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Interobserver agreement in interpretation of chest radiographs for pediatric community acquired pneumonia: Findings of the pedCAPNETZ-cohort

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Abstract

Although chest radiograph (CXR) is commonly used in diagnosing pediatric community acquired pneumonia (pCAP), limited data on interobserver agreement among radiologists exist. PedCAPNETZ is a prospective, observational, and multicenter study on pCAP. $N = 233$ CXR from patients with clinical diagnosis of pCAP were retrieved and $n = 12$ CXR without pathological findings were added. All CXR were interpreted by a radiologist at the site of recruitment and by two external, blinded pediatric radiologists. To evaluate interobserver agreement, the reporting of presence or absence of pCAP in CXR was analyzed, and prevalence and bias-adjusted kappa (PABAK) statistical testing was applied. Overall, $n = 190$ (82%) of

CXR were confirmed as pCAP by two external pediatric radiologists. Compared with patients with pCAP negative CXR, patients with CXR-confirmed pCAP displayed higher C-reactive protein levels and a longer duration of symptoms before enrollment ($p < .007$). Further parameters, that is, age, respiratory rate, and oxygen saturation showed no significant difference. The interobserver agreement between the onsite radiologists and each of the two independent pediatric radiologists for the presence of pCAP was poor to fair (69%; PABAK = 0.39% and 76%; PABAK = 0.53, respectively). The concordance between the external radiologists was fair (81%; PABAK = 0.62). With regard to typical CXR findings for pCAP, chance corrected interrater agreement was highest for pleural effusions, infiltrates, and consolidations and lowest for interstitial patterns and peribronchial thickening. Our data show a poor interobserver agreement in the CXR-based diagnosis of pCAP and emphasized the need for harmonized interpretation standards.

KEYWORDS

antibiotic therapy, imaging, infections: pneumonia, TB, viral

1 | INTRODUCTION

Pediatric community-acquired pneumonia (pCAP) is the most common infectious disease in children aged 1–59 months, causing substantial global morbidity and mortality.[1] Hospital admissions in children with pCAP is a considerable burden on healthcare systems worldwide.[2] In Europe, pCAP affects 30/10,000 children and adolescents until the age of 16 years.[3] The incidence is inversely correlated with age, ranging from 111/10,000 in the first year of life to 25/10,000 in early childhood (2–5 years) to 12.5/10,000 in school-aged children (5–16 years).[4] Disease patterns vary in localization, degree of infestation, and age of the child.[5,6]

Chest radiograph (CXR) remains the most available and common imaging modality to confirm the diagnosis and classify pCAP in children.[7,8] pCAP typically presents radiologically as one of three patterns: "lobar pneumonia," "multifocal bronchopneumonia," and focal or diffuse "interstitial pneumonia." These patterns allow distinction from other forms of lower respiratory tract infections such as bronchiolitis.[9] Although guidelines suggest that CXR should not routinely performed in mild or uncomplicated cases of pCAP,[10–12] it is still commonly performed in children.[10] CXR is not routinely recommended in the outpatient setting due to a lack of evidence for substantial impact on clinical outcomes.[13] However, radiographic findings can provide useful prognostic information and may predict disease severity.[14,15] Although CXR is used to confirm the diagnosis of pCAP, the variability in diagnosing pCAP based on CXR including the interobserver agreement among pediatric radiologists is a recognized problem.[16–18] While radiographic findings are commonly accepted as the gold standard for diagnosing pCAP, there are no validated definitions for CXR interpretation in clinical practice.[7] Therefore, the aim of this investigation was to analyze interobserver agreement in the interpretation of CXR for the diagnosis of pCAP in children in Germany. Specifically, we wonder whether CXR-based diagnosis of pCAP in a multicenter study design needs to be revised by independent external reviewers.

2 | METHODS

2.1 | Study design and participants

Between December 2014 and July 2017, study data of $n = 233$ patients with pCAP were collected in private practices, outpatient clinics, and hospitals across Germany as part of the pedCAPNETZ study, an observational, multicenter study on pCAP.[19] All patients or their legal guardians gave informed consent to participate in this study. Inclusion criteria for inclusion into the analysis were the presence of at least one of the following signs or symptoms: cough, tachypnea, fever, or abnormal findings on auscultation plus pCAP radiographically confirmed by a local radiologist at the site of recruitment.[19] Exclusion criteria were hospitalization for any other reason within the last 28 days, congenital or acquired immunodeficiency, cytostatic therapy during past 28 days, neutropenia (<1000/μl), other relevant immunosuppressive treatment, a concomitant respiratory disease with impaired mucociliary clearance such as cystic fibrosis, primary ciliary dyskinesia, tracheostomy, or other severe lung diseases including pulmonary tuberculosis.[19]

2.2 | Clinical history and laboratory procedures

Detailed data on demographic background, case history, clinical presentation, quality of life, physical examination, diagnostic findings, treatment, socioeconomic measures, and other patient-

related items were collected by means of an electronical case report form.[19] Moreover extensive biosampling is conducted including the collection of blood sample, nasopharyngeal aspirate or swab in the upper airway tract (UAT), and sputum or deep throat swab in the lower airway tract (LAT).[19] Spectrum of pathogen of pCAP is studied in the collected biosamples of the UAT, LAT by Multiplex polymerase chain reaction (PCR) pathogen screen (Multiplex panel see Table S2) and microbiome culture.[19] Nasopharyngeal swabs were analyzed using a multiplex real-time RT-PCR panel according to Bierbaum et al.[20] This included testing for respiratory viruses (adenovirus, bocavirus, coronavirus [CoV] OC43, CoV 229E, CoV HKU1, CoV NL63, enterovirus, influenza virus A+B, human metapneumonvirus, parainfluenza virus 1–4, human parechovirus, respiratory syncytial virus A+B, and rhinovirus) and atypical bacteria (*Bordetella pertussis*, *Legionella pneumophila*, and *Mycoplasma pneumoniae*). Microbial cultures of respiratory samples were performed to standard laboratory procedures in each center (certified clinical microbiology departments).

2.3 | Evaluation of CXR

A total of $n = 245$ CXR were rated by a local radiologist. Images were downloaded as Digital Imaging and Communications in Medicine (DICOM) images from the hospital's Picture Archiving and Communication System (PACS, Picture Archiving and Communication System/IMPAX EE R20 XVII/Agfa HealthCare/Belgium). After pseudonymization using IQ View 3.0 Image information system (IQ View Image information system/3.0. trial version/IMAGE Information Systems Europe GmbH/Germany), two independent specialized pediatric radiologists reviewed all images and completed a standardized CXR interpretation form (Table S1). Main outcome measure was the presence or absence of pCAP on radiographs, defined as evidence of an infiltrate. Furthermore, we analyzed the interobserver agreement of radiographic findings commonly described in childhood pneumonia. Therefore, the two independent radiologists were requested to report diagnostic findings using the clinical pedCAPNETZ-item-catalog (peribronchial thickening, interstitial pattern, infiltrate, atelectasis, and dystelectasis, pleural effusion[19])

TABLE 1 Interobserver agreement of pediatric radiologists, prevalence and bias-adjusted kappa (PABAK) with 95% confidence interval and Cohens Kappa (κ) with 95% confidence interval evaluating chest radiographs in children

	Observed agreement (%)	PABAK	95% Confidence Interval	Cohens Kappa (κ)	95% Confidence Interval
Radiologists					
Local pediatric radiologists/external pediatric radiologist (1)[a]	76	0.53	0.41–0.63	0.23	0.15–0.31
Local pediatric radiologists/external pediatric radiologist (2)[a]	69	0.39	0.26–0.50	0.17	0.10–0.24
External pediatric radiologist (1)/external pediatric radiologist (2)[a]	81	0.62	0.51–0.71	0.56	0.44–0.69
Radiographic changes: WHO-Classification[21]					
Consolidation[b]	75	0.49	0.37–0.60	0.45	0.33–0.58
Other infiltrates[b]	57	0.13	0.00–0.26	0.14	0.02–0.25
Pleural effusion[b]	88	0.76	0.67–0.84	0.64	0.52–0.77
Radiographic changes:pedCAPNETZ-item-catalogue					
Peribronchial thickening[b]	62	0.25	0.11–0.37	0.23	0.10–0.36
Interstitial pattern[b]	64	0.28	0.15–0.41	0.17	0.06–0.29
Hyperinflation[b]	71	0.41	0.29–0.53	0.41	0.28–0.54
Infiltrate[b]	80	0.59	0.48–0.69	0.51	0.38–0.63
Atelectasis/dystelectasis[b]	72	0.45	0.32–0.56	0.25	0.12–0.38
Pleural effusion[b]	88	0.76	0.66–0.84	0.64	0.52–0.77
Radiographic pattern					
Lobar pneumonia[b]	88	0.75	0.65–0.83	0.56	0.43–0.69
Bronchopneumonia[b]	78	0.55	0.43–0.66	0.30	0.17–0.42
Interstitial pneumonia[b]	84	0.68	0.57–0.77	0.03	−0.09 to 0.14

[a]Interobserver agreement in the interpretation of CXR for the diagnosis of pCAP by local pediatric radiologists and two external pediatric radiologists.
[b]Interobserver agreement of radiographic findings commonly described in childhood pneumonia by two external pediatric radiologists.

and the WHO-classification (consolidation, other infiltrates, and pleural effusion[21]). In addition to describing individual diagnostic findings, pediatric radiologists were asked to further classify CXR based pCAP diagnoses into specific subtypes: lobar pneumonia, bronchopneumonia, interstitial pneumonia,[9] or "other pattern" (-Table 1). In addition, normal chest X-rays from healthy controls were randomly placed into the conspicuous chest radiographs of children with clinical pneumonia. In contrast to the local radiologists, who judged the chest X-rays based on clinical information, the two external radiologists independently read all chest radiographs and were blinded to each other's interpretations.

2.4 | Statistical analysis

Data analysis was performed using Statistical Package for the Social Sciences (SPSS,[22]) and R V4.0.3.[23] Interobserver agreement was assessed using observed percent agreement, prevalence and bias-adjusted kappa (PABAK) with 95% confidence interval[24] and Cohens Kappa (κ) with 95% confidence interval. The interpretation of PABAK and Cohens Kappa is based on the criteria (<0.41: poor, <0.75: fair, and <1: excellent) defined by Fleiss.[23] Next, we assessed interobserver agreement specifically for different radiographic findings in our investigation. Based on the main outcome measure children were divided into two groups. Children with radiographic confirmed pCAP by both or at least one external pediatric radiologist were classified as "pneumonia." Children with CXR judged as negative for pCAP by both external pediatric radiologists were classified as "non-pneumonia." Depending on data distribution, Mann–Whitney-U- or *t*-testing was samples were applied to assess differences between these two groups. In addition, viral and bacterial etiology of pCAP was studied in the collected bio samples of the UAT, LAT, and urogenital tract. The groups of pneumonia and non-pneumonia were descriptively compared regarding previously described biosamples.

3 | RESULTS

Characteristics of the study population are shown in Table 2. The median age of children with clinical signs of pCAP included into this analysis was 2 years ($n = 233$, range 1 month–17 years, interquartile range [IQR] 1–6 years), and 47% were female. Nearly all children (97%) suffered from cough and 85% presented with fever at the enrollment visit. For control purposes, $n = 12$ CXR of children without findings suspicious of pCAP were added. Their median age was 3.5 years (IQR 1.3–12) and 67% were female.

All radiologists agreed that all chest radiographs were suitable for interpretation. All 12 control CXR were assessed by the two external radiologists as inconspicuous for pCAP. Amongst the CXR of the pCAP patients, $n = 190$ (82%) CXR were assigned as "pneumonia" by at least two out of three involved radiologists (Figure 1).

Interobserver agreement between radiologists was assessed using observed percent agreement, the PABAK and Cohens Kappa (κ) in the main outcome measure presence or absence of pneumonia on radiographs. Our results and calculated interobserver agreement for various findings and categories are presented in Tables 3 and 1 and in Supplement (S2–S4). Chest X-ray examples for selected pathologies listed in the tables showing agreement and disagreement between reviewers are displayed in Figure 2.

TABLE 2 Study population characteristics and symptoms of an acute airway tract infection at inclusion

Patients' characteristics	pedCAPNETZ-cohort *n* = 233 (95%)	Study cites				Healthy controls *n* = 12 (5%)
		Lübeck *n* = 99 (43%)	Hannover *n* = 71 (31%)	Oldenburg *n* = 49 (21%)	Dresden *n* = 14 (6%)	
Gender: male *n* (%)	124 (53)	51 (52)	40 (56)	25 (51)	8 (57)	4 (33)
Age, years median (IQR)	2 (1–6)	2 (1–4)	3 (1–6)	3 (1.5–5.5)	2 (1–9)	3.5 (1.3–12)
Inpatient *n* (%)	189 (81)	96 (97)	31 (44)	49 (100)	13 (93)	n.a.
Clinical signs and symptoms						
Cough *n* (%)	225 (97)	96 (97)	71 (100)	45 (92)	13 (93)	n.a.
Tachypnea* *n* (%)	130 (56)	66 (67)	28 (39)	27 (55)	9 (64)	n.a.
Abnormal findings on auscultation *n* (%)	203 (87)	85 (86)	61 (86)	45 (92)	12 (86)	n.a.
Fever** *n* (%)	199 (85)	87 (88)	59 (83)	39 (80)	14 (100)	n.a.

Abbreviation: IQR, interquartile range.

*Tachypnea (respiratory rate > 60/min for infants less than 2 month old; respiratory rate > 50/min for children aged 2–11 months; respiratory rate: > 40/min for those 1–18 years old)[3,25]

**Fever (≥ 38.5°C [rectal] or 38.0°C [tympanic, axillary, and oral]).[19]

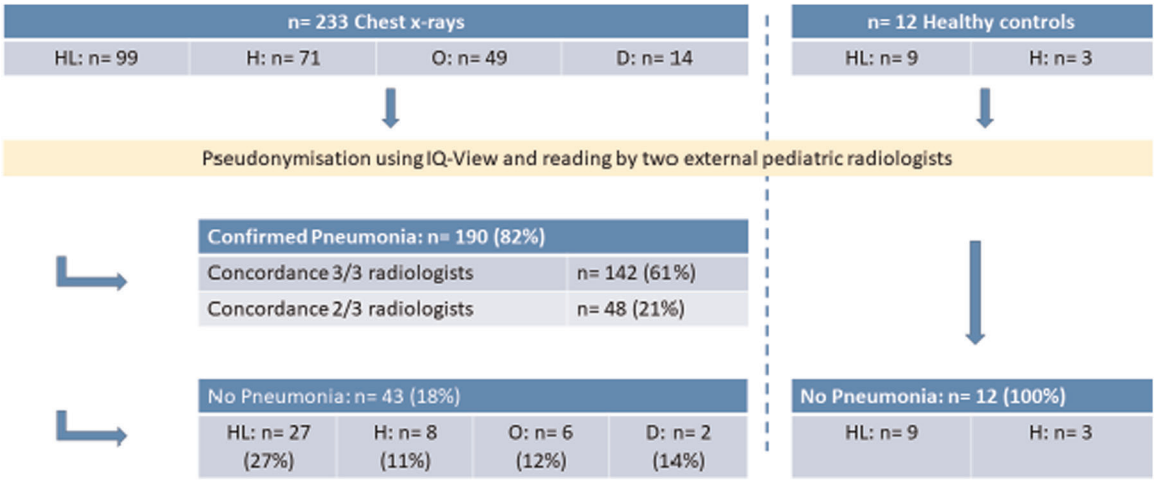

FIGURE 1 Course of study. D, Dresden; H, Hannover; HL, Study center Luebeck; O, Oldenburg [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Concordance analysis on the question of pneumonia between the local radiologist and external pediatric radiologist 1 and 2 and between the external pediatric radiologists 1 and 2

		Local pediatric radiologists		
		No	Yes	Total
External pediatric radiologist (1)	No	12	0	12
	Yes	58	175	233
	Total	70	175	245

Note: Observer agreement = 76%, PABAK = 0.53, κ= 0.23.

		Local pediatric radiologists		
		No	Yes	Total
External pediatric radiologist (2)	No	12	0	12
	Yes	75	158	233
	Total	87	158	245

Note: Observer agreement = 69%, PABAK = 0.39, κ= 0.17.

		External pediatric radiologist (1)		
		No	Yes	Total
External pediatric radiologist (2)	No	55	15	70
	Yes	32	143	175
	Total	87	158	245

Note: The observer agreement, the prevalence and bias-adjusted kappa (PABAK) and Cohens Kappa (κ) is reported. Observer agreement = 81%, PABAK = 0.62, κ = 0.56.

Next, we analyzed whether the children with CXR confirmed pCAP (grouped as "pneumonia") displayed a distinct phenotype from those children with CXR judged as "no pneumonia." Indeed, patients in the CXR confirmed "pneumonia" group displayed higher C-reactive protein levels and longer symptom duration before enrollment (Table 4). The radiological findings showed that consolidation was exclusively ascribed in the group of pneumonia. Further parameters such as age, temperature, respiratory rate, oxygen saturation, and white blood cell count demonstrated no significant difference.

To analyze the pathogenic spectra, viral and bacterial pathogens were studied in the UAT and the lower airway tract by multiplex PCR (UAT: n = 216 children; 93%; LAT: n = 184; 79%) and microbiological culture (UAT: n = 69; 30%; LAT n = 198; 85%).

Overall a potential causative agent was found in 74% and 66% of the conducted multiplex PCR of the UAT and LAT, respectively, while conventional culture revealed 62% and 58% positive results. We observed no significant differences between the confirmed versus no pneumonia groups in terms of numbers or patterns of identified pathogens in UAT or LAT samples (Table 5).

4 | DISCUSSION

This study shows high interrater variability in the interpretation of CXR for the diagnosis of pCAP. This may be a significant confounder variable in multicenter trials. Two independent, external, blinded pediatric radiologists rejected 18% of the CXR-based pCAP diagnoses in a large cohort of children and adolescents. Chance adjusted agreement between local pediatric radiologists and the two external pediatric radiologists was poor. The interobserver agreement showed high variability between the study sites.

Our result highlights the need to revise the CXR-based diagnosis of pCAP in a multicenter study design. Based on our data we additionally suggest using standardized radiographic interpretation forms in the initial assessment and to set up a compulsory training course in multicenter studies. A modified pedCAPNETZ-item-catalogue[19] can be used to further evaluated and improve the interobserver agreement.

One of the aims of the pedCAPNETZ study is to characterize children and adolescents with pCAP using comprehensive epidemiological, clinical, and biological analyses to improve care and

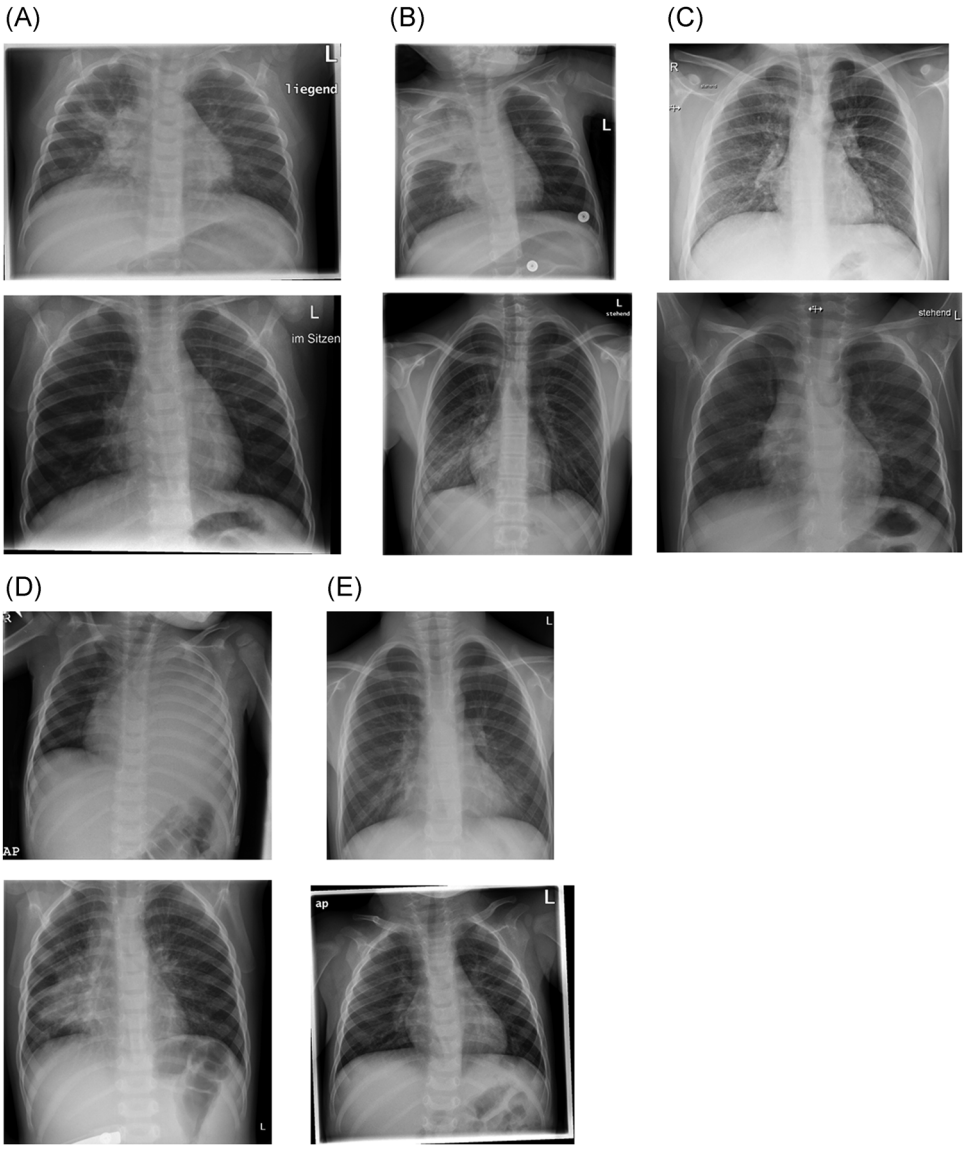

FIGURE 2 X-ray examples for selected pathologies listed in table showing agreement (upper row) and disagreement (lower row) between reviewers: (A) bronchopneumonia, (B) consolidation, (C) interstitial pneumonia, (D) lobar pneumonia, and (E) other infiltrates [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 4 Patient characteristics in patients with pneumonia and nonpneumonia

Patient characteristics	Pneumonia (n = 190)	Nonpneumonia (n = 43)	p value
Age, years median (IQR)	2.5 (1–6)	1 (1–5)	.173
Days since onset of symptoms median (IQR)	5 (3–9)	3 (1–6)	.004
Highest temperature median (IQR)	39.6 (39–40)	39.5 (39–40)	.918
Respiratory rates/min mean (*SD*)	41 (15.73)	46.7 (21.45)	.178
SpO_2 in % median (IQR)	95 (90–97)	93 (91–95)	.353
Leukocytes 10^3/µl median (IQR)	13 (10–19)	13 (9–15)	.116
CRP g/dL median (IQR)	34 (10–84)	14 (5–41)	.003

Abbreviations: CRP, C-reactive protein; IQR, interquartile range.

TABLE 5 Detected viral and bacterial pathogens in upper and lower airways of children with radiological confirmed pCAP and nonconfirmed pCAP

Location	Upper airway tract			Lower airway tract		
Group	All *n* (%)	Pneumonia *n* (%)	Nonpneumonia *n* (%)	All *n* (%)	Pneumonia *n* (%)	Nonpneumonia *n* (%)
PCR[a]	**160**	**129**	**31**	**122**	**97**	**25**
RSV A/B	**50 (21)**	**41 (21)**	**9 (19)**	**35 (25)**	**26 (23)**	**9 (30)**
Rhinovirus	39 (16)	29 (15)	10 (21)	18 (13)	15 (14)	3 (10)
Human bocavirus	33 (14)	26 (13)	7 (14)	14 (10)	10 (9)	4 (13)
Mycoplasma pneumoniae	30 (13)	27 (14)	3 (6)	30 (21)	28 (25)	2 (6)
Human metapneumovirus A/B	20 (8)	15 (8)	5 (11)	7 (5)	3 (3)	4 (13)
Human coronavirus (HKU 1, NL 63, 229E, OC43)	17 (7)	14 (7)	3 (6)	9 (6)	7 (6)	2 (7)
Parainfluenzavirus	16 (7)	13 (7)	3 (6)	5 (4)	5 (5)	0 (0)
Adenovirus	11 (5)	9 (5)	2 (4)	1 (1)	1 (1)	0 (0)
Enterovirus	10 (4)	6 (3)	4 (9)	10 (7)	5 (5)	5 (17)
Influenza-A-virus	7 (3)	7 (4)	0 (0)	5 (4)	5 (5)	0 (0)
Influenza-B-virus	6 (3)	5 (3)	1 (2)	5 (4)	4 (4)	1 (3)
Parechovirus	1 (0)	1 (1)	0 (0)	2 (1)	2 (2)	0 (0)
Total	240 (100)	193 (100)	47 (100)	141 (100)	111 (100)	30 (100)
Microbiological culture	43	28	15	114	90	24
Haemophilus influenzae	20 (34)	12 (32)	8 (38)	34 (23)	27 (23)	7 (21)
Moraxella catarrhalis	12 (21)	7 (19)	5 (24)	2 (1)	2 (2)	0
Staphylococcus aureus	9 (16)	6 (16)	3 (14)	14 (9)	13 (11)	1 (3)
ORSA/MRSA	1 (2)	1 (3)	0	0	0	0
Streptococcus pneumoniae	6 (10)	3 (8)	3 (14)	4 (3)	3 (3)	1 (3)
Enterobacter	2 (3)	2 (5)	0	12 (8)	10 (9)	2 (6)
Pseudomonas spp.	1 (2)	1 (3)	0	1 (1)	0	1 (3)
Klebsiella oxytoca	1 (2)	1 (3)	0	5 (3)	3 (3)	2 (6)
Klebsiella pneumoniae	0	0	0	2 (1)	2 (2)	0
E. coli	0	0	0	4 (3)	1 (1)	3 (9)
Haemophilus parainfluenzae	0	0	0	23 (15)	19 (16)	4 (12)
Haemophilus spp.	0	0	0	8 (5)	4 (3)	4 (12)
Haemophilus haemolyticus	0	0	0	6 (4)	5 (4)	1 (3)
Actinetobacter spp.	0	0	0	11 (7)	8 (7)	3 (9)
Candida albicans	0	0	0	8 (5)	6 (5)	2 (6)
Others[b]	6 (10)	4 (10)	2 (10)	15 (10)	13 (11)	2 (6)
Total	58 (100)	37 (100)	21 (100)	149 (100)	116 (100)	33 (100)

Note: Total numbers of detects and percentage in relation to samples with positive proof are reported.

Abbreviations: ORSA/MRSA, oxacillin-resistant *Staphylococcus aureus*/methicillin-resistant *Staphylococcus aureus*; pCAP, pediatric community-acquired pneumonia; PCR, polymerase chain reaction.

[a]In some children, the multiplex PCR analyses of the upper and/or lower airway tract displayed multiple pathogenic agents. Total numbers of detects and percentage in relation to samples with positive proof are reported.

[b]*Streptococcus pyogenes*; *Streptococcus* (ß-häm) non-A, non-B; *Streptococcus viridans*; *Streptococcus pyogenes*; *Bacillus* species; *Propionibacterium acnes*; *Streptococcus mitis*; *Corynebakterium*; *Haemophilus parahaemolyticus*; *Pantoea* sp.; *Serratia marcescens*; *Stenotrophomonas maltophilia*; *Candida guilliermondii*; nonfermenting bacteria.

quality of life.[19] However, a concurring diagnosis is a prerequisite for subsequent in-depth analysis in the pedCAPNETZ cohort. Nonspecific clinical symptoms make it difficult to distinguish pneumonia from other respiratory diseases.[11] Accuracy of radiograph interpretation is important for clinical decision-making.

Similar to previous studies, chance-adjusted diagnostic concordance between external radiologists was moderate in our study. An Australian study on variability and accuracy in interpretation of CXR in diagnosing pCAP in more than 3000 children under the age of five found an interobserver agreement similar to that observed in our cohort.[17] Another study from Israel focused on pediatric CXR with discordant interpretations between emergency physician and radiologist's final interpretation.[26] A subgroup analysis of interobserver agreement revealed low kappa scores comparable to those found in our investigation with the best level of agreement between radiologists and senior emergency physicians.

Overall, our findings are in line with previous studies of interobserver agreement in the interpretation of CXR for the diagnosis of pCAP.[16,27,28] However, direct comparison is limited as most studies differ in number and age of participants, fluid intake of the child (e.g., for demarcation of infiltrates), extent of radiographic findings noted in the chest radiography interpretation form, specialty of the investigator reading the CXR, or extent of further analysis of the patient characteristics and microbiological correlate.

A strength of our study lies in the multicenter study design, which enabled the comparison of interobserver agreement between different study sites. In addition, the detailed radiographic interpretation form used in our analysis allowed us to compare interrater variability in high granularity. Furthermore, the broad clinical data collection and biosampling enabled us to correlate CXR based observation with multiple other variables. Possible limitations of our work could lie in the fact that the external radiologists, based on their knowledge of the study design, may have been biased to diagnose pCAP. Moreover, the sample size might be a limitation, and that is the low number of normal CXR might have biased our results. However, for ethical reasons, the recruitment of normal CXR is challenging.

The interobserver agreement varied depending on specific findings recorded in the standardized chest radiograph interpretation form. We decided to include the WHO-classification in our standardized chest radiograph interpretation form to enable the comparison to previous international studies about interobserver agreement. Similar to previous studies, pleural effusion and consolidation are findings with high interobserver agreement,[29] whereas interobserver agreement regarding other infiltrates was poor.

Nevertheless, it is important to point out that the WHO standardized criteria were developed with the goal to improve the interobserver agreement for epidemiological studies on pneumonia and bacterial vaccine efficacy trials.[21] The central aim of the pedCAPNETZ initiative to analyze current applied diagnostic and therapeutic strategies in hospital and outpatient care across Germany and evaluate their importance for accuracy in clinical pCAP management.[19] The WHO classification was not designed for use in individual patient clinical management because of its emphasis on specificity on bacterial pneumonia at the expense of sensitivity for overall pCAP.

The clinical pedCAPNETZ-item-catalogue showed a range of interobserver agreement from poor for the interstitial pattern to good for the pleural effusion for its findings. Overall, pleural effusion, infiltrate, and consolidation seemed to be the findings with most interobserver concordance rates in CXR.

CXR should not be the driving force to decide whether e.g. an antibiotic treatment is indicated. A study from Finland on the differentiation of bacterial and viral pneumonia in children showed that an interstitial infiltrate was likewise associated with viral and bacterial pneumonia.[30] This fits our observation and is in line with other findings reporting on nonspecific CXR patterns for different types of pCAP causing pathogens.[31] Only for the CXR pattern of lobar pneumonia, a significant association with bacterial infection has been described.[30] There was no significant difference between the pathogen spectrum in the group with pneumonia and no pneumonia in our descriptive analysis. However, it should be mentioned that a further limitation of our work is the incomplete collection of biological samples of every patient enrolled in the study, as we focused on analyzing interobserver agreement in the interpretation of chest radiographs for pCAP. Moreover, the difficulty to differentiate between colonization and infection of potential causative agents remains. Nevertheless, potential causative agents concerning the etiology of pCAP will be subject to future analysis of the pedCAPNETZ cohort to possibly improve individual treatment and adjust the use of antibiotics.

In conclusion, the extensive interrater variability in our study illustrates the necessity of a standardized interpretation of CXR for pCAP in clinical practice. This emphasizes the need for uniform definitions on simple criteria and adequate training to improve interobserver agreement.[32,33] In addition, our data suggest that the diagnosis of pCAP should be based on the integration of a number of related observations, that is, clinical signs and symptoms, laboratory parameters, and CXR. Clinicians should take into account the great interrater variability of CXR interpretation for the diagnosis pCAP when making clinical decisions. Finally, our data support current guidelines suggesting that CXR should not routinely performed in mild or uncomplicated cases of pCAP.

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CONFLICT OF INTERESTS

M.V. Kopp has received a speaker honorarium or consultant fees from the following companies: ALK-Abelló, Allergopharma, Boehringer-Ingelheim, Chiesi; Glaxo; Infectopharm; Sanofi-Aventis, Leti Pharma, Novartis Pharma, Vertex. G. Voigt has nothing to declare.

AUTHOR CONTRIBUTIONS

Gesche Maria Voigt: formal analysis (equal); investigation (equal); writing original draft (supporting). **Dominik Thiele**: data curation (supporting); formal analysis (lead); methodology (equal); validation (equal). **Martin Wetzke**: investigation (equal); writing original draft (supporting); writing review & editing (supporting). **Jürgen Weidemann**: investigation (equal); methodology (equal); validation (equal); writing original draft (supporting). **Patricia-Maria Parpatt**: investigation (equal); methodology (equal); validation (equal); writing review & editing (supporting). **Tobias Welte**: conceptualization (equal); methodology (equal); resources (equal); writing review & editing (equal). **Jürgen Seidenberg**: investigation (equal); supervision (equal); writing review & editing (equal). **Christian Vogelberg**: conceptualization (supporting); investigation (supporting); writing review & editing (supporting). **Gernot Rohde**: conceptualization (supporting); supervision (equal); writing review & editing (equal). **Gesine Hansen**: conceptualization (equal); funding acquisition (equal); investigation (equal); methodology (equal); project administration (equal); resources (equal); supervision (equal); writing review & editing (equal). **Matthias Volkmar Kopp**: conceptualization (equal); formal analysis (equal); funding acquisition (equal); investigation (equal); project administration (equal); supervision (equal); writing original draft (lead); writing review & editing (lead).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The trial design was approved by the Ethic committees of the MH Hannover. The trial was conducted in accordance with the trial protocol, the International Conference on Harmonization guideline for Good Clinical Practice, applicable local regulations and the Declaration of Helsinki. Patients willing to participate in the trial were asked to provide written informed consent after being given sufficient time to consider participation.

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REFERENCES

1. Liu L, Johnson HL, Cousens S, et al. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet*. 2012;379(9832):2151-2161. https://doi.org/10.1016/S0140-6736(12)60560-1
2. Nair H, Simões EA, Rudan I, et al. Global and regional burden of hospital admissions for severe acute lower respiratory infections in young children in 2010: a systematic analysis. *Lancet*. 2013;381(9875):1380-1390.
3. Liese JG. Pneumonie. In: Berner R, Bialek R, Forster J, eds. *Deutsche Gesellschaft für Pädiatrische Infektiologie, DGPI Handbuch, Infektionen bei Kindern und Jugendlichen*. Vol 7. Auflage: Georg Thieme Verlag; 2018:220-226.
4. Weigl JAI, Puppe W, Belke O, Neusüß J, Bagci F, Schmitt HJ. Population-based incidence of severe pneumonia in children in Kiel, Germany. *Klin Padiatr*. 2005;217(4):211-219.
5. 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. *Lancet Infect Dis*. 2015;15(4):439-450.
6. Stein RT, Marostica PJC. Community-acquired pneumonia: a review and recent advances. *Pediatr Pulmonol*. 2007;42(12):1095-1103.
7. Cherian T, Mulholland E, Carlin J, Ostensen H. Standardized interpretation of paediatric chest radiographs for the diagnosis of pneumonia in epidemiological studies variability in the interpretation of chest radiographs! standardized method for identifying radiological pneumonia would facilitate read. *Bull World Heal Organ*. 2004;83(5):353-359.
8. Mahomed N, Fancourt N, de Campo J, et al. Preliminary report from the World Health Organisation chest radiography in epidemiological studies project. *Pediatr Radiol*. 2017;47(11):1399-1404.
9. Franquet T. Imaging of community-acquired pneumonia. *J Thorac Imaging*. 2018;33(5):282-294.
10. Bowen SJM, Thomson AH. British Thoracic Society Paediatric Pneumonia Audit: a review of 3 years of data. *Thorax*. 2013;68(7):682-683.
11. Rose M, Liese J, Barker M, et al. S2k-Leitlinie: management der ambulant erworbenen pneumonie bei kindern und jugendlichen (pädiatrische ambulant erworbene Pneumonie, pCAP). *AWMF*. 2017;(048):1-51. https://www.awmf.org/uploads/tx_szleitlinien/048-013l_S2k_pCAP_ambulant_erworbene_Pneumonie__Kinder_Jugendliche_2017-06.pdf
12. Bradley JS, Byington CL, Shah SS, et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America Pediatric Community Pneumonia Guide. *Clin Infect Dis*. 2011;53(7):25-76. https://academic.oup.com/cid/article-abstract/53/7/e25/424286
13. Swingler GH, Swingler GH, Hussey GD, Zwarenstein M. Randomised controlled trial of clinical outcome after chest radiograph in ambulatory acute lower-respiratory infection in children. *Lancet*. 1998;351:404-408.
14. Kelly MS, Crotty EJ, Rattan MS, et al. Chest radiographic findings and outcomes of pneumonia among children in Botswana. *Pediatr Infect Dis J*. 2016;35(3):257-262.
15. McClain L, Hall M, Shah SS, et al. Admission chest radiographs predict illness severity for children hospitalized with pneumonia. *J Hosp Med*. 2014;9(9):559-564.
16. Elemraid MA, Muller M, Spencer DA, et al. Accuracy of the interpretation of chest radiographs for the diagnosis of paediatric pneumonia. *PLoS One*. 2014;9(8):6-10.
17. Williams GJ, Macaskill P, Kerr M, et al. Variability and accuracy in interpretation of consolidation on chest radiography for diagnosing pneumonia in children under 5 years of age. *Pediatr Pulmonol*. 2013;48(12):1195-1200.
18. Johnson J, Kline JA. Intraobserver and interobserver agreement of the interpretation of pediatric chest radiographs. *Emerg Radiol*. 2010;17(4):285-290.
19. Wetzke M, Kopp MV, Seidenberg J, et al. PedCAPNETZ – prospective observational study on community acquired pneumonia in children and adolescents. *BMC Pulm Med*. 2019;19(1):238.
20. Bierbaum S, Forster J, Berner R, et al, CAPNETZ study group. Detection of respiratory viruses using a multiplex real-time PCR assay in Germany, 2009/10. *Arch Virol*. 2014;159(4):669-676. https://doi.org/10.1007/s00705-013-1876-3
21. World Health Organization. Standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children/World Health Organization Pneumonia Vaccine Trial Investigators' Group. 2001; Available from: http://www.who.int/iris/handle/10665/66956

22. IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.
23. R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/
24. Byrt T, Bishop J, Carlin JB. Bias, prevalence and kappa. *J Clin Epidemol*. 1993;46:423-429.
25. World Health Organization. Intergrated Management of Childhood Illness; Chart Booklet. 2014:1-76. Available from: https://apps.who.int/iris/bitstream/handle/10665/104772/9789241506823_Chartbook_eng.pdf;jsessionid=0FF4E6A5C4DAC6656C30364CD04E0648?sequence=16
26. Fleiss JL. *Statistical Methods for Rates and Proportions*. 2nd ed. New York, USA: Wiley; 1981.
27. Ben Shimol S, Dagan R, Givon-Lavi N, et al. Evaluation of the World Health Organization criteria for chest radiographs for pneumonia diagnosis in children. *Eur J Pediatr*. 2012;171(2):369-374.
28. Neuman MI, Lee EY, Bixby S, et al. Variability in the interpretation of chest radiographs for the diagnosis of pneumonia in children. *J Hosp Med*. 2012;7(4):294-298.
29. Test M, Shah SS, Monuteaux M, et al. Impact of clinical history on chest radiograph interpretation. *J Hosp Med*. 2013;8(7):359-364.
30. Virkki R, Rikalainen H, Svedström E, Juven T, Mertsola J, Ruuskanen O. Differentiation of bacterial and viral pneumonia in children. *Thorax*. 2002;57(5):438-441.
31. Korppi M, Don M, Valent F, Canciani M. The value of clinical features in differentiating between viral, pneumococcal and atypical bacterial pneumonia in children. *Acta Paediatr Int J Paediatr*. 2008;97(7):943-947.
32. Berbaum KS, Franken EA, Dorfman DD, Lueben KR. Influence of clinical history on perception of abnormalities in pediatric radiographs. *Acad Radiol*. 1994;1(3):217-223.
33. Levinsky Y, Mimouni FB, Fisher D, Ehrlichman M. Chest radiography of acute paediatric lower respiratory infections: experience versus interobserver variation. *Acta Paediatr*. 2013;102(7):e310-e314. https://doi.org/10.1111/apa.12249

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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