 135 were enrolled in the study. The reason for cases not recruited is given in Fig. 1. Among those enrolled, there were 74.8% (n = 101) cases of pneumonia with LCI and 25.2% (n = 34) cases of severe pneumonia. Hypoxia defined as $SpO_2 < 92\%$ was found in 54/135 (40%) patients of CAP. Among patients of

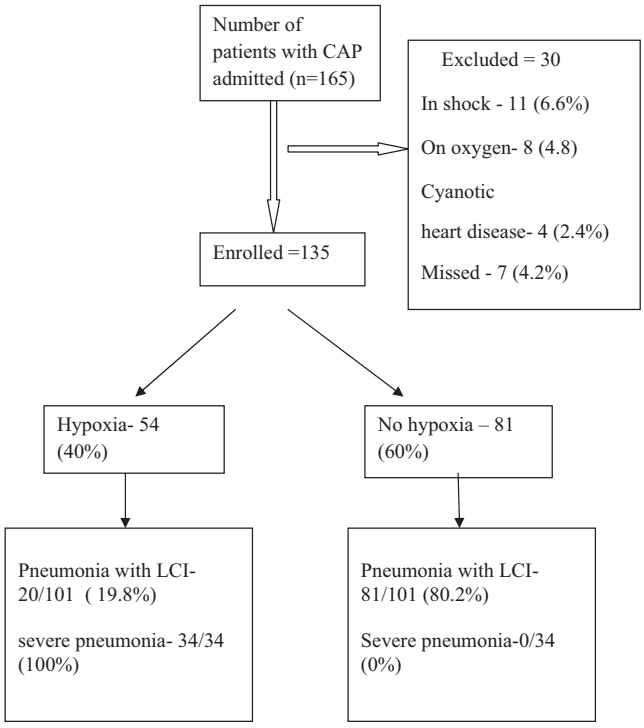

Fig. 1 – Flow diagram for inclusion of study subjects.

pneumonia with LCI, 19.8% (20/101) were hypoxic and 100% (34/34) of severe pneumonia patients were hypoxic.

The mean age of patients with hypoxia was 17.2 ± 18.3 months, and for patients without hypoxia, it was 19.1 ± 17.1 months ($p = 0.543$). Mean height/length of patients with and without hypoxia was 68 ± 5.4 cm and 76 ± 13.4 cm ($p = 0.056$), respectively. Patients with hypoxia had statistically significant lesser weight than patients without hypoxia at admission (7.08 ± 3.6 kg vs 9.3 ± 4.0 kg, p value = 0.001). As shown in Table 1, compared to those having no malnutrition, the odds of having hypoxia were significantly higher among those having moderate and severe malnutrition ($\chi^2 = 48.587$; $p < 0.001$). The clinical features of hypoxic and non-hypoxic patients were compared, and sensitivity and specificity for diagnosis of hypoxia have been calculated and given in Table 2.

In hypoxic children, the mean serum albumin was 3.3 ± 2.9 mg/dl as compared to the non-hypoxic children, which was 3.2 ± 0.7 mg/dl ($p = 0.816$). Levels of C-reactive protein in patients of pneumonia with LCI was 40.8 ± 27 mg/l, and in those with severe pneumonia, it was 76.7 ± 23.3 mg/l ($p < 0.001$). However, on comparison of C-reactive protein of hypoxic and non-hypoxic patients, no difference was observed (67 ± 27.16 mg/l vs 58 ± 30.3 mg/l, $p = 0.068$).

An increasing trend of hypoxia prevalence was observed with anaemia and its severity ($\chi^2 = 48.587$; $p < 0.001$), as seen in Table 3. In the unconditional logistic model, adjusted risk of hypoxia with malnutrition (<−2 SD weight/height) was 12.1 ((95% CI) 5.0–29.4, p value <0.001), and with anaemia (Hb < 10 g/dl) it was 4.5 ((95% CI) 1.8–11.2, p value 0.001).

On chest X-ray, pleural effusion was found to be significantly higher in hypoxic patients when compared to non-hypoxic patients (37% vs 21%, $p = 0.041$). Patients with hypoxia at admission required longer duration of oxygen (61.14 ± 44.6 h vs 29.6 ± 37.02 h, $p < 0.001$) and therefore had longer hospital stay (11.8 ± 8.3 days vs 8.9 ± 8.6 days, p value 0.051).

Table 1 – Baseline characteristics of the study population.

Characteristics	Hypoxia ($N = 54$)	No hypoxia ($N = 81$)
Mean age	17.2 ± 18.3 months	19.1 ± 17.1 months
Mean height/length	68 ± 5.4 cm	76 ± 13.4 cm
Mean weight	7.08 ± 3.6 kg	9.3 ± 4.0 kg

4. Discussion

The present study was conducted on 135 patients with CAP aged 1 month to 5 years. Using SpO_2 at ambient air <92% as cut-off value for detecting hypoxia, we found 40% prevalence of hypoxia in this study. Other studies have reported a wide variation in prevalence of hypoxia in different regions of India ranging from 24.5% to 62%.[5,6] The reason for this variation may be due to different cut-off values of hypoxia, variation in baseline characteristic of the study population, variation in altitude and study setting in which they were conducted. We found higher hospital prevalence as higher cut-off for defining hypoxia was used, which increased the sensitivity for detecting hypoxia. Other studies found hypoxia to be more frequent and more severe in children who live at high altitude, as normal SpO_2 values at plains and high altitude differ.[14–17]

We found that no symptoms or signs were both sufficiently sensitive and specific to identify hypoxia. Hence, accurate detection of hypoxia could only be done by a simple instrument, the pulse oximeter, a non-invasive, inexpensive, safe and easy to use method.[3,14,18,19] As found in our study, other workers had also found no symptoms or signs to be significant enough to identify hypoxia.[4–7,16]

Table 2 – Association of nutritional status with hypoxia in patients of community-acquired pneumonia.

S. no.	WHO grade of nutritional status (wt/ht)	Hypoxia ($N = 54$)		No hypoxia ($N = 81$)		Odds ratio (95% CI)	p value
		n	%	n	%		
1.	No malnutrition	15	27.8	68	84.0	Ref.	
2.	Moderate malnutrition (<−2 SD)	20	37.0	12	14.8	7.56 (3.05–18.74)	$p < 0.001$
3.	Severe malnutrition (<−3 SD)	19	35.2	1	1.2	86.13 (10.68–694.41)	$p < 0.001$

χ^2 for trend = 48.587; $p < 0.001$.

Table 3 – Association of clinical characteristics with hypoxia in patients of community-acquired pneumonia at the time of admission.

Clinical characteristics	Hypoxia (N = 54) n, %	No hypoxia (N = 81) n, %	p value	Sensitivity (95% CI)	Specificity (95% CI)
Fever	54, 100	81, 100	–	100	0
Cough	23, 42.6	23, 28.4	0.088	42.6	71.6
Fast breathing	54, 100	81, 100	–	100	0
Cyanosis	32, 59.3	0, 0	<0.001	59.3	100
Chest indrawing	54, 100	52, 64.2	<0.001	100	35.8
Nasal flaring	48, 88.9	64, 79	0.135	88.9	21.0
Wheezing	5, 9.3	9, 11.1	0.730	9.3	88.9

Table 4 – Association of severity of anaemia with hypoxia in patients of community-acquired pneumonia.

S. no.	WHO grading of anaemia	Hypoxia (N = 54)		No hypoxia (N = 81)		Odds ratio (95% CI)	p value
		n	%	n	%		
1.	No anaemia (≥11 g/dl)	5	9.3	17	21.0	Ref.	
2.	Mild anaemia (10–10.9 g/dl)	7	13.0	32	39.5	0.74 (0.205–2.701)	$p = 0.652$
3.	Moderate anaemia (7–9.9 g/dl)	32	59.3	28	34.6	3.89 (1.27–11.89)	$p = 0.014$
4.	Severe anaemia (<7 g/dl)	10	18.5	4	4.9	8.50 (1.84–39.23)	$p = 0.004$

χ^2 for trend = 20.843; $p < 0.001$.

As was expected with increasing severity of pneumonia, the proportion of cases with hypoxia increased ($p < 0.001$) in our study. These results were corresponding with other Indian studies.[6,7] Studies from South Asia and Africa showed a lower prevalence in patients of pneumonia with LCI, which may be related to earlier presentation of patients in a health facility.[20,21] Therefore, screening in this group for hypoxia may prove cost effective and reduce health care facility burden.

Malnutrition was found to be a statistically significant predictor for hypoxia in logistic regression. Our findings were corresponding with reports by other workers.[22] On extensive literature review, anaemia has not been reported as a risk factor for hypoxia in patients of CAP. In this study, an increasing trend of hypoxia prevalence was observed with anaemia and its severity (Table 4). Anaemia is an integral part of malnutrition; however, in our study, both were found as independent predictors for hypoxia.

Inclusion and exclusion criteria were well defined and strictly followed and standard WHO classification was used, which added to the strength of the study. $SpO_2 < 92\%$ was used as cut-off for hypoxia, and this increased the sensitivity. The use of pulse oximeter instead of the clinical criteria for assessment of hypoxia increased the reliability and is also a non-invasive method in comparison to arterial blood gas measurement. However, the study was conducted at a tertiary care, referral centre so it may not reflect the actual conditions, as many patients due to delay in referral may develop complications like shock and receive oxygen therapy leading to their exclusion. Total hospital stay reported and the duration of oxygen requirement are likely to be biased, as discharge policies are not standardized. This is an intrinsic weakness of the present study.

5. Conclusions

Our study provides evidence for promoting the use of pulse oximetry at peripheral health care level in cases of CAP for early detection of hypoxia and timely referral/intervention. Presence of malnutrition and anaemia (haemoglobin <10 g/dl) are independent risk factors for hypoxia in children with CAP. Primary prevention of malnutrition and anaemia in children less than 5 years of age will contribute significantly in reducing prevalence of hypoxia and thus related mortality among those developing CAP. Thus, this would help in achieving millennium development goal-4.

Conflicts of interest

The authors have none to declare.

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