

RESEARCH ARTICLE

Clinical predictors of radiological pneumonia: A cross-sectional study from a tertiary hospital in Nepal

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Abstract

Background

Despite readily availability of vaccines against both *Hemophilus influenzae* and *Pneumococcus*, pneumonia remains the most common cause of morbidity and mortality in children under the age of five years in Nepal. With growing antibiotic resistance and a general move towards more rational antibiotic use, early identification of clinical signs for the prediction of radiological pneumonia would help practitioners to start the treatment of patients. The main aim of this study was to reassess the clinical predictors of pneumonia in Nepal.

Methods

This cross-sectional study was conducted between June 2015 and November 2015 at Tribhuvan University Teaching Hospital, a tertiary hospital in Kathmandu, Nepal. Children aged 3–60 months with a clinical diagnosis of pneumonia by a physician were enrolled in the study. Radiological pneumonia was identified and categorized as per World Health Organization guidelines by an experienced radiologist blinded to patient characteristics. We calculated sensitivity and specificity of clinical signs and symptoms for radiological pneumonia.

Results

Out of 1021 children with fever, 160 cases were clinically diagnosed as pneumonia and were enrolled for this study. Among the enrolled patients, 61% had radiological pneumonia. Tachypnea had the highest sensitivity of 99%, while bronchial breathing had the highest specificity of 100%. During univariate analysis, grunting, wheezing, nasal discharge, decreased breath sounds, noisy breathing and hypoxemia were associated with radiological pneumonia. Only hypoxemia remained an independent predictor when adjusted for all the factors.

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Conclusion

Tachypnea was the most sensitive sign, whereas bronchial breathing was most specific sign for radiological pneumonia.

Introduction

Pneumonia is one of the most common causes (followed by prematurity related deaths) of childhood infections attributed to about 2 million children deaths worldwide [1]. The diagnosis of pneumonia in children remains an important yet difficult clinical problem, particularly in resource poor setting. Although fast breathing has been recommended as a predictor of childhood pneumonia, no clinical sign can solely predict pneumonia [2].

The World Health Organization (WHO) uses tachypnea (age 2–11 months, $\geq 50/\text{min}$; age 1–5 years, $\geq 40/\text{min}$) and/or lower chest indrawing as a sole criterion to diagnose pneumonia in children with a cough or breathing difficulty [3]. In low- and middle-income countries (LMICs), including Nepal, chest x-ray usually remains the diagnostic test of choice and often, health workers, including treating physicians, use WHO guidelines to diagnose and treat pneumonia [4]. Due to difficulty in obtaining appropriate specimens from the lower respiratory tract for culture and microbiological evaluation, radiography has been considered as the best method available for diagnosing pneumonia [4–6]. However, there is still a dilemma regarding when to order a chest x-ray in a case of suspected pneumonia. Earlier studies reported the clinical predictors of radiological pneumonia when the cases associated with radiological pneumonia were usually caused by bacterial agents mostly *Streptococcus pneumoniae* and *Hemophilus influenzae* [7–9]. WHO guidelines developed earlier for the detection and management of childhood pneumonia targeted bacterial agents [3, 10].

Currently, with the introduction of *Hemophilus influenzae type b* (Hib) and pneumococcal conjugate vaccines (PCV) and global expansion of their coverage, bacterial agents are on the decline and out-numbered by viral and atypical bacteria [11, 12]. The clinical presentation and the radiographic signs of pneumonia may not be the same as found earlier. Considering the change in the epidemiological pattern, the clinical predictors of pediatric pneumonia need reassessment. Hence, this hospital-based study was conducted to find the predictors of radiological pneumonia.

Methods

Study design, hospital setting, participants and diagnosis

This cross-sectional study was conducted from June 2015 to November 2015 in Tribhuvan University Teaching Hospital (TUTH), a tertiary healthcare centre in Kathmandu, Nepal, which lies at an altitude of 1400 meters (4600 ft) from the sea level. Children aged 3–60 months who visited the TUTH at an outdoor patient department or emergency unit and presented with fever, cough, and difficulty or fast breathing were enrolled in this study. All the clinical pneumonia cases included were community-acquired (CAP). No hospital-acquired pneumonia cases were included in the study. Children with pre-existing cardiac disease, chronic respiratory disease (cystic fibrosis/bronchopulmonary dysplasia), known asthma or presenting with asthma (requiring >1 bronchodilator or systemic steroids), history of foreign body aspiration, history of receiving antibiotics >1 week and with chest x-ray outside TUTH (in private clinics)

were excluded from the study. Etiological diagnosis (bacterial versus viral) was not performed in the present study.

Parents of all children enrolled in this study provided vaccination history details, including *Hib* and *PCV* vaccines. The youngest child included in this study was three months and had received at least one dose of *Hib* and *PCV-10* vaccines. A respiratory physician examined the children for the presence of tachypnea, nasal flaring, grunting, chest indrawing, decreased air entry, bronchial breath sounds and hypoxemia. Experienced medical officers from emergency departments or senior pediatric residents blinded to radiological findings of the children, screened them at the out-patient clinic.

Study definitions and variables

WHO cut-off points were taken to define age-adjusted tachypnea- children between 2–11 months (50 or more breaths/min) and 12–59 months (40 or more breaths/min) [3]. Clinical pneumonia was defined as a child having a fever, cough, difficult and/or fast breathing. Hypoxemia was defined as oxygen saturation less than 90% in the pulse oximeter (Mini SPO₂, Criticare Systems, USA) measured by the pediatric probe.

Fever was defined as an axillary temperature of 100.4 ° F or more. All x-rays were carried out using the same portable digital x-ray machine (SHEMADZU 500mA Shandong, Mainland China). All x-ray films were interpreted by an experienced radiologist, blinded to the clinical features of the child's condition. The presence of consolidation, asymmetrical infiltrates, or air bronchograms was considered as radiological pneumonia. A diagnostic agreement was made between the evaluating pediatrician and radiologist in all cases.

Study outcomes

Clinical pneumonia was categorised as radiological and non-radiological pneumonia based on the x-ray findings. The sensitivity and specificity of each of the clinical predictors were then calculated.

Ethical approval

The study was approved by the Institute's Research Committee (IRC) of Tribhuvan University Teaching Hospital (TUTH), Institute of Medicine, Kathmandu, Nepal [reference number-37 (6-11-0)], dated 26th August 2014]. Written and oral consent were obtained from the parents.

Statistical analysis

Descriptive statistics were used to report the characteristics of all children enrolled in this study. The heterogeneity between different baseline characteristics for children with radiological versus non-radiological pneumonia were tested using Chi-square test for categorical variables and t-test for continuous variables. We calculated the crude odds ratio for clinical signs and symptoms of radiological pneumonia using regression analysis. A multivariable regression analysis was carried out after adjusting for all the clinical signs and symptoms. SPSS software (version 21.0 IBM, Armonk, NY, USA) was used for data entry and analysis. Sensitivity and specificity of each variable for radiological pneumonia were calculated.

Results

Out of 4211 children visiting the out-patient and emergency unit of the pediatric department of TUTH, 1021 patients had a fever and were screened for the presence of clinical pneumonia

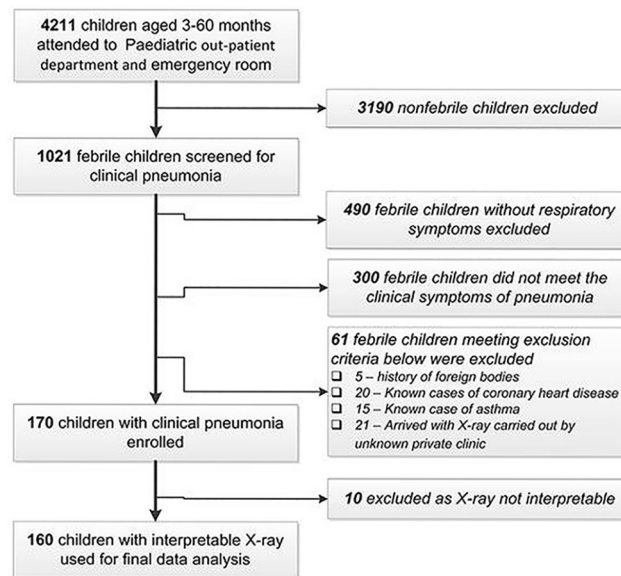


Fig 1. Flow chart showing the selection of pneumonia participants.

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(fever, cough and fast or difficulty breathing). Fig 1 shows the flow diagram of the enrolled children in this study.

Out of a total of 160 children enrolled, 68% were males, and about 60.6% had radiological pneumonia. Table 1 shows the baseline characteristics of children with radiological pneumonia and non-radiological pneumonia. The proportion of children with radiological pneumonia was greater in both males (59.6% versus 40.4%) and females (62.7% versus 37.3%) children when compared to non-radiological pneumonia (Table 1). Oxygen saturation (<90%) and high total leukocyte counts were found to be significantly associated with radiological pneumonia.

Children with radiological pneumonia had complications such as empyema, myocarditis, parapneumonic effusion, respiratory failure and septic shock. The common signs and symptoms present in the enrolled children are reported in Figs 2 and 3, respectively. Noisy breathing and refusal to feeds were common clinical presentation in children with pneumonia and was predominant in children ≤ 12 months (Fig 2). On examination, tachypnea (99% in 3–12 months and 96% in 13–60 months), crepitation (75% in 3–12 months and 71% in 13–60 months), retraction (72% in 3–12 months and 45% in 13–60 months) and hypoxemia (68% in 3–12 months and 51% in 13–60 months) were common clinical signs noticed and was predominantly more in children aged 3–12 months (Fig 3).

Table 2 shows the statistical comparison of clinical features between children with and without radiological pneumonia. Noisy breathing ($p = 0.02$) and nasal discharge ($p = 0.02$) were the clinical symptoms which were significantly associated with radiological pneumonia. The sensitivity and specificity of noisy breathing were 44.3% and 30.2% respectively whereas for nasal discharge were 15.5% and 69.8% respectively. Among the clinical signs, grunting ($p = 0.044$), hypoxemia ($p = 0.005$), wheezing ($p < 0.001$), decreased breath sounds ($p < 0.001$), and bronchial breath sounds were significantly associated with radiological pneumonia in the children. No significant association of radiological pneumonia was observed with tachypnea, nasal flaring, retraction and crepitation (Table 2). Among various clinical variables, age-adjusted tachypnea had the highest sensitivity (99%) with low specificity (6.35%). Grunting

Table 1. Baseline characteristics of children enrolled with and without radiological pneumonia.

Parameters	Radiological pneumonia	Non-radiological pneumonia	p-value
	(Mean ± SE) or [n (%)]	(Mean ± SE) or [n (%)]	
N	97 (60.6)	63 (39.4)	
Age (months)	22.6 ± 1.8	21.4 ± 2.3	0.339
Gender			
Male	65 (59.6)	44 (40.4)	0.707
Female	32 (62.7)	19 (37.3)	
Birth weight (kg)	2.8 ± 0.04	3.0 ± 0.05	0.019
Height for age (z-score)			
+2 to +3	14 (60.9)	9 (39.1)	0.927
0 to +2	38 (58.5)	27 (41.5)	
0 to -2	34 (64.2)	19 (35.8)	
-2 to -3	11 (57.9)	8 (42.1)	
Weight for height			
+2 to +3	4 (50.5)	4 (50.0)	0.346
0 to +2	21 (55.3)	17 (44.7)	
0 to -2	64 (66.0)	33 (34.0)	
-2 to -3	8 (47.1)	9 (52.9)	
History of family smoking (Yes)	7 (63.6)	4 (36.4)	0.832
Temperature (deg F)	100.6 ± 1.1	100.7 ± 0.1	0.95
Respiratory rate (per min)	60.1 ± 1.0	58.7 ± 1.7	0.232
Oxygen saturation (%)	88.3 ± 0.5	90.6 ± 0.7	0.006
Heart rate (per min)	139.8 ± 1.8	143.3 ± 2.3	0.231
Heart sound (abnormal)	9 (69.2)	4 (30.8)	0.508
Blood examination			
Hemoglobin (g/dl)	10.5 ± 0.2	10.6 ± 0.2	0.801
Total leucocyte count (per mm ³)	14094.1 ± 1005.9	11735.3 ± 730.0	0.049
Absolute neutrophil count (per mm ³)	-	-	-
Platelets (per mm ³)	333664.9 ± 1689.1	303379.3 ± 16429.8	0.116
Complications (Yes)			
No	74 (58.3)	53 (41.7)	0.002
Yes	22 (91.7)	2 (8.3)	
Empyema	9 (100.0)	0	0.441
Myocarditis	4 (80.0)	1 (20.0)	
Parapneumonic effusion	4 (100.0)	0	
Respiratory failure	3 (100.0)	0	
Septic shock	2 (66.7)	1 (33.3)	

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(96.8%), bronchial breathing (100%) and decreased breath sounds (92.1%) had the highest specificity (Table 2).

Table 3 shows the validity of a combination of clinical variables for the prediction of pneumonia. Tachypnea alone has a high sensitivity but poor specificity (6%). The addition of hypoxia increased its specificity to 59% while further addition of various auscultatory findings (crepitations, bronchial breathing sounds, decreased air entry) increased specificity to 100%.

Univariate regression analysis, it was found that noisy breathing (OR 0.34; 95% CI 0.17–0.67), nasal discharge (OR 0.42; 95% CI 0.20–0.91), wheezing (OR 0.29; 95% CI 0.15–0.57), decreased breath sounds (OR 7.15; 95% CI 2.63–19.46), and hypoxemia (OR 2.54; 95% CI 1.32–4.88) were significantly associated with radiological pneumonia (Table 4). Following

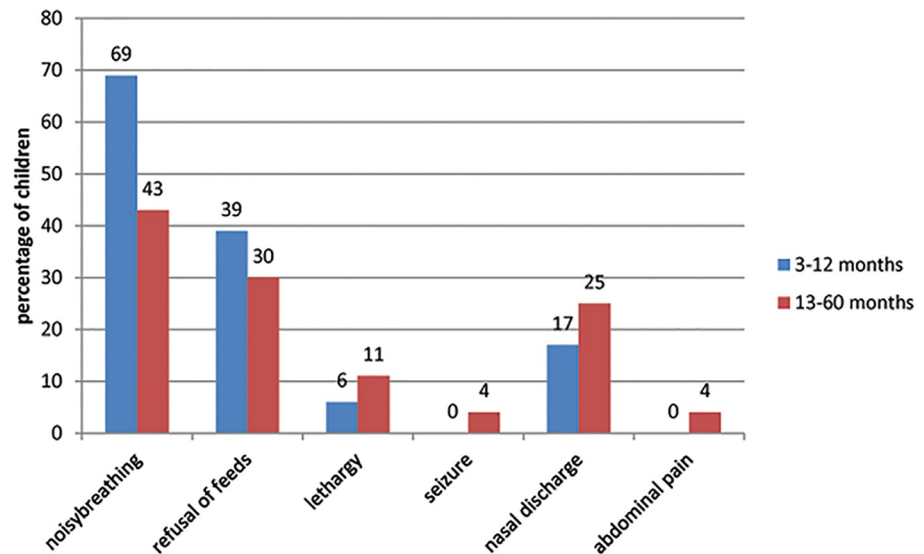


Fig 2. Common presenting symptoms of enrolled children.

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adjustment for all the clinical signs and symptoms, only hypoxemia (AOR 3.41; 95% CI 1.47–7.92) was independently associated with radiological pneumonia (Table 4).

Discussion

In our study, tachypnea had high sensitivity and poor specificity for the diagnosis of radiological pneumonia. Although radiography is the gold standard in the diagnosis of pneumonia in low-income countries, including in Nepal, the unavailability of x-ray machines in majority of rural health settings poses a diagnostic challenge. Equally, it is not feasible to undergo a chest x-ray examination in all children with cough due to its high frequency and radiation hazards. We, therefore, still rely on simple clinical signs as laid out by WHO for diagnosing and treating

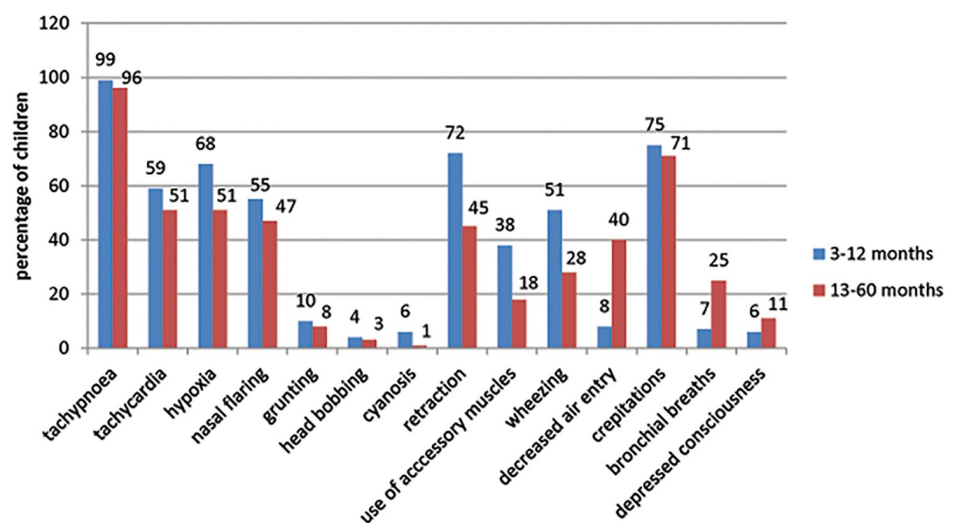


Fig 3. Commonly observed signs in enrolled children.

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Table 2. Comparison of clinical features between children with and without radiological pneumonia.

Clinical features	Radiological pneumonia			Sensitivity [95% CI]	Specificity [95% CI]
	Yes (N, %)	No (N, %)	p-value*		
Symptoms					
Noisy breathing	43 (49.4)	44 (50.6)	0.002	43/97 (44.3) [34.2–54.8]	19/63 (30.2) [19.2–43.0]
Refusal of feeds	33 (60.0)	22 (40.0)	0.907	33/97 (34.0) [24.7–44.3]	41/63 (65.1) [52.0–76.7]
Lethargy	8 (57.1)	6 (42.9)	0.78	8/97 (8.3) [3.6–15.6]	57/63 (90.5) [80.4–96.4]
Nasal discharge	15 (44.1)	19 (55.9)	0.026	15/97 (15.5) [8.9–24.2]	44/63 (69.8) [57.0–80.8]
Signs					
Tachypnea	96 (61.9)	59 (38.1)	0.059	96/97 (99.0) [94.4–100.0]	4/63 (6.35) [1.76–15.5]
Nasal flaring	54 (66.7)	27 (33.3)	0.113	54/97 (55.7) [45.2–65.8]	36/63 (57.1) [44.0–69.5]
Grunting	12 (85.7)	2 (14.3)	0.044	12/97 (12.4) [6.6–20.6]	61/63 (96.8) [89.0–99.6]
Hypoxemia	65 (69.9)	28 (30.1)	0.005	65/97 (67) [56.7–76.2]	35/63 (55.6) [42.5–68.1]
Retraction	60 (65.9)	31 (34.1)	0.114	60/97 (61.9) [51.4–71.5]	32/63 (50.8) [37.9–63.6]
Wheezing	26 (42.6)	35 (57.4)	<0.001	26/97 (26.8) [18.3–36.8]	28/63 (44.4) [31.9–57.5]
Decreased breath sound	37 (88.1)	5 (11.9)	<0.001	37/97 (38.1) [28.5–48.6]	58/63 (92.1) [82.4–97.4]
Bronchial breath	27 (100.0)	0	<0.001	27/97 (27.8) [19.2–37.9]	63/63 (100.0) [94.3–100.0]
Crepitations	73 (62.9)	43 (37.1)	0.332	73/97 (75.3) [65.5–83.5]	20/63 (31.7) [20.6–44.7]

CI, confidence interval;

*Chi square test (categorical variables).

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pneumonia. WHO defines tachypnea as a sensitive sign of pneumonia; however, it has a poor specificity [13]. Hence, using only tachypnea as a guideline to define pneumonia leads to over-diagnosis of pneumonia resulting in over-prescription of antibiotics [14, 15]. Therefore, chest retraction was added in the definition of pneumonia, along with fast breathing in the WHO pocket book [3]. Chest retraction had a sensitivity of 62% in diagnosing radiological pneumonia with a specificity of 50.8% in the present study. This tachypnea based algorithms also significantly under-diagnose wheezy diseases. Likewise, specific signs like nasal flaring, retraction, hypoxemia, crepitations and wheezing may be present in asthma and cardiac diseases [15–17]. Using these specific signs may under-diagnose pneumonia cases. Therefore, a combination of clinical variables (signs and symptoms) that define pneumonia is required for its effective management [15, 18].

The prevalence of radiological pneumonia in this study was 61%, as has also been reported by earlier studies [19–21]. However, this was in contrast to other studies where the prevalence of radiological pneumonia was low [22–25]. Our study had strict inclusion criteria (cough, fever of 100.4° F or more, fast or difficulty breathing) in defining clinical pneumonia, whereas other studies used the earlier WHO definition of pneumonia (only cough and fast breathing)

Table 3. Validity of combination of variables.

Combination of variables	Sensitivity	Specificity
Tachypnea + hypoxemia	67	59
Tachypnea + auscultatory findings	20	100
Hypoxemia+ wheezing	43	50
Hypoxemia + bronchial breath sounds	44	100
Wheezing+ bronchial breath sounds	4	100
Wheezing + hypoxemia + bronchial breath sounds	7	100

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Table 4. Associations between clinical variables (signs and symptoms) with radiological pneumonia.

Variables	Crude Odds ratio (95% CI)	Adjusted Odds ratio* (95% CI)
Noisy breathing	0.34 (0.17–0.67)	0.46 (0.17–1.25)
Tachypnea	6.51 (0.71–59.64)	-
Nasal discharge	0.42 (0.20–0.91)	0.85 (0.30–1.98)
Grunting	4.30 (0.93–19.94)	1.94 (0.26–14.46)
Wheezing	0.29 (0.15–0.57)	0.72 (0.28–1.87)
Decreased breath sounds	7.15 (2.63–19.46)	3.68 (0.99–13.76)
Hypoxemia	2.54 (1.32–4.88)	3.41 (1.47–7.92)
Refusal to feed	0.96 (0.49–1.87)	0.77 (0.30–1.98)
Lethargy	0.85 (0.28–2.59)	0.15 (0.02–1.01)
Nasal flaring	1.67 (0.88–3.17)	1.72 (0.74–3.99)
Retraction	1.67 (0.88–3.18)	2.15 (0.87–5.31)
Creptitations	1.41 (0.70–2.86)	2.98 (0.06–8.12)

CI, confidence interval;

*Each clinical variables were mutually adjusted for each other.

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as their entry criteria. This might be the reason for the high prevalence of radiological pneumonia in the present study.

Although tachypnea, in the current study, was found to be the most sensitive sign to define pneumonia, its specificity was low, and the predictability of radiological pneumonia was insignificant. Similarly, in a study by Lynch *et al.* (2004) [21] and others [22–24], tachypnea had a sensitivity of above 95%, but was unable to distinguish children with and without radiological pneumonia. Likewise, Palafox *et al.* (2000) found that tachypnea had a sensitivity of 74% and concluded that tachypnea might be used as a useful screening clinical sign for identifying pneumonia in children [25].

Among various signs, the specificity of bronchial breath sound was 100% in diagnosing pneumonia in the present study. Similarly, grunting and decreased breath sounds had excellent specificities of 96% and 92%, respectively. This was similar to the study by Lozano *et al.* (1994), where decreased breath sounds had a specificity of 97% [18]. Lynch *et al.* (2004) concluded grunting had 100% specificity [21].

Although noisy breathing, nasal discharge, wheezing, decreased breath sounds, and hypoxemia were significantly associated with radiological pneumonia on univariate analysis, only hypoxemia was found to be independently associated with radiological pneumonia following adjustment of all the clinical signs and symptoms.

Using hypoxemia as a clinical sign had higher sensitivity (67%) with the specificity of 55.6% in predicting radiological pneumonia in the present study. In the present study, the clinical variable (hypoxemia) significantly associated with radiological pneumonia was similar to those reported by Lynch *et al.* (2004) [21] and Bilkis *et al.* [26]. The previous study conducted in the higher altitude of Nepal by Basnet *et al.* (2006–2008) found hypoxia in the majority proportion of children (62%) with pneumonia and predicted it as a sign of treatment failure and admission duration [27].

The sensitivity and specificity of chest retraction in predicting radiological pneumonia in the present study was about 62% and 51%, respectively with no significance in differentiating it from non-radiological pneumonia ($p = 0.114$). Hence, chest indrawing is probably an early indicator of respiratory distress that could be due to different disorders like pneumonia and

bronchiolitis. Although using chest indrawing only as a sole clinical sign is insufficient for a diagnosis of radiological pneumonia, it might still be useful to recognise children with a high risk of hypoxemia and would benefit from oxygen therapy rather than the provision of antibiotics [28].

No single clinical signs have been able to truly predict radiological pneumonia the revised WHO definition of pneumonia suggests tachypnea and/or retractions be used widely in the resource-poor settings to identify children with pneumonia. In the present study, tachypnea had high sensitivity but poor specificity, and its association with radiological pneumonia ($p = 0.079$) was statistically insignificant. Similar results were found in a study done by Lozano *et al.* (1994), where the specificity was low (20%) when tachypnea alone was used to diagnose radiological pneumonia. Wingerter *et al.* (2012) applied the WHO criteria to an urban population visiting the emergency department and found that only 111 met the WHO case definition of pneumonia out of 324 children diagnosed with radiological pneumonia (sensitivity 34.3%, 95% confidence interval: 29.1–39.7) suggesting that WHO criteria was neither sensitive nor specific in predicting pneumonia in younger children [29]. On a combination of clinical signs (tachypnea + auscultatory findings; hypoxemia + bronchial breath sounds) (Table 4), the specificity of predicting radiological pneumonia was 100% in the present study. Rothrack *et al.* suggested that the absence of each of the four signs (respiratory distress, tachypnea, rales, and decreased breath sounds) excludes the diagnosis of pneumonia in children [30]. Therefore, due care needs to be taken while ordering a chest x-ray or prescribing antibiotics to any children presenting with tachypnea alone.

The current study has a few limitations. First, as the present study included children up to 5 years with pneumonia, this result may not be valid for children above five years of age; however, excluding children above five years of age would not take into account the changing epidemiology and the clinical presentation of pneumonia in this age group. Second, this study did not attempt to search the etiological agents. Therefore, our study is not in a position to ascertain with a greater degree of certainty whether the change in epidemiological pattern and variation of clinical presentation of radiological pneumonia is bacterial or viral agents. Thirdly, as this study was conducted in a tertiary care hospital (respiratory physician and radiologist interpreted the data), it may be a challenge to apply these findings in the community setting where these facilities are lacking.

Conclusion

Hypoxemia was the only independent predictor for radiological pneumonia. Tachypnea was the most sensitive sign, whereas bronchial breathing was the most specific sign of radiological pneumonia in the present study. This changing pattern in the clinical presentation and epidemiology of pediatric pneumonia could be due to the introduction of new vaccines which requires a reassessment of clinical predictors of pediatric pneumonia. A larger multi-centric study along with etiological diagnosis is necessary to re-define this changing clinical pattern of pediatric pneumonia to formulate new diagnostic guidelines and empirical antibiotics. The clinician should not rely only on a single sign or symptom and should consider a combination of clinical variables before diagnosing and treating pneumonia in children.

Supporting information

S1 Checklist. STROBE checklist.
(DOC)

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References

1. Rudan I, Boschi-Pinto C, Biloglav Z, et al. Epidemiology and etiology of childhood pneumonia. *Bulletin of the World Health Organization* 2008; 86(5):408–16 <https://doi.org/10.2471/blt.07.048769> PMID: 18545744
2. Lozano JM, Steinhoff M, Ruiz JG, Mesa ML, Martinez N, Dussan B. Clinical predictors of acute radiological pneumonia and hypoxaemia at high altitude. *Archives of disease in childhood*. 1994 Oct 1; 71(4):323–7. <https://doi.org/10.1136/adc.71.4.323> PMID: 7979525
3. World Health Organization. Pneumonia. Pocketbook of hospital care for children: Second edition. 2013. 80–81 p. https://www.who.int/maternal_child_adolescent/documents/child_hospital_care/en/.
4. Ayieko P, English M. Case management of childhood pneumonia in developing countries. *The Pediatric infectious disease journal* 2007; 26(5):432–40. <https://doi.org/10.1097/01.inf.0000260107.79355.7d> PMID: 17468655
5. Koran LM. The reliability of clinical methods, data and judgments (second of two parts). *The New England journal of medicine* 1975; 293(14):695–701. <https://doi.org/10.1056/NEJM197510022931405> PMID: 1160937
6. Koran LM. The reliability of clinical methods, data and judgments (first of two parts). *The New England journal of medicine* 1975; 293(13):642–6. <https://doi.org/10.1056/NEJM197509252931307> PMID: 1097917

7. Falade AG, Mulholland EK, Adegbola RA, et al. Bacterial isolates from blood and lung aspirate cultures in Gambian children with lobar pneumonia. *Annals of tropical paediatrics* 1997; 17(4):315–9 <https://doi.org/10.1080/02724936.1997.11747904> PMID: 9578790
8. Forgie IM, O'Neill KP, Lloyd-Evans N, et al. Etiology of acute lower respiratory tract infections in Gambian children: II. Acute lower respiratory tract infection in children ages one to nine years presenting at the hospital. *The Pediatric infectious disease journal* 1991; 10(1):42–7 <https://doi.org/10.1097/00006454-199101000-00009> PMID: 2003054
9. Forgie IM, O'Neill KP, Lloyd-Evans N, et al. Etiology of acute lower respiratory tract infections in Gambian children: I. Acute lower respiratory tract infections in infants presenting at the hospital. *The Pediatric infectious disease journal* 1991; 10(1):33–41 <https://doi.org/10.1097/00006454-199101000-00008> PMID: 1848364
10. Hazir T, Nisar YB, Qazi SA, et al. Chest radiography in children aged 2–59 months diagnosed with non-severe pneumonia as defined by World Health Organization: descriptive multicentre study in Pakistan. *BMJ* 2006; 333(7569):629. <https://doi.org/10.1136/bmj.38915.673322.80> PMID: 16923771
11. De Wals P, Robin E, Fortin E, et al. Pneumonia after implementation of the pneumococcal conjugate vaccine program in the province of Quebec, Canada. *The Pediatric infectious disease journal* 2008; 27(11):963–8. <https://doi.org/10.1097/INF.0b013e31817cf76f> PMID: 18845982
12. Scott JA, English M. What are the implications for childhood pneumonia of successfully introducing Hib and pneumococcal vaccines in developing countries? *PLoS medicine* 2008; 5(4):e86 <https://doi.org/10.1371/journal.pmed.0050086> PMID: 19226734
13. Castro AV, Nascimento-Carvalho CM, Ney-Oliveria F, et al. Additional markers to refine the World Health Organization algorithm for diagnosis of pneumonia. *Indian pediatrics* 2005; 42(8):773–81 PMID: 16141478
14. Anadol D, Aydin YZ, Gocmen A. Overdiagnosis of pneumonia in children. *The Turkish journal of pediatrics* 2001; 43(3):205–9 PMID: 11592510
15. Banstola A, Banstola A. The epidemiology of hospitalization for pneumonia in children under five in the rural western region of Nepal: a descriptive study. *PloS one* 2013; 8(8):e71311. <https://doi.org/10.1371/journal.pone.0071311> PMID: 23940739
16. Gupta D, Mishra S, Chaturvedi P. Fast breathing in the diagnosis of pneumonia—a reassessment. *Journal of tropical pediatrics* 1996; 42(4):196–9. <https://doi.org/10.1093/tropej/42.4.196> PMID: 8816029
17. Brandstetter RD. *Pulmonary Disorders Mimicking Infectious Pneumonia*. The Pneumonia. New York, NY: Springer New York, 1993:277–87.
18. Lozano JM, Steinhoff M, Ruiz JG, et al. Clinical predictors of acute radiological pneumonia and hypoxaemia at high altitude. *Archives of disease in childhood* 1994; 71(4):323–7 <https://doi.org/10.1136/adc.71.4.323> PMID: 7979525
19. Lucero MG, Dulalia VE, Nillos LT, et al. Pneumococcal conjugate vaccines for preventing vaccine-type invasive pneumococcal disease and X-ray defined pneumonia in children less than two years of age. *The Cochrane database of systematic reviews* 2009(4):CD004977. <https://doi.org/10.1002/14651858.CD004977.pub2> PMID: 19821336
20. Lynch T, Gouin S, Larson C, et al. Does the lateral chest radiograph help pediatric emergency physicians diagnose pneumonia? A randomized clinical trial. *Academic emergency medicine: official journal of the Society for Academic Emergency Medicine* 2004; 11(6):625–9
21. Lynch T, Platt R, Gouin S, et al. Can we predict which children with clinically suspected pneumonia will have the presence of focal infiltrates on chest radiographs? *Pediatrics* 2004; 113(3 Pt 1):e186–9 <https://doi.org/10.1542/peds.113.3.e186> PMID: 14993575
22. Neuman MI, Graham D, Bachur R. Variation in the use of chest radiography for pneumonia in pediatric emergency departments. *Pediatric emergency care* 2011; 27(7):606–10. <https://doi.org/10.1097/PEC.0b013e3182225578> PMID: 21712748
23. Neuman MI, Lee EY, Bixby S, et al. Variability in the interpretation of chest radiographs for the diagnosis of pneumonia in children. *Journal of hospital medicine* 2012; 7(4):294–8. <https://doi.org/10.1002/jhm.955> PMID: 22009855
24. Neuman MI, Monuteaux MC, Scully KJ, et al. Prediction of pneumonia in a pediatric emergency department. *Pediatrics* 2011; 128(2):246–53 <https://doi.org/10.1542/peds.2010-3367> PMID: 21746723
25. Palafox M, Guiscafre H, Reyes H, et al. Diagnostic value of tachypnoea in pneumonia defined radiologically. *Archives of disease in childhood* 2000; 82(1): 41–5. <https://doi.org/10.1136/adc.82.1.41> PMID: 10630911
26. Bilkis MD, Gorgal N, Carbone M, et al. Validation and development of a clinical prediction rule in clinically suspected community-acquired pneumonia. *Pediatr Emerg Care*.2010; 26(6):399–405 <https://doi.org/10.1097/PEC.0b013e3181e05779> PMID: 20502390

27. Basnet S, Sharma A, Mathisen M, Shrestha PS, Ghimire RK, Shrestha DM, et al. Predictors of duration and treatment failure of severe pneumonia in hospitalized young Nepalese children. *PloS one*. 2015 Mar 23; 10(3):e0122052. <https://doi.org/10.1371/journal.pone.0122052> PMID: 25798907
28. Rambaud-Althaus C, Althaus F, Genton B, D'Acremont V. Clinical features for diagnosis of pneumonia in children younger than 5 years: a systematic review and meta-analysis. *The Lancet infectious diseases*. 2015 Apr 1; 15(4):439–50. [https://doi.org/10.1016/S1473-3099\(15\)70017-4](https://doi.org/10.1016/S1473-3099(15)70017-4) PMID: 25769269
29. Wingerter SL, Bachur RG, Monuteaux MC, Neuman MI. Application of the world health organization criteria to predict radiographic pneumonia in a US-based pediatric emergency department. *The Pediatric infectious disease journal*. 2012 Jun 1; 31(6):561–4. <https://doi.org/10.1097/INF.0b013e31824da716> PMID: 22333702
30. Rothrock SG, Green SM, Fanelli JM, Cruzen E, Costanzo KA, Pagane J. Do published guidelines predict pneumonia in children presenting to an urban ED? *PediatrEmergCare*. 2001; 17(4):240–243