ARTÍCULO ORIGINAL

COVID-19 in pediatric patients from Pinar del Rio province

Enfermedad por coronavirus 2019 en pacientes pediátricos de Pinar del Río

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ABSTRACT

Introduction: coronaviruses are named for the peculiar crown-shaped viral particles that cover their surface, several species are newly investigated and there is little information about transmission, severity and clinical effects.
Objective: to characterize pediatric patients with COVID-19 attended in Pinar del Río province.
Methods: an observational, descriptive and cross-sectional study of 15 patients with COVID-19 admitted to Dr. Leon Cuervo Rubio Clinical-Surgical Teaching Hospital was conducted from March 26th to May 12th, 2020. The studied was completed by means of a non-probabilistic sampling. Descriptive statistical methods were applied to process the information collected.
Results: the most represented age group was seven -12 years old and male gender (60 vs. 40 %); 53,3% of patients developed a non-complicated infection and bronchial asthma was the most frequent comorbidity. The most reported symptom on admission was fever (60 %). In the chest X-ray the hilar thickening showed a greater presentation, without significant alterations in the laboratory studies. The total number of cases studied was treated with oral Oseltamivir.
Conclusions: COVID-19 has rapidly become a global health threat. Male schoolchildren were more prone to infection and the disease presented non-severe clinical syndromes.

Keywords: Coronavirus; Epidemiology; Respiratory system; Child; Molecular Biology; Pediatrics.

RESUMEN

Introducción: los coronavirus llevan su nombre por las peculiares partículas virales con forma de corona que recubren su superficie, varias especies son de reciente investigación y existe poca información sobre la transmisión, gravedad e impacto clínico.
Objetivo: caracterizar pacientes pediátricos con COVID-19 atendidos en Pinar del Río.
Métodos: se realizó un estudio observacional, descriptivo y transversal de 15 pacientes con enfermedad por coronavirus 2019, ingresados en el Hospital Clínico-Quirúrgico Docente "León Cuervo Rubio", desde el 26 de marzo hasta el 12 de mayo de 2020. La muestra fue seleccionada mediante un muestreo no probabilístico. Para el procesamiento de la información obtenida se emplearon las técnicas de estadística descriptiva.
Resultados: el grupo de edad más representado fue el de siete a 12 años y el sexo masculino (60 vs 40 %). El 53,3 % de los pacientes debutó con infección no complicada y el asma bronquial resultó la comorbilidad más frecuente. El síntoma más notificado al ingreso fue la fiebre (60 %). En la radiografía de tórax el engrosamiento hiliar mostró mayor presentación, sin alteraciones significativas en los estudios de laboratorio. El total de casos estudiados recibió tratamiento con Oseltamivir oral.
Conclusiones: la enfermedad por coronavirus 2019 se ha convertido rápidamente en una amenaza mundial para la salud. Los escolares masculinos fueron más propensos al contagio y debutaron como síndromes clínicos no severos.

Palabras clave: Coronavirus Humano; Epidemiología; Sistema Respiratorio; Niño; Biología Molecular; Pediatría.

INTRODUCTION

Coronaviruses belong to the family Coronaviridae, which includes similar genogroups of single-stranded RNA-positive viruses with a helical nucleocapside and crown-shaped tips on the surface. Thirty-nine species of coronavirus have been recorded to date. Several species are of recent research, as they had not been identified in humans. Concerning its transmission, severity and clinical effects, there is little information. Coronaviruses that affect humans can range from a common cold to more serious illnesses such as severe acute respiratory syndrome (SARS) or Middle Eastern respiratory syndrome (MERS). In some cases, zoonotic transmission may occur. [1]

Most coronaviruses spread to susceptible hosts by respiratory or fecal-oral routes, and replication occurs initially in epithelial cells. SARS-CoV-2 binds with high affinity to angiotensin-converting enzyme 2 (ACE2), which is used as a gateway receptor to invade cells. This enzyme is abundant in type-II pneumocytes and also in enterocytes of the small intestine, which may help to better understand the routes of infection and manifestations of the disease. [2]

The exact incubation period is unknown. It is presumed to be 2-14 days after exposure, and most cases are reported after five days. The most frequent symptoms at the beginning of the disease vary according to age and the presence of comorbidities; they include: fever, hacking cough, asthenia, headache, pharyngeal pain, rhinorrhea, myalgia, gastrointestinal symptoms and dyspnea. In pediatric patients, clinical expression is usually slight. This is associated with

a less developed humoral and cellular immune response and reduced expression of ACE2 receptors. [3]

As in previous pandemics, corticosteroids are not routinely recommended because they delay viral clearance and may exacerbate lung injury associated with coronavirus disease 2019 (COVID-19). Accumulated evidence suggests that a subgroup of patients with severe disease may have a cytokine-storm syndrome. However, in hyperinflammation, immunosuppression is likely to be beneficial. [4]

No specific analytical and radiographic alterations have been described in child population affected by COVID-19. Clinical syndromes associated with acute viral respiratory infection include: non-complicated infection (limited to the upper respiratory tract), mild lower respiratory tract infection (cough and tachypnea, but no signs of clinical severity), severe lower respiratory tract infection (tachypnea), and at least one of the following: central cyanosis or pulse oximetry < 92 %, moaning, flaring of nostrils, severe thoracic retraction, sensory disturbances or convulsions), acute respiratory distress syndrome (ARDS) (PaO2 / FiO2 ≤ 300 mmHg or SpO2 / FiO2 ≤ 264), sepsis (suspected or proven infection and two or more criteria of systemic inflammatory response syndrome, one of which must be dysthermia or abnormal white blood cell count. It is serious, if the child presents cardiovascular dysfunction, ARDS or two dysfunctions of the rest of the organs), septic shock (signs of peripheral hypoperfusion requiring vasoactive drugs to maintain adequate blood pressure after a correct volume expansion). [5]

Antibiotic therapy will be used in treatment if bacterial over-infection is suspected and in case of sepsis or septic shock. Systemic corticoids are indicated in patients with ARDS, encephalitis, meconium aspiration syndrome (MAS), and when signs of bronchospasm are observed. No specific antiviral has been shown to be effective in coronavirus infection. There are several drugs that are experimentally used. Inhaled interferon alpha is recommended in association with Lopinavir/Ritonavir. Remdesivir may be the best potential drug for the treatment of COVID-19. Other drugs such as chloroquine (antimalarial) have been considered as possible therapeutic options. Oseltamivir is not recommended at this time. [6]

Since COVID-19 is an emerging, rapidly evolving situation and the information about its pathogenic mechanism, clinical expression and more effective treatment is limited; the objective of this study is to characterize clinical, epidemiological and radiological the coronavirus disease 2019 in pediatric patients from Pinar del Rio province.

METHODS

Observational, descriptive, cross-sectional study on COVID-19 in pediatric patients from Pinar del Río province, admitted to Dr. Leon Cuervo Rubio Clinical-Surgical Teaching Hospital, from March 26 to May 12, 2020. The target group consisted of the 220 patients with suspected disease who were admitted for epidemiological surveillance in the period analyzed. The sample included 15 patients under 18 years old, with a confirmed diagnosis by means of molecular biology techniques and clinical history with complete data.

The variables studied were age, gender, clinical syndromes, associated comorbidities, symptoms on admission, and findings on chest X-ray, laboratory results and therapeutic interventions. For data collection, the clinical histories of the patients were reviewed. The statistical processing was done by distributing frequencies in absolute and relative percentage values.

All the data collected were used for strictly scientific purposes. The established ethical principles of Beneficence, Non-maleficence, Justice and Respect for people were met; for this type of documentary studies without the intervention of individuals.

RESULTS

The 6,8 % of the children admitted for epidemiological surveillance were confirmed cases. Regarding the frequency of COVID-19 according to age groups and gender, it was found that the most represented group was from 7 to 12 years old (53,3 %) and male gender (60 %). (Table 1)

Table 1. Distribution of pediatric patients with COVID-19 according to age groups and sex. Dr. Leon Cuervo Rubio Clinical-Surgical Teaching Hospital. Pinar del Rio. March 26th - May 12th, 2020

Age brackets (years old)	Female		Male		Total	
	No.	%	No.	%	No.	%
0-6	3	20	-	-	3	20
7-12	3	20	5	33,3	8	53,3
> 12	-	-	4	26,7	4	26,7
Total	6	40	9	60	15	100

Source: Clinical History

Of the sample studied, 53,3 % of the patients developed a non-complicated infection and 26.7 % of them were asymptomatic during hospitalization. Bronchial asthma was the comorbidity with the highest frequency of presentation at 20 %. (Table 2)

Table 2. Distribution of pediatric patients with COVID-19 according to clinical syndromes and associated comorbidities.

Clinical syndromes	No.	%
Non-complicated infections	8	53,3
Asymptomatic	4	26,7
Moderate infections of the lower respiratory tract	3	20
Comorbidities	**No.**	**%**
Bronchial asthma	3	20
Allergic rhinitis	1	6,7
Celiac disease	1	6,7

Source: Clinical History

There is evidence that 60% of children with COVID-19 had fever on admission. Dyspnea was reported only in one patient with a history of bronchial asthma and evolving bilateral para-cardiac bronchopneumonia. Gastrointestinal symptoms were represented in 20 % of them. (Table 3)

Table 3. Distribution of pediatric patients with COVID-19 according to symptoms on admission.

Symptoms on admission	No.	%
Fever	9	60
Pharyngeal pain	5	33,3
Hacking cough	5	33,3
Rhinorrhea	5	33,3
Diarrhea	3	20
Dyspnea	1	6,7

Source: Clinical History

In chest X-ray, hilar thickening was the one with the highest presentation (60 %); while alveolar condensation was reported in 6,7 % of the patients. With respect to laboratory studies, low percentages of positivity were observed, as important findings: mild leukopenia and augmented erythrocyte sedimentation rate in 20 % of the children studied. (Table 4)

Table 4. Distribution of pediatric patients with COVID-19 according to findings on the chest X-ray and laboratory results.

Chest X-rays	No.	%
Hilar thickening	9	60
Non-pleuropulmonary alterations	3	20
Interstitial infiltrate	2	13,3
Condensed infiltrate	1	6,7
Leukocyte count		
Normal	10	66,7
Mild leukopenia	3	20
Lymphopenia	2	13,3
Erythrocyte sedimentation rate		
Normal	12	80
Augmented	3	20
Platelet count		
Normal	14	93,3
Mild Thrombopenia	1	6,7
Creatinine		
Normal	15	100
Augmented	0	0
Aminotransferases		
Normal	13	86,7
Higher than 60 UI	2	13,3
Lactate dehydrogenase [LDH]		
Normal	14	93,3
Higher than 250 UI	1	6,7

Source: Clinical History

Oral oseltamivir was prescribed in the total of the sample studied. Lopinavir/ritonavir, chloroquine and subcutaneous recombinant interferon alpha-2b were used in 60 % of the children. The use of Ceftriaxone was limited to patients with inflammatory lung lesions (20 %). (Table 5)

Table 5. Distribution of pediatric patients with COVID-19 according to therapeutic interventions.

Treatment	No.	%
Oseltamivir	15	100
Lopinavir/ritonavir	9	60
Chloroquine	9	60
Recombinant interferon	9	60
Ceftriaxone	3	20

Source: Clinical History

DISCUSSION

The genes that code for the synthesis of immunoglobulins are located on the X chromosomes, which explains why male gender is a risk factor for infections in a general sense, especially those involving the respiratory system. Based on the experience of Pinar del Río province, COVID-19 most frequently affects patients over 35 years old.

The results of the present study resemble to those of Guan W and col,[6] who studied 1099 confirmed patients in 30 provinces of China. They reported in relation to gender, 58,1 % of male and 41,9 % of female patients. In terms of age, they found a higher prevalence of individuals between 15 and 49 years old (55,1 %), only 0,9 % of the patients were under 15 years old.

This research does not coincide with that reported by Olmos GC et al., [7] in an epidemiological review conducted in Chile up to April 14th, 2020, where they reported 478 patients under 20 years old; 257 of them were women (53,8 %), indicating a slight predominance of this gender. With respect to age, 92 patients from 0 to 4 years old, 72 from 5 to 9 years old, 107 from 10 to14 years old and 207 from 15 years old and over, were diagnosed with COVID-19.

The associated comorbidities and their control is a determining factor in the clinical behavior of COVID-19. The pathologies considered as risk by the Spanish Academy of Pediatrics (AEP) are mentioned below: primary immunodeficiencies, solid organ transplantation or hematopoietic parents, treatment with chemotherapy or immunosuppressant, HIV infection with detectable viral load, heart diseases with hemodynamic repercussion, cystic fibrosis, bronchopulmonary dysplasia (BPD), patients with oxygen therapy or mechanical ventilation at home, bronchial asthma, sickle cell disease, type I diabetes mellitus with poor metabolic control, severe malnutrition, short bowel, severe encephalopathies, myopathies and inborn error of metabolism. [8]

The study by Zhou F et al., [9] on the clinical course and risk factors for mortality, shows that, of 191 patients included in the research, 91 (48 %) had associated comorbidities. In order of frequency: high blood pressure (30 %), diabetes mellitus (19 %) and coronary disease (8 %).

These results do not coincide with those presented in the current study, which are mainly related to the age of the patients analyzed.

Studied 2449 patients diagnosed with COVID-19 from February 12 to March 16, 2020. They reported that the risk for severe illness and death increases with age. All patients under 19 years old (123) started with non-severe clinical syndromes, with no need for intensive care admissions or deaths. Similar results were found in the current research.[10]

The study does not coincide with what was reported in relation to symptoms on admission. The researchers reported hacking cough in 68 % of patients, fever in 44 %, and dyspnea in 19 % in addition to pharyngeal pain in 15 %.[11]

Hosseiny M et al., [12] recorded in their research that 85 % of the patients presented imaging studies with acute parenchymal alterations at diagnosis. The most represented findings: asymmetric opacities (patchy or diffuse), mainly towards the pulmonary periphery in the chest X-ray and tarnished glass pattern in the CT-scan. No evidence of cavitation or lymphadenopathy. These results are not similar to those presented in this study.

With respect to blood biometry,[13] showed that the evolution of the percentage of lymphocytes can be useful as a predictor of severity. If the percentage is less than 5 % the patient is at high risk of critical illness. Other authors, [7] reported lymphopenia in 82,2 % of hospitalized patients. The series under study showed low percentage of positivity.

The pharmacological treatment underwent several modifications during the period analyzed, as the National Pediatric Group readjusted the protocol based on the international scientific evidence. Initially, patients who were asymptomatic and had uncomplicated infections without comorbidities were treated with oseltamivir. The current protocol proposes treatment with lopinavir/ritonavir, chloroquine and recombinant interferon for all confirmed pediatric patients. The indication for oseltamivir was maintained because a large group of children studied were positive for influenza. [14]

Sanders JM and collaborators [15] reviewed 1315 articles on the therapeutic modality used and its effectiveness. The researchers concluded that early combined antiviral treatment slows disease progression, although such antiviral treatments have not been independently evaluated. In addition, the most promising therapy is Remdesivir because of its potent in-vitro activity against SARS-CoV-2. Oseltamivir was not shown to be effective. The results of the current study are consistent with regard to combined antiviral therapy, but Oseltamivir was prescribed in the totality of the sample.

It was concluded that COVID-19 has rapidly become a global health threat. Male schoolchildren were more likely to be infected and presented non-severe clinical syndromes. Fever was the most frequent symptom on admission, with low positivity in chest X-ray and blood tests. The therapeutic interventions were adjusted to the current protocol of action.

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The authors do not declare conflicts of interest in this study.

Author's contribution
All the authors contributed in equal measure in the conception, design, writing and revision of the final version of the manuscript.

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