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Analysis of radiological interobserver agreement in the diagnosis of pneumonia in children: a challenge in clinical practice

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Abstract

Background: Despite the 2001 standardized interpretation criteria established by the World Health Organization, the radiological identification of pneumonia in childrenremains challenging, with significant inter-observer variability persisting.***Objectives:*** To describe the epidemiological and clinical characteristics of community-acquired pneumonia in children and to evaluate inter-observer radiological agreement in the diagnosis of pneumonia in children under five years of age. ***Materials andMethods:*** A descriptive, observational study

involving452 patientshospitalized in a pediatric referral centerbetween October 2010 and September 2013. Clinical and sociodemographic variables were evaluated. Two independent radiologists evaluated the images according to the World Health Organization's standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children, modified to take not only consolidation, alveolar infiltrate and pleural effusion into consideration, but also interstitial infiltrate.***Results:*** Around 70% of the children were under two years of ageand family income was one minimum salary or less in half the households. Pneumonia was classified as severe or very severe in 83.9% and complicated in 22.6%. The deathrate was 1.5%. Inter-observer agreement was almost perfectfor pleural effusion (kappa 0.825). Consolidation was the most common finding (66.8%),with inter-observer agreement considered substantial (kappa 0.696). Conversely, agreement was poor for interstitial or alveolar infiltrate (kappa 0.533). ***Conclusion:*** Agreement was high for the radiographicfinding of pleural effusion; however, interstitial and alveolar infiltrates proved difficult to interpret. Consolidation was the most common abnormality in hospitalized children with severe pneumonia.

Keywords: pneumonia; epidemiology; chest radiography; inter-observer agreement.

Introduction

Pneumonia is characterized by inflammation of the pulmonary parenchyma induced by alower respiratory tract infection. When the disease is acquired outside a hospital environment it is referred to as community-acquired pneumonia (CAP). Currently, around 150.7 million new cases of CAP occur annually worldwide in children under five years of age. Of these, 11 to 20 million cases(7-13%) are severe enough to require hospitalization [1] andaround 1.8 million deaths occur annually.Althoughthis number has been in decline over recent decades, CAP remains one of the principal causes of death in children under five years of age [2,3].

Pneumonia is often preceded by a viral upper respiratory tract infection [1]. One of the most common clinical symptoms of CAP is tachypnea. The younger the child, the more severe the symptom. Fever, cough and prostration are also present.

Although chest radiography is considered the optimal complementarymethod for diagnosing pneumonia due to its low cost and wide availability compared to other imaging methods [4], consensuses and guidelines on CAP in childhood have stated thatradiology is superfluous for reaching diagnosis and should be reserved for the more severe cases requiring admission to hospital. Indeed, radiologicalresults do not normally affect clinical outcome, since the exam cannot determine the etiological agent responsible and is unable to clearly differentiate between a viral and a bacterial infection [5,6]. Consequently, the findings do not effectively change patient management insofar as the administration of antibiotics is concerned, with these being prescribed according to the most probable etiology for each age group and the patient's clinical presentation [7,8]. Furthermore, radiologists are not available at all healthcare services, and diagnosis tends to bemade by emergency pediatricians with varying degrees of experience and training [9]. Therefore, the clinical diagnostic criteria proposed by the World Health Organization (WHO)should be sufficient to initiate treatment, particularly in the case of outpatient care [1].On the other hand, chest x-rays remaincrucialin the case of severe pneumonia requiringhospitalization, especially for diagnosing complications such as pleural effusion, pneumatocele, pneumothorax, necrotizing pneumonia and atelectasis [1].

Chest x-rayinterpretation of pulmonary diseases varies significantlyamong observers [10],as reported in cases of pneumoconiosis [11], lung cancer [12]and, particularly, pneumonia [13]. Cohen's kappa coefficient is the most commonly used method for the evaluation of inter-observer agreement. This method measures the proportion of agreement between observers, eliminating the possibility of chance agreement [8,14].

Inter-observer agreement was considered moderate (kappa 0.41)in a study in which a pediatric radiologist, a pediatric pneumologist and a pediatrician examined 60 chestx-rays from children under five years of age with a clinically suspected lower respiratory tract infection.The best agreement was for the findings of pleural opacities and the poorest for peribronchial cuffing [8].

In 2001, the WHO developed a set of criteria to standardize the interpretation of chest x-rays in the diagnosis of pneumonia in children. The criteria weredesigned for use in epidemiological studies, with the ultimateaimof generating comparable results [4].

Even with the WHO standardization, inter-observervariability continues to be a problem. Twentyobservers, including radiologists and clinicians, interpreted 208 pediatric chest x-rays.The finding of pneumonia as an endpoint ranged from 8 to 16%. Thirteen of the

observers had a kappa coefficient of>0.6, with a mean of 0.65 for the clinicians and 0.73 for the radiologists [15]. In a similar study conducted in Philadelphia and Boston, six different radiologists evaluated 100 x-rays performed on children admitted to emergency departments. Agreement was substantial for alveolar infiltrate (kappa coefficient 0.69), moderate for any infiltrate and for pleural effusion (kappa 0.47 and 0.45, respectively), fair for air bronchogram (kappa 0.32) and slight for interstitial infiltrate (kappa 0.14) [9].

A study conducted in England with two observers classified abnormalities as a function of their location and found substantial inter-observer variations (kappa 0.70), particularly for findings in the peribronchial (48.8%) and perihilar (28.1%) regions. In cases of pleural effusion, the variation was of 11.8% (kappa 0.57) [16].

In a comparison of medical specialties,one studyreported a greater incidence of error in the interpretation of imaging tests among emergency room physicians compared to radiologists and radiology residents [17]. In addition, varying degrees of agreement were foundin the diagnoses reached by radiology residents [18]. One study evaluated agreement between radiology residents and an experienced radiologist and reported precision of more than 95% [19].A slight reduction in the rate of error has been identified as residents progress through their years of residency [19,20].

The objective of the present study was to evaluate inter-observer agreement with respect to the radiology findings associated with pneumonia in children and to describe the distribution of the sociodemographic and clinical variables of hospitalized patients with pneumonia.

Methods

Study design

A descriptive, observational study was conducted to evaluate inter-observeragreement in the interpretation of chest x-rays of children with clinical signs of pneumonia. The observers were a radiologist and a second-year radiology resident. Data on the patients in the present study and their relevant radiology examswere extracted from a database originally used in a previous case-control study on risk factors for CAP [21].

Study population

A total of 452 children agedbetweenone month andfive yearswith an initial clinical diagnosis of pneumonia reached in accordance with the WHO criteria were included in the studyand

their chest x-rays were examined. The children were hospitalized in wards or in the intensive care unit (ICU) of the *Instituto de Medicina Integral Prof. Fernando Figueira* (IMIP) between October 2010 and September 2013.

Criteria and procedures for the selection of the study participants

Inclusion criteria

Children of either sex aged>29 days and <5 years, with a clinical diagnosis of pneumonia, who were receiving care at IMIP's emergency department, who had been admitted to a hospital ward or to the pediatric ICU and whose chest radiographies were available for examination, were included in the study.

Exclusion criteria

Children with concomitant underlying diseases including heart disease, chronic lungdiseases, kidney disease, neuropathies, hemoglobinopathies, liver disease, immunodeficiency, cystic fibrosis or congenital lung malformations were excluded from the study to avoid any ambiguity in the interpretation of abnormalities. Patients with hospital-acquired pneumonia were also excluded.

Definition of terms and variable management

Pneumonia

The diagnosis of pneumonia was defined at the time of data collection and based on the WHO clinical criteria [22] and on the Brazilian Guidelines on Community-Acquired Pneumonia in Pediatric Medicine [1]. The presence of pneumonia was established clinically as a history of coughing and tachypnea at clinical examination in accordance with the established parameters for age (≥ 60 breaths per minutein children under two months old; ≥ 50 breaths per minutein children aged 2 months to 1 year; and ≥ 40 breaths per minutein those aged from 1 to 4 years). Severe pneumonia was defined as the presence of the criteria for pneumonia together with lower chest wall indrawing or stridor,while very severe pneumonia was defined as inability to drink, very difficult breathing and central cyanosisin addition to the criteria for severe pneumonia. Pneumonia was considered complicated when pleural effusion, atelectasis, pneumothorax, pneumatocele or abscesses were present or when the patient progressed with other conditionsresulting from pneumonia such as shock or respiratory failure [23].

Radiological variables

The radiological variables were defined in accordance with the WHO standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children [4], as follows:

Consolidation: Especially dense, often homogeneous, confluent alveolar infiltrate sometimes may encompass an entire lobe or large segment, fluffy, mass-like, cloud-like density, erases heart and diaphragm borders (silhouette sign); often contains air bronchograms.

Interstitial infiltrate: Includes peribronchial thickening and tiny areas of atelectasis (thought to be typical of viral infection).

Alveolar infiltrate: Alveoli filled with fluid (pus, edema, etc.).

*Pleural effusion:*Fluid collecting in the pleural space around the lung, seen as a dense rim (the same density as the chest-wall muscles) interposed between the lung and the ribs.

The endpoints for the diagnosis of pneumonia are: the presence of consolidation, pleural effusion or alveolar infiltrate. Non-endpoint: Other infiltrates (interstitial), with peribronchial thickening and areas of atelectasis.

Data collection instrument

The patients'sociodemographic data were collected: sex, age, number of individuals living in the family home(to assess household crowding), whether the child attended a day-care center, whether there were any smokers in the household, and the mother's age and education level. Data on the patient's clinical history included: birthweight, prematurity and whether breastfed. The variables regarding diagnosis and outcome were: the classification of pneumonia, the presence of complication (pleural effusion requiring pleural fluid drainage, pneumatocele, pneumothorax, necrotizing pneumonia or sepsis), need for the patient to be transferred to the ICU, and death.

Each observer was given a questionnaire containing objective questions on the presence or absence of the following findings: consolidation, interstitial or alveolar infiltrate and pleural effusion.

Data processing and analysis

The Statistical Package for the Social Sciences, version 20.0, was the software used to calculatethe absolute and relative frequencies of the variables on a nominal or ordinal scale, and to calculate contingency and inference.The chi-square test or Fisher's exact test and Student's t-test were used as appropriate. Significance level was established at $p<0.05$.

Cohen's kappa coefficient was used to analyze agreement in accordance with its standard interpretation. The reference indicators proposed by Landis and Koch were used, as follows: <0.0 = poor agreement; 0.0-0.20 = slight agreement; 0.21-0.40 = fair agreement; 0.41-0.60 = moderate agreement; 0.61-0.80 = substantial agreement; 0.81-1.0 = almost perfect agreement [14].

Ethical aspects

In compliance with the Brazilian National Health Council's Resolution 196 of 1996and its amended Resolution 466 of2012, the original study protocol was approved by the internal review board of the *Instituto de Medicina Integral Prof. Fernando Figueira*under reference number 1860,CAAE 0128.0.099.000-10, on August 31, 2010.Agreement to participate in the study was obtained from the patients' parents or guardians, who signed an informed consent form.

Results

Of the 452 children included in the study, 51.8% were male and 26.8% were under six months old. Approximately half the families earned one minimum salary or less, and 97% of the children did not attend a day-care center. In 30.1% of the cases, the patient lived in a home in which someone smoked. Of the smokers,76.4% smoked over 20 cigarettes a day. Most of the mothers (61.6%) had failed to complete elementary school (Table 1).

Table 2 showsthe patients' clinical history, revealing that only 49.6% of the patients were breastfed exclusively for 4-6 months. The diagnosis for 81.4% of the childrenwas severe pneumonia, and 22.6% were considered to have complicated pneumonia.In3.8% of the cases, transferal to the ICU was required, whiledeath was the outcome in 1.5% of the cases (Table 3).

The best inter-observer agreement was with respect to pleural effusion, with a kappa of 0.82, indicative of almost perfect agreement. The poorest agreement was for alveolar or interstitial infiltrate, with a kappa of 0.533, indicating moderate agreement. Consolidation was the most commonly diagnosed abnormality, foundon 67.1% of x-rays,with a kappa coefficient of 0.69for this finding(Table 4).

Discussion

There wasa slight predominance of males in the study sample. For some diseases, the higher frequency of males can be explained by the better Th1 response in girls; however, there is no consensus in the literature with respect to sex as a risk factor for pneumonia [24,25]. In agreement with other published studies, most of the children in the present sample wereunder two years of age. Children in thisage group are ata greater risk of pneumonia because their airways are narrower and their immune systems immature [21,26].

Most of the study population had a family income of one minimum salary or less, reflecting the association between poverty and pneumonia, with a greater frequency of the disease having been reported in populations with poorer socioeconomic conditions and more difficult access to the healthcare system [21,27,28]. Additionally, most of the mothers had failed to complete elementary school, a factor that is associated with increased morbidity and mortality from pneumonia in infancy [26].

The presence of smokers in the child's home represents an important risk factor [21,29] that was present in a third of this sample population. Half the children had beenbreastfed exclusivelyand this factorhas beenassociated with milder forms of pneumonia and a lower risk of death [30].

Complications are reported to occur in 30% of children hospitalized with CAP, with the most common clinical complication being pleural effusion [23]. Several studies have found an increase in the severity of pneumonia in recent years, with more complications being registered [23,31,32].

Comparison of the radiography findings showed a reasonable degree of inter-observer agreement for findings consistent with pneumonia when the standardized interpretation criteria were applied. In line with the results of other studies, agreement was highest for pleural effusion, showing a high degree of reliability in the inter-observer evaluation [8,33]. In the radiological interpretation of effusion, certain data are particularly relevant: the extent of the effusion, which could obstruct the costophrenic angles, an increase in the distance from the gastric air bubble to the base of the lung, or even completelyopacified hemithorax with deviation of the mediastinum. Another factor that should be taken into consideration is the patient's position, whether orthostatic or decubitus [34].

The kappa statistic, used to measure inter-observer reliability, is based on the difference between actual (observed) agreement and what would be expected to occur merely by chance (expected agreement). However, its results are affected by the prevalence of the findings in question, i.e. it may not be appropriate to compare kappa coefficients between different studies or populations [14].

Inter-observer agreementregarding the presence of interstitial or alveolar infiltrate was considered moderate;however,it was poorerfor this finding than for any of the other abnormalities present. This problem is compounded by the poor reliability of radiography for the detection of interstitial infiltrate, with data in the literature confirmingthe poor level of agreement for this finding [9,33]. Conversely, agreement has beenfound to be high for alveolar infiltrate alone [9,15].

A major criticism of the WHO standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children is that having been designed based specifically on epidemiological studies conducted to validatethe effectiveness of vaccines,it would need to be amplified to be suitable for studies conducted in clinical settings [16,35].

The kappa coefficient values found in the present study are higher than those described in other previous studies on pneumonia in children [8,9,33]. This can be explained as a function of observer experience in a pediatric referral center, even considering that one of the observers was a second-year resident. Another possible explanation concerns the smaller proportion of radiographic abnormalities found in previous studies [15,16]. Because in this department radiography is indicated only for cases of severe or complicated pneumonia, radiographic findings may tend to be more obvious, reflecting the greater percentage of more severe cases.

One of the strongpoints of the present study was the number of patients in the sample. However, having only two observers represents a limiting factor compared to other studies [8,9,15,16].

From a practical viewpoint, a finding of pleural effusion would provide the physician with greater certainty when making a diagnosis, whereas a finding of infiltrate would lead him/her to reflect further on clinical data that may deserve greater attention. Analysis of the radiographic abnormalities for which inter-observer agreement was poorer may serve to encouragenew and more precise methods to be developed.

Conclusion

Good inter-observer agreement was found for pleural effusion (almost perfect agreement), consolidation (substantial agreement) and alveolar/interstitial infiltrate (moderate agreement). Infiltrate was the diagnosis with the poorest inter-observer agreement, while agreement was highest in cases of pleural effusion.

Compliance with Ethical Standards

Funding: None.

Disclosure of potential conflicts of interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in this study were inaccordance with the ethical standards of the institutional andnational research committeesand with the 1964 Helsinki declaration and its later amendments.

Informed consent: Informed consent was obtained from the parents or guardians of all individual participants included inthe study.

Tables

Table 1: Sociodemographic characteristicsof the 452 children hospitalized due to community-acquired pneumonia. IMIP, Recife, Pernambuco, Brazil. October 2010 to September 2013.

Sociodemographic Characteristics	n	%
Sex		
Male	234	51.8
Female	218	48.2
Age (months)		
< 6	121	26.8
6 - 12	66	14.6
12 - 24	127	28.1
> 24	138	30.5
Household crowding		

Sociodemographic Characteristics	n	%
Yes	118	26.8
No	322	73.2
Family income		
≤ 1 minimum salary	224	49.5
> 1 minimum salary	177	39.2
Data missing	51	11.3
Attends a day-care center		
Yes	14	3.0
No	438	97.0
Smoker in the household		
No	312	69.9
Yes	140	30.1
< 20 cigarettes/day	47	23.6
> 20 cigarettes/day	93	76.4
Mother's age		
< 19 years	42	9.4
≥ 19 years	410	90.6
Mother's education level		
< 11 years of schooling	270	61.6
≥ 11 years of schooling (elementary school)	182	38.4

Table 2: Clinical history of the 452 children hospitalized due to community-acquired pneumonia. IMIP, Recife, Pernambuco, Brazil. October 2010 to September 2013.

Clinical History	n	%
Birthweight		
< 2,500 g	47	11.3

≥ 2,500 g	405	88.7
Prematurity		
Yes	36	8.5
No	416	91.5
Breastfed		
Never breastfed	32	7.0
Non-exclusive breastfeeding from birth	196	43.4
Exclusive breastfeeding (for 4-6 months)	224	49.6

Table 3: Diagnosis and outcome for the 452 children hospitalized due to community-acquired pneumonia. IMIP, Recife, Pernambuco, Brazil. October 2010 to September 2013.

Diagnosis and outcome	n	%
Classification of pneumonia		
Pneumonia	73	16.2
Severe pneumonia	368	81.4
Very severe pneumonia	11	2.4
Complicated pneumonia		
Yes	102	22.6
No	350	77.4
Transferred to the intensive care unit		
Yes	17	3.8
No	435	96.2
Death		
Yes	7	1.5
No	445	98.5

Table 4: Agreement between radiologists for each radiological finding in the 452 children hospitalized due to community-acquired pneumonia. IMIP, Recife, Pernambuco, Brazil. October 2010 to September 2013.

Radiological Finding		Radiologist 2		Total, n (%)	*Kappa*
	Radiologist 1	Yes	No		
Consolidation	Yes	273	15	288 (63.0)	0.696
	No	46	118	164 (37.0)	
	Total	319 (70.6)	133 (29.4)	452	
Interstitial or alveolar infiltrate	Yes	115	61	176 (38.9)	0.533
	No	37	239	276 (61.1)	
	Total	152 (33.6)	300 (66.4)	452	
Pleural effusion	Yes	125	14	139 (30.8)	0.825
	No	20	293	313 (69.2)	
	Total	145 (32.1)	307 (67.9)	452	

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