ORIGINAL ARTICLE

Pulmonary Imaging Findings of the Pediatric Novel Coronavirus Disease (COVID-19) in Two Tertiary Centers in the Philippines: A Local Experience

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ABSTRACT

Objective:
To describe the demographic and clinical profiles as well as the various pulmonary imaging findings of pediatric patients in St. Luke's Medical Center afflicted with SARS-CoV-2 infection (COVID-19)

Methods:
This descriptive, retrospective, cross-sectional study reviewed the hospital databases and pulmonary imaging studies of patients less than 19 years old who tested positive for SARS-CoV-2 infection based on viral RNA rt-PCR swab tests in St. Luke's Medical Center from March 1, 2020 to August 31, 2021.

Results:
A total of 196 patients were included in this study. The disease was most frequent in the adolescent age group (39%) with a slight male preponderance. Most common reported symptoms in decreasing order of frequency were cough, fever, and rhinorrhea. Leukocytosis and lymphopenia were the most common abnormal laboratory findings. 134 (68%) had normal chest radiograph findings. 62 patients (32%) were found to have abnormal radiographs with the most common showing bilateral ground-glass opacities.

Conclusion:
The majority of pediatric cases yielded normal chest radiograph findings and less extensive lung involvement, while those with abnormal radiographs most commonly showed bilateral ground-glass opacities. The results, along with the demographic and clinical profile in this population, are congruent with the findings in the literature. Through this study, further knowledge is gained on how the COVID-19 infection affects the pediatric population especially during the surge of cases in this time period. This also assesses the typical and atypical pulmonary imaging findings that radiologists and pediatricians should be aware of to ensure a prompt and accurate diagnosis.

Keywords: children, coronavirus infection, diagnostic imaging

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) emerged in Wuhan, Hubei province, China in December 2019, and was caused by a novel coronavirus, since named severe acute respiratory syndrome - coronavirus 2 (SARS-CoV-2) [1]. SARS-CoV-2 is the seventh member of enveloped RNA coronavirus besides coronavirus 229E, OC43, NL63, HKU1, SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV) [2]. It is a highly infective disease which has rapidly spread all over the world, affecting both adults and children. The World Health Organization (WHO) declared the outbreak a global health emergency on January 3, 2020 [3]. Since then, the disease affected more than 177 countries globally [4].

Initially considered to primarily affect the elderly especially those with comorbidities, the virus has undergone several mutations over the subsequent several months with emerging variants that have become endemic to certain countries. In the late 2020 to mid-2021, more pediatric patients have been found to have been infected by the virus. It resulted in a spectrum of manifestations ranging from mild upper respiratory tract infection to severe pneumonitis, acute respiratory distress syndrome (ARDS), septic shock and even death [5]. Fortunately, the disease predominantly occurs in the milder end of the spectrum, with fewer symptoms in children compared to the adult counterparts [6,7]. The clinical presentation is non-specific, with the most common presenting symptoms including fever, cough, nasal congestion, and rhinorrhea [8-12].

Although the diagnosis of COVID-19 is primarily based on reverse transcription - polymerase chain reaction (rt-PCR) assay swab tests, imaging modalities including chest x-ray (CXR) and computed tomography (CT) are also used to detect abnormal lung changes [13]. The imaging features are diverse, ranging from normal to diffuse changes [14]. Because the time between onset of symptoms and the development of ARDS can be as short as 9 days among initial patients with COVID-19 pneumonia [15], early recognition of the disease is essential for the management of these patients.

While more data are emerging, the clinical presentation and course of COVID-19 as well as imaging findings in Filipino children remain poorly characterized since most reports in the literature dealt with foreign patients [16–21]. Knowledge of the imaging findings of COVID-19 is helpful in early detection of the disease process. Given the non-specific clinical presentation, imaging studies are likely to play an important role in diagnostic work-up for affected pediatric patients, especially in children with other co-morbidities such as congenital heart, lung and airway disease, malnutrition and tumors among others, who are vulnerable to severe infection [22].

The purpose of this study is then to describe the demographic and clinical characteristics of pediatric patients with COVID-19, as well as to characterize the different imaging findings among these patients. Given that this pandemic has been happening since the end of 2019, it has been observed that more cases have affected more pediatric patients in 2021. This therefore emphasizes the need for continued data gathering about the disease and to learn about any possible trend changes in the Philippine setting. Continuing surveillance is vital so that radiologists become aware of the latest updates on specific imaging findings to look for, especially since this viral disease continues to evolve. More importantly, this will also broaden the comprehension on how this disease affects the local pediatric population, and at the same time compare these findings to the relevant information being gathered in other countries.

METHODS

This was a descriptive, retrospective, cross-sectional study among pediatric cases from March 1, 2020 to August 31, 2021 in two tertiary hospitals in the Philippines. All patients less than 19 years old who tested positive for SARS-CoV-2 infection using the viral RNA rt-PCR test and who underwent chest imaging studies in this institution during the specified time period were included. Convenience sampling was utilized in this study.

Demographic data such as age and gender, type of imaging study performed, presenting signs and symptoms, pertinent laboratory findings and presence of co-morbidities were extracted from the hospitals' HealthCare System and Radiology Information System – Picture Archiving and Communication System (RIS-PACS). Patients were categorized by age into the following: newborn (<1 month), infant to toddler (1 month to <2 years), preschool child (2 years to <6 years), middle school child (6 years to <13 years) and adolescent (13 years to <19 years). These age categories were based from integrated age groups developed by Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) [23]. Pertinent complete blood count (CBC) findings were also collected.

The chest imaging findings were reviewed independently by pediatric radiology fellows-in-training, and a fellowship-trained pediatric radiologist practicing for 15 years, and a consensus was made if there is a discrepancy. These radiographs were assessed for certain findings such as lung parenchymal opacities including consolidation or ground-glass opacities, interstitial lung involvement and for pleural involvement.

Patients with incomplete medical records and those with suboptimal imaging studies, i.e. taken in obliquity, with motion artifact, and those with poorly visualized lungs, were excluded.

Categorical variables which include patient's demographic data, clinical presentation, and imaging findings were reported as frequency and percentage of findings among the study. Age was also reported as mean, median and interquartile range.

RESULTS

A total of 196 pediatric patients satisfied the criteria and were included in the study. Patient age ranged from newborn to 18 years old, with a mean age of 10 years and median age of 9 years (interquartile range, 5-16 years). COVID-19 was most frequently seen in the adolescent age group (n = 76/196, 39%), and slightly more in boys than girls with a male-to-female ratio of 1.4:1 (Table 1).

Table 1. Demographics of the 196 patients included in this study

Demographics	Frequency (n)	Percentage (%)
Age Distribution*		
Newborn (<1 month)	6	3
Infant to Toddler (1 mo. to <2 years)	29	15
Preschool to child (2 to 6 years)	31	16
Middle School (6 to 13 years)	54	28
Adolescent (13 to < 19 years)	76	39
Gender		
Male	116	59
Female	80	41

* Modified from integrated age groups developed by Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) [23]

Of the 196 pediatric patients, nine (4.5%) were asymptomatic, seven of which had known exposure to confirmed COVID-19 infected individuals, while the two had no known exposure but with recent history of trauma (Table 2). All asymptomatic patients had unremarkable chest radiographic findings.

The most common presenting symptoms were cough (44%), fever (41%) and nasal congestion or rhinorrhea (18%) (Table 2). Other symptoms that were manifested included ageusia, dyspnea, anosmia, sore throat, abdominal pain, and few with diarrhea, skin rashes, and headache/myalgia. There were no emergency warning signs for COVID-19 infection detected in any of the patients, such as cyanosis, inability to wake up, and swelling of the distal extremities [24].

Majority of the patients had no known co-morbidities (168/196, or 86%). The co-morbidities found among these cases were respiratory diseases (4) such as atypical Mycoplasma pneumonia, asthma and concomitant influenza A pneumonia, malignancy (3), heart disease (3), and prematurity (1). Others included one case each of seizure disorder, laceration, multiple fractures, arthrogryposis, and neuroleptic malignant syndrome. Six (3%) patients had concomitant dengue fever, one of which had the severe type, while the rest (5) had the mild form with no warning signs. Another six (3%) patients presenting with abdominal pain were found to have acute appendicitis (3) and mesenteric lymphadenitis (3). Chronic kidney disease and chronic liver disease, which are postulated to increase the risk for severe COVID-19 infection in pediatric patients [4, 23], were not recorded in this study.

Complete blood count (CBC) test was performed in 135 of 196 patients (69%), wherein 59 cases (43%) yielded normal results. The most common abnormal CBC findings were leukocytosis (33), lymphopenia (32), anemia (18), leukopenia (14), thrombocytosis (10), and thrombocytopenia (9). One patient with a known hematologic malignancy showed severe anemia with leukocytosis, lymphocytosis, and atypical mononuclear cells.

Table 2. Presenting symptom of the 196 cases

Presenting Symptom	Frequency (n)	Percentage (%)
Cough	86	44
Fever	80	41
Nasal congestion or rhinorrhea	36	18
Ageusia	25	13
Shortness of breath	23	12
Anosmia	20	10
Sore throat	9	4.5
Abdominal pain	8	4
Diarrhea	4	2
Skin rash	4	2
Headache	2	1
Muscle ache	1	1
Decreased sensorium	1	1
Asymptomatic	9	4.5

CHEST X-RAY FINDINGS

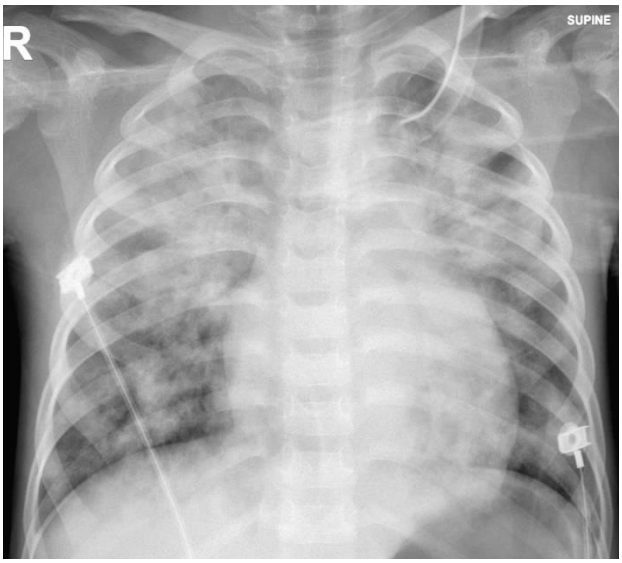
134 of 196 patients (68%) exhibited normal chest radiograph findings. The most frequent abnormal findings (Table 3) in decreasing order were bilateral ground-glass opacities (Fig. 1), subsegmental atelectasis or non-specific beginning pneumonia appearing as subtle haziness or linear opacities predominantly affecting one of the lower lobes (Fig. 2), air space consolidation or opacity, pulmonary hyperaeration, increased interstitial lung

markings with peribronchial cuffing, and minimal unilateral pleural effusion.

Table 3. Frequency of chest radiographic findings in the 196 patients

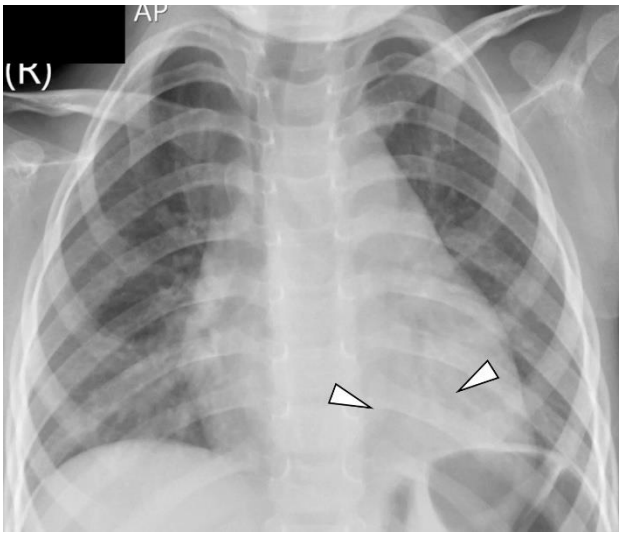
Findings	Frequency (n)	Percentage (%)
Bilateral ground-glass opacities	26	13
Subsegmental atelectasis or non-specific beginning pneumonia	17	9
a. Right upper lobe	2	1
b. Middle lobe	2	1
c. Right lower lobe	6	3
d. Left lower lobe	7	4
Air-space consolidation or opacity	9	5
a. Bilateral	4	2
b. Right lower lobe	3	1.5
c. Left lower lobe	2	1
Hyperaeration without focal opacities	6	3
Increased interstitial lung markings with peribronchial cuffing	3	2
Minimal pleural effusion, unilateral	2	1
Unremarkable	134	68

Fig. 1 A frontal view radiograph of a 5-year-old boy with known leukemia and COVID-19 shows ground-glass opacities and patchy consolidations in both lungs



Among the 62 patients (32%) with symptoms and positive chest radiographic findings, 21 were adolescents, 14 infants, 14 middle-school children, 10 preschool, and 3 neonates. 12 patients had progression of the imaging findings. In these cases, fifty patients (81%) showed subsequent resolution or did not have any follow-up radiographs done in this institution.

Fig. 2 Two-year-old girl with confirmed coronavirus disease. Frontal view of the chest shows the atypical findings of atelectasis or beginning pneumonia (arrowheads) in the left lower lobe



Among the remaining cases that had disease progression on follow-up x-ray, there were four notable patients worth mentioning in this paper. One adolescent, a 16-year-old boy, presented with difficulty of breathing. The chest radiograph initially showed hazy air-space and streaky lung opacities in both mid to lower lungs. Symptoms rapidly worsened and the patient was subsequently intubated. A chest CT scan was done which demonstrated multifocal bilateral ground-glass opacities and areas of consolidation in keeping with severe COVID-19 pneumonia possibly relating to acute respiratory distress syndrome (ARDS) (Fig. 3a–d).

Another 15-year-old boy, also with similar presentation of dyspnea, initially had diffuse hazy and confluent airspace opacities involving the middle and both lower lungs. Follow-up chest x-rays showed progression of these opacities, with subsequent development of minimal left-sided pleural effusion and pneumothorax. The patient was also categorized as having severe COVID-19 pneumonia with ARDS.

One patient, a 7-year-old girl, presented with decreased sensorium. Her complete blood count showed leukocytosis and lymphocytosis. Initial x-ray only showed minimal streaky opacities in the left retrocardiac region. Due to the altered level of consciousness, a brain MRI was also done which showed subtle frontoparietal leptomeningeal enhancement suggestive of an

inflammatory process. Follow-up chest radiographs only showed minimal progression of the lung disease. The patient was signed out with a diagnosis of COVID-19 infection with viral encephalopathy.

A 5-year-old boy known to have acute lymphocytic leukemia (ALL) presented with difficulty in breathing. His initial CXR showed patchy hazy opacities scattered in both lungs. The patient was intubated and had marked progression of the bilateral lung opacities on his subsequent radiographs. This patient eventually succumbed, and was the only casualty in this study.

DISCUSSION

Among the pediatric patients with coronavirus disease, majority belonged to the adolescent age group. This is similar to the data by Hasan, et al [4]. Increased incidence of COVID-19 was noted among male patients, with male-to-female ratio of 1.4:1, which is in close proximity to that from other previously published international studies from China by Dong and colleagues [25], and Lu and colleagues [26] with male-to-female ratio of 1.3:1 and 1.55:1, respectively.

Majority of the chest radiograph findings for children with COVID-19 were normal, as seen in 68% of 196 patients. This is likewise concordant with the single-center study done by Bayramoglu, et al. [27] wherein 81% of 69 patients had normal chest radiographs. These rates are also similar to the rates of normal chest CT findings in children with the same condition, as demonstrated in studies done by Steinberger and colleagues (77%) [28] and by Chen and colleagues (50%) [29]. Bayramoglu and colleagues analyzed the discrepancy between the findings on chest radiographs and chest CT studies of pediatric patients with COVID-19 and concluded that the majority of the causes for normal-appearing chest radiographs in COVID-19 infected patients with abnormal chest CT studies were attributed to low-density opacities, small-sized opacities, or basal opacities obscured by the diaphragm and hepatic dome on frontal chest radiographs [27].

Positive chest radiograph findings, such as nonspecific opacities suggestive of either subsegmental atelectasis or beginning pneumonia, and air-space consolidation or opacity, most frequently involved only one lobe. Among patients who demonstrated subsegmental atelectasis or beginning pneumonia, the lower lobes were the most commonly involved. According to the structured chest

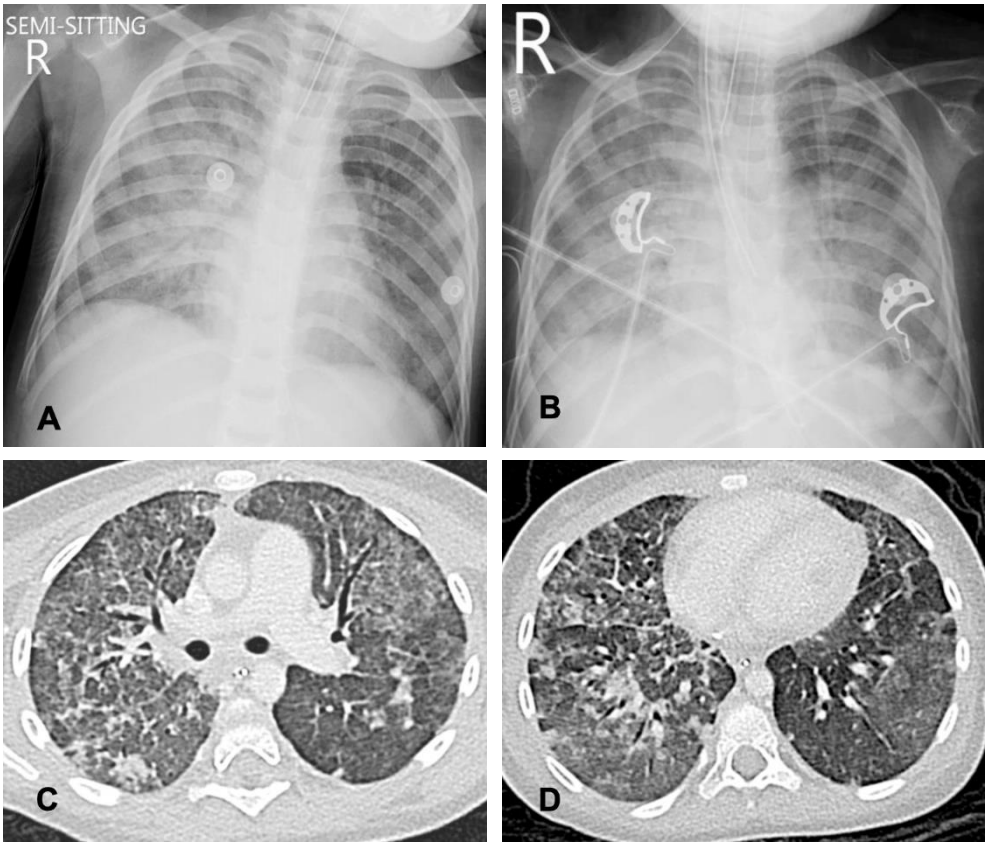


Fig. 3a-d Frontal view chest radiographs (**a**–**b**) and axial chest CT images in lung window setting (**c**–**d**) of a 16-year-old male show hazy air-space and streaky lung opacities with rapid progression in both mid to lower lungs in only two days (**a** to **b**) with extensive bilateral ground-glass opacities (**c** and **d**) compatible with the clinical impression of bilateral pneumonia with acute respiratory distress syndrome

radiographic reporting algorithm for pediatric COVID infection [21], lobar consolidation is uncommon and classified as atypical of COVID-19. This structured reporting system was adapted from the Radiological Society of North America expert consensus statement on reporting adult COVID-19. However, according to the study done by Bayramoglu, et al., this reporting system seems not to be applicable to children because imaging findings revealed different and heterogeneous opacity patterns compared to those in adults. It was also noted that pediatric COVID-19 related imaging findings were subtle or less extensive both on chest radiography and chest CT examinations [29, 30], as compared to those among infected adults.

A meta-analysis performed by De Rose and his colleagues among infants six months and below showed bilateral ground-glass opacities as a common imaging finding [5]. In this study, bilateral diffuse ground-glass opacities were noted in one patient who was born prematurely at 36 weeks. However, there was improvement after surfactant administration, with further regression after 4- and 11-day follow-up. Hence, this is more in keeping with surfactant deficiency, and less likely from COVID-19.

Two adolescent subjects developed severe pneumonia with imaging findings showing diffuse multifocal ground-glass opacities and consolidation in both lungs which raise the possibility of ARDS. The Pediatric Acute Lung Injury Consensus Conference (PALICC) has recommended the pediatric-focused definition and management for ARDS, in which the primary etiology is pneumonia [30, 31]. ARDS manifests as pulmonary inflammation, alveolar edema, and hypoxemic respiratory failure. It defines pediatric ARDS as those who develop respiratory failure and pulmonary edema within seven days of the known clinical insult, not fully explained by cardiac failure or fluid overload, and with chest imaging findings of new infiltrates consistent with acute pulmonary parenchymal disease. However, in contrast to the earlier adult-based definitions, the PALICC definition eliminates the requirement for bilateral pulmonary infiltrates on chest imaging due to a lack of evidence that etiology, management, and outcomes differ between patients with unilateral versus bilateral disease. Hence, ARDS remains primarily a clinical diagnosis.

Almost all of the patients with positive chest radiograph findings had at least one clinical symptom. Among the pediatric study population as well as among those with positive chest radiograph findings, the most common presenting symptoms encountered were cough and fever, consistent with the prior studies [2, 4, 10, 15], as well as nasal congestion or rhinorrhea.

There were nine patients who had an x-ray done but were asymptomatic. These COVID-19 positive cases had household exposure. The international consensus statement of the Radiological Society of North America on chest imaging in pediatric COVID-19 patients as postulated by Foust, et al. [21], states that imaging studies are actually not indicated for well-appearing immunocompetent patients greater than three months old who present with no symptoms. Initial imaging studies should only be reserved for those who have risk factors for disease progression or those with moderate to severe acute respiratory illness symptoms that are not responding to outpatient treatment and requiring hospitalization. This therefore emphasizes the importance of proper clinical history and physical examination to determine whether a chest radiograph is indeed warranted and in turn should obviate any unnecessary imaging studies. This decision-making becomes particularly important when considering cumulative radiation dose in pediatric patients. It is also important to keep in mind that the disease may still be in its early acute stages such that a normal CXR among positive COVID-19 patients does not essentially rule out pulmonary involvement at the time of examination. These asymptomatic cases yielded normal CXR results and had no disease progression, which did not necessitate any immediate follow-up imaging studies in our institution.

CONCLUSION

The COVID-19 pandemic, in the more recent years, has shown a surge of infection in pediatric patients. This emphasizes the need for further studies particularly in the field of pediatric radiology where it is crucial in finding a timely and accurate diagnosis.

In this series, adolescents were the most commonly affected followed by middle-school children, and is slightly more common in boys than in girls. Most common clinical symptoms presented were cough, fever, and nasal congestion or rhinorrhea, in decreasing order of frequency; lymphopenia and leukopenia were the predominant abnormal laboratory findings. Majority of pediatric patients with COVID-19 in this study exhibited normal chest radiograph findings. Among those with positive chest radiographic findings, initially bilateral ground-glass opacities were the most commonly seen. The lower lobes were most frequently affected.

Overall, these findings seen in children with COVID-19 infection in St. Luke's Medical Center are similar to the trends in the previously published international studies.

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