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Pantig FM & Gatchalian S. Comparison of Various Methods of Detection of Hypoxemia and Correlation of Hypoxemia with Clinical Features Among Pediatric Patients 3 Months to 5 Years Old with Community-Acquired Pneumonia at a Tertiary Hospital Emergency Room

ORIGINAL ARTICLE

COMPARISON OF VARIOUS METHODS OF DETECTION OF HYPOXEMIA AND CORRELATION OF HYPOXEMIA WITH CLINICAL FEATURES AMONG PEDIATRIC PATIENTS 3 MONTHS TO 5 YEARS OLD WITH COMMUNITY-ACQUIRED PNEUMONIA AT A TERTIARY HOSPITAL EMERGENCY ROOM

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The authors declare that the data presented are original material and has not been previously published, accepted or considered for publication elsewhere; that the manuscript has been approved by all authors, and all authors have met the requirements for authorship.

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ABSTRACT

Introduction: Pulse oximetry is frequently utilized as a rapid, non-invasive, point-of-care alternative to arterial blood gas analysis in measuring oxygen saturation of children with pneumonia.

Objectives: To compare portable fingertip pulse oximetry saturation (SpO_2^{PF}), handheld pulse oximetry saturation (SpO_2^{H}) and arterial oxygen saturation (SaO_2) in detection of hypoxemia, and correlate hypoxemia with clinical features in children with pneumonia.

Methodology: This was a prospective, observational, cross-sectional study involving patients 3 months to 5 years old with pneumonia. Oxygen saturation was measured using a portable fingertip pulse oximeter, a handheld pulse oximeter, and arterial blood gas analysis.

Results: Eighty-six children were included. SpO_2^{PF} underestimated oxygen levels by 0.126% (95% CI -0.240 to 0.491), while SpO_2^{H} underestimated it by 0.323% (95% CI -0.075 to 0.721). Between portable and handheld readings, the mean difference was 0.198% (95% CI -0.089 to 0.484). Across the three methods, limits of agreement ranged from -3.388 to +4.035%. There was no statistically significant difference in variance among the three measurements. Children with tachypnea (cOR 2.623, 95% CI 1.06 – 6.48, p = 0.037), difficulty breathing (cOR 6.316, 95% CI 1.96 – 20.34, p = 0.002), and subcostal retractions (cOR 2.842, 95% CI 1.05 to 7.69, p = 0.040) were more likely to have hypoxemia.

Conclusion: Pulse oximetry closely correlates with arterial blood gas analysis within acceptable limits of agreement and with no significant differences in variance among measurements. Difficulty breathing, tachypnea and subcostal retractions were significantly more likely to be observed in hypoxemic children.

KEYWORDS: *community-acquired pneumonia; pulse oximetry; hypoxemia*

INTRODUCTION

Pneumonia is defined by the World Health Organization (WHO) as an acute disease episode with cough or difficult breathing combined with age-adjusted tachypnea.[1,2] In 2015, the WHO reported 920,000 deaths due to pneumonia globally in the under-five age group. This translates to 16% of all deaths under five years for the said year. While this is a substantial decline from the reported 1.7 million deaths in the year 2000, pneumonia mortality rates have decreased at a significantly slower rate compared with declines in other childhood illnesses such as diarrhea, malaria, and AIDS.[3] In the Philippines, 12,224 deaths were reported due to pneumonia in the under-five age group in the year 2015, accounting for 19% of all childhood deaths, which is slightly higher than the worldwide mortality rate.[4]

Hypoxemia in pneumonia has been shown to be a predictor of mortality, with a reported two- to five-fold increase in death due to pneumonia in patients with hypoxemia.[5,6] The gold standard for detection of hypoxemia is arterial blood gas (ABG) analysis.[7] The procedure is invasive as it requires taking an arterial blood sample from the patient, which also poses a potential risk for needlestick injury in health care workers. Blood gas analyzers are expensive, chemical reagents add to the cost, and a laboratory facility with trained personnel is necessary, which may be unaffordable and prohibitive for hospitals and patients with limited resources. Furthermore, high-level skill is needed in clinical interpretation of blood gas analysis results. Thus, arterial blood gas analysis may not be suitable or feasible for most hospitals with limited resources, and is mostly unavailable in primary care and local health care facilities.

Pulse oximetry has been identified as a simple and effective intervention for identifying children in urgent need of oxygen, thus preventing child deaths from lack of oxygen supplementation.[3] It is a cost-effective tool that can identify 20-30% more cases of hypoxemic children than using clinical signs alone. In addition to averting mortalities, oximetry helps to identify children requiring referral, increases the incidence of correct identification of severe pneumonia cases, decreases unnecessary oxygen supplementation, and reduces the incidence of incorrect diagnosis and inappropriate treatment with antibiotics.[8] Indeed, the introduction of pulse oximetry in clinical practice has led to an advancement in patient assessment and monitoring, because it allows for a simple, non-invasive, and reasonably accurate estimation of arterial oxygen saturation for the detection of hypoxemia. Pulse oximetry has proved to be a simpler, inexpensive, non-invasive, point-of-care alternative method to arterial blood gas analysis in measuring the oxygen saturation in arterial blood. It is non-invasive, causes less pain and distress to patients, allows for continuous monitoring or regular spot-checks, and does not require highly technical and clinical skill in its use and interpretation. The technology is affordable, sustainable and highly cost-effective for developing countries.[9] Knowledge of the oxygen saturation, correlated with the patient's presenting signs and symptoms, has been shown to alter a physician's decision on treatment, need for and level of admission, diagnostic investigation, and therapeutic interventions. With the widespread use of pulse oximetry at the frontline of patient assessment at the emergency room, this study aimed to compare portable fingertip pulse oximetry oxygen saturation (SpO_2^{PF}), handheld pulse oximetry oxygen saturation (SpO_2^{H}) and arterial oxygen saturation (SaO_2), and correlate these SpO_2^{PF}, SpO_2^{H} and SaO_2 with clinical features in children 3 months to 5 years old diagnosed with community-acquired pneumonia.

METHODOLOGY

Study Subjects

This study was a prospective, observational, cross-sectional study involving patients 3 months to 5 years of age admitted at the Pediatric Emergency

Room (PER) of the Philippine General Hospital from April to July 2018 with an admitting impression of pediatric community-acquired pneumonia of any severity. Non-probability, quota sampling was applied. Recruitment of eligible patients proceeded until the required number of participants was achieved. The inclusion criteria included: 1) patients 3 months to 5 years old admitted at the PER for 48 hours or less at the time of study enrolment; and 2) patients who satisfied the 2016 Philippine Academy of Pediatric Pulmonologists (PAPP) definition and criteria for diagnosis of pneumonia[10], and were decided by the attending pediatrician to be treated as such. The exclusion criteria were: 1) patients with any of the following conditions: pulmonary anatomic abnormality, existing cardiac condition, chronic lung conditions (bronchial asthma, bronchopulmonary dysplasia, congenital pulmonary adenomatoid malformation, pulmonary tuberculosis, chronic lung disease, lung malignancy, and others as diagnosed by the attending pediatrician); 2) patients discharged from another institution within 48 hours of admission in the PER to exclude patients with possible healthcare-associated pneumonia.

Patients were assessed by the triage officer upon arrival at the PER, and those warranting admission were admitted to the PER following standard protocol. Patients who satisfied the inclusion criteria were approached by the primary investigator who provided the parents/legal guardians with the information sheet regarding the study, and answered any questions raised by the parents/legal guardians pertaining to the study. A written informed consent was obtained from parents/legal guardian. Patients who did not consent to participate in the study continued to receive routine patient care.

Sample Size

A minimum of 76 pediatric patients were required for this study based on 80% power (101 patients for 90% power), a level of significance of 5%, assumed clinically significant difference of SpO_2 and SaO_2 equal to 1, and their standard deviation equal to ± 2.19. The values used were from a reference article by Ross and Helms.[11]

Intervention

Patient demographic data were obtained upon admission and were recorded on the data collection form. Pertinent details in the clinical history, physical examination, and degree of severity of signs and symptoms upon admission were noted and recorded on the data collection form.

After primary assessment by the attending physician, stabilization of the patient, and institution of initial therapy and other interventions, the primary investigator measured the SpO_2^{PF} level on the thumb (right or left) of the subject using the portable fingertip pulse oximeter (ChoiceMMed® Health Care MD300C21C LED Fingertip Pulse Oximeter, manufactured by Beijing Choice Electronic Tech Co., Ltd., China). This was followed by measurement of the SpO_2^{H} level on the same digit using the handheld pulse oximeter (Contec® CMS60D handheld pulse oximeter, manufactured by Contec Medical Systems Co. Ltd., Qinhuangdao, China). For both readings, the sensor was attached to the child's digit and the reading was taken after 30 seconds to allow ample time for stabilization of reading. The portable fingertip pulse oximeter did not require routine calibration or maintenance, while the handheld pulse oximeter was calibrated before leaving the factory and needed to be calibrated once a year.[12,13] The fingertip pulse oximeter and handheld pulse oximeter probe was cleaned according to manufacturer's recommendations before and after use on each patient. Pulse oximeters used were purchased specifically for the study; these were not provided/sponsored by the company. Choice of pulse oximeter brands was based on availability at the time of purchase.

The SaO_2 was measured via arterial blood sample drawn by the primary investigator from the radial artery of the same extremity. A heparinized

1cc syringe was used, prepared as follows: heparin was taken in the syringe to lubricate the inner wall of the syringe, and then was expelled from the syringe completely.[14] One (1) ml of arterial blood sample was collected, and was transported in ice to the ABG laboratory. The blood sample was processed using the institution's arterial blood gas analyzer (Nova PHOX Blood Gas Analyzer, manufactured by Nova Biomedical, Waltham Massachusetts, USA). The blood sample used was then disposed following the institution's standard protocol for disposal of biological material. The ABG tests were included in the patient's allocated funds for diagnostic tests.

In the event that venous blood was drawn instead of an arterial blood, a repeat blood extraction was performed by the primary investigator following the procedure previously described. A venous blood gas sample was determined based on, but not limited to, the following characteristics: dark red color, slow flow of blood into the syringe, non-pulsatile blood flow, and other characteristics as determined by the primary investigator.

The portable fingertip and handheld pulse oximetry results and the arterial blood gas results were relayed to the attending physician of the patient for appropriate intervention and management of the patient. Standard medical care was given to all patients upon the discretion of the attending physician. The primary investigator collected and recorded data on the treatment given that included, but was not limited to, oxygen supplementation either via nasal cannula, or face mask, endotracheal intubation, among others.

The study did not in any way cause any undue delay in the provision of standard of care to patients. Hence, if the attending physician deemed it necessary to perform an arterial blood gas determination, the attending physician proceeded with the procedure and other necessary interventions. A patient who already underwent ABG was still included in the study if his/her attending physician deemed it necessary to perform another arterial blood gas determination and had made a reorder for the test.

Only one-time determination of SpO_2^{PF}, SpO_2^{H} and SaO_2 was performed by the primary investigator. The fraction of inspired oxygen (FiO_2, in percent) upon measurement of SpO_2^{PF}, SpO_2^{H} and SaO_2 was documented. All pulse oximeter readings preceded arterial blood sampling to reduce patient irritability, resistance, and motion artifacts in measuring saturation that may alter results. The subject's participation in the study lasted from completion of the informed consent form up to the release of arterial blood gas results.

This study was approved by the hospital Research Ethics Board. The investigators reported no conflicts of interest.

Definition of terms

Hypoxemia was determined by using the partial pressure of oxygen in arterial blood (PaO_2) determined by blood gas analysis, and is defined as a PaO_2 less than 80 mm Hg in patients breathing room air (FiO_2 0.21). In patients on oxygen supplementation, the minimally predicted PaO_2 for that level of inspired oxygen computed by Shapiro et al. was used. A measured value that was less than the predicted value presumes that the patient will be hypoxemic breathing room air. [15]

Non-hypoxemic is defined as a PaO_2 of 80 mm Hg or higher in patients breathing room air (FiO_2 0.21), or a PaO_2 that is equal to or greater than the computed predicted value for patients on oxygen supplementation.

Statistical Analysis

Descriptive statistics were used to summarize the general and clinical characteristics of the participants. Frequency and proportion were used for nominal variables, median and range for ordinal variables, and mean and standard deviation for interval/ratio variables.

Independent sample t-test, Mann-Whitney U test and Fisher's Exact/Chi-square test were used

to determine the difference of mean, median and frequency between groups, respectively.

A Bland Altman analysis was performed to see limits of agreement and the mean difference between the portable fingertip and handheld pulse oximetry saturation (SpO_2) and arterial blood oxygen saturation (SaO_2).

Odds ratio and the corresponding 95% confidence interval from binary logistic regression were computed to determine the significant predictor of hypoxemia.

All valid data were included in the analysis. Missing variables were neither replaced nor estimated. Null hypothesis was rejected at 0.05α-level of significance. STATA 15.0 was used for data analysis.

RESULTS

During the course of the study, 86 children were included, 55 (63.9%) of whom were classified as hypoxemic while the rest were non-hypoxemic. Table 1 shows that the socio-demographic and clinical data of both groups were comparable except for the following findings: more children in the hypoxemic group presented with tachypnea, difficulty of breathing and subcostal retractions; most of them also stayed in the ER for 24 hours or less (58.7% admitted to general wards, 41.3% discharged from the PER).

Table 1. Socio-demographic and clinical data of children with PCAP ages 3 months to 5 years (n = 86)

	Hypoxemic children (n = 55)	**Non-hypoxemic children (n = 31)**	**P-value**
	Frequency (%); Median (Range)		
Age	1 (0.25 – 4)	1 (0.25 – 3.83)	0.907*
Age distribution			0.897†
<1 year	24 (43.64)	13 (41.94)	
1 – 3 years	26 (47.27)	14 (45.16)	
>3 years	5 (9.09)	4 (12.90)	
Sex			0.423‡
Male	35 (63.64)	17 (54.84)	
Female	20 (36.36)	14 (45.16)	
Temperature on admission			0.341‡
< 37.8°C	11 (20)	9 (29.03)	
≥ 37.8°C	44 (80)	22 (70.97)	
Cough			1.000†
None	7 (12.73)	3 (9.68)	
Present	48 (87.27)	28 (90.32)	
Tachypnea			**0.034‡**
None	19 (34.55)	18 (58.06)	
Present	36 (65.45)	13 (41.94)	
Alar flaring	32 (58.18)	15 (48.39)	0.381‡
Head bobbing	12 (21.82)	6 (19.35)	0.787‡
Stridor	1 (1.82)	3 (9.68)	0.131†
Grunting	3 (5.45)	2 (6.45)	1.000†

	Hypoxemic children (n = 55)	Non-hypoxemic children (n = 31)	P-value
	Frequency (%); Median (Range)		
Cyanosis	13 (23.64)	4 (12.90)	0.230‡
Apnea	1 (1.82)	1 (3.23)	1.000†
Difficulty in breathing	50 (90.9)	19 (61.29)	**0.001**‡
Difficulty in swallowing	4 (7.27)	2 (6.45)	1.000†
Ear complaints	4 (7.27)	4 (12.90)	0.451†
Eye complaints	7 (12.73)	3 (9.68)	1.000†
Vomiting	20 (36.36)	14 (45.16)	0.423‡
Diarrhea	8 (14.55)	8 (25.81)	0.198‡
Seizure	5 (9.09)	6 (19.35)	0.193†
Retractions			
Subcostal	45 (81.82)	19 (61.29)	**0.036**‡
Intercostal	3 (5.45)	1 (3.23)	1.000†
Suprasternal	3 (5.45)	2 (6.45)	1.000†
Supraclavicular	3 (5.45)	1 (3.23)	1.000†
Breath sounds			0.533‡
Normal	11 (20)	8 (25.81)	
Abnormal	44 (80)	23 (74.19)	
WBC count			0.499‡
$\leq 12 \times 10^9$ / L	14 (25.45)	10 (32.26)	
$> 12 \times 10^9$ / L	41 (74.55)	21 (67.74)	
Outcome			0.683†
Discharged from PER	25 (45.45)	17 (54.84)	
Admitted to ward	29 (52.73)	14 (45.16)	
Admitted to ICU	1 (1.82)	0	
Length of ER stay			**0.012**‡
$\leq$ 24 hours	35 (63.64)	11 (35.48)	
> 24 hours	20 (36.36)	20 (64.52)	

Table 2 shows oxygen supplementation of children included in the study: 1) no oxygen supplementation, 2) low flow oxygen delivery, via either nasal cannula or oxygen face mask, and 3) endotracheal intubation.

In this study, 91% of hypoxemic children received oxygen therapy delivered via various methods (nasal cannula, face mask or intubation), while 9% of hypoxemic children were not given oxygen supplementation. In contrast, 48.4% of non-hypoxemic children were managed with oxygen therapy, while the remaining did not receive oxygen.

In the hypoxemic group that received oxygen therapy, 67.27% received low flow oxygen delivery either via nasal cannula or facemask, and 23.63% had assisted ventilation via endotracheal intubation. In the non-hypoxemic group, 51.61%

received no oxygen supplementation, the 48.4% that received oxygen therapy, 41.93% received low flow oxygen delivery, while 6.45% were intubated.

The hypoxemic group required oxygen supplementation, greater FiO_2 concentrations, and needed endotracheal intubation and mechanical ventilation, compared to their non-hypoxemic counterpart.

Table 2. Oxygen supplementation of children with PCAP ages 3 months to 5 years (n = 86)

	Hypoxemic children (n = 55)	**Non-hypoxemic children (n = 31)**	**P-value**
	Frequency (%); Median (Range)		
No oxygen supplementation (n = 21)	5 (9.09)	16 (51.61)	**<0.001**‡
Oxygen supplementation (n = 65)	50 (90.9)	15 (48.39)	
Low flow oxygen delivery (n = 50)	n = 37 (67.27)	n = 13 (41.93)	**0.033**‡
Route			
Nasal cannula	13 (35.14)	9 (6.23)	
Face mask	24 (64.86)	4 (30.77)	
FiO_2 (liters per minute)	6.27 ± 3.56	3.24 ± 1.96	**0.006**§
FiO_2 (%)	44.65 ± 14.31	31.69 ± 5.99	**0.003**§
Endotracheal intubation (n = 15)	n = 13 (23.63)	n = 2 (6.45)	
Route			
Mechanical ventilation	11 (20)	0	**0.006**†
Bag-valve ventilation	2 (3.64)	2 (6.45)	0.617†
FiO_2 (liters per minute) (bag-valve ventilation)	10	10	-
FiO_2 (%) (bag-valve ventilation)	80	80	-
FiO_2 (%) (mechanical ventilation)	83.64 ± 22.92	-	-

The agreement between the three different methods of measuring oxygen saturation was assessed (Table 3, Figures 1-3). On the average, SpO_2^{PF} underestimated oxygen levels by 0.126% (95% CI -0.240 to 0.491), while SpO_2^{H} underestimated it by 0.323% (95% CI -0.075 to 0.721). Between portable and handheld readings, the mean difference was at 0.198% (95% CI -0.089 to 0.484). The limits of agreement indicate how closely the estimation agrees with the actual oxygen saturation. Across the three methods, limits of agreement ranged from -3.388 to +4.035%. However, these limits of agreement are applicable only for approximate oxygen saturations of 93% to 99%. The variances of the estimates from the three methods were analyzed. In all three cases, p-values were >0.05 which means there was no statistically significant difference in variance among measurements.

Table 3. Comparison of Bland-Altman statistic portable fingertip and handheld pulse oximetry saturation (SpO_2) and arterial blood oxygen saturation (SaO2) of children with PCAP ages 3 months to 5 years (n = 86)

	Mean difference	Limits of Agreement	Range	Pitman's Test of difference in variance (r)	P-Value
SaO_2 and Portable fingertip (SpO_2^{PF})	0.126 (-0.240 to 0.491)	-3.282 to 3.533	93.20 to 99.85	0.150	0.168
SaO_2 and Handheld (SpO_2^{H})	0.323 (-0.075 to 0.721)	-3.388 to 4.035	93.20 to 99.65	0.008	0.943
Portable fingertip ($SpO2^{PF}$) and Handheld ($SpO2^{H}$)	0.198 (-0.089 to 0.484)	-2.474 to 2.869	93.00 to 99.50	-0.166	0.126

Figure 1. Bland-Altman plot depicting agreement between portable fingertip (SpO_2^{PF}) and SaO_2

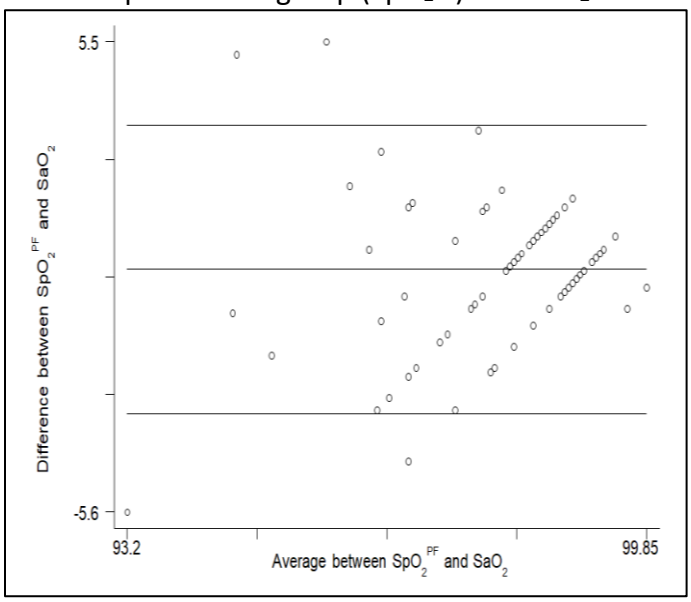

Figure 2. Bland-Altman plot depicting agreement between handheld pulse oximetry oxygen saturation (SpO_2^{H}) and SaO_2

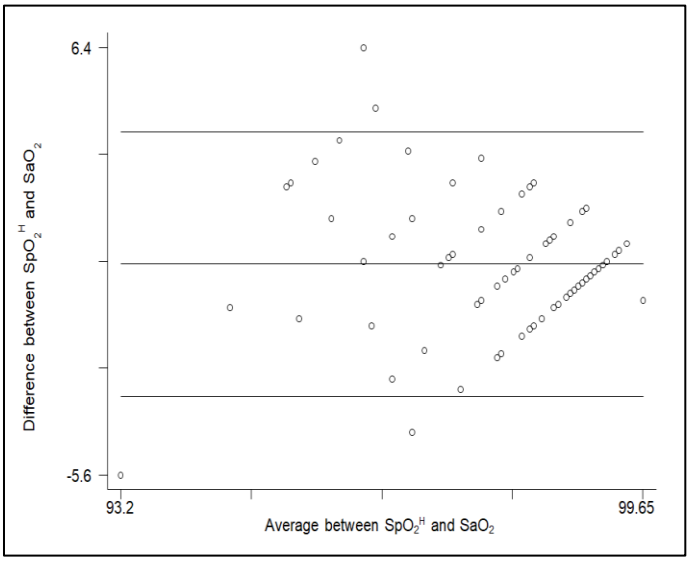

Figure 3. Bland-Altman plot depicting agreement between portable fingertip (SpO_2^{PF}) and handheld pulse oximetry oxygen saturation (SpO_2^{H})

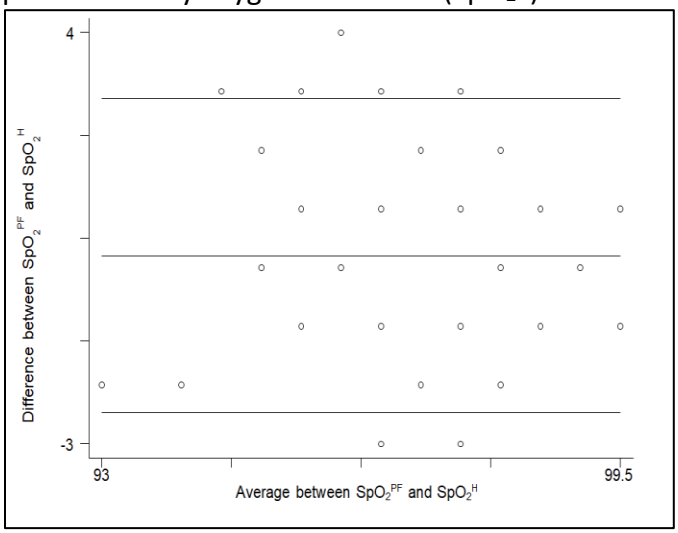

Table 4 shows the factors associated with hypoxemia. Children with tachypnea were 2.6 times more likely to have hypoxemia compared to those with normal respiratory rates (cOR 2.623, 95% CI 1.06 – 6.48, p = 0.037). Children perceived to have difficulty in breathing were 6.3 times more likely to have hypoxemia compared to those without difficulty breathing (cOR 6.316, 95% CI 1.96 – 20.34, p = 0.002). Children who present with subcostal retractions were 2.8 times more likely to have hypoxemia compared to those without (cOR 2.842, 95% CI 1.05 to 7.69, p = 0.040).

Table 4. Factors associated with hypoxemia among children with PCAP ages 3 months to 5 years (n = 86)

	Hypoxemic children (n = 55)	Non-hypoxemic children (n = 31)	Odds Ratio (95% CI)	P-value
	Frequency (%); Mean ± SD; Median (Range)			
Age (years)	1 (0.25 – 4)	1 (0.25 – 3.83)	1.091 (0.70 – 1.70)	0.700
Sex				
Male	35 (63.64)	17 (54.84)	(reference)	-
Female	20 (36.36)	14 (45.16)	0.694 (0.28 – 1.70)	0.424
Fever				
Absent	11 (20)	9 (29.03)	(reference)	-
Present	66 (76.74)	22 (70.97)	1.636 (0.59 – 4.53)	0.343
Cough				
None	7 (12.73)	3 (9.68)	(reference)	-
Present	48 (87.27)	28 (90.32)	0.735 (0.18 – 3.07)	0.673
Tachypnea				
None	19 (34.55)	18 (58.06)	(reference)	-
Present	36 (65.45)	13 (41.94)	**2.623 (1.06 – 6.48)**	**0.037**
Alar flaring	32 (58.18)	15 (48.39)	1.484 (0.61 – 3.60)	0.382
Head bobbing	12 (21.82)	6 (19.35)	1.163 (0.39 – 3.48)	0.788
Stridor	1 (1.82)	3 (9.68)	0.172 (0.02 – 1.74)	0.136
Grunting	3 (5.45)	2 (6.45)	0.837 (0.13 – 5.30)	0.850
Cyanosis	13 (23.64)	4 (12.90)	2.089 (0.62 – 7.08)	0.237
Apnea	1 (1.82)	1 (3.23)	0.556 (0.03 – 9.20)	0.682

Difficulty in breathing	50 (61.29)	19 (61.29)	**6.316 (1.96 – 20.34)**	**0.002**
Difficulty in swallowing	4 (7.27)	2 (6.45)	1.137 (0.20 – 6.59)	0.886
Ear complaints	4 (7.27)	4 (12.90)	0.529 (0.12 – 2.28)	0.394
Eye complaints	7 (12.73)	3 (9.68)	1.361 (0.33 – 5.69)	0.673
Vomiting	20 (36.36)	14 (45.16)	0.694 (0.28 – 1.70)	0.424
Diarrhea	8 (14.55)	8 (25.81)	0.489 (0.16 – 1.47)	0.203
Seizure	5 (9.09)	6 (19.35)	0.417 (0.12 – 1.50)	0.180
Retractions				
Subcostal	45 (81.82)	19 (61.29)	**2.842 (1.05 – 7.69)**	**0.040**
Intercostal	3 (5.45)	1 (3.23)	1.731 (0.17 – 17.39)	0.641
Suprasternal	3 (5.45)	2 (6.45)	0.837 (0.13 – 5.30)	0.850
Supraclavicular	3 (5.45)	1 (3.23)	1.731 (0.17 – 17.39)	0.641
Breath sounds				
Normal	11 (20)	8 (25.81)	(reference)	-
Abnormal	44 (80)	23 (74.19)	1.391 (0.49 – 3.94)	0.534
WBC count				
$\leq 12 \times 10^9$ / L	14 (25.45)	10 (32.26)	(reference)	-
$> 12 \times 10^9$ / L	41 (74.55)	21 (67.74)	1.395 (0.53 – 3.67)	0.500

Final analysis (Table 4.1) shows difficulty of breathing as a final predictor, where children presenting with difficulty of breathing are 6.3 times more likely to be hypoxemic (95% CI 1.96 – 20.34, p value 0.002). This model explains 9.45% in the variation of hypoxemia, and was statistically significant at $p < 0.0001$.

Table 4.1 Final prediction model of hypoxemia among of children with PCAP ages 3 months to 5 years (n = 86)

	Adjusted Odds Ratio	**95% Confidence Interval**	**p – value**
Difficulty in breathing	6.316	1.96 – 20.34	0.002

R2 = 9.45%, p-value = <0.0001

DISCUSSION

This study in children ages 3 months to 5 years old with community-acquired pneumonia of different severity demonstrated that 63.9% of children presented with hypoxemia, who required oxygen supplementation, greater FiO_2 concentrations, and needed assisted ventilation, compared to non-hypoxemic children. Difficulty breathing, tachypnea and subcostal retractions were significantly more likely to be observed in hypoxemic children. Comparing oxygen saturation values measured using pulse oximetry and arterial blood gas analysis showed no significant differences among measurements.

The prevalence of hypoxemia obtained in this study was higher compared to that reported in the systematic review by Subhi et al. in 2009 of a range of 9.4 to 13.3% measured by pulse oximetry.[16] A more recent cross-sectional study by Alwadhi et al. in 2017 reported a prevalence of 50.9% by pulse oximetry in children 2 months to 5 years old with severe pneumonia/very severe disease by WHO definition.[17] Wide variations in reported prevalence

of hypoxemia in children with pneumonia may be due to differences in characteristics of study populations, severity of pneumonia, cut-off values and definitions of hypoxemia, methods of measurement of hypoxemia, presence of comorbid conditions, and geographic region and altitude of study setting. [16,18]

Numerous studies have recognized the need to identify predictors of hypoxemia in resource-limited settings, each with varying results. This present study identified difficulty breathing, tachypnea, and subcostal retractions as significantly more likely to be observed in those with hypoxemia. These findings are consistent with previous studies conducted on predictors of hypoxemia.[18,19,20,21,22] Final prediction model in this study showed difficulty in breathing as a final predictor of hypoxemia.

Lower chest wall indrawing or subcostal retraction was found to be correlated to mortality in a multi-hospital, retrospective cohort study by Agweyu et al. involving over 16,000 children 2 months to 5 years old with pneumonia.[23] This clinical sign has been studied with great interest recently since the WHO revised the classification of pneumonia in 2013, downgrading lower chest wall indrawing from a vital physical sign previously used to identify severe pneumonia warranting referral to a facility and injectable antibiotics, to a sign of non-severe pneumonia which warrants oral antibiotic therapy and home care.[24,25,26] Moore et al. implemented the revised WHO recommendations at a developing country capital's general hospital and assessed the feasibility of outpatient management of 120 children 1 month to 12 years old with pneumonia with chest indrawing.[27] Their study concluded that there was a 95% treatment success rate with outpatient management, with no adverse events and no mortalities. However, the study emphasized that several safeguards were in place to identify high-risk children – those with severe malnutrition, HIV infection, danger signs, or hypoxemia by pulse oximetry. In this study and similar to other studies, chest indrawing was identified as a predictor of hypoxemia, and may remain to be a strong indicator for hospital admission, despite the wide variability in its sensitivity and specificity to detect hypoxemia. [28]

Oxygen therapy is essential for the management of hypoxemia in children with pneumonia, yet different guidelines have varying recommendations and cut-off values for providing oxygen supplementation.[1,10,29] The WHO listed several conditions that must be satisfied for hypoxemic children to receive oxygen supplementation: 1) the child must be recognized as hypoxemic by a trained health care provider on the basis of clinical signs or with a pulse oximeter; and 2) the hypoxemic child must receive adequate, uninterrupted oxygen therapy for an adequate duration.[9] In this study, half of non-hypoxemic children were given oxygen therapy, implying a need for reevaluation of practices of emergency room pediatricians on judicious use of oxygen in children with pneumonia, and the benefit of pulse oximetry at the frontline of patient assessment. Unnecessary oxygen entails additional cost and may cause oxygen toxicity leading to acute lung injury due to hyperoxia, which presents with signs and symptoms similar to pneumonia causing undue confusion in the recognition of these features as either pneumonia progression or manifestations of oxygen toxicity.[30] Previous studies reported two infants given supplementary oxygen to have pneumocephalus as severe adverse event to oxygen therapy. [28] A model was proposed by Wu et al. on titration of oxygen flow rates in children receiving oxygen therapy for pneumonia as a method to prevent oxygen toxicity and for oxygen conservation in resource-limited settings.[31] This model involves fixed schedules of titration which translated to oxygen savings of 8% to 12%; however, oxygen titration in children with pneumonia cannot be restricted to a standardized protocol but must be guided by improvement or deterioration of clinical signs and symptoms supported by objective

measurement of oxygenation status. Further, the significant potential risk of non-hypoxemic children to develop hypoxemia during the course of hospital admission must be recognized, and continued observation and monitoring cannot be overemphasized. The computation for hypoxemia in this study was not done real-time; instead, it was evaluated during data analysis. The attending pediatrician was not aware of the fact that a non-hypoxemic patient was on oxygen therapy or vice-versa, as this study did not involve standard medical care administered to the patients. The ABG results were at the disposal of the attending pediatricians to guide them on their medical management.

This study compared oxygen saturation values measured using pulse oximetry and arterial blood gas analysis. Both portable fingertip and handheld pulse oximeters underestimated arterial blood gas oxygenation, although only by 0.136% - 0.323%. No significant statistical differences were noted among measurements indicating that any method of measuring oxygen saturation is acceptable, and either portable fingertip or handheld pulse oximetry closely correlates with the gold standard.

Limits of agreement estimate the interval within which a proportion of the differences between measurements lie. Acceptable limits must be defined or postulated based on clinical necessity, biological considerations, or according to the objective of the study.[32] The limits of agreement of all three methods of measurement were computed to range from -3.388 to 4.035%, with the widest range observed between SaO_2 and SpO_2^H, and the narrowest range seen between SpO_2^{PF} and SpO_2^H. In all three cases, there was no statistically significant difference in variance among measurements. However, since the subjects recruited in this study demonstrated oxygen saturations of 93% and above, these results are applicable only for approximate oxygen saturations of 93-99% as reported in this study, and generalizability is limited to this range of oxygen saturations. This may further be supported by relating these findings to the oxygen-hemoglobin dissociation curve, which demonstrates a steep drop in PaO_2 as the oximeter reading falls below 90%.[33] Furthermore, this generalization is only limited to the particular models of pulse oximeters used in this study; varying results may be generated using different models.

Arterial blood gas still remains to be the gold standard in determination of oxygen saturation, and it has the added advantage of determining acidosis and hypercapnia which are clinically significant parameters in the management of children with pneumonia. However, for the purpose of detecting oxygen saturation, pulse oximetry is an acceptable alternative especially in low-resource settings.

CONCLUSIONS AND RECOMMENDATIONS

Pulse oximetry, either using portable fingertip pulse oximeter or handheld pulse oximeter, closely correlates with arterial blood gas analysis within acceptable limits of agreement and with no significant differences in variance among measurements. Difficulty breathing, tachypnea and subcostal retractions were significantly more likely to be observed in hypoxemic children.

Further studies can be done using a larger sample population to increase the power of the study or a wider age range involving the neonatal and the older pediatric population. Because clinical features may be observer-dependent, standardized evaluation may be used to ensure uniformity in assessment of clinical findings. Further studies can also be done to evaluate the effect of pulse oximetry measurement on the management and outcomes of children with pneumonia. Likewise, investigating the use of pulse oximetry in patients stratified according to pneumonia severity may be done to further evaluate the utility of pulse oximetry across the spectrum of symptom severity.

The applicability of this study is limited to the pulse oximeter models used, and other pulse

oximeter models available in different settings may be evaluated by adapting a similar protocol.

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