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Clinical presentation and outcomes of hospitalized children with COVID-19 in Mexico City

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Abstract

We describe the demographic, clinical, radiological, and laboratory findings relating them also to the severity and clinical outcome of 129 children (0–18 years) who were admitted to a tertiary care pediatric hospital in Mexico City due to severe acute respiratory syndrome coronavirus 2 infection between April 1, 2020 and March 31, 2021. The infection was confirmed using reverse transcription-polymerase chain reaction Fever (82.2%), tachypnea (72.1%), and cough (71.3%) were the most reported signs at the moment of hospitalization. The most frequent radiological pattern that stood out was the interstitial pattern (66.7%). History of oncologic pathology (25.6%) was the most frequent past medical history. Non-steroidal anti-inflammatory drugs (93%), antibiotics (57.4%), and steroids (40.3%) were the most common medication given. The average hospitalization stay was 14.2 days, and 21.7% of the total patients required transfer to the intensive care unit. At discharge, 20.2% required oxygen on an outpatient basis, and unfortunately, 7.0% of the patients who were admitted to the institute for COVID-19 died. Our findings confirm that COVID-19 in children has a mild presentation except for patients with hematologic/oncologic comorbidities who had severe presentations.

KEYWORDS
COVID-19, Pediatric

1 | INTRODUCTION

In Mexico, the first COVID-19 case was reported on February 27, 2020,[1] and from there 2 years later 4.6 million cases and 300,000 deaths have been documented in this country[2] with around 2.3 million contagions during the first year of the pandemic.[3] Worldwide children account for up to 13% of laboratory-confirmed cases[4] therefore, it is essential to understand the clinical manifestations of COVID-19, especially in children. Mexico has been one of the most affected countries in the world by the COVID-19 pandemic due that the real impact of the pandemic has been underestimated by the authorities of the country increasing mortality.[5] Racial and ethnic minority groups are disproportionately affected, perhaps in relation to underlying health conditions and economic and social conditions. Among reports from other countries in America, for those

hospitalized with COVID, the cumulative hospitalization rate was 16.9 per 100,000 population for Hispanic children, 10.5 per 100,000 for non-Hispanic Black children, and 2.1 per 100,000 population for White children.[4] Since the first pediatric COVID-19 case was identified on January 20, 2020, several studies have described the epidemiological and clinical features of COVID-19 in pediatric patients.[6]

The symptoms of COVID-19 are similar in children and adults, but the frequency of symptoms varies, overlapping with many other respiratory clinical syndromes. At least a third of infections in pediatric patients are asymptomatic, and symptoms in children may not be recognized even before diagnosis.[7]

During the acute phase of the disease, pediatric patients, according to their clinical manifestations, receive symptomatic supportive care some requiring oxygen therapy with mild symptoms, as well as those

moderately symptomatic or with pneumonia who receive empirical antibiotics and, if very serious, even invasive mechanical ventilation.[8]

The reasons that led us to investigate the characteristics of respiratory and radiological clinical manifestations in children and requiring hospitalization, emerge from the scarcity of pediatric reports in this country. As a result of this situation, the present investigation is justified by the need to know the main respiratory and demographic, clinical characteristics, past medical history related comorbidities, the need for oxygen use as well as the evolution during said hospitalization of the pediatric patient with COVID-19 to inform diagnosis, treatment, and follow-up of these patients in the future.

2 | METHODS

A retrospective review from April 1, 2020 to March 31, 2021, was done in the National Pediatrics Institute, a national referral hospital, in Mexico City which during the pandemic did not exclusively serve COVID-19 patients. This was a single study center. The National Pediatrics' Institute (Instituto Nacional de Pediatría) is a 251-bed hospital national referral hospital in downtown Mexico City receiving ~129,859 outpatient visits every year and ~5493 admissions and referrals. It is solely dedicated to the attention, diagnosis, and treatment of the pediatric population of Mexico, and it has a national endowment of nearly 8 million USD quarterly.[9]

The data were manually collected from electronic records using Microsoft Excel and were analyzed using STATA 14. Descriptive clinical variables were collected and tabulated in frequencies as shown in the tables. Student's t-test analysis was employed for continuous variables and Fisher's exact was used for categorical or binary variables. A significance threshold of $p < 0.05$ was used.

The inclusion criteria were: age 0–18-year-old, presenting to the hospital with respiratory symptoms or fever and/or being admitted to the COVID area, and having a positive polymerase chain reaction (PCR) test for COVID-19. Exclusion criteria included not having a radiological imaging study within the first 72 h of admission and not having an electronic medical record.

2.1 | ETHICS

This study was approved by the Institute's Central Ethics committee (GA/062/2021).

3 | RESULTS

3.1 | Demographic and epidemiological characteristics

A total of 129 patients who were reported with a positive PCR test for severe acute respiratory syndrome coronavirus 2. and were hospitalized in the "COVID ward" entered the analysis. Of these

TABLE 1 Demographics and clinical presentation of patients

Demographic	n (%)
Sex	
Male	73 (56.6)
Female	56 (43.4)
Age (years)	
<1	15 (11.6)
1–4	22 (17.1)
5–9	19 (14.7)
10–14	47 (36.4)
15–18	26 (20.2)
Proven state	
Ciudad de México	73 (56.6)
Estado de México	40 (31.0)
Other	16 (12.4)
Positive contact	42 (32.6)
Sign/symptom	
Tachypnea	93 (72.1)
Dyspnea	52 (40.3)
Cough	92 (71.3)
Fever	106 (82.2)
Rhinorrhea	50 (38.8)
Wheezing	7 (5.4)
Sneezing	6 (4.7)
Crackles	33 (25.6)
Anosmia	9 (7.0)
Odynophagia	35 (27.1)
Oxygen saturation	87.3 ± 7.60
Underlying disorders	
None	33 (25.6)
Hemato-oncology	33 (25.6)
Cardiovascular	6 (4.7)
Respiratory	6 (4.7)
Neurologic	10 (7.8)
Gastrointestinal	4 (3.1)
Endocrinologic	15 (11.6)
Inmunologic	10 (7.8)
Nephrological	4 (3.1)
Other[a]	8 (6.2)
Radiological pattern	
Normal	28 (21.7)
Perihilar infiltrate	46 (35.7)
Interstitial pattern	86 (66.7)

TABLE 1 (Continued)

Demographic	n (%)
Lobular vonsolidation	31 (24.0)
Pleural effusion	14 (10.9)
Chest tube	3 (2.3%)

[a]Specific comorbidities were not available to the investigators.

patients, 56.6% (n = 73) are male. Within the assigned age ranges, 36.4% (n = 47) and representing the largest number of patients are between 10 and 14 years old, with a mean of 9.1 years. 56.6% (n = 73) of the patients were from Mexico City state (Table 1).

3.2 | Clinical characteristics

Of the total number of patients, only 32.6% stated at the time of hospital admission that they had had contact with patients previously diagnosed with COVID-19. Regarding the clinical manifestations reported at the time of hospital admission, the cardinal sign that appeared in 82.2% was fever, followed by tachypnea in 72.1%. Cough was described in 71.3%, these three being the only ones to occur in more than 50% of the patients. The other signs or symptoms presented were dyspnea (40.3%), rhinorrhea (38.8%), odynophagia (27.1%), crying (25.6%), anosmia (7.0%), wheezing (5,4%), and sneezing (4.7%). The mean oxygen saturation on admission was 87.3 ± 7.60% (Table 1).

Regarding previous pathologies, it stands out that 25.6% had no comorbidities. Only 11.6% suffered from some endocrine alteration, and following in frequency both patients with neurologic and immunologic affection presented in 7.8%. Finally, the rest of the conditions presented as follows: cardiovascular (4.7%), respiratory (4.7%), nephrologic (3.1%), gastrointestinal (3.1%), and others (6.2%) (Table 1).

3.3 | Radiological findings

Among the most frequent radiological findings, the radiological pattern that stood out the most was the interstitial pattern, presenting 66.7%. In 35.7% para-hilar infiltrates were found, followed by lobar consolidation with 24% and only 10.9% presented pleural effusion, in which only three patients required the placement of an endo-pleural catheter. Chest X-ray was normal in 21.7% of patients (Table 1).

3.4 | Laboratory findings

Erythroid sedimentation rate (ESR) was the only laboratory value significantly associated with a severity of 27.82 mm/h (SD ± 23.83). The rest of the variables there were not statistically different in severity.

There were nonsignificant associations between laboratory ordered and intensive care unit (ICU) admission (Table 2).

TABLE 2 Laboratory findings and ICU admission

Parameter	Mean (SD)	95% CI	p Value
Leukocytes (cells/ml)	8385 ± (6867)	5722–11,048	0.33
Lymphocytes (cells/ml)	2328 ± (3952)	796–3861	0.19
Neutrophils (cells/ml)	5435 ± (5833)	3173–7697	0.51
Platelets (cells/ml)	169,250 ± (107,222)	127–210	0.58
LDH (UI/L)	758 ± (1602)	−38–1554	0.093
ESR (mm/h)	27.82 ± (23.83)	15–40	**0.015**
CRP (mg/dl)	10.78 ± (10.96)	5–15	0.1
Fibrinogen (mg/dl)	345.28 ± (97.68)	304–385	0.073
Ferritin (ng/dl)	2025 ± (3622)	458–3592	0.49
D dimer(mg/ml)	2.96 ± (4.61)	1.05–4.87	0.33

Note: Bold value indicates a significance threshold of $p < 0.05$ was used. Abbreviations: CI, confidence interval; CRP, C-reactive protein, ESR, erythroid sedimentation rate; ICU, intensive care unit; LDH, lactate dehydrogenase; SD, standard deviation.

TABLE 3 Treatment and outcomes

Medications administered	n (%)
NSAID	120 (93.0)
Steroids	52 (40.3)
Antibiotics	74 (57.4)
IVIG	39 (30.2)
Nebulized/inhaled therapy	18 (14.0)
	Mean (SD)
Oxygen use (days)	10.7 ± (23.8)
Intrahospital stay (days)	14.2 ± (25.0)
Mechanical ventilation (days)	2.1 ± (6.6)
	n (%)
Transfer to ICU	28 (21.7)
Ambulatory oxygen	26 (20.2)
Transfer to another institution	13 (10.1)
Death	9 (7.0)

Abbreviations: ICU, intensive care unit; IVIG, intravenous immunoglobulin; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation.

3.5 | Characteristics during hospitalization and medical outcome

Among the medications used as part of in-hospital medical management, it is worth noting that 93% (n = 120) of the patients were administered non-steroidal anti-inflammatory drugs (NSAIDs) as supportive therapy. Antibiotics were also part of the most frequently

indicated medical therapy for patients since they were administered to 57.4% (n = 74) of patients. Steroids were administered to 40.3% (n = 52) of patients. The use of intravenous immunoglobulin was administered to 30.2% (n = 39) and only 14% (n = 18) required the use of nebulized therapy. Inhaled therapy usually includes albuterol, budesonide, and less commonly ipratropium (Table 3).

The days of hospital stay averaged 14.2 days, and from those, 10.7 days of supplemental oxygen use. Of the 28 (21.7% of the total) patients who required transfer to the ICU, the mean number of days on mechanical ventilation was 2.1 ± 6.6 days. At discharge, 20.2% (n = 26) required oxygen on an outpatient basis. 10.1% of the patients were transferred to another institution, and unfortunately, 7.0% (n = 9) of the patients who were admitted to the institute for COVID-19 died (Table 3).

4 | DISCUSSION

This study is one of the few comprehensive clinical characterizations of COVID-19 in the pediatric population in Mexico, being one of the most affected countries in America, just behind the United States, Brazil, Peru, and Chile.[5] It is comparable to prior reports in low- and middle-income countries but some contrasts are worth noting. The demographic characteristics described by She et al.[10] have reported a higher incidence in males similar to the data herein reported. The age range most affected and that required hospitalization was found between 10 and 14 years, with a mean of 9.1 years, unlike Lu et al.[8] where the average age was lower, reporting 6.7 years. Other reports from the Mexican pediatric population state the median age for diagnosis was 12 years.[11]

Similar values are reported of the admitted patients in terms of contact with another positive patient for COVID-19; Haslak et al.[12] report that 40% of their patients have had contact with relatives with positive tests. In this study, 32% of those hospitalized had previous contact, with a family member or another acquaintance with a diagnosis of COVID-19.

The most frequent sign is the presence of fever, as indicated by Wang et al.[13] where 98.6% of 138 patients presented fever. In this study, 82.2% of hospitalized patients presented fever as an initial symptom before admission. Other reports among Mexican children reported that 100% of the patients had a fever as the predominant symptom.[14]

Among the other prominent symptoms, cough, as in the study, was found as one of the first three main symptoms, in this study it was reported in 71%, and as reported by Wang et al.[13] in 59.4% of their sample.

As in published meta-analyses, symptoms such as rhinorrhea and odynophagia were presented to a lesser extent, as mentioned in the publication by Cui et al.[15] where it was found that odynophagia occurred in 16% of patients and rhinorrhea in 14%, in this study rhinorrhea was present in 38.8% and odynophagia in 27.1%. It is noteworthy that in this publication, tachypnea is reported only in 9%, unlike the findings where tachypnea was found as the second

relevant clinical finding, occurring in 72% of patients. Other studies, such as the one carried out by Al Yazidi et al.[16] report that none of the hospitalized patients presented anosmia, unlike what was found in this study where 7% of the patients did present anosmia. Finally, 14% of its population presented dyspnea, unlike what was found in the studied population, where it was found in 40.3% of the patients. Patel et al.[17] found that 13.7% of the studied population presented sneezing unlike what was found where only 4.7% presented it, this being something important since it is one of the most important routes of contagion. Similarly, the oxygen saturation at hospital admission has been reported below 92%, such as the case reported in Ayinbuomwan et al.[18] where the mean arterial oxygen saturation was 86.9%, and that of this study 87.3%.

Although in meta-analyses published such as the one carried out by Kumar et al.),[19] it is reported that computed tomography (CT) was the most common imaging modality performed in children with confirmed COVID-19, in our setting the modality was a chest X-ray. Unlike other studies carried out, such as the one published by Biko et al.[20] where most of the imaging studies requested for hospitalized children are reported, they were chest X-rays, these were normal in more than half of the cases (67%), being normal only in 21.7% of our population. It is worth mentioning that the interstitial and alveolar opacities in the radiographs were the main radiological patterns found, in the same way, reported by Lopez Aguilar et al.[14] among Mexican children with COVID-19. Other rare findings such as pleural effusion occurred mainly in those who developed complications associated with COVID-19. As in the study by Biko et al.[20] the need for a chest tomography to evaluate COVID-19 was not evident, which supports the pediatric consensus recommendations to use it in cases where there is concern about progression an alternative diagnosis, or poor clinical improvement.[21]

Of the associated comorbidities of hospitalized patients, there are publications such as that by Oliveira et al.[22] where the most frequent comorbidities associated with hospital admission were mainly respiratory and malignancies, agreeing with our study where 25% of hospitalized patients had a hematologic or oncologic pathology, especially Leukemia, according to other reports where admission and mortality were related to having comorbidities.[23] It is important to mention that 25% of the patients were formerly healthy and only 4.7% had a history of previous respiratory disease.

The laboratory findings can be compared with other published studies such as that of Mania et al.[24] where, as in our study, the presence of alterations in the value of leukocytes at the time of admission is not reported, without finding initial alterations in the neutrophil and lymphocyte count initially on average. In turn, the number of platelets was within normal ranges. Inflammatory markers were generally found to be high at the time of admission, being similar to those found in publications such as those previously published by Mania et al.[24] In our study, ESR was associated with ICU admission, however, patients being admitted to the ICU were more likely to have this laboratory parameter.

Regarding the treatment carried out, during hospitalization, there are cohorts of hospitalized patients with COVID-19, we find where it

is reported that up to 56.6% were treated with early empirical antibacterial therapy,[25] very similar to what was found in our study where 57.4% of the patients, antibiotics were started empirically. The use of NSAIDs, as initial therapy in symptomatic management, has been used globally as mentioned by Drake et al.[26] in their study, and it is important to emphasize that their use did not lead to an increase in the severity of the illness. Steroids were used in 40.3% of the patients, being used mainly in those who presented moderate or severe disease described by Dulek et al.[27] The use of therapy with immunomodulators was mainly focused on those who developed the multisystemic inflammatory syndrome, as they did in their study Verdoni et al.[28] Initially, inhaled therapy was contraindicated, so it was not administered to patients, but after the publication of guidelines,[29] hospitalized patients who required the use of inhaled therapy as asthmatics or with cystic fibrosis continued their mainstay management.

Unlike other studies where the days of hospital stay were counted, for example, Ng et al.[30] report a mean of 7 days, compared to our study where the mean was 14 days, but it should be noted that none of these patients studied were admitted to intensive care, nor did they die. In other reports such as the description by Lopez Aguilar et al.[14] among Mexican children, the median hospital stay was 11 days. Of the hospitalized patients, unlike the study carried out by Götzinger et al.[31] where at the time of the end of the study only 4% needed respiratory assistance.

5 | STRENGTHS AND LIMITATIONS

The strength of our study is that it describes the clinical and radiological characteristics of the pediatric Mexican population, being one of the first nationwide databases of hospitalized children and adolescents with laboratory-confirmed COVID-19. The main limitations of this study are the retrospective observational nature of the analyses, the small sample size, and that were only studied in a single center. Also, chest radiographs were performed on the vast majority of patients, unlike high-resolution CT which would provide more in-depth characteristics.

6 | CONCLUSIONS

This study showed that COVID-19 in children was associated with mild symptoms and a good prognosis. Although fever, tachypnea, and cough, none of them were related to severity. Lastly, the radiological pattern that stood out the most was the interstitial pattern. Children with hematologic and oncologic comorbidity had a more severe presentation. In the early stages of the pandemic, mortality in children may have been underestimated.

AUTHOR CONTRIBUTIONS

David Rodriguez Diaz collected the data and prepared the manuscript. Samuel Urrutia analyzed the data and prepared the manuscript. Gabriel Gutierrez and Francisco Cuevas participated in project conception, data collection, and approval of the final manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Raw data is available upon sensible request.

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