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Multicenter study of hypoxemia prevalence and quality of oxygen treatment for hospitalized Malawian children

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Abstract

Background—Although hypoxemic children have high mortality, little is known about hypoxemia prevalence and oxygen administration in African hospitals. We aimed to determine the hypoxemia prevalence and quality of oxygen treatment by local clinicians for hospitalized Malawian children.

Methods—The study was conducted in five Malawian hospitals during January–April 2011. We prospectively measured the peripheral oxygen saturation (SpO_2) using pulse oximetry for all children <15 years old and also determined clinical eligibility for oxygen treatment using WHO criteria for children <5 years old. We determined oxygen treatment quality by Malawian clinicians by comparing their use of WHO criteria for patients <5 years old using two standards: hypoxemia (SpO_2 <90%) and the use of WHO criteria by study staff.

Results—Forty of 761 (5.3%) hospitalized children <15 years old had SpO_2 <90%. No hospital used pulse oximetry routinely, and only 9 of 40 (22.5%) patients <15 years old with SpO_2 <90% were treated with oxygen by hospital staff. Study personnel using WHO criteria for children <5 years old achieved a higher sensitivity (40.0%) and lower specificity (82.7%) than Malawian clinicians (sensitivity 25.7%, specificity 94.1%).

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Ethical approval: This study was approved by the National Health Sciences Research Committee in Malawi and the University of North Carolina-Chapel Hill School of Medicine Institutional Review Board (USA).

Conclusion—Although hypoxemia is common, the absence of routine pulse oximetry results in most hospitalized, hypoxemic Malawian children not receiving available oxygen treatment.

Keywords

Pneumonia; Pediatrics; Hypoxemia; Pulse oximetry; Integrated Management of Childhood Illness; Africa

Introduction

Despite recent efforts, global mortality rates for children continue to be high, especially in developing countries.[1] Hypoxemia is a common complication of treatable, fatal childhood illnesses,[2] and the treatment of hypoxemia with oxygen is a priority of WHO Integrated Management of Childhood Illness (IMCI) and Emergency Triage Assessment and Treatment (ETAT) guidelines.[3,4] Pulse oximetry and oxygen concentrators are critical to the accurate detection and effective treatment of hypoxemia, but are not yet widely available.[5–8] As a result, IMCI and ETAT guidelines instead use clinical signs associated with an increased risk of hypoxemia to prioritize oxygen treatment for those children most likely to be hypoxemic.[3,4]

In Malawi, a HIV-endemic southern African country, HIV infection is common in hospitalized Malawian children and severe respiratory illness is a major cause of death in those infected with HIV, irrespective of age.[9,10] Although Malawian pediatric wards care for children up to the age of 15 years, the prevalence of hypoxemia in these children is not known. Since WHO clinical criteria, rather than pulse oximetry, guide oxygen treatment decisions and these apply to children <5 years old only, we hypothesized that many hypoxemic Malawian children are not correctly receiving oxygen treatment despite oxygen concentrator availability. Thus, the aims of this study were to determine the prevalence of hypoxemia in Malawian pediatric hospital wards regardless of age, to assess the existing hospital resources available for hypoxemia detection and oxygen provision, and to ascertain the quality of oxygen treatment by Malawian healthcare providers when using the current clinical criteria for children <5 years old during routine program conditions.

Materials and methods

Study setting

This study included five hospitals from the central region of Malawi, four randomly selected district hospitals and one referral hospital, serving an estimated population of 1 500 000 children <15 years old.[11] The hospitals represent urban (Lilongwe), rural coastal (Salima), rural mountainous (Dedza) and rural inland (Ntchisi and Mchinji) catchment areas.

Study design

We conducted a prospective, multicenter observational study of 761 consecutive pediatric ward admissions. We included all hospitalized children aged 0–15 years assessed <18 h after admission. To best approximate the maximum clinically determined oxygen requirements, we conducted the study during the rainy season, January–April 2011, because

hospitalizations are highest due to hyperendemic malaria and children with malaria are often clinically indistinguishable from those with pneumonia.[12–14]

At admission, clinical and nursing staff at each hospital recorded the patient history, one primary diagnosis and any number of secondary admission diagnoses using IMCI guidelines, and prescribed treatment, including oxygen, for each patient according to current recommendations.[3,4] Since we aimed to assess oxygen treatment during routine program conditions, we did not train any of the hospital staff. However, study personnel included a pediatrician and general clinician who were clinically standardized prior to the study. Diagnostic criteria for pneumonia classifications and clinical oxygen eligibility criteria are outlined in Box 1.[3]

Box 1

WHO diagnostic classifications for pneumonia[3]

WHO pneumonia classification

Non-severe

- Cough or difficulty breathing
- Fast breathing for age
- No signs or symptoms of severe or very severe pneumonia

Severe

- Cough or difficulty breathing
- Lower chest wall indrawing
- No signs or symptoms of very severe pneumonia

Very severe

- Cough or difficulty breathing
- One of the following signs or symptoms:
  1. Central cyanosis
  2. Inability to breastfeed or drink
  3. Vomiting all oral intake
  4. Presence or history of convulsions during this illness
  5. Severe respiratory distress
  6. Grunting

WHO clinical oxygen eligibility criteria

Age <5 years with any one of the following signs:

- Central cyanosis
- Inability to breastfeed or drink
- Severe lower chest wall indrawing
- Respiratory rate ≥70 breaths per min
- Grunting in infants <2 months old
- Head nodding
- Very severe pneumonia classification

After the hospital staff completed their assessment, study staff then used a Rad-57 Pulse Oximeter (Masimo Corp., Irvine, CA, USA) to record peripheral oxygen saturation (SpO_2) measurements. SpO_2 values were documented after a quality signal was obtained while the child breathed room air. Patients were defined as hypoxemic if their SpO_2 was <90%.[3] Study staff also measured axillary temperature, respiratory and heart rate, weight and height, mid-upper arm circumference, Blantyre coma scale, and made observations with respect to skin turgor, severe lower chest wall indrawing, grunting, nasal flaring, cyanosis, head nodding and lethargy. HIV testing of patients was according to each hospital's procedures and Malawi national guidelines.[15] Study staff initiated oxygen therapy for hypoxemic patients if the hospital staff did not.

Individual written consent was not required since the study was within routine operations and involved no risk for patients.

Statistical analysis

Normally distributed variables were reported as mean ± SD, and comparisons between two groups were made with Student's *t*-tests. Non-parametric variables were given as median with IQR, and comparisons were made with Mann–Whitney *U* tests. Two groups of categorical variables were compared using either Pearson's χ^2 tests or Fisher's exact tests. As there was no existing hypoxemia prevalence for Malawian children, health facility pneumonia rates (9.9%) were used as a proxy to determine the sample size of 152 patients per hospital.[11] All statistical analyses were performed using SPSS 17.0 (SPSS Inc., Chicago, IL, USA).

Results

Study staff prospectively enrolled a total of 761 consecutive admissions to the pediatric wards of five hospitals. The majority of patients were male (436; 57.3%), with a median age of approximately 26 months (Table 1). Children <5 years old comprised 80.4% (612) of patients. The two most common primary and secondary admission diagnoses were malaria and severe anemia. Respiratory illnesses, including all classifications of pneumonia, comprised 23.7% (180/761) of primary or secondary hospital diagnoses, while 13.0% (99/761) of patients met anthropomorphic criteria for moderate to severe malnutrition that was clinically determined at admission. Eighty-seven (11.4%) children were tested for HIV and 18 (20.7%) were HIV positive.

The overall prevalence of hypoxemic children at hospital admission was 5.3% (40/761) (Table 1). Children aged <5 and 5–15 years had a hypoxemia prevalence of 5.7% (35/612) and 3.4% (5/149), respectively, and of the five hospitals, Mchinji reported the highest prevalence (13/153; 8.5%). We found that the prevalence of hypoxemia, as measured by pulse oximetry, differed greatly from the proportion of children aged <5 years clinically eligible for oxygen. Specifically, WHO clinical criteria identified three times more children <5 years old as eligible for oxygen treatment (114/612; 18.6%) than pulse oximetry (35/612; 5.7%).

This study also assessed the oxygen delivery capacity at each facility relative to the measured hypoxemia prevalence and clinical oxygen eligibility. We found that all of the pediatric wards had at least one functioning oxygen concentrator with a power cord, flow splitter device, available nasal prongs, and a minimum of one IMCI-trained or ETAT-trained healthcare provider. Only Ntchisi hospital lacked a backup power source. All of the hospitals had the capacity to deliver oxygen to at least three patients simultaneously, while Lilongwe could administer oxygen to a total of 13 children at any one time. We attempted to determine whether each facility's oxygen capacity was sufficient by multiplying the average number of daily hospitalizations per facility by either its hypoxemia prevalence or clinical oxygen eligibility prevalence. Next we compared both calculations with the total number of patients each hospital could provide oxygen to concurrently. We found that all of the hospitals had sufficient oxygen capacity to meet needs when SpO_2 <90% alone was considered (0.4 [Dedza and Salima] to 2.3 [Ntchisi] admissions/day). On the other hand, only two of the five sites (Lilongwe [9.3 clinically eligible admissions/day] and Dedza [0.8 clinically eligible admissions/day]) also had the capacity to meet oxygen needs when clinical criteria were used to determine oxygen eligibility.

While all of the pediatric wards had oxygen concentrators, three departments had operational pulse oximeters prior to the study period (Lilongwe, Dedza and Salima), and none of those departments routinely screened children for hypoxemia at admission. Only local clinicians at the Lilongwe site performed pulse oximetry at admission, checking the SpO_2 in 20 of 152 (13.2%) new patients they identified as clinically suspicious for hypoxemia. Although study personnel found a total of 114 children to be clinically eligible for oxygen, only 25 (21.9%) were managed with oxygen by hospital staff. The majority of these 25 children needed oxygen only transiently and did not occupy all oxygen sources (data not shown), suggesting that a lack of oxygen availability did not account for this finding. Additionally, of all patients found by study personnel to be hypoxemic with a pulse oximetry reading of SpO_2 <90%, 9 of 40 (22.5%) were prescribed oxygen by the hospital staff.

To study the role of hypoxemia in the presentation of patients to hospital we assessed the relationship of hypoxemia to admission diagnoses and to individual patient characteristics. We found that patients classified with a primary respiratory diagnosis had a lower median SpO_2 than those with a non-respiratory condition (96.5% vs 99.0%; $p < 0.001$; Table 2). Very severe pneumonia represented the lowest (93.0%) and both malaria and severe anemia revealed the highest (99.0%) median SpO_2. Although the proportion of severely anemic children with SpO_2 <90% was low (1/31; 3.2%), non-hypoxemic patients with severe anemia may still benefit from oxygen supplementation since treatment increases oxygen carrying capacity. Seventeen percent of patients (27/159) hospitalized with a primary respiratory diagnosis were found to be hypoxemic; children with a non-respiratory primary diagnosis were seven times less likely to be hypoxemic (13/602; 2.2%; $p < 0.001$). No hypoxemic child with a non-respiratory diagnosis received a secondary respiratory diagnosis to account for their hypoxemia. Additionally, more patients with a respiratory illness were clinically eligible for oxygen, compared with those with non-respiratory diagnoses (43/145 [29.7%] vs 71/467 [15.2%]; $p < 0.001$). Forty-one of 761 (5.4%) children died in the hospital with 8 (19.5%) identified as hypoxemic at initial presentation by the study team.

Compared with normoxic children, patients with SpO_2 <90% were younger, and a greater proportion presented with cough, difficulty breathing, tachypnea for age, severe lower chest wall indrawing, nasal flaring, lethargy and malnutrition determined by mid-upper arm circumference measurement (Table 3). No study patient, irrespective of SpO_2 measurement, was found to be cyanotic. Together these results highlight the importance of hypoxemia in children hospitalized with respiratory illnesses.

Lastly, this study sought to determine the quality of oxygen treatment by comparing Malawian providers' use of the WHO clinical criteria and the study staff's use of the same criteria for children <5 years old. Both groups were judged against the gold standard of hypoxemia defined by a pulse oximetry reading SpO_2 <90%. We found that the WHO clinical criteria applied by the study staff had a higher sensitivity (40.0%) and lower specificity (82.7%) in determining which children had a SpO_2 <90% compared with the same criteria used by Malawian clinicians (sensitivity 25.7%, specificity 94.1%) (Table 4).

Discussion

This multicenter prospective study demonstrated that hypoxemia is often present in hospitalized children in a HIV-endemic country, with a higher prevalence found in children with respiratory compared with non-respiratory illnesses. Furthermore, sufficient oxygen capacity exists to treat hospitalized, hypoxemic Malawian children, but both poor provider adherence to WHO clinical criteria and limited pulse oximetry use results in oxygen not getting to those who need it the most.

Our study from southern Africa reports a hypoxemia prevalence similar to reports from West Africa (The Gambia, 5.8%)[16] and East Africa (Kenya, 6.4%),[17] but lower than Asia (Papua New Guinea, 52.0%).[18] It is difficult to draw direct comparisons, however, due to differences of study design, location and duration. Specifically, the previous studies were completed at single facilities, either a referral or district hospital, in contrast to the one referral and four district hospitals from which we are reporting. The Gambia, Kenya and Papua New Guinea cohorts included higher proportions of patients with neonatal disease or a severe respiratory illness, and the Papua New Guinea study altitude (1600 m asl) was also higher than any of the sites we sampled. Notably, age, respiratory illness and altitude are all associated with higher rates of hypoxemia.[16,19]

Although we found hypoxemia to be commonly present in hospitalized children, we also found the quality of hypoxemia detection and oxygen treatment to be severely lacking. Malawian healthcare providers had poor adherence to the WHO clinical criteria for prescribing oxygen and this was likely due to a combination of factors including lack of ongoing training with WHO clinical oxygen eligibility criteria, prioritization of other treatments like antibiotics, inadequate supervision and insufficient staffing. Additional study is needed to further understand this quality of care gap. Nonetheless, 78.1% (89/114) of children clinically eligible for oxygen were not administered oxygen. While routine use of pulse oximetry is not the standard of care in Malawi, the current standards resulted in 77.5% (31/40) of hypoxemic patients determined by pulse oximetry not receiving oxygen. This finding raises concerns given the strong evidence from developing countries showing that

hypoxemia is associated with an increased risk of death in hospitalized children,[16,20,21] and that oxygen treatment in hypoxemic children with pneumonia reduces mortality.[6]

Even if we had found high provider adherence to the WHO clinical criteria, our results highlight the limitations of using these criteria instead of pulse oximetry. Clinical predictor models for hypoxemia in children with pneumonia can achieve sensitivities >95%, but only by combining multiple clinical signs and thereby lowering the specificity.[22,23] Low specificities can result in the incorrect use of limited oxygen resources such that children without hypoxemia inappropriately receive oxygen at the expense of hypoxemic patients not meeting clinical criteria.

Furthermore, most clinical predictor models use age-specific ranges with different clinical variables, including heart rate and respiratory rate, in order to maximize sensitivity and specificity. This can create more complicated criteria that may explain low provider adherence. Using age ranges can also leave out important subsets of children. For example, the WHO criteria targets patients <5 years old. However, 19.6% (149/761) of hospitalized children in this study were older than 5 years, with 3.4% (5/149) found to be hypoxemic and not clinically eligible for oxygen simply due to age. Due to these shortcomings, we would expect there to be lower rates of error if providers routinely used pulse oximetry rather than clinical algorithms. Additional operational research is needed to investigate this possibility in both inpatient and outpatient settings, where even earlier identification of hypoxemic patients with pulse oximetry may further improve outcomes.

Compared with pulse oximetry, additional refinement of the clinical criteria for hypoxemia diagnosis is unlikely to provide the most efficient use of oxygen resources. Our results show that oxygen use would not have been feasible if the WHO clinical criteria were accurately applied to this patient cohort as demands would have outstripped existing capacity to deliver oxygen at most facilities. Instead, we recommend the following measures to improve oxygen allocation at admission. First, hospitals should allocate sufficient funds to procure enough pulse oximeters so that routine screening at admission is feasible. Second, providers need additional pre-service and in-service training in oximetry use and maintenance to ensure competent utilization and maximum longevity of the device. Third, adequate ongoing facility supervision and operational research is necessary to assess provider use of oximetry and oxygen concentrators, with corrective guidance provided as necessary.

There are limitations to this study. We may have underestimated the prevalence of hypoxemia for two reasons. First, five patients during the study period died shortly after hospitalization before SpO_2 could be recorded and were therefore excluded from analysis. Second, oximetry measurements were limited to patients hospitalized for <18 h. This exclusion criterion was governed by study resources and our focus on admission-related treatment decisions since the majority of hospital mortality occurs <24 h after admission.[24] To comprehensively collect hypoxemia data and facilitate recruitment of participants, patients were examined up to 18 h after admission by the study staff. Although the study team evaluated nearly all patients immediately after the hospital staff, it is possible that the physical findings of some patients may have changed between evaluations. We also acknowledge the inherent subjectivity of certain physical examination findings.[25] Lower

chest wall indrawing, for example, is a clinical sign that generates low rates of interprovider agreement.[26] This could create the appearance that Malawian providers were more non-adherent to the WHO criteria than they actually were. However, the study staff's application of the WHO criteria generated similar sensitivity and specificity values to other reports,[23] suggesting that the disparity noted in this study is most likely due to the local clinicians' use of the WHO criteria rather than changes in the clinical findings between examinations or the misinterpretation of clinical signs.

Conclusions

While hypoxemia is a common problem found in children hospitalized in Malawi, the absence of routine pulse oximetry use during hospital admission results in the majority of hypoxemic children not receiving available oxygen treatment. By increasing healthcare provider access to pulse oximeters, training for their use, and supervising oxygen delivery, mortality in children due to hypoxemia and respiratory infections may be reduced.

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Table 1

Hypoxemia prevalence and quality of oxygen provision for hospitalized Malawian children by hospital

	Lilongwe (n = 152)	Dedza (n = 153)	Mchinji (n = 153)	Ntchisi (n = 152)	Salima (n = 151)	Total (n = 761)
Characteristic						
Age (months) [median (IQR)]	26.1 (13.1–59.6)	30.0 (14.7–48.1)	24.5 (11.0–48.0)	22.5 (7.8–47.4)	24.3 (14.2–45.3)	25.9 (11.9–48.3)
Female [n/N (%)]	66/152 (43.4)	63/153 (41.2)	70/153 (45.8)	68/152 (44.7)	58/151 (38.4)	325/761 (42.7)
Weight-for-height Z-score[a] [mean ± SD]	−0.69±1.34	−0.47±1.56	−0.50±1.40	0.26±1.45	−0.66±1.43	−0.40±1.48
SpO_2 [median (IQR)]	98.5 (97.0–99.5)	98.0 (96.0–99.5)	98.5 (97.0–99.5)	98.0 (96.0–99.5)	99.0 (98.0–100.0)	98.5 (97.0–99.5)
SpO_2 <90% [n/N (%, 95% CI)]						
All patients	4/152 (2.6, 0.8–6.8)	10/153 (6.5, 3.5–11.8)	13/153 (8.5, 4.9–14.1)	10/152 (6.6, 3.5–11.8)	3/151 (2.0, 0.06–5.0)	40/761 (5.3, 3.9–7.1)
Patients 0–2 months old	0/6 (0.0, 0.0–44.3)	3/11 (27.3, 9.2–57.1)	2/7 (28.6, 7.6–64.8)	2/8 (25.0, 6.3–59.9)	0/2 (0.0, 0.0–71.0)	7/34 (20.6, 10.1–37.1)
Patients 0–5 years old	3/114 (2.6, 0.6–7.8)	8/124 (6.5, 3.1–12.4)	12/123 (9.8, 5.5–16.4)	9/122 (7.4, 3.8–13.6)	3/129 (2.3, 0.5–6.9)	35/612 (5.7, 4.1–7.9)
Patients 5–15 years old	1/38 (2.6, <0.01–14.7)	2/29 (6.9, 0.9–23.0)	1/30 (3.3, <0.01–18.1)	1/30 (3.3, <0.01–18.1)	0/22 (0.0, 0.0–17.6)	5/149 (3.4, 1.2–7.8)
Oxygen eligible per WHO clinical criteria[b] [n/N (%)]	25/114 (21.9)	17/124 (13.7)	21/123 (17.1)	19/122 (15.6)	32/129 (24.8)	114/612 (18.6)
Mortality [n/N (%)]	9/152 (5.9)	12/153 (7.8)	7/153 (4.6)	2/152 (1.3)	11/151 (7.3)	41/761 (5.4)
Indicators for quality of oxygen care [n/N (%)]						
Obtained admission pulse oximetry reading[c]	20/152 (13.2)	0/153	0/153	0/152	0/151	20/761 (2.6)
Correctly prescribed oxygen per WHO clinical criteria[d]	3/25 (12.0)	11/17 (64.7)	3/21 (14.3)	3/19 (15.8)	5/32 (15.6)	25/114 (21.9)
Correctly prescribed oxygen per SpO_2 <90%	2/4 (50.0)	3/10 (30.0)	2/13 (15.4)	1/10 (10.0)	1/3 (33.3)	9/40 (22.5)

SpO_2: peripheral oxygen saturation.

[a] Weight-for-height Z-score could not be calculated for some children due to edema: Lilongwe, 9; Dedza, 20; Mchinji, 4; Ntchisi, 1; Salima, 8.

[b] WHO clinical criteria for children <5 years old includes any of the following: very severe pneumonia, central cyanosis, unable to drink, severe lower chest wall indrawing, respiratory rate ≥70 breaths per min, grunting in infants <2 months old or head nodding.

[c] Mchinji and Ntchisi District Hospitals did not have operational pulse oximeters.

[d] According to study staff.

Table 2

Hypoxemia prevalence and quality of oxygen provision for hospitalized Malawian children by primary hospital diagnosis

	Primary hospital diagnosis												Overall total	p value
	Respiratory					Non-respiratory								
	Pneumonia			Other	Total	Malaria[a]	Sepsis	Severe acute malnutrition	Severe anemia	Gastro-enteritis[b]	Other	Total		
	Non-severe	Severe	Very severe											
No.	13	113	25	8	159	427	29	19	31	29	67	602	761	
Characteristic														
SpO_2 [median (IQR)]	98.0 (97.0–99.0)	96.5 (93.5–98.5)	93.0 (88.0–97.0)	95.5 (94.0–97.0)	96.5 (93.0–98.5)	99.0 (97.5–99.5)	98.5 (97.5–99.0)	98.5 (97.0–100.0)	99.0 (98.0–100.0)	98.5 (98.0–99.5)	99.5 (98.5–100.0)	99.0 (97.5–99.5)	98.5 (97.0–99.5)	<0.001
SpO_2 <90% [n/N (%, 95% CI)]	2/13 (15.4, 3.1–43.5)	17/113 (15.0, 9.5– 22.9)	7/25 (28.0, 14.1–47.8)	1/8 (12.5, 0.1–49.2)	27/159 (17.0, 11.9– 23.6)	8/427 (1.9, 0.9–3.7)	1/29 (3.4, <0.01–18.6)	1/19 (5.3, <0.01–26.5)	1/31 (3.2, <0.01–17.6)	0/29 (0.0, 0.0–13.9)	2/67 (3.0, 0.2–10.9)	13/602 (2.2, 1.2–3.7)	40/761 (5.3, 3.9–7.1)	<0.001
Oxygen eligible per WHO clinical criteria[c] [n/N (%)]	4/12 (33.3)	16/105 (15.2)	23/23 (100.0)	0/5	43/145 (29.7)	50/341 (14.7)	2/25 (8.0)	4/17 (23.5)	7/25 (28.0)	3/25 (12.0)	5/34 (14.7)	71/467 (15.2)	114/612 (18.6)	<0.001
Mortality [n/N (%)]	0/13	2/113 (1.8)	3/25 (12.0)	1/8 (12.5)	6/159 (3.8)	20/427 (4.7)	3/29 (10.3)	5/19 (26.3)	1/31 (3.2)	0/29	6/67 (9.0)	35/602 (5.8)	41/761 (5.4)	NS
Mortality and SpO_2 <90% [n/N (%)]	0/0	1/2 (50.0)	1/3 (33.3)	1/1 (100.0)	3/6 (50.0)	2/20 (10.0)	0/3	1/5 (20.0)	1/1 (100.0)	0/0	1/6 (16.7)	5/35 (14.3)	8/41 (19.5)	NS
Indicators for quality of oxygen care [n/N (%)]														
Obtained admission pulse oximetry reading	0/13	5/113 (4.4)	1/25 (4.0)	1/8 (12.5)	7/159 (4.4)	10/427 (2.3)	2/29 (6.9)	0/19	1/31 (3.2)	0/29	0/67	13/60 (2.2)	20/761 (2.6)	NS
Correctly prescribed oxygen per WHO clinical criteria[d]	0/4	1/16 (6.3)	15/23 (65.2)	0/0	16/43 (37.2)	8/50 (16.0)	0/2	1/4 (25.0)	0/7	0/3	0/5	9/71 (12.7)	25/114 (21.9)	0.002
Correctly prescribed oxygen per SpO_2 <90%	0/2	0/17	7/7 (100.0)	0/1	7/27 (25.9)	2/8 (25.0)	0/1	0/1	0/1	0/0	0/2	2/13 (15.4)	9/40 (22.5)	NS

NS: not significant; SpO_2: peripheral oxygen saturation.

[a] 6 and 8 patients were assigned a secondary diagnosis of pneumonia and severe pneumonia, respectively.

[b] 1 patient was assigned a secondary diagnosis of pneumonia.

[c] WHO clinical criteria for children <5 years old includes any of the following: very severe pneumonia, central cyanosis, unable to drink, severe lower chest wall indrawing, respiratory rate ≥70 breaths per min, grunting in infants <2 months old or head nodding.

[d] According to study staff.

Table 3

Comparison of hypoxemic and non-hypoxemic hospitalized Malawian children

	SpO_2 ≥90% (n = 721)	SpO_2 <90% (n = 40)	p value
Patient characteristic			
Age (months) [median (IQR)]	27.3 (12.6–48.8)	12.2 (4.0–33.6)	<0.001
Female [n (%)]	309 (42.9)	16 (40.0)	NS
Presenting symptoms			
Respiratory [n/N (%)]			
Cough	227/286 (79.4)	27/28 (96.4)	0.024
Difficulty breathing	80/156 (51.3)	14/14 (100.0)	<0.001
Non-respiratory [n/N (%)]			
Fever	573/580 (98.8)	25/25 (100.0)	NS
Vomiting	180/275 (65.5)	2/8 (25.0)	0.026
Diarrhea	96/211 (45.5)	5/8 (62.5)	NS
Convulsions	136/285 (47.7)	5/19 (26.3)	NS
Not drinking	64/204 (31.4)	4/14 (28.6)	NS
Pallor	248/307 (80.8)	8/9 (88.9)	NS
Presenting signs			
Respiratory [n/N (%)]			
Tachypnea for age	400/720 (55.6)	33/40 (82.5)	<0.001
Chest indrawing	200/716 (27.9)	35/40 (87.5)	<0.001
Grunting	1/721 (0.1)	1/40 (2.5)	NS
Nasal flaring	86/721 (11.9)	18/40 (45.0)	<0.001
Head nodding	1/721 (0.1)	1/40 (2.5)	NS
Non-respiratory			
Weight-for-height Z-score [mean ± SD]	−0.41±1.47	−0.29±1.58	NS
Weight-for-height Z-score ≥2 SD below median [n/N (%)]	67/538 (12.5)	7/33 (21.2)	NS
MUAC Z-score [mean ± SD]	−0.94±1.23	−0.92±1.26	NS
MUAC ≥2 SD below median [n/N (%)]	80/535 (15.0)	8/25 (32.0)	0.022
Temperature ≥37.5°C [n/N (%)]	251/720 (34.9)	17/40 (42.5)	NS
Tachycardic for age [n/N (%)]	494/720 (68.6)	25/40 (62.5)	NS
Lethargy [n/N (%)]	326/720 (45.3)	29/40 (72.5)	0.001
Skin pinch ≥2 s [n/N (%)]	6/718 (0.8)	1/40 (2.5)	NS
Blantyre coma scale ≤3 [n/N (%)]	25/707 (3.5)	3/38 (7.9)	NS

MUAC: mid-upper arm circumference; NS: not significant; SpO_2: peripheral oxygen saturation.

Table 4

Performance of WHO clinical oxygen eligibility criteria compared with hypoxemia by pulse oximetry for hospitalized Malawian children <5 years old

Model	No. with SpO_2 <90%	No. with SpO_2 ≥90%	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Model 1 WHO clinical criteria by study staff[a]						
No. with signs	14	100	40.0	82.7	12.3	95.8
No. without signs	21	477				
Model 2 WHO clinical criteria by Malawian clinicians[a]						
No. with signs	9	34	25.7	94.1	20.9	95.4
No. without signs	26	543				

NPV: negative predictive value; PPV: positive predictive value; SpO_2: peripheral oxygen saturation.

[a]WHO model for children <5 years old includes any one of the following clinical criteria: very severe pneumonia, central cyanosis, not drinking or sucking, severe lower chest wall indrawing, respiratory rate ≥70 breaths per min, grunting in infants <2 months old and head nodding.