



Prevalence, clinical features and outcomes of neonatal Covid-19 infection at a tertiary center in Turkey

Erbu Yarci^{a,*}, Sefika Elmas Bozdemir^b

^aDepartment of Neonatology, Dortcelik Childrens Hospital, Bursa, Turkey

^bDepartment of Pediatric Infectious Diseases, Dortcelik Childrens Hospital, Bursa, Turkey

ARTICLE INFO

Keywords:

Covid-19; newborn; outcome; prevalence

Received: Aug 23, 2021

Accepted: Nov 10, 2021

Available Online: Feb 15, 2022

DOI: [10.5455/annalsmedres.2021.08.530](https://doi.org/10.5455/annalsmedres.2021.08.530)

Abstract

Aim: Newborns constitute a special and sensitive group within the pediatric age group due to their unique characteristics and disease. We evaluated the prevalence, clinical features and outcomes of neonates admitted to emergency department and hospitalized with suspected SARS-CoV-2 infection.

Materials and Methods: In this retrospective, single centre study all neonates admitted to emergency department with suspected SARS-CoV-2 infection between March 11, 2020 and March 11, 2021 were enrolled.

Results: Fifty-five newborns were hospitalized in (Neonatal Intensive Care Unit) NICU with a suspicion of SARS-CoV-2 infection during the study period. PCR was positive in 14 newborns out of 55 hospitalized newborns (25.5%). Thirteen (92.8%) newborns with a positive SARS-CoV-2 PCR had household contact. The most common findings on admission were fever (43%), feeding intolerance (29%) and tachypnea (14%). One (7%) newborn was asymptomatic on admission. Three newborns (21%) had lymphopenia. Seven (50%) newborns had leukopenia, but none of them had neutropenia. D-dimer levels of nine (64%) SARS-CoV-2 positive newborns were elevated but none of these patients had coagulation disorders or problems needing treatment. Five of fourteen PCR positive newborns (35%) needed supplemental oxygen, while a newborn baby (7%) needed non-invasive mechanical ventilation.

Conclusions: Fever is a common symptom in SARS-CoV-2 infected newborns but new symptoms will be encountered in the course of the pandemics. Clinical information and course of SARS-CoV-2 in newborns has an obscurity. In the pandemic conditions all newborns, especially having a contact with a SARS-CoV-2 infected person must be tested for SARS-CoV-2 even if having no symptoms.



Copyright © 2022 The author(s) - Available online at www.annalsmedres.org. This is an Open Access article distributed under the terms of Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Introduction

Coronavirus disease-19 (COVID-19) which is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), started in the initial days of December 2019 as an outbreak in Wuhan, China and it was declared as a pandemic on 11 March 2020 by The World Health Organization (1). In the pediatric population, especially in the younger, morbidity and mortality rates were prominently lower than the adults (2). Newborns constitute a special and sensitive group within the pediatric age group due to their unique characteristics and diseases (3). A multicenter study from Turkey was carried out presenting the clinical course of disease in 37 newborns with community-acquired SARS-CoV-2. The most frequent findings in that study were fever (49%), hypoxemia (41%), and cough (27%), respectively (4). There are some other case series reports on outcomes of newborns born to SARS-CoV-2 positive mothers all over the world. It was reported that two newborns were found to be

SARS-CoV-2 PCR positive born from 70 SARS-CoV-2 PCR positive mothers in a study by Ng et al. In another study, 2 of 49 newborns were detected to be SARS-CoV-2 positive, born from SARS-CoV-2 PCR positive mothers. Most of the SARS-CoV-2 positive newborn babies had pulmonary symptoms or sepsis like syndrome. While different clinical presentations due to SARS-CoV-2 are under-described even in children, different clinical courses in newborns are even less defined (5-7).

Also, there are no reports on the prevalence of SARS-CoV-2 in newborns admitted to emergency department and hospitalized with suspected SARS-CoV-2 infection in Turkey. In this study, we evaluated the clinical spectrum of COVID-19 disease and outcomes of newborns hospitalized. The clinical spectrum of the newborns in this study comprised sepsis like disease, pneumonia, myocarditis and encephalitis, which distinguishes this study from others.

Materials and Methods

This retrospective, single centre observational study was conducted in a level III neonatal intensive care unit (NICU) in Bursa, the fourth largest city of Turkey. The study conformed

*Corresponding author:

Email address: erbuyarci@yahoo.com (Erbu Yarci)

to the Declaration of Helsinki and was initiated upon approval of Institutional Ethical Review Board, and the Ministry of Health and parental informed consent was obtained from each patient included in the study. All neonates admitted to emergency department with suspected SARS-CoV-2 infection between March 11, 2020 and March 11, 2021 were enrolled. In the NICU, suspected or proven COVID-19 newborns were placed in 4-bed-COVID-19 NICU distinct from other newborns.

Neonates;

1. developing symptoms suggestive of COVID-19 after household contact with a COVID-19 patient,
2. having clinical or radiologic evidence of pneumonia, acute respiratory distress syndrome or influenza-like illness,
3. having fever $\geq 37.5^{\circ}\text{C}$ and at least one of the following respiratory symptoms, which must be of acute onset: persistent cough (with or without sputum), hoarseness, nasal discharge or congestion, shortness of breath, sore throat, wheezing, sneezing
4. seizures were tested by nasopharyngeal and oropharyngeal PCR swabs. The management of neonates with the diagnosis of COVID-19 was in accordance with the guidelines issued by the Turkish Ministry of Health and the Turkish Neonatal Society (8, 9).

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) for Windows, version 20.0 (SPSS Inc., Chicago, IL) was used for analysis of the data. We presented continuous values as the mean \pm standard deviation (SD) or median (minimum–maximum) according to the homogeneity of the distribution, which was evaluated by the Kolmogorov–Smirnov test. We presented categorical values as the number and percentage, and analyzed them by the χ^2 test. The Student's t test was used for continuous variables with normal distribution, and the Mann-Whitney U test and Kruskal–Wallis test were used for continuous variables which did not exhibit a normal distribution. Correlation between the independent parameters was investigated by bivariate (Pearson and Spearman) correlation analysis. A p value of < 0.05 was considered to indicate statistical significance.

Results

Fifty-five newborns were hospitalized in NICU between 11 March 2020 and 11 March 2021 with a suspicion of SARS-CoV-2 infection. Demographic and clinical characteristics of newborns at admission are summarized in Table 1.

All newborns were outpatients admitted to our emergency department/policlinics or newborns referred from other hospitals to our centre for hospitalization. Forty-two infants were term newborns (76%) and the remaining was late preterms (24%). Of 55 newborns, 48 (87%) were Turkish citizens; seven were Syrian refugees (13%).

At least one parent of 16 newborns were smokers. PCR was positive in 14 newborns out of 55 hospitalized newborns (25.5%). Thirteen (92.8%) newborns with a positive SARS-CoV-2 PCR had household contact and one had a history of symptomatic non-household contact. Number of SARS-CoV-2 PCR positive mothers was 18 (33%) and nine of them (50%) had SARS-CoV-2 PCR positive newborn. The mothers of five SARS-CoV-2 PCR positive newborns had negative tests for SARS-CoV-2 PCR, but at least one person living at the same home had a positive PCR test for SARS-CoV-2 (5/38, %13). The most common

findings on admission were fever (43%), feeding intolerance (29%) and tachypnea (14%). On the other hand, one (7%) newborn was asymptomatic on admission. Hemoglobin, platelet counts, urea, creatinin, CRP, procalcitonin, LDH, Troponin-I, CK-MB, ferritin, PT, PTT and INR levels did not differ between SARS-CoV-2 positive and SARS-CoV-2 negative newborns ($p > 0.05$). Although there was no difference between SARS-CoV-2 positive and negative newborns in terms of mean lymphocyte counts, three newborns (21%) had lymphopenia among SARS-CoV-2 positive newborns. Median WBC and neutrophil levels of SARS-CoV-2 positive newborns were significantly lower than SARS-CoV-2 negative newborns ($p = 0.006$ and $p = 0.014$ respectively). Seven of SARS-CoV-2 positive newborns (50%) had leukopenia, but none of them had neutropenia.

SARS-CoV-2 positive newborns had higher albumin levels compared to SARS-CoV-2 negative newborns (3.76 ± 0.52 g/dl vs 3.49 ± 0.34 g/dl; $p = 0.047$). SARS-CoV-2 positive newborns had higher median ALT levels compared to SARS-CoV-2 negative newborns within the normal range ($p = 0.038$). Only one (7%) of the SARS-CoV-2 positive newborns had elevated ALT level. Median AST levels did not differ between the SARS-CoV-2 positive and negative newborns, but three (21%) newborns had elevated AST levels among the SARS-CoV-2 positive newborns.

D-dimer levels of nine (64%) SARS-CoV-2 positive newborns were elevated but none of these patients had coagulation disorders or problems needing treatment. Median d-dimer levels of SARS-CoV-2 negative newborns did not differ from the positive group ($p = 0.45$). One newborn had jaundice on admission and he had dysmorphic appearance and was found to have direct hyperbilirubinemia. On further examinations he was found to have pulmonary stenosis on echocardiography and butterfly vertebra was diagnosed on X-ray examination. He was referred to a university hospital with a diagnosis of Alagille syndrome. Before referral, a PCR test was carried on and resulted positive for SARS-CoV-2. One newborn was admitted to pediatric emergency policlinic with complaint of afebrile seizure on postnatal third day. He was hospitalized and further evaluation was performed. Cranial MRI was found to be consistent with neonatal viral encephalitis. The nasopharyngeal swab for SARS-CoV-2 PCR was positive. SARS-CoV-2 in CSF was negative. A nasopharyngeal swab sample was inoculated in cell culture for SARS-CoV-2 grew positive. To rule out other common neurotrophic viruses; including herpes simplex 1-2, enteroviruses (echovirus, coxsackievirus and poliovirus), mumps and varicella-zoster virus in CSF were tested and resulted negative. Also, rotavirus in stool was found to be negative. He was treated with ampicillin and gentamicin. The seizures were treated with oral phenobarbital. Cranial MRI on day 15 showed that the previous neuroradiologic findings exhibited no longer. Throughout his hospitalization, he did not have respiratory symptoms. The patient was discharged on day 16 without any neurologic deficit.

Four newborns were admitted to emergency department with complaints of fever and tachypnea. After clinical and laboratory evaluation they were found to have fever, tachycardia, prolonged capillary refilling time (> 2 seconds) and elevated levels of troponin-I. Echocardiography was performed and intravenous immunoglobulin (IVIG) treatment was recommended for myocarditis. All of these four newborns were given

Table 1. Demographic and clinical characteristics of the newborns at admission

Variable	COVID-19 PCR (+) n = 14 Mean ± SD or Median (min-max)	COVID-19 PCR (-) n=41 Mean ± SD or Median (min-max)	p
Maternal age (years)	29.1±4.7	27.9 ± 5.7	0.50
Birth weight (gr)	3205 ± 428	3047 ± 569	0.39
Gestational age (weeks)	38 (35-41)	38 (34-41)	0.37
Length of hospital stay (days)	7 (3-25)	10 (4-25)	0.18
Age at admission (days)	9 (2-27)	10.5 (3-27)	0.78
Delivery mode, CS (n, %)	8 (57)	23 (56)	1
Term birth (n, %)	13 (92.8)	29 (70)	0.04
Sex (male,%)	8 (57)	22(53)	0.73
Nationality, Turkish (n, %)	12 (71.5)	35 (85.3)	0.47
History of COVID-19 positive household contact (n, %)	13 (92.8)	15 (36.6)	0.002
Maternal COVID-19 PCR(+) (n, %)	9 (64)	9 (21)	0.023
Smoker parents (n, %)	10 (71)	6 (14)	0.002
Complaints at admission			NA
Fever	6 (43)	15 (36.5)	
Poor feeding	4 (29)	11 (27)	
Tachypnea	2 (14)	7 (17)	
Seizure	1 (7)	0	
Diarrhea	0	2 (5)	
Cough	0	5 (12)	
Rhinorrhea	0	1 (2.5)	
Asymptomatic	1(7)	0	

COVID-19, Coronavirus disease 2019; CS, Cesarean section; PCR, Polymerase chain reaction; SD, Standard deviation

IVIIG treatment and were evaluated with consecutive echocardiographic examination. They all had normal cardiac functions in follow-up and were discharged without any sequelae.

One newborn was admitted to emergency department on postnatal 13 th day with complaint of fever. Although not having a history of contact or symptoms in the parents he was found to have a positive PCR for SARS-CoV-2. Nasopharyngeal swap specimens of the parents for SARS-CoV-2, resulted positive for both. The chest X-ray was normal on admission. On postnatal 17th day he had fever, coughs and needed non-invasive mechanical ventilation. On chest X-ray a new infiltration on the right appeared and the treatment was changed to vancomycin and amikacin from ampicillin and gentamicin. Although he had a levels of ferritin 880 ng/ml on admission (normal range 21-274 ng/ml), on 17 th day ferritin levels increased to 1749 ng/ml and 5045 ng/ml on 18th day consecutively. There was no cardiac dysfunction on cardiac examinations, but his respiratory symptoms worsened with persistent fever. Dexamethasone treatment with a dose of 0.6 mg/kg/day was given for five days and ferritin levels decreased to the normal level (239 ng/ml) and there was no need for respiratory support. He was discharged on postnatal 27 th day. All newborns had chest radiograph, of whom 5 (36%) had positive radiographic findings and only one neonate was evaluated with computed tomography. Five of fourteen PCR positive newborns (35%) needed supplemental oxygen, while a newborn baby (7%) needed non-invasive mechanical ventilation.

One 27-day-old newborn was brought from home with fever and tachypnea. Both of her parents were SARS-CoV-2 PCR positive for five days, but her SARS-CoV-2 PCR resulted negative. She had a chest X-ray on admission showing bilateral



Figure 1. Chest X-ray on admission showing bilateral pneumonic infiltration more on the left

pneumonic infiltration more on the left (Figure 1).

She was evaluated with chest computed tomography revealing pleural based widespread areas of ground glass opacity, consolidations and nodular infiltrates tending to coalesce, extending into the upper zones, consistent with viral pneumonia (Figure 2).

In the pandemic conditions she was treated as if she had SARS-CoV-2 pneumonia. She needed oxygen treatment with nasal canula and Lopinavir-Ritonavir was added to her antibiotic treatment. She was discharged after 15 days of treatment without any sequelae.



Figure 2. Chest computed tomography revealing pleural based widespread areas of ground glass opacity, consolidations and nodular infiltrates tending to coalesce, extending into the upper zones, consistent with viral pneumonia

Only two patients were searched for accompanying respiratory viruses which resulted negative. Azitromycin and oseltamivir were not used but all newborns except the newborn with a diagnosis of Alagille syndrome were given ampicillin antibiotic treatment. There were no complications including disseminated intravascular coagulopathy, multiple organ failure, and intracranial hemorrhage or necrotizing enterocolitis.

Discussion

In this single center retrospective study, we evaluated hospitalized newborns with suspected SARS-CoV-2. Fourteen (25.5%) were found to have positive PCR results for SARS-CoV-2 out of 55 hospitalized newborns. In a case series including 70 outpatient newborns, the rate of SARS-CoV-2 positive newborns was reported to be 11.4% (7).

In these proven SARS-CoV-2 cases, one newborn was asymptomatic and admitted to hospital with a complaint of jaundice, diagnosed with Alagille Syndrome and was found to have a positive PCR for SARS-CoV-2 incidentally. The most common findings on admission were fever, feeding intolerance and tachypnea. Fever and cough were reported to be most common symptoms in a series by Kanburoglu et al., but they reported no asymptomatic neonates (4). Nanavati et al. reported 21 SARS-CoV-2 infected neonates 14 (66%) of whom were asymptomatic (6). Similarly, a nation-wide study from Spain reported 20% asymptomatic newborns out of 26 community acquired Covid-19 cases (10). Also a review by Karabay et al. reported nearly 17% of asymptomatic newborn SARS-CoV-2 cases (11). In our opinion it will be better to test newborns for SARS-CoV-2 on hospital admission with any complaint in the pandemic conditions.

Five (35%) of SARS-CoV-2 cases needed supplemental oxygen and one (7%) needed non-invasive mechanical ventilation. This finding was similar to results reported by Kanburoglu et al (4). Of the proven fourteen SARS-CoV-2 cases, four had myocarditis, one had encephalitis and one had pneumonia requiring mechanical ventilation. Although the numbers of SARS-CoV-2 cases were small, there were wide-spread clinical findings. These were contrary to reported less severe clinical course in

children by Dong et al. and Bai et al (12, 13). Also the rates of severe cases were higher than reported by Kanburoglu et al (4). Clinicians will have to face many different clinical entities in the course of the pandemics and must always keep in mind SARS-CoV-2 as an etiological factor. In a review, lymphopenia and leukopenia were reported to be 35% and 11% respectively. In the present study lymphopenia was lower (21%) and leukopenia was higher (50%) than reported. Neutropenia was reported to be 19% in the same review, while none of the SARS-CoV-2 positive newborns had neutropenia in our study (11).

Karabay et al. reported raised ALT and AST levels in 9% and 58% of the SARS-CoV-2 newborns respectively while only one newborn (7%) had elevated ALT level and three (21%) had elevated AST level among SARS-CoV-2 positive newborns in this study (11). CRP and procalcitonin are markers of infection widely used in all age groups including newborns in the discrimination of infection. The CRP and procalcitonin levels of proven SARS-CoV-2 cases were not higher than those with suspected SARS-CoV-2. Two newborns (14%) had elevated CRP levels and five newborns (35%) had elevated procalcitonin levels. Previously, Kanburoglu et al. reported that CRP and PT values can be used to differentiate disease severity but that was not compatible with our findings. They reported elevated CRP and procalcitonin levels in 27% and 50% in SARS-CoV-2 positive newborns which were higher than our results (4). Also Whittaker et al. reported that CRP levels were higher in children with shock during the SARS-CoV-2 compared to children without shock. In the present study, there were no patients having shock during the course of infection with SARS-CoV-2 (14).

Nine (64%) of SARS-CoV-2 positive newborns had elevated levels of d-dimer. Elevated levels of d-dimer were reported to indicate poor prognosis in adults (15, 16), however in the present study there were no complications related to blood coagulation anomalies, similar to a recent case series reported from Brazil (5). Newborns having PT levels lower than 14 seconds were reported to be less likely to be in severe/critical state or supplemental oxygen demand (4). Contrary to this report, in the present study, all of the SARS-CoV-2 positive newborns had PT levels lower than 14 seconds but four had myocarditis, one had encephalitis and one needed non-invasive mechanical ventilation and steroid treatment due to pneumonia.

In the literature there is very limited data on household contact in newborns. Kanburoglu et al. reported a household contact rate of 76% but in the present study it was 92.8% (4). This rate was lower than a previously reported systematic review of children (98.7%)(17). All newborns had chest radiograph. Five (36%) neonates had positive radiographic findings, which was similar to reported by Kanburoglu et al (4). Only one neonate was evaluated with computed tomography; although he had a negative PCR for SARS-CoV-2, his parents were positive for SARS-CoV-2. Xia et al. reported that 20% of 20 children with SARS-CoV-2 pneumonia had no abnormalities on chest CT (18). Similarly, reported by Kanburoglu et al (4). CT should be preserved for selected cases, not only in SARS-CoV-2 positive cases, but also in patients with a high suspicion of SARS-CoV-2 infection having a contact with a SARS-CoV-2 infected person as mentioned above.

Myocarditis in newborn period is a rare entity and treatment with either steroids or IVIG is controversial (19). Similarly,

the optimal management for myocardial injury associated with SARS-CoV-2 patients of either adults or children has not been determined, yet (20, 21). Because there is a big and deep gap of data for management of newborns with myocarditis due to SARS-CoV-2, we considered these newborns as a candidate of multisystem inflammatory syndrome in children and used IVIG for treatment. We chose the newborns whose clinical findings did not improve during the follow-up period and who had an increase in both troponin I levels and acute phase reactants. We did not perform any further evaluation for the other respiratory viruses because these newborns had either SARS-CoV-2 PCR positivity or a parent with COVID-19 disease.

HIV protease inhibitor lopinavir, boosted with ritonavir, has been offered for the treatment of SARS-CoV-2 at the beginning of the pandemic. Guidelines issued by the Turkish Ministry of Health and the Turkish Neonatal Society also offered to use Lopinavir-Ritonavir for neonates with the diagnosis of SARS-CoV-2 (8, 9). In the lightning of these guidelines we used Lopinavir-Ritonavir for a newborn with SARS-CoV-2 pneumonia. As we used Lopinavir-Ritonavir for only one newborn we could not comment on its benefit. Later in the following studies data obtained from large clinical trials did not support using lopinavir/ritonavir to treat SARS-CoV-2 in hospitalized patients.

Dexamethasone is the only drug associated with decreased mortality in adult patients, however trials in children are ongoing and the benefits and risks are uncertain. For selected children with severe or critical SARS-CoV-2 who require mechanical ventilation or those who require supplemental oxygen and have risk factors for disease progression low-dose glucocorticoids (dexamethasone, prednisolone, methylprednisolone or hydrocortisone) may be given up to 10 days or until discharge, whichever is shorter. Dexamethasone is preferred in treatment if available (22). Based on this information we used dexamethasone in the treatment of one newborn with worsening respiratory symptoms.

Limitations

This study has limitations. First, it is a single centre study. Secondly it has a small sample size which may cause conflicting results from previously published data. Besides its small sample size it has a wide variety of severe clinical presentations.

Conclusion

In conclusion, fever is a common symptom in SARS-CoV-2 infected newborns but new symptoms concerning different organs and systems will be encountered in the course of the pandemics. Clinical information and course of SARS-CoV-2 in newborns has an obscurity. In the pandemic conditions all newborns, especially having a contact with a SARS-CoV-2 infected person must be tested for SARS-CoV-2 even if having no symptoms. Necessary precautions should be taken to protect newborn infants from SARS-CoV-2, especially in the presence of infected mothers and/or household contacts. Further studies with higher sample size are needed to learn more about SARS-CoV-2 infection management not only in newborns, but also in all age groups.

Ethical Approval

This study conformed to the Declaration of Helsinki and was initiated upon approval of Institutional Ethical Review Board, and the Ministry of Health and informed consent was obtained from each family prior to the study. (Approval date: 07.04.2021, No:2021-6/3).

References

- Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *NEJM* 2020;382:727-33.
- Morand A, Fabre A, Minodier P, et al. COVID-19 virus and children: what do we know? *Arch Pediatr* 2020;27:117-8.
- Williams K, Thomson D, Seto I, et al. StaR Child Health Group. Standart 6: Age groups for pediatric trials. *Pediatrics* 2012;129:153-60.
- Kanburoglu MK, Tayman C, Oncel MY, et al. A Multicentered Study on Epidemiologic and Clinical Characteristics of 37 Neonates With Community-acquired COVID-19. *Pediatr Infect Dis J* 2020;39:e297-e302.
- dos Santos Beozzo GPN, de Carvalho WB, Krebs VLJ, et al. Neonatal manifestations in COVID-19 patients at a Brazilian tertiary center. *Clinics* 2020;75:e2407.
- Nanavati R, Mascarenhas D, Goyal M, et al. A single-center observational study on clinical features and outcomes of 21 SARS-CoV-2-infected neonates from India. *Eur J Pediatr* 2021;180:1895-906.
- Ng KF, Bandi S, Bird PW, et al. COVID-19 in Neonates and Infants: Progression and Recovery. *Pediatr Infect Dis J* 2020;39:e140-e2.
- Turkish Ministry of Health. COVID-19 Yeni Koronavirüs Hastalığı [Online]. 2020. Available at: <https://covid19bilgi.saglik.gov.tr/tr>. Accessed June 23, 2020.
- Erdeve O, Cetinkaya M, Bas AY, et al. The Turkish Neonatal Society proposal for the management of COVID-19 in the neonatal intensive care unit. *Turkish Archives of Pediatrics* 2020;55:86-92.
- Colomer BF, Manuel Sánchez-Luna M, de Alba Romero C, et al. Neonatal Infection Due to SARS-CoV-2: An Epidemiological Study in Spain. *Front Pediatr* 2020;8:580-4.
- Karabay M, Cinar N, Suzan OK, et al. Clinical characteristics of confirmed COVID-19 in newborns: a systematic review. *J Matern Fetal Neonatal Med* 2020;1-12.
- Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. *Pediatrics* 2020;145:e20200702.
- Bai K, Liu W, Liu C, et al. Clinical analysis of 25 COVID-19 infections in children. *Pediatric Infectious Disease Journal* 2020;39:e100-e3.
- Whittaker E, Bamford A, Kenny J, et al. for the PIMS-TS Study Group and EUCLIDS and PERFORM Consortia Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2. *JAMA* 2020;324:259-69.
- Zheng Z, Peng F, Xu B, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *J Infect* 2020;81:e16-e25.
- Zhang L, Yan X, Fan Q, et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. *J Thromb Haemost* 2020;18:1324-9.
- Panahi L, Amiri M, Pouy S. Clinical Characteristics of COVID-19 Infection in Newborns and Pediatrics: A Systematic Review. *Arch Acad Emerg Med* 2020;18;8:e50.
- Xia W, Shao J, Guo Y, et al. Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. *Pediatric Pulmonology* 2020;55:1169-74.
- Yen CY, Hung MC, Wong YC, et al., Role of intravenous immunoglobulin therapy in the survival rate of pediatric patients with acute myocarditis: A systematic review and meta-analysis. *Sci Rep* 2019;18;9:10459.
- Son MBF, Friedman K. Covid-19: Multisystem Inflammatory Syndrome in Children (Mis-C) Clinical Features, Evaluation, and Diagnosis. UpToDate 2021. Available online: <https://www.uptodate.com/contents/covid-19-multisystem-inflammatory-syndrome-in-children-mis-c-clinical-features-evaluation-and-diagnosis> (accessed on 15 May 2021)
- Caforio AL. COVID-19: Cardiac manifestations in adults. In: Mancini D & Dardas TF. UpToDate 2021. Available online: <https://www.uptodate.com/contents/covid-19-cardiac-manifestations-in-adults>.
- Deville JG, Song E, Ouellette CP. COVID-19: Management in children. In: Mancini D & Dardas TF. UpToDate 2021. Available online: <https://www.uptodate.com/contents/covid-19-management-in-children>.