ECUATORIAN JOURNAL OF PEDIATRICS
rev-sepp.ec

ORIGINAL RESEARCH

Laboratory findings in patients with COVID-19 treated in the pediatric emergency area of the Hospital General IESS del Sur from April to June 2020

Amparo Enríquez[1], **Patricia Sanafria**[1], **José Charro**[1], **Mary Salazar**[2]
https://orcid.org/0000-0002-7494-3138 https://orcid.org/0009-0000-1132-1043 https://orcid.org/0000-0001-6000-7392

1. Pediatric Emergency Service, Hospital General IESS del Sur, Quito, Ecuador.
2. Postgraduate Degree in Pediatrics, Pontificia Universidad Católica del Ecuador, Quito, Ecuador.

Received: July 12, 2020
Accepted: August 12, 2020
Published: August 31, 2020

Bibliographic letterhead:

Enríquez A, Sanafria P, Charro J, Salazar M. Laboratory findings in patients with COVID-19 treated in the pediatric emergency area of the Hospital General IESS del Sur of April to June 2020. Rev. Ecuat. Pediatr. 2020;21(1): Article 12: 1-7. doi: 10.52011/0024

DOI:
https://doi.org/10.52011/0024

Abstract

Introduction: SARS-CoV-2 is less prevalent in children, and it mostly has a mild clinical presentation. The aim of the present study was to describe the findings from blood, urine, and stool test results in patients with COVID-19 who were treated in the pediatric emergency area of the Hospital General del Sur de Quito from April to June 2020.

Methods: This was a descriptive, cross-sectional study. Depending on the clinical case, from mild to critical disease, hematic biometry, blood chemistry, coagulation times, and inflammatory reactants such as C-reactive protein and procalcitonin, elemental and microscopic urine, and coprological tests were performed. Participants were confirmed using nasopharyngeal swabbing and the real-time reverse transcription polymerase chain reaction test for COVID-19. Descriptive statistics were used.

Results: Fifty-four patients aged between 29 days and 17 years 11 months were included. Blood counts were normal in 72% of patients, C-reactive protein was <5 ng/dL in 71% of patients, and procalcitonin was <0.5 ng/mL in 100% of patients. Aspartate aminotransferase and alanine aminotransferase were normal in 79% and 85% of patients, respectively. Partial thromboplastin time and prothrombin time were normal in 56% of children.

Conclusions: Laboratory tests are nonspecific in patients with COVID-19. However, they are a tool for timely decision-making.

Keywords: Laboratory tests, coronavirus infections, clinical laboratory techniques, child.

* Corresponding author.

Email: amparitoe2510@hotmail.com (Amparo Enríquez) / Telephone: 09 87285646, Quito, Ecuador.

Introduction

The new SARS-CoV-2 coronavirus causes the disease called COVID-19, which has rapidly spread worldwide, and it was first detected in Wuhan, China, in November 2019. It was declared a pandemic in March 2020 by the World Health Organization (WHO) [1-3].

Since the first confirmed case in Ecuador on February 29, 2020, a rapid spread of the disease has been observed in the most populated cities such as Guayaquil, Quito, and Cuenca. Since then, a daily increase in new cases has been reported in the country [4].

According to Pan American Health Organization (PAHO)/WHO data, in its report 14 dated June 29, 2020, 5,136,705 confirmed cases of COVID-19 were recorded in the Region of the Americas [5]. The National Emergency Operations Committee (NEOC) of Ecuador reported 56,342 confirmed cases on June 30, 2020, of which 7.220 (15.2%) correspond to the province of Pichincha [4].

Current worldwide data reflect an COVID-19 infection rate 1% to 5% in the pediatric age group (2). In China, 2.1% of confirmed cases were reported in children under 19 years old [6]. In Ecuador, we found a prevalence of 4.2% in patients under 19 years old [4].

In humans, SARS-CoV-2 causes mainly respiratory and gastrointestinal symptoms. Clinical manifestations in pediatric patients range from uncomplicated disease to severe disease such as pneumonia, acute respiratory distress syndrome, sepsis, and septic shock, which can lead to multiple organ failure and death [7].

COVID-19 disease has had less severe symptomatology in children and a less lethal outcome compared to the adult population; however, children are just as likely as adults to become infected with the virus [3]. Severe or complicated patients were those younger than 1 year of age or who had comorbidities [6]. "Mild clinical symptoms or absence of symptoms in children is observed even with high viral loads despite the presence of important radiological alterations" [8].

Limited expression of angiotensin converting enzyme 2 (ACE2) in childhood, which is a period when the lungs are developing, could protect children from the most severe forms of COVID-19. Children as well as adult males have higher ACE2 levels, which could explain the higher infection rates in males [9].

For an etiological diagnosis, swabs are performed, preferably from the nasopharyngeal and oropharyngeal region, to identify viral RNA using real time reverse transcription-polymerase chain reaction (RT-PCR). This test helps to confirm or rule out the disease, but it does not provide information on its severity. Thus, there is a need to complement the diagnosis with laboratory studies including surveillance, therapeutic follow-up, and prognosis, especially because there are co-infections and comorbidities in children [6].

In addition to the tests for SARS-CoV-2, in patients with acute respiratory infection who require hospitalization, tests to detect other types of viruses such as respiratory syncytial virus and influenza, including the H1N1 strain, are suggested, as well as regular laboratory tests such as the following: blood gas, hematic biometry, electrolytes, and blood cultures; inflammatory markers such as C-reactive protein (CRP), procalcitonin (PCT), and lactate; renal function tests such as creatinine, urea nitrogen, and urinary volume; liver function tests such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT); and cardiac enzymes, clotting times, and D-dimer. Other recommended tests are elemental and microscopic urine and coprological testing [7].

"The most common hematological findings are: lymphopenia, neutrophilia, eosinophilia, and mild thrombocytopenia, and a few cases of thrombocytosis have been described" [10].

Lymphocyte counts can be used to predict the disease evolution in patients. The following model based on the lymphocyte count at two time points has been proposed: patients with a lymphocyte count lower than 20% on days 10–12 after symptom onset and less than 5% on days 17–19 have the worst prognosis. There may be both thrombocytosis and thrombocytopenia, which is associated with a poor prognosis [11, 12].

In the population under 19 years old, hematic biometric analysis studies reflect abnormal leukocyte values in 69.2% of patients, neutrophilia in 4.6%, neutropenia in 6%, lymphopenia in 3%, elevated procalcitonin in 13.6%, and CRP in 10.6% [12].

Data concerning the clinical and laboratory diagnosis of COVID-19 disease in the pediatric population

are minimal and insufficient to understand its evolution towards severe and critical cases without comorbidities. Thus, the present study aimed to describe the laboratory findings in children who were treated in the Pediatric Emergency area to determine if abnormal data that will alert and allow us to provide timely care in the event of an eventual presentation of multi-organ failure and death.

Population and methods

Study design

The design was an observational, cross-sectional, retrospective study.

Scenario

The study was conducted in the Pediatric Emergency Department of the Hospital General del Sur de Quito of the Instituto Ecuatoriano de Seguridad Social (IESS), from April 1 to June 30, 2020 in the city of Quito, Ecuador. The study period included a recruitment and an exposure period. Follow-up was completed on July 7, 2020, and the data collection period ended on July 10, 2020.

Participants

A database search of pediatric patient records was conducted for patients aged 28 days to 17 years 11 months who were diagnosed with COVID-19 and had a positive RT-PCR test for SARS-CoV-2 via nasopharyngeal/oropharyngeal swab and who attended the institution's emergency department within the study inclusion period. Patients with complete medical record data were selected.

Variables

Variables included descriptive demographic and clinical laboratory variables.

Reference values for hematological analysis were taken from practical hematology including interpretation of the hemogram and coagulation tests [13].

All patients who were admitted with gastrointestinal symptoms underwent a coprological examination.

The following laboratory tests were investigated in the present study: hematic biometry, CRP, PCT, ALT, AST, electrolytes (sodium, potassium, and chlorine), creatinine, urea, lactic dehydrogenase (LDH), D-dimer, creatine phosphokinase (CPK), clotting times (prothrombin time [PT] and thromboplastin time [PTT]), elemental and microscopic examination of urine (EMO), and coprological testing and investigation of polymorphonuclear cells and pyocytes.

Data sources and measurement

For each variable, the institutional software AS400 that was available at the IESS was used as a data source, the electronic medical record was consulted, and the physical emergency records were additionally consulted to obtain data crossover. The data were compiled in an electronic sheet to be later transferred to the statistical software.

Controlling sources of bias.

Medical records with incomplete data were excluded, and imputation of missing or excluded data was avoided. The protocol for this study was approved by the Institutional Teaching Committee.

Study size

The sample was non-probabilistic, in which all potentially eligible cases from the hospital were included.

Handling quantitative variables

The quantitative variables in scale are presented as the mean and standard deviation. Nominal quantitative variables are presented as the frequency and percentage, and 95% confidence intervals are presented for a proportion.

Statistical methods

Descriptive statistics were used. The statistical package used was SPSS v.22 for Windows.

Results

Participants

There were 54 patients included in this study. The patients who were not included in the study are presented in Fig. 1.

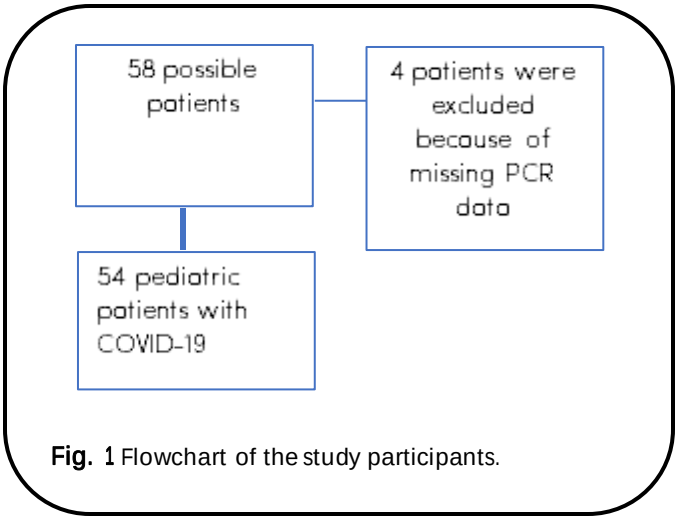

Fig. 1 Flowchart of the study participants.

Characteristics of the study population

Fifty-four patients were included in the study population, and 31/54 (57.41%) patients with COVID-19 were males and 43% were females. Five patients (9.2%) were young infants, which was the least affected age group (shown in Fig. 2).

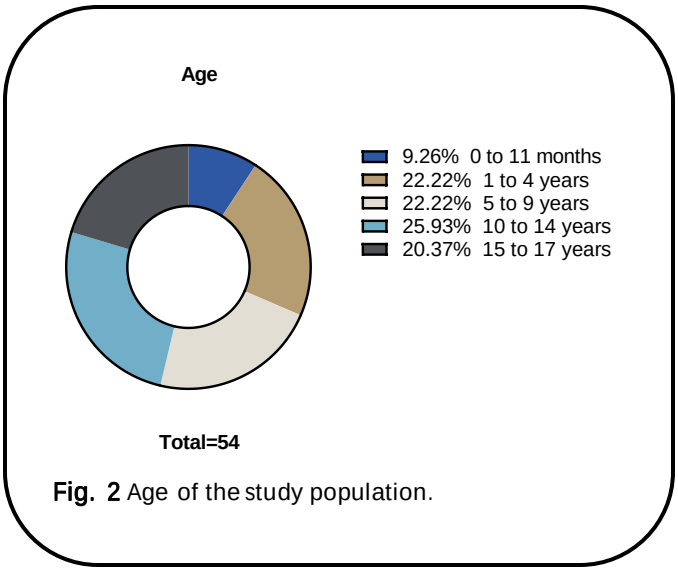

Fig. 2 Age of the study population.

Main results

Hematic biometry was performed on 98% of the participants and values within the normal range for age were found in 72% of patients. Additionally, 28% of the participants showed some degree of abnormality (see Table 1).

Table 1 Laboratory findings for hematic biometry in children with SARS-CoV-2.

*	n=54	Total %	% within sample	95% CI
Normal	13	24.01%	24.53%	22.94-26.12
Leukopenia	8	14.81%	15.09%	13.70-16.42
Leukocytosis	7	12.96%	13.21%	11.96-14.46
Lymphopenia	7	12.96%	13.21%	11.96-14.46
Neutropenia	7	12.96%	13.21%	11.96-14.46
Thrombocytosis	7	12.96%	13.21%	11.96-14.46
Thrombopenia	4	7.41%	7.55%	6.57-8.52
Not performed	1	1.85%		

* Absolute values that were identified in practical hematology were used as the reference: interpretation of the hemogram and coagulation tests [13]. CI, confidence interval

Furthermore, 65% of pediatric patients underwent inflammatory marker testing such as CRP and/or PCT shown in Table 2. In 11 patients, PCT studies were performed, and all of them showed values below 0.5 ng/mL, i.e. corresponding to a significantly improbable bacterial infection as a low risk of progression to severe disseminated infection. Liver function tests were performed in 87% of the participants (see Table 2).

Table 2 CRP, and liver function test results

		N= 54	total %	% within the sample performed	95% CI
CRP mg/L	CRP ≥5	10	18.52	28.57	26.04–31.1
	CRP <5	25	46.29	71.43	68.9–73.96
	NP	19	35.19	-	
AST U/L	AST ≥34	10	18.52	21.28	19.57–22.98
	AST <34	37	68.52	78.72	77.02–80.43
	NP	7	12.96	-	
ALT U/L	ALT ≥52	7	12.96	14.89	13.41–16.38
	ALT <52	40	74.07	85.11	83.62–86.59
	NP	7	12.96	-	

ALT, alanine aminotransferase AST, aspartate aminotransferase; CRP, C-reactive protein; CI, confidence interval. NP: Not performed

The basic coagulation parameters such as PT, PTT, and D-dimer were assessed. Eighteen patients underwent coagulation time, of whom eight patients had some alteration for their age, as follows: five patients had abnormal PT and PTT values, and three patients had alterations in PT. D-dimer was performed in five patients, four of whom showed elevated values.

In the biochemical analysis, both urea and creatinine were found to be within normal ranges for age. LDH was investigated in nine participants, and all of them showed normal results. A CPK study was performed in three patients, and the results showed high values over 308 U/L in one participant.

Urine elemental and microscopic studies were analyzed for proteinuria in 31 patients, among whom nine patients were positive (29.03%; 95% CI 26.16–31.90%).

Of seven participants who underwent stool tests, two patients showed infectious parameters.

Discussion

Although most children with COVID-19 present mild or asymptomatic clinical forms, it is necessary to investigate the measures that are used for infection control and prevention.

Worldwide, the number of patients who are infected by this disease is increasing, and health care facilities are also becoming overcrowded. Thus, etiological diagnosis is essential as is biochemical analysis to evaluate the severity and prognosis of patients who are infected with SARS-Cov-2 and to monitor the effectiveness of the therapeutic intervention.

Laboratory findings in pediatric patients with COVID-19 are not specific, as expected in viral diseases. However, several hematological disorders have been described in this disease, which were shown as variable and inconclusive results in other retrospective studies. This variability is probably due to the smaller number of pediatric patients who were included because mild to moderate clinical forms were mostly observed.

Sun et al. (2020) investigated the clinical features of severe COVID-19 pediatric patients in Wuhan, China [14]. Laboratory findings showed normal or slightly increased leukocyte, lymphocyte, neutrophil, platelet, and hemoglobin counts (7/8 patients), increased C-reactive protein, procalcitonin, and lactate dehydrogenase (6/8 patients), and abnormal liver function (4/8 patients) [14]. In the present study, leukocyte, lymphocyte, neutrophil, and platelet counts were within normal parameters in 38 of 53 patients, increased CRP was found in 10 of 34 patients, and abnormal liver function was observed in 17 of 47 patients.

A systematic review by Liguoro et al. (2020) included 38 studies comprising 655 children, and they reported leukopenia in 17.1% of patients, lymphopenia or neutropenia in 13.3%, elevated inflammatory markers (CRP or PCT) in 31.1%, elevated CPK in 14.5%, and alteration of liver enzymes in 12.4% [15]. Our study showed similar results (leukopenia in 15% of patients, lymphopenia or neutropenia in 13%, increased CRP in 29%, and increased liver function test results in 18%).

Xu et al. (2020) showed that lymphopenia was a common feature in the pathological findings of COVID-19 patients with acute respiratory distress syndrome, and it may be a critical factor that is associated with disease severity and mortality [16]. These results are in contrast to those of our study where a critically ill patient who died had initially presented biometry results that were within normal parameters.

De Francisco and Perez Canga (2020) in their complete update on kidney and the coronavirus indicated that there was an acute kidney disease with a relatively low incidence, and one of the published articles showed that 59 adults who were infected with SARS-CoV-2 reported renal involvement with early proteinuria (63% of the patients) [17]. In the present study, elemental and microscopic urine examination was performed in 31 children, among whom nine (29%) patients showed some degree of proteinuria (four patients were admitted to the intensive care unit and one patient died).

Leora et al. (2020) is the first article to describe multisystemic inflammatory syndrome in American children and adolescents, and they showed that most patients (171 patients; 92%) had four or more elevated inflammation biomarker levels; elevated erythrocyte sedimentation rate, CRP, ALT, International Normalized Ratio (INR), D-dimer, and ferritin; and lymphocytopenia, neutrophilia, and thrombocytopenia [18]. In this study, we found that markers such as PCT and CRP were within normal parameters, which is likely because 48 (88.8%) patients did not require special care and were discharged because they presented mild to

moderate symptoms. Only six (11%) patients required attention in the intensive care unit.

Conclusions

In our pediatric population, the disease caused by SARS CoV-2 occurred in 57% of males, with a greater involvement in the age group between 10 and 14 years. Laboratory test results were nonspecific in patients with this disease. However, they can be a tool for timely decision-making.

Normality in the results that were obtained from laboratory tests does not always correlate with the severe condition in pediatric patients with COVID-19, and therefore, these results cannot be correlated with the patient's prognosis.

Future studies should standardize blood tests in all patients regardless of their degree of clinical involvement, and a comparative analysis between initial blood test and follow-up test results during hospitalization should be performed in patients with severe disease to determine their impact on patient prognosis.

Because the disease was more prevalent in male patients, the investigation of ACE2 could be expanded in future studies and its relationship to more severe clinical presentations could be observed.

Abbreviations

CRP, C reactive protein
NEOC, National emergency operations committee
PCT, procalcitonin
RT-PCR, real time polymerase chain reaction reverse transcription.

Acknowledgments

The authors would like to thank the young patients who have bravely faced this pandemic throughout Ecuador without any complaints, and who have remained inside their homes despite adversity. The authors would also like to thank the IESS Quito Sur hospital, which allowed us to collect information to complete this work.

Authors' contributions

AE: Research idea, article writing, critical analysis, editorial corrections
PS: Data compilation, bibliographic review, critical analysis
JC: Research idea, data collection, critical analysis
MS: Critical analysis, data collection, statistical analysis, editorial corrections
All authors read and approved the final version of the manuscript

Authors information

Amparo Enríquez, Attending Physician at the Pediatric Emergency Service, Quito, Ecuador; Email: amparitoe2510@hotmail.com Orcid: https://orcid.org/0000-0003-3993-0195
Patricia Sanafria, Attending Physician at the Pediatric Emergency Service, Quito, Ecuador
José Charro, Pediatric Emergency Resident Physician, Quito, Ecuador
Mary Salazar, Postgraduate Physician, Pediatrics Service, Pontificia Universidad Católica del Ecuador, Quito, Ecuador

Funding

The authors financed the expenses incurred in the production of this article.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due participant confidentiality but are available from the corresponding author on reasonable request.

Ethical statements

Protection of persons

The authors declare that the procedures followed were in accordance with the ethical standards of the responsible human experimentation committee and in accordance with the World Medical Association and the Declaration of Helsinki.

Confidentiality of the data

The authors declare that they have followed the protocols of their work center on the publication of patient data.

Consent for publication

The authors have obtained the informed consent from the guardians of the patient referred to in the article. This document is in the possession of the corresponding author. The parents have signed the authorization for publication of this case.

Competing interests

The authors have no competing interests to declare.

References

1. Hasöksüz M. Kiliç S. Coronaviruses and SARS-COV-2. Turkish Journal of Medical Sciences. 2020;50:549-556. **SU**: PMC7195990

2. Tezer H, Bedir Demirdağ T. Novel coronavirus disease (COVID-19) in children. Turk J Med Sci. 2020 Apr 21;50(SI-1):592-603. **DOI**: 10.3906/sag-2004-174. **PMID**: 32304191; PMCID: PMC7195991.

3. Zimmermann P, Curtis N. Coronavirus Infections in Children Including COVID-19: An Overview of the Epidemiology, Clinical Features, Diagnosis, Treatment and Prevention Options in Children. Pediatr Infect Dis J. 2020 May;39(5):355-368. **DOI**: 10.1097/INF.0000000000002660. **PMID**: 32310621; PMCID: PMC7158880.

4. Servicio Nacional de Gestión de Riesgos y Emergencias [Internet]. Ecuador: Informes de Situación e Infografías – COVID 19; 30 Junio 2020 [Citado 05 Jul 2020]. SU: INFOGRAFIA30062020

5. Organización Panamericana de la Salud. Organización mundial de la Salud. Covid-19.Respuesta de la OPS/OMS. 29 de junio del 2020. Informe n.° 14 [Internet]. 2020. [Consultado 05 Jul 2020]. **SU**: paho/reporte/jun20

6. Henry B. Lippi G. Laboratory abnormalities in children with novel coronavirus disease 2019. Clinical Chemistry and Laboratory Medicine (CCLM) 2020;58(7)1135-1138. **DOI**: 10.1515/cclm-2020-0272

7. Coordinación de Emergencias Pediátricas - Subdirección de Docencia e Investigación - Hospital General del Sur de Quito - IESS. Protocolo de manejo de pacientes pediátricos con sospecha o confirmación de COVID-19 en Emergencias Pediátricas. 2020

8. Ministerio de Sanidad. centro de control de alertas y emergencias sanitarias. INFORMACION CIENTIFICA TÉCNICA. Enfermedad por coronavirus, COVID – 19 actualización 3 julio del 2020, PAG 42. **SU**: mscbs.gob.es

9. Safadi MAP. The intriguing features of COVID-19 in children and its impact on the pandemic. J Pediatr (Rio J). 2020 May-Jun;96(3):265-268. **DOI**: 10.1016/j.jped.2020.04.001. Epub 2020 Apr 14. **PMID**: 32305211; PMCID: PMC7195056.

10. Espinoza G, Granda M, Heredia M, León C, Orquera A, Ortega M. Consenso de recomendaciones de Hematología sobre el tratamiento de Covid19. MSP [Internet]. 2020 [Consultado 05 Jul 2020]:1-73. **SU**: salud.gob.ec/COVID19

11. Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. Signal Transduct Target Ther. 2020 Mar 27;5(1):33. **DOI**: 10.1038/s41392-020-0148-4. **PMID**: 32296069; PMCID: PMC7100419.

12. Quishpe E, Jimbo R. COVID-19 en niños. Resumen de evidencia Científica. Pontificia Universidad Católica del Ecuador. [Internet]. 2020 [Consultado 05 Jul 2020]. **SU**: puce.edu.ec/covid19

13. Huerta Aragonés J, Cela de Julian E. Hematología practica: interpretación del hemograma y de las pruebas de coagulación .En: AEPap (ed.).Curso de actualización pediatría 2018.Madrid:Lua Ediciones 3.0;2018:507-526.

14. Sun D, Li H, Lu XX, Xiao H, Ren J, Zhang FR, et al. Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center's observational study. World J Pediatr. 2020 Jun;16(3):251-259. **DOI**: 10.1007/s12519-020-00354-4. Epub 2020 Mar 19. **PMID**: 32193831; **PMCID**: PMC7091225.

15. Liguoro I, Pilotto C, Bonanni M, Ferrari ME, Pusiol A, Nocerino A, Vidal E, Cogo P. SARS-COV-2 infection in children and newborns: a systematic review. Eur J Pediatr. 2020 Jul;179(7):1029-1046. **DOI**: 10.1007/s00431-020-03684-7. Epub 2020 May 18. Erratum in: Eur J Pediatr. 2021 Feb 1;: **PMID**: 32424745; **PMCID**: PMC7234446.

16. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020 Apr;8(4):420-422. **DOI**: 10.1016/S2213-2600(20)30076-X. Epub 2020 Feb 18. Erratum in: Lancet Respir Med. 2020 Feb 25;: **PMID**: 32085846; **PMCID**: PMC7164771.

17. De Francisco ALM y Perez Canga JI Coronavirus y Riñón. Actualización Completa 09 de junio de 2020 ,del servicio de nefrología ,hospital universitario valdecilla Disponible en : https://www.nefrologiaaldia.org/es-articulo-coronavirus-rinon-actualizacion-completa-09-305

18. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Overcoming COVID-19 Investigators; CDC COVID-19 Response Team. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. N Engl J Med. 2020 Jul 23;383(4):334-346. **DOI**: 10.1056/NEJMoa2021680. Epub 2020 Jun 29. **PMID**: 32598831; **PMCID**: PMC7346765.

DOI: Identificador de objeto digital
PMID: identificador de PubMed
SU: Short URL

Publisher 's Note