WHAT TO LOOK FOR IN CHEST X-RAYS OF PEDIATRIC PATIENTS WITH COVID-19: INSIGHTS FROM A COLOMBIAN COHORT.

Melisa Sofía Naranjo Vanegas[1], Claudia Burgos[2], Laura Melissa Mendez[2], María Margarita Rodriguez[2], Arianna Martinez[2], Paola Sanchez[2], Carolina Tovar[2], Pablo Vasquez-Hoyos[3], María Lucia Mesa-Rubio[2], Gustavo Triana[2], Mónica Royero-Arias[4], Jessica Echeverry[5], Tamara Gamo[5], Luz Ángela Moreno[4], Olga Lucía Baquero Castañeda[5], Sonia Restrepo-Gualteros[2], Sergio Moreno-Lopez[1], Clara Galvis[6], CINTA MORALEDA[7], ALFREDO TAGARRO[7], Andrea Ramirez[1], Gabriela Friedrich[8], Luz Marina Mejía[9], Luis Miguel Navarro Ramirez[8], Juan Gabriel Piñeros[10], Carlos Alvarez-Moreno[11], Alejandro Díaz-Díaz[12], Iván Gutierrez-Tobar[13], José Manuel Nieto[14], and Irati Gastegi[15]

[1]Universidad de los Andes Facultad de Medicina
[2]Hospital Universitario de la Fundacion Santa Fe de Bogota
[3]Red colaborativa pediátrica de Latinoamérica (LaRed Network
[4]Fundacion HOMI Hospital de la Misericordia
[5]Clinica Infantil Colsubsidio
[6]Hospital Militar Central
[7]Hospital Universitario 12 de Octubre Centro de Investigacion Biomedica
[8]Universidad de los Andes Facultad de Medicina Santiago, CL
[9]Instituto de Ortopedia Infantil Roosevelt Bogota, CO 110001
[10]Hospital Universitario de la Fundacion Santa Fe de Bogota Bogota, CO
[11]Universidad Nacional de Colombia
[12] Hospital Pablo Tobon Uribe Medellin, CO
[13]Clinica Colsanitas SA Bogota, CO 111176
[14]Hospital Regional de la Orinoquía Yopal, CO
[15]Hospital Universitario 12 de Octubre Centro de Investigacion Biomedica Madrid, ES 28041

September 20, 2023

Abstract

Background: Despite advancements in vaccination and the transition from pandemic to endemic, SARS-CoV-2 continues to pose a medical challenge, particularly among children. In this context, imaging diagnostics, such as chest x-rays, are crucial to the initial treatment of patients. This study aims to characterize the radiological findings in pediatric patients with confirmed SARS-CoV-2 infection in Colombia between April 2020 and November 2021, as well as their potential association with intensive care admission. **Methods:** In Colombia, a multicenter cohort comprised patients aged 29 days to 17 years with confirmed SARS-CoV-2 infection and chest X-ray administered within 72 hours of hospitalization. In two separate groups, four radiologists evaluated the images. A fifth radiologist reviewed all the X-rays; and subsequently, these readings were used to calculate the kappa coefficient and to resolve discrepancies among the other radiologists. The results were compared to admission to intensive care. **Results:** Analysis was conducted on 392 patients with a mean age of 2 years, the majority of whom (42%) were infants. Sixty-eight percent of the radiographs had normal results. Peribronchial thickening and interstitial opacity were the most common aberrant findings (59%), followed by alveolar opacity (12%). 88 percent of findings were bilateral. The most common association between peribronchial thickening and intensive care admission was ventilatory failure. Interobserver agreement was low for peribronchial thickening (kappa = 0.1), but higher for consolidations and alveolar opacities (kappa = 0.4 and 0.5, respectively). **Conclusion:** In pediatric patients with SARS-CoV-2, radiological findings are nonspecific and interobserver agreement is minimal. Although consolidation and alveolar opacities demonstrated greater concordance, they were not associated with clinical differences; therefore, chest radiography is not considered useful for determining the severity of COVID-19 in children.

INTRODUCTION

Since 2013, COVID-19 has posed a challenge to the medical community worldwide. Since March of 2020, it began as a pandemic and is now in transition to its endemic phase . Despite all efforts and the introduction of vaccines, it still considered a significant public health concern because it has affected more than 760 million people and caused 6.8 million fatalities worldwide . In addition, infants and adolescents continue to account for 21% of the infected population . Given the supporting evidence for brief and long-term multisystemic complications of COVID-19 , early detection and treatment of this disease in pediatrics and related fields will continue to be essential. Thoracic diagnostic imaging has been an instrument for evaluation of patients with COVID-19 in context of respiratory disease. A growing number of adult and pediatric investigations have focused on describing findings on chest radiography (CXR) and computed tomography (CT) scans.

COVID-19 has been examined using CXR as a diagnostic tool. Current American College of Radiology guidelines, mention this imaging technique as first line for the diagnosis of pediatric patients with COVID-19 who have mild symptoms and comorbidities, or moderate to severe symptoms . Although medical literature characterizes CT scan for this disease mostly normal, when there is a finding the most common ones were glass ground and parabronchial opacities as well as consolidations. This imaging modality has been widely utilized for adult patients; however, it must be considered that the majority of pediatric patients were less likely to have positive chest CT results . In addition, CT is utilized less frequently than CXR due to the elevated risks associated with sedation (when necessary) and the long-term carcinogenic risk for pediatric patients posed by exposure to ionizing radiation .

A group of experts issued a consensus statement on the imaging manifestations of COVID-19 in the pediatric population in 2020, categorizing findings as typical, indeterminate, atypical, and negative . In addition, other pediatric and radiology specialists have attempted to address other general imaging findings in CXR , such as characteristics focusing on zonal predominance , their relationship with specific complications, such as multisystem inflammatory syndrome in children (MIS-C) and even the use of ultrasound (US) and artificial intelligence as alternative tools. Even though there is substantial evidence from studies in the adult population, there is less evidence from studies and smaller sample sizes in the pediatric population.

However, it is essential to recognize that the reported low concordance of radiographic findings in patients with lower respiratory disease is a potential limitation of radiology. This limitation may impact the accuracy and dependability of radiologists 'interpretations of COVID-19 in pediatric patients. This limitation must be addressed and comprehended in order to ensure the correct application and interpretation of radiological findings in clinical practice.

This study´s primary objective is to characterize the radiological findings in pediatric in-patients with confirmed SARS-CoV2 infection in Colombia between March 2020 and November 2021, with a focus on their relationship to clinical presentation, treatment, and outcomes. In addition, as a secondary objective, we intend to assess the concordance of these radiological findings among radiologists in order to ascertain their true impact on clinical practice.

METHODOLOGY

Study design and settings

This study is part of a multicenter cohort study from Colombia and Spain, called EPICO (Epidemiological study of respiratory infections caused by SARS-CoV-2 infection in pediatric population). This cohort´s results included data collected between April 2020 and November 2021 from 13 institutions in Colombia (distributed in 5 cities) and 55 institutions in Spain (distributed in 13 provinces). From this cohort, a subsample of Colombian children was selected to examine the association between radiology findings (chest x-rays) and clinical presentation, treatment, and outcomes throughout their hospital course. After excluding institutions in which remote visualization of chest radiographs in a PACS (Picture Archiving Communication System) program was unavailable, a total of 7 hospitals were included. Most of these hospitals (6 out of 7) were located in Bogotá, and all of them were private institutions providing fourth level of care.

Participants

Children (ages 29 days to 17 years) with confirmed COVID-19 infection prior to or during hospitalization (PCR, antigen, or IgG/IgM+) who underwent chest X-ray between admission and 72 hours after hospitalization were included in this sample. Chronic lung disease with possible confounding radiological findings (bronchiolitis obliterans, bronchopulmonary dysplasia, ciliary dyskinesia, tuberculosis, cystic fibrosis, congenital pulmonary malformations, intestinal disease, among others) was among the exclusion criteria. Also, chest-radiographs that could not be retrieved from the PACS system (Picture Achieving communication system) or that could not be found, were excluded from the reading list. For more information about data analysis X-ray selection flowchart, please see supplementary appendix 1.

Variables

Investigators and pediatric specialists from each institution reviewed electronic health records to compile data. Variables were chosen to describe demographic characteristics, comorbidities, signs and symptoms upon admission, laboratory and imaging, and disease core variables (severe clinical manifestation, treatment, and outcomes). These variables were recorded in REDcap (electronic data capture system) and variables regarding clinical presentation, treatment and outcomes and radiological findings were recategorized for the analysis (Figure 1).

[INSERT FIGURE 1 ABOUT HERE]

Radiological Findings

To define clinically relevant categories for describing X-ray findings, we conducted a rapid literature review in PubMed, Web of Science, Cochrane, and Scopus databases. Medical subject heading terms (MESH-term) were used for the search, and only articles in Spanish or English were included. Three pairs of authors carefully reviewed all selected publications.

Based on the insights gathered from the literature review, a group consisting of pediatricians, epidemiologists, and radiologists collaborated to develop patterns of radiological findings (as depicted in Figure 2). The categories for these radiological findings were established using the definitions provided in the Glossary of terms for chest imaging suggested by the Fleischner Society and the International Expert Consensus Statement on Chest Imaging in Pediatric COVID-19 Patient Management .

[INSERT FIGURE 2 ABOUT HERE]

A comprehensive database was constructed for the study, and the radiologists' performed evaluations on various aspects of the chest X-rays. Specifically, they assessed the presence or absence of interstitial or focal opacities, the distribution and affection of the lungs, as well as the presence of any complications related to COVID-19, such as pleural effusion or consolidations.

The initial group consisted of four radiologists with varying clinical experience. Their experience as radiologists ranged from 8 to 22 years, while their experience as pediatric radiologists ranged from 5 to 22 years. To ensure an unbiased evaluation, this group was divided into two subgroups, and half of the X-ray images were randomly assigned to each subgroup for assessment. In addition to the initial group, an additional radiologist with 30 years of experience independently reviewed all the X-ray images and was considered the gold standard for the study. This expert's evaluation served as a reference for comparison with the assessments made by the initial group of radiologists.

In order to maintain consistency and establish a standardized interpretation, the images were categorized according to their level of quality, dividing them into three groups: "excellent", "optimal" and "suboptimal" quality. These categories were defined based on previously agreed criteria supported by the literature, specifically the European Commission guidelines on quality criteria for diagnostic radiographic image . In performing the classification, several technical aspects were considered, including image alignment and rotation, adequate penetration, correct anatomical coverage and the presence of motion artifacts. A chest radiograph that complied with all the technical aspects was classified as "excellent quality"; if it showed an alteration in at least one of the characteristics, it was classified as "optimal"; and if it showed more than two alterations, it was designated as "suboptimal".

This standardization ensured that the quality of the images did not impact the accuracy of the radiological interpretations. Here are some examples (Figure 3) of X-ray classifications to provide visual representations of the radiological findings and classifications.

[INSERT FIGURE 3 ABOUT HERE]

Data analysis

In order to assess the inter-observer agreement, we calculated the kappa coefficient weekly for the interpretation of alveolar pattern, which is known for its use as a standard tool for inter-observer agreement according to literature. The Fleiss Kappa was used to assess the inter-observer agreement of the chest X-rays findings between three raters. Subsequently, we compared each radiologist's findings with those of the gold standard radiologist using Cohen's Kappa to identify the radiologist with the least agreement with the gold standard. Descriptive analysis of the variables, including radiological findings and relevant clinical variables, was performed using frequencies and measures of central tendency and dispersion. To explore potential associations between radiological findings and clinical variables, we conducted bivariate analysis using Pearson Chi-Square test, Fisher's exact test, or Kruskal-Wallis rank sum test, as appropriate based on the type of data. All analyses were performed in R.

RESULTS

Demographics and clinical data

A total of 392 radiographs were included in the study, representing patients who met inclusion criteria for the study from March 2020 to November 2021. Age range was between 1 month and 18 years, with a median age of 2 years old. Toddlers was the predominant age group (42%). Gender was distributed 53% male and 47% female. Regarding readmission, it was observed in 10% of the cases. Additionally, the presence of comorbidities such as asthma, malnutrition, and malignant neoplasms was documented. More than half of the patient had fever for more than 3 days, cough and runny nose. Codetection was assessed, revealing bacterial-viral infections in 17% (9/392) of cases, and viral-viral infections in 83% (43/329) of cases. The most frequently isolated viruses were Syncytial Respiratory Virus, Influenza A and B, Adenovirus, and Rhinovirus. General demographic data and clinical characteristics regarding evolution, treatment and outcomes are shown in Table 1.

[INSERT TABLE 1 ABOUT HERE]

Interobserver concordance

The results of the Fleiss kappa assessed for alveolar pattern yielded a value of 0.421 for the first group and 0.49 for the second group, which represents a moderate agreement. The highest Cohen kappa values were 0.524 within group 1 and 0.44 within group 2, both corresponding to alveolar opacities. For more information about Fleiss Kappa and Cohen Kappa values please see supplementary appendix 2.

Quality and radiological findings

The radiological patterns, summarized in Table 3, revealed that almost half of the chest x-rays (47%) were classified as high quality, 35% were categorized as medium quality, and 16% were considered low quality. Additionally, nearly one-third of the chest x-rays (31%) were interpreted as normal. The most frequently encountered findings were peribronchial thickening and interstitial opacities, each occurring in 59% of the cases. Alveolar opacities followed as the next most frequent, found in 12% of the patients, consolidation in sixteen patients and eight patients exhibited pleural effusion. The most frequent location was bilateral, and distribution was mainly central.

[INSERT TABLE 2 ABOUT HERE]

Clinical presentation, treatment, and outcomes

In Toddlers and preschoolers, the frequency of peribronchial thickening and interstitial opacities was higher than in the other age groups. Regarding to clinical findings, patients that presented with fever for more than 3 days did not have a predominant radiological pattern. When comparing the group with SARS-CoV-2 alone to the group with codetection, there was a significant difference in the frequency of peribronchial thickening and interstitial opacities (56% versus 79%, respectively p= 0.002). On the other hand, virus-virus isolation showed a higher frequency of peribronchial thickening and interstitial opacities compared to virus-bacteria isolation. Furthermore, there was not difference in consolidation pattern between different isolation groups ($p > 0.9$). (Table 3)

[INSERT TABLE 3 ABOUT HERE]

When treatment was assessed, it was observed that among the 126 patients who received antibiotic therapy, only 8.1% exhibited a consolidation pattern, which was significantly higher than the frequency observed in the group that did not receive antibiotics (1.9%) (P=0.02). Antibiotic treatment was given to eleven of the sixteen patients (69%) that had a consolidation pattern. Conversely, there was no significant difference in the radiograph findings between patients who received corticosteroids and those who did not.

Out of 267 patients on oxygen therapy, 25% had normal chest x-rays, compared to 45% of the 125 patients who did not receive oxygen therapy. The requirement of oxygen was not associated with a different pattern in the chest x-ray. However, patients presenting with respiratory failure had higher (32%) of alveolar opacities in comparison to patients that did not present respiratory failure.

Location of radiological findings did not have a variation in frequency among different outcomes assessed. Nevertheless, difusse distribution had a higher frequency in patients with ventilatory failure (37%). Patients admitted to PICU had lower percentage of normal radiological results compared to those in standard care. From the ones that had abnormal radiological findings, peribronchial thickening was the most common pattern. There was not a significant difference of radiological pattern in relation to the duration of stay in the PICU as well as in standard care.

Mortality was observed in 11 patients, with alveolar opacities being the most common finding at 45%, followed by peribronchial thickening at 36%. Meanwhile, among the group of patients who survived, predominant pattern was peribronchial thickening followed by normal pattern was found in 32%.

DISCUSSIONTo our knowledge, compared to other studies conducted in Colombia regarding this topic, this study involves a greater number of patients. Our findings shed light on key aspects related to patient demographics and clinical features, as well as the interobserver agreement among radiologists in interpreting the radiographs. In contrast to previous studies, different populations reported average ages ranging from 5 to 7 years (27)(28). We found that the median age of our patients was 2 years old. However, our clinical characteristics, including main symptoms, microorganism codetection, hospitalization days, and admission to pediatric intensive care units (PICU), were in line with other studies conducted in Colombia and internationally

Regarding the interobserver agreement, we found a moderate kappa coefficient for alveolar opacities. Previous studies have indicated that interobserver variability may be influenced by the level of expertise, lack of precise definitions for findings other than consolidation, and occasionally the quality of the image . Interestingly, we observed that the quality of the image did not significantly impact kappa's value in our study, which is an essential consideration for future interpretations.

Alveolar opacities emerged as the category with the best interobserver concordance in our study. This finding contrasts with the study developed by Ugas-Charcape et al., where peribronchial thickening showed the highest interobserver agreement

In our cohort, we also identified peribronchial thickening as the most common radiological finding, in line with previous studies . Interestingly, we did not observe a significant association between oxygen requirement and specific radiological findings, which contrasts with the study by Mania et al., where interstitial and/or ground-glass opacities were more frequent in patients receiving oxygen therapy . This can be explained by considering that, in the aforementioned study, the average age is higher than that of this group, this difference in age could account for the observed radiological findings lacking specificity. Presumably, older children may exhibit patterns akin to those established as typical in adults, such as ground glass opacities.

Regarding the location of radiological findings, we did not find significant variation among assessed outcomes. However, central distribution was more frequent in patients with ventilatory failure. A descriptive study by Oterino Serrano et al. in 2020, evaluating chest tomography and X-ray findings, reported that unfavorable outcomes were more common with extensive involvement, characterized by peribronchial thickening, ground-glass opacities, and bilateral or diffuse consolidation . While our study did not provide a specific definition for unfavorable outcomes, it is important to consider these radiological patterns in the context of clinical assessment.

In our cohort, peribronchial thickening was the most common radiological pattern and was associated with admission to PICU, antibiotic prescription, isolated viral or bacterial detection, and a fever lasting more than three days. Although this finding is nonspecific, fever has consistently been reported as the most frequently observed symptom in different studies .

A noteworthy finding in our cohort of patients who died was the higher occurrence of alveolar opacities as the main pattern on their chest x-rays. While there is limited literature that directly relates these variables, a retrospective cohort study with 110 patients MIS-C described diffuse bilateral coalescent opacities observed in three patients admitted to the intensive care unit with severe respiratory distress, with one of these patients deteriorating on the fourth day of admission to the PICU. A similar pattern has been studied in adults, where it has been associated with mortality.Although the presence of this pattern does not necessarily imply a different treatment approach from the clinical indications, it may work as an alert to closely and strictly monitor the patient.

Limitations and strengths

Despite having employed strategies to reduce interpretational variations, including image classification based on quality, randomized assessment of radiographs, reviews by different professionals, and contrasting readings with radiologists of differing years of experience; we acknowledge certain limitations.

The study highlights a moderate to low interobserver agreement, possibly attributed to the lack of standardized definitions for radiological findings of pneumonia and inherent limitations in chest radiography specificity. It is noteworthy that certain x-ray images were excluded from the study due to variations in the quality and accessibility of chest radiographs across different hospitals.

Futures perspectives

The radiological findings in pediatric patients with COVID-19 infection can be nonspecific, and their correlation with the patient's outcome is difficult to establish. However, determining the role of radiography in the disease is inherent to each patient, and it can be used as a tool to provide a basis for assessing the disease status or establishing an alternative diagnosis .

The swift progress since the emergence of the disease makes it unclear how external factors, such as vaccine introduction, may influence radiological findings and clinical evolution. These findings can be used as a baseline for making comparisons with future studies developed post pandemic era .

CONCLUSION

Our study provides unique insights into the radiological characteristics of pediatric COVID-19 patients in Colombia. The demographic differences in our population contribute to varying radiological patterns. While alveolar opacities showed the best interobserver concordance, the radiological findings may not significantly predict clinical outcomes, treatment decisions, or disease progression. Therefore, the utility of chest radiography in hospitalized pediatric COVID-19 patients appears limited, emphasizing the need for comprehensive clinical evaluation in managing these cases.

Acknowledgments

We thank the entire EPICO-AEP, EPICO-Colombia and ORCHESTRA working groups for all the entire work. We also thank pediatric residents from the Pediatric Department at Universidad de los Andes that collaborate throughout the process.

Funding

This study was fund by the Pediatrics Department at the Universidad de los Andes and Fundación Santa Fe de Bogotá and Pan American Health Organization. The sponsors were not directly involved in the study, meaning that they had no role in the study design, data collection, and report writing.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval

The study was performed according to the Declaration of Helsinki of 1975 and the ethical standards of the local Ethics Committee. The Ethics committee of the Colombian institutions approved the study (protocols CCEI-12686-2020, CEIFUS 1852-20, CEIFUS 1853-20, CEIFUS 1851-20, CEIFUS 1903-20, CEISH 0629-2020, SDM-034-20). All these actions were carried out to comply with organic law 3/2018, of December 5, on the protection of personal data and guarantee of Digital Rights.

Competing interest

The authors declare they were no competing interests.

REFERENCES

TABLES AND FIGURES

Figure 1. Variables included in the analysis.

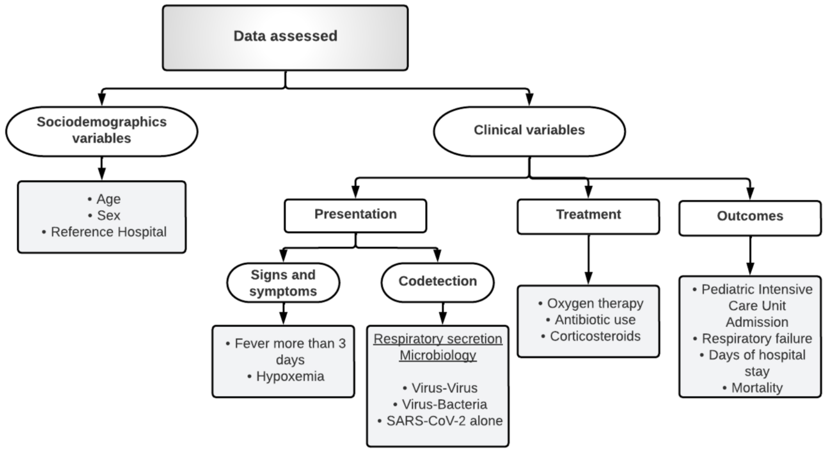


Figure 2. Variables Linked to Radiological Findings

Figure 2. Stepwise development of radiological classification format.

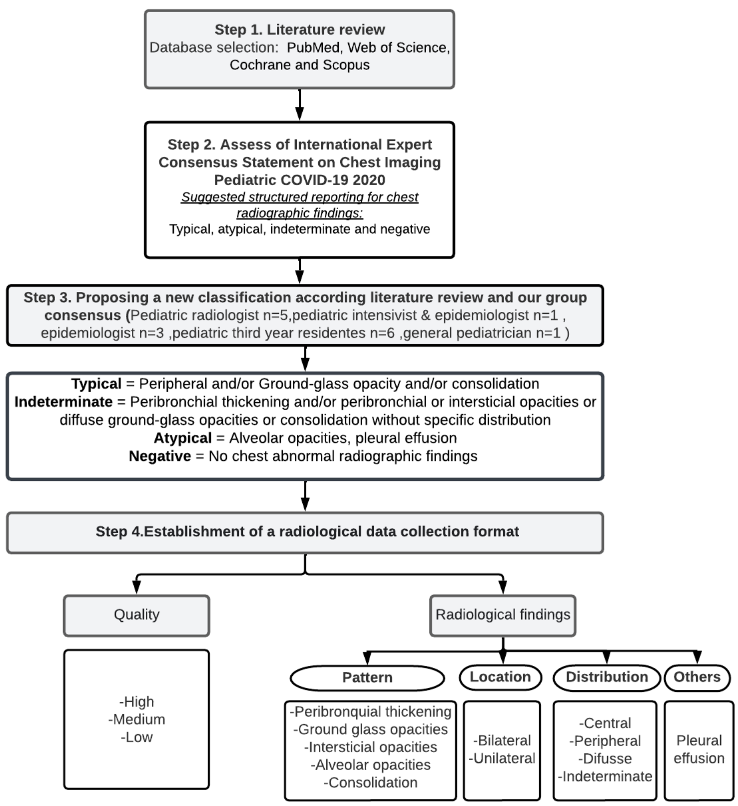


Figure 3. Stepwise development of radiological classification format

Figure 3. **A)** main pattern: alveolar opacities, unilateral location, undefined distribution. **B)** Main pattern:

Peribronchial thickening. One-sided location. central distribution.**C)** main pattern: ground glass opacities. One-sided location. Undefined distribution. **D)** main pattern: Consolidation. One-sided location. peripheral distribution. **E)** main pattern: interstitial opacities. bilateral-sided location. Central distribution.**F)** Other findings: right pleural effusion.

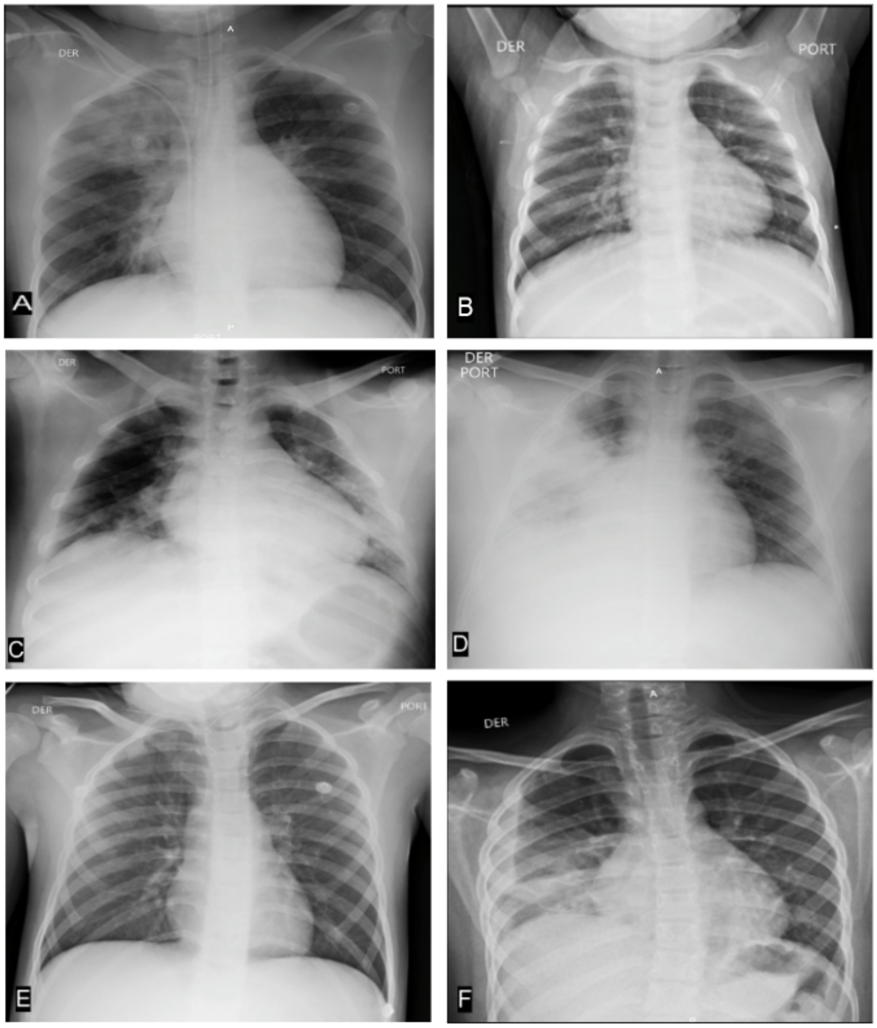


Table 1. Demographics and clinical characteristics of the study population

Table 1 Demographics and clinical characteristics of the study population

Finding	N= 392 (%)
Demographics, comorbidities	**Demographics, comorbidities**
Age in months, median (IQR)	27 (7, 126)
Sex	Sex
Female	183 (47)
Male	209 (53)
Chronic cardiac disease, including congenital heart disease (no hypertension)	0 (0)
Hypertension	1 (0.3)
Asthma (or recurrent wheezing)	47 (12)

Immunosupressors	8 (2.0)
Symptoms and labs	**Symptoms and labs**
Fever days >= 3	224 (57)
Oxygen saturation %, median (IQR)	391 -93.0 (90.0, 96.0)
Cough	264 (67)
Sorethroat	76 (19)
Runny nose	251 (64)
Wheezing	94 (24)
Chest pain	29 (7.4)
Myalgia	44 (11)
Jointpain	30 (7.7)
Fatigue	132 (34)
Dyspnea	162 (41)
C reactive protein mg/L, median (IQR)	7 (2, 34)
Procalcitonin ng/mL, median (IQR)	1 (0, 13)
PCR obtained for 16 viruses in respiratory secretion	59 (15)
Codetection	
Yes	52 (13)
No	260 (66)
Unknown due to lack of microbiological data	80 (20)
Codetecion type	
Virus-Bacteria	9 (17)
Virus-Virus	43 (83)
Unknown	340
Evolution	**Evolution**
Oxygen therapy	267 (68)
Oxygen therapy time in days, median (IQR)	4 (3, 7)
High-flow therapy	56 (14)
High-flow therapy time in days, median (IQR)	4 (2, 6)
PICU admission	89 (23)
PICU time in days, median (IQR)	5 (3, 8)
Mechanical ventilation	27 (30)
Non-invasive mechanical ventilation	5 (19)
Invasive mechanical ventilation	23 (85)
Complications	53 (14)
Pleural effusion	14 (26)
Effusion type	
Complicated (pH< 7 and/or partitions)	2 (14)
Not complicated	12 (86)
Pneumatocele abscess	1 (1.9)
Pneumothorax	3 (5.7)
Sepsis	20 (38)
Death	11 (2.8)

Table 2. Quality and radiological findings

Table 3 Quality and radiological findings

Variable	N= 392
Quality	
Excellent	186 (47.57%)

Optimal	66 (16.88%)
Suboptimal	139 (35.55)
Radiological Findings	
Peribronchial thickening	232 (59%)|
Ground-glass opacities	44 (11%)
Interstitial opacities	232 (59%)
Alveolar opacities	48 (12%)
Consolidation	16 (4.1%)
Localization	
Bilateral	237 (88%)
Unilateral	32 (12%)
Unknown	123
Distribution	
Central	226 (84%)
Difusse	19 (7.1%)
Undefined	3 (1.1%)
Peripheral	21 (7.8%)
Unknown	123
Pleural effusion	8 (2.0%)
Main pattern	
Consolidation	3 (1.1%)
Peribronchial thickening	214 (80%)
Ground-glass opacities	27 (10%)
Alveolar opacities	23 (8.6%)
Interstitial opacities	1 (0.4%)
Unknown	124

Table 3. Comparison of the different radiological patterns with clinical features, treatment and outcomes.

Table 4. Comparison of the different radiological patterns with clinical features, treatment and outcomes

Variable		Peribronchial thickening	Ground glass opacities	Interstitial opacities	Alveolar opacites	Consolidation	Pleural Effusion
Clinical features							
Fever for > 3 days N=224	Number (%)	126 (56%)	27 (12%)	126 (56%)	28 (12%)	9 (4%)	6 (2,7%)
	p value	*0.2*	*0.5*	*0.2*	*0.9*	*>0.9*	*1.5*
Codetection N=52	Number (%)	41 (79%)	6 (12%)	41 (79%)	7 (13%)	1 (1.9%)	1 (1.9%)
	p value	*0.002*	*>0.9*	*0.02*	*0.8*	*0.7*	*>0.9*
Leukocytosis N=306	Number (%)	166 (54%)	28 (27%)	166 (54%)	42 (14%)	12 (3.9%)	8 (2.97%)
	p value	*0.004*	*0.07*	*0.04*	*0.7*	*0.3*	*0.7*
Treatment							
Oxygen Therapy N=267	Number (%)	168 (63%)	36 (13%)	168 (63%)	42 (16%)	16 (6%)	8 (3%)
	p value	*0.028*	*0.031*	*0.028*	*0.002*	*0.005*	*0.059*
Antibiotics N=127	Number (%)	74 (58%)	15 (12%)	74 (58%)	24 (19%)	11 (8.7%)	6 (4.7%)
	p value	*0.8*	*0.8*	*0.8*	*0.005*	*0.002*	*0.016*
Corticosteroids N=136	Number (%)	84 (62%)	14 (10%)	84 (62%)	29 (21%)	10 (7.4%)	5 (3.7%)
	p value	*>0.4*	*0.7*	*0.4*	*<0.001*	*0.017*	*0.3*
Outcomes							
Hospital Stay	Number (%)	5 (4.7%)	7 (3.14%)	8 (8.8%)	5 (4.8%)	9 (7.1%)	-
	p value	0.08					
Ventilatory failure N=57	Number (%)	39 (68%)	11 (19%)	39 (68%)	18 (32%)	7 (12%)	4 (7.1%)
	p value	0.12	0.037	0.12	< 0.001	0.004	0.017
PICU Admission N=89	Number (%)	55 (62%)	16 (18%)	55 (62%)	17 (19%)	9 (10%)	5 (5.7%)
	p value	*0.6*	*0.022*	*0.6*	*0.025*	*0.003*	*0.016*
PICU Days of stay	Number (%)	6 (3.9%)	6 (4.15%)	4 (4.6%)	-	5 (5.5%)	-
	p value	*0.6*					
Mortality N=11	Number (%)	4 (36%)	3 (27%)	4 (36%)	5 (35%)	1 (9.1%)	1 (9.1%)
	p value	*0.13*	*0.11*	*0.13*	*0.06*	*0.4*	*0.2*

SUPPLEMENTARY APPENDIX

Supplementary appendix 1. Data analysis X-ray selection flowchart

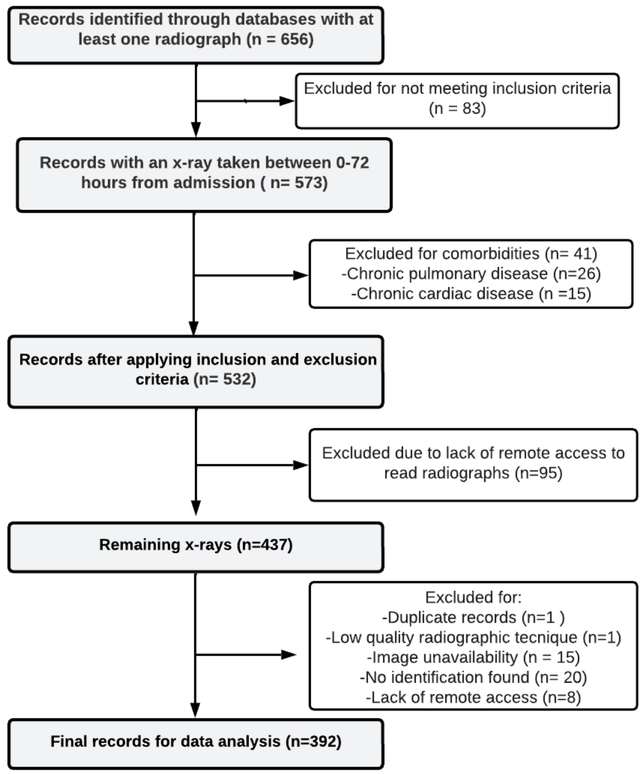


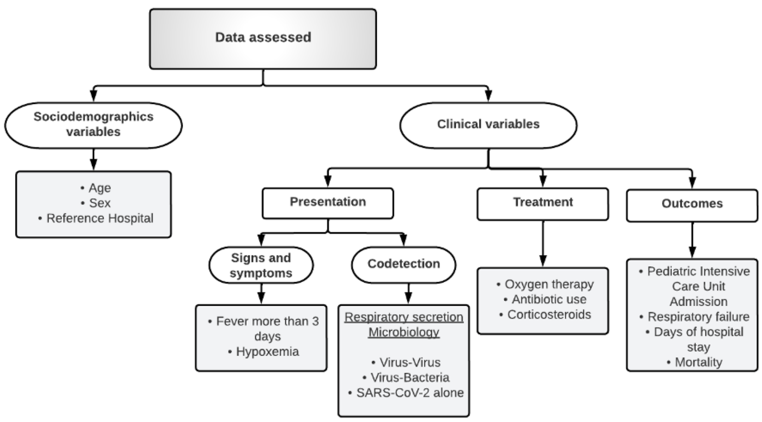
Figure 1. Process of x-ray selection for data analysis

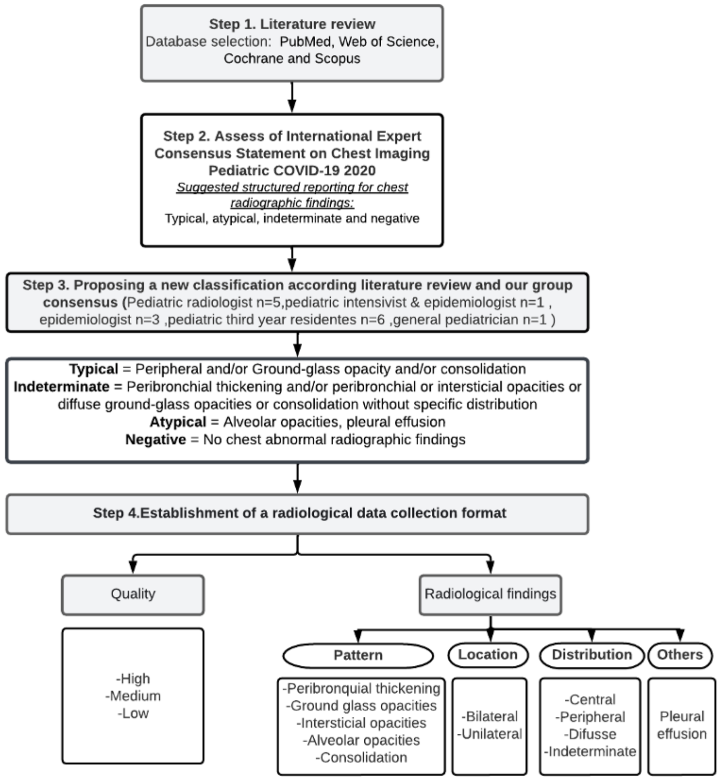
Supplementary appendix 2. Fleiss kappa and Cohen Kappa values.

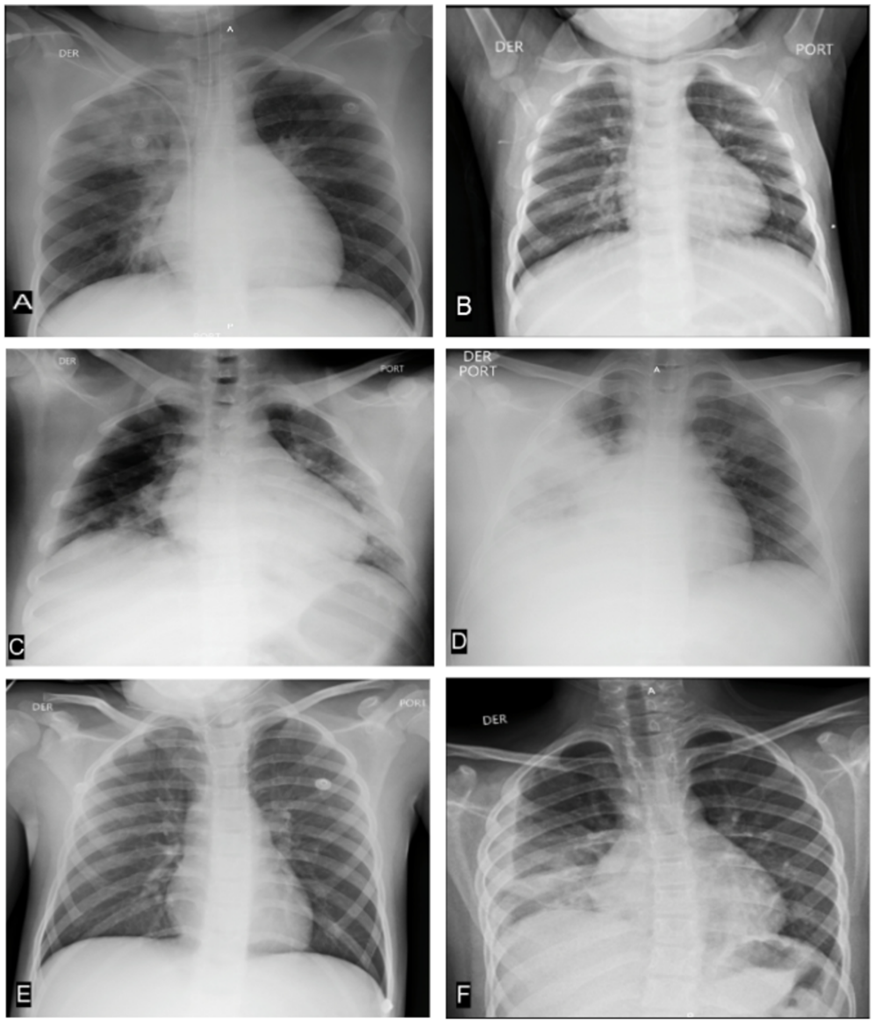
Inter-observer agreement

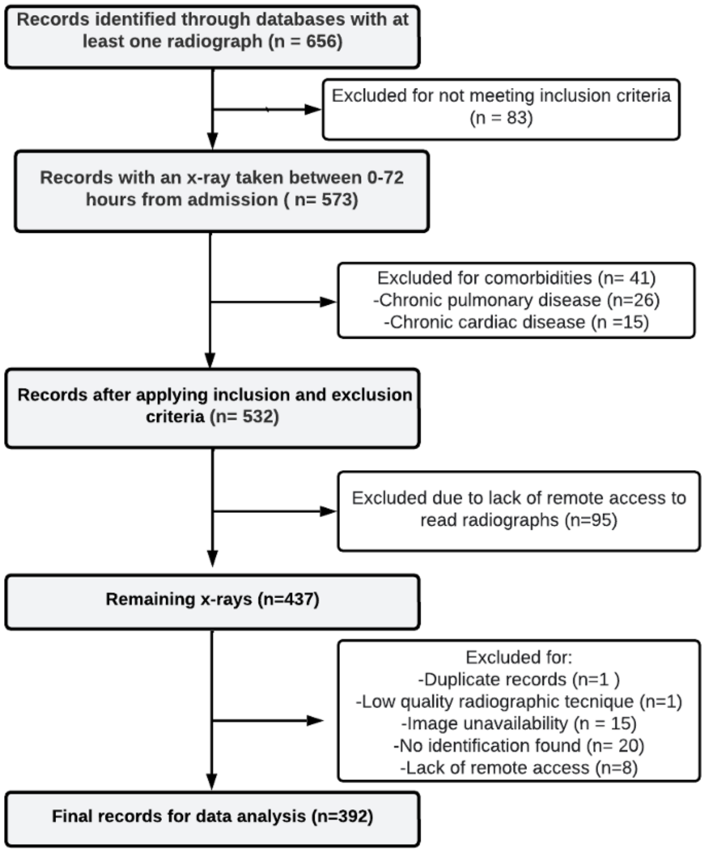
Variable	Group 1 Fleiss'Kappa coefficient All	Group 1 Cohen'Kappa coefficient Rater 1 vs Gold standard	Group 1 Cohen'Kappa coefficient Rater 2 vs Gold standard	Group 2 Fleiss'Kappa coefficient All	Group 2 Cohen'Kappa coefficient Rater 1 vs Gold standard	Group 2 Cohen'Kappa coefficient Rater 2 vs Gold standard
Peribronchial thickening	-0,0146	0,0601	0,165	0,247	0,296	0,291
Ground-glass opacities	0,174	0,308	0,147	0,301	0,265	0,316
Interstitial opacities	-0,0497	0,0355	0,047	0,307	0,172	0,383
Alveolar opacities	0,383	0,524	0,348	0,462	0,399	0,44
Consolidation	0,421	0,447	0,368	0,209	0,0896	0,146

Localization	0,245	0,0544	0,35	0,254	0,349	0,295
Distribution	0,115	0,235	0,109	0,18	0,114	0,303
Pleural effusion	0,318	0,234	0,235	0,507	0,444	0,384
Main pattern	0,0377	0,224	-0,00941	0,0103	0,0868	-0,012
Interstitial Subgroup	0,0444	0,0601	0,184	0,346	0,273	0,392
Alveolar Subgroup	0,421	0,504	0,373	0,497	0,502	0,413
Normal pattern	0,105	0,0152	0,278	0,405	0,372	0,496




Step 1. Literature review
Database selection: PubMed, Web of Science, Cochrane and Scopus
Step 2. Assess of International Expert Consensus Statement on Chest Imaging Pediatric COVID-19 2020
Suggested structured reporting for chest radiographic findings:
Typical, atypical, indeterminate and negative
Step 3. Proposing a new classification according literature review and our group consensus (Pediatric radiologist n=5,pediatric intensivist & epidemiologist n=1 , epidemiologist n=3 ,pediatric third year residentes n=6 ,general pediatrician n=1)
Typical = Peripheral and/or Ground-glass opacity and/or consolidation
Indeterminate = Peribronchial thickening and/or peribronchial or intersticial opacities or diffuse ground-glass opacities or consolidation without specific distribution
Atypical = Alveolar opacities, pleural effusion
Negative = No chest abnormal radiographic findings
Step 4.Establishment of a radiological data collection format
Quality
-High
-Medium
-Low
Radiological findings
Pattern
-Peribronquial thickening
-Ground glass opacities
-Intersticial opacities
-Alveolar opacities
-Consolidation
Location
-Bilateral
-Unilateral
Distribution
-Central
-Peripheral
-Difusse
-Indeterminate
Others
Pleural effusion


DER
A
DER
PORT
B
DER
PORT
C
DER
PORT
D
DER
PORT
E
DER
F



Hosted file

`tables.docx` available at https://authorea.com/users/666466/articles/667308-what-to-look-for-in-chest-x-rays-of-pediatric-patients-with-covid-19-insights-from-a-colombian-cohort