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Mortality Rate in Hospitalized Pediatric Patients with COVID-19 Infection in Iran: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: There is little data on the mortality rate and severity of COVID-19 infection among pediatrics. This knowledge is particularly significant because pneumonia is the main underlying cause of death in children worldwide. This systematic review and meta-analysis aims to evaluate the mortality rate of COVID-19 in the pediatric population in Iran.

Methods: A systematic review and meta-analysis of the publications was conducted based on the PRISMA guidelines to search for COVID-19 child mortality. PubMed, Google Scholar, Embase, Medline databases, and Persian database were searched for publications on pediatric COVID-19 infections published in Iran with a focus on mortality in children with COVID -19 infection in Iran between January 1st to April 30th, 2021. Articles representing at least one Pediatric with and without comorbidities, COVID-19 infection, and informed outcomes were examined.

Results: Eight studies including three case series, and five retrospective cross-sectional studies altogether representing a total of 238 pediatric patients with COVID-19 were included in this meta-analysis. Of this population, 14 patients had died. In this study, the mean age of the study sample was 6.7 years. The mortality rate among children hospitalized with COVID-19 was 9% (95% CI 0.055-0.146). Also, children with comorbidities had a higher risk of COVID-19 related mortality.

Conclusion: Unlike adults, most infected children are asymptomatic and are not usually hospitalized. Children with underlying conditions are at increased risk of severe COVID-19 related mortality than children without underlying illness. More attention should be paid to children with comorbidities and children of young age.

Introduction

Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-COV2) infection is accountable for the new coronavirus infection (COVID-19) and the famous pandemic of the time. It was first initiated at Wuhan in December 2019.[1,2] The outbreak of SARS-COV-2 has been announced as a global public health emergency by the World Health Organization (WHO).[3] COVID-19 mainly targets the respiratory tract and lungs and the most typical presentations of the infection involve fever, fatigue, dyspnea and dry cough, however gastrointestinal presentations may also be prevalent.[1,4] Therefore COVID-19 has a more variable clinical period than the common cold. COVID-19 is directly transmissible from person to person via respiratory droplets and possibly manipulates the ACE2 receptor to infect humans.[5] COVID-19 appears to be less threatening in pediatric patients and is associated with milder symptoms than in adults.[6] Numerous studies have demonstrated that pediatrics and adolescents comprise a small ratio of the verified case.[7] Nevertheless, the infection course in pediatrics can be indistinct, with the most typical clinical symptoms and signs being fever, sore throat, and headaches.[8] On the other hand, it has been speculated that asymptomatic pediatric carriers may play a role in maintaining virus circulation in the society. The varied status of immune competence may account for the differences in the clinical manifestation and prevalence of COVID-19 infection in children and adults.[9,10] A more distinct feature seen in children with COVID-19 is referred to as "Multisystem Inflammatory Syndrome associated with COVID-19 (MIS-C)" or "Pediatric inflammatory multisystem syndrome (PIMS)".[11] The clinical presentations of MIS-C and PIMS-TS are both distinguishable from one another while resembles other inflammatory syndromes, like Kawasaki disease, which is a toxic shock syndrome.[8] Children with MIS-C more usually tested positive for COVID-19 antibody than for the actual virus via nasopharyngeal real-time reverse transcription polymerase chain reaction (rRT-PCR) assay. Inspite of the lack of absolute knowledge on the pathogenesis of COVID-19, immune misdirection is thought to precipitate viral proliferation and tissue injuries.[12] Thus, early detection and control of PIMS are essential to minimize the risk of long-term consequences, morbidity, and mortality.[13]

Although the prodromal period is more often less serious, fatal SARS-CoV-2 infection with acute respiratory distress syndrome (ARDS) and multiple organ failure is still very likely.[14] Immune compromising conditions like diabetes, cardiovascular disease and hypertension are known to trigger severe SARS-CoV-2 infections and related mortality.[5,15,16,8] Although prior investigations have documented pre-existing comorbidities as key determinants for severe COVID-19 in adults, this is yet to be confirmed in the pediatric population with regards to comorbidities and related SARS-CoV-2 outcomes.[8] Numerous analytical studies on SARS-CoV-2 disease in children report varied results in terms of clinical manifestations, mortality and infection rates unlike in adults. Acute disease in pediatrics and adults generally manifest in a similar manner with severe pneumonia marked by respiratory distress, blood oxygen saturation less than 92%, and septic shock. These patients require mechanical ventilation, immunomodulatory regimens and treatment with antivirals.

Despite many investigations on children, little is known about the prevalence and features of fatality among children in Iran. Although several studies in Iran, have studied children with SARS-CoV-2 and fatal outcomes, there exists limited data on the demographics and clinical characteristics of children infected with COVID-19. This systematic review and meta-analysis was conducted to evaluate and estimate the

mortality rate in hospitalized pediatric patients with COVID-19 Infection in Iran.

Materials and Methods

Search Strategy: The main purpose of this Systematic Review and Meta-Analysis study was the estimation and characterization of mortality rate in hospitalized pediatric cases with SARS-CoV-2 infection in Iran. In particular, the primary analysis focused on age, clinical manifestations, and outcomes of children with COVID-19. For this, databases such as Web of Sciences, Scopus, PubMed/Medline, Embase, Iranian Scientific Information Database (SID), and IranMedex were searched for both English and Persian language articles published from January 1st, 2020 until April 30th, 2021.

After searching for the relevant words in the Medical Subject Headings (MeSH) database, finally, the keywords like "COVID-19", "SARS-CoV-2", "novel coronavirus", and "coronavirus" and "child", "children" "pediatric", "paediatrics", "teenage", "adolescent", "infant", and "newborn" were typed to retrieve articles related to COVID-19 infection. To obtain articles pertaining to COVID-19 infection in pediatric patients, the terms "mortality", "death" and "dying", "fatality" "rate" were queried along with the coronavirus search. In order to extract articles possibly missed by our systematic search, Google Scholar was queried for articles on the mortality associated with SARS-CoV-2 infection in pediatric patients. References were scrutinized with mendeley software (version 1.19.8) which was also used to omit duplicates. The systematic literature search was done in agreement with the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines to improve comprehensibility and clarity of reporting.

Inclusion Critetia: Articles reporting pediatric patients with COVID-19 and its outcomes and articles depicting the outcomes and severity of COVID-19 infection in pediatric patients was retained. In addition we gathered case-control, case reports, cross-sectional studies, case series, and letters to the editors that included clinical, laboratory and imaging of pediatric patients infected with COVID-19.

Exclusion Criteria: The exclusion criteria are as follows: 1) articles not stating pediatric outcome; 2) only adult studies; 3) systematic reviews, meta-analyses, and pre-existing reviews were excluded, just original articles were included; 4) articles with patients without confirmed diagnosis of SARS-CoV-2; 5)basic science investigations; 6) clinical recommendations, discussions, and guidelines; 7) clinical presentation studies 8) studies not reporting comorbidities 9) articles which data on the comorbidity was indistinguishable from adult comorbidity data; and 10) studies on other coronavirus.

Data Extraction: Eventually, studies that stated the outcome of children with COVID-19, from any part of Iran referring to clinics, hospitals, or neonatal intensive care units (NICU) were extracted. The collected data consisted of the number of patients, outcomes, demographics, signs and symptoms, imaging results, laboratory markers, and medications. Risk of bias for observational studies was eliminated through the quality assessment tool published by the National Institute of Health and in order to avoid any form of bias, data was assessed independently by at least two investigators and the disagreements were resolved by a third researcher. Then, the following information was extracted: first author name, date of publication, Study type, city, total number of COVID-19 Infection, number of mortality, median age and gender of affected children (Table 1). Also the study aim, number of COVID-19 infections without comorbidities, number of COVID-19 with comorbidities, type of comorbidities in patients who died, and the overall prevalent comorbidities was sorted from the literature (Table 2).

Statistical Analyses: All statistical calculations were performed using Comprehensive Meta- Analysis (CMA) software version 2.0 (Biostat, USA). Random-effect model meta-analysis was

Table 1. Summary and Characteristics of the Eight Studies Included in This Systematic Review and Meta-Analysis

Study	Study type	City	Total number COVID-19 Infection (n = 236)	Mortality (N = 14)	Median age	Male n = (%)	Female n = (%)
Mamishi 2020[17]	Cross-sectional	Qom	24	3	6	11(46%)	13 (54%)
Mamishi 2020[12]	Retrospective	Tehran, Qom and Mazandaran	45	0	7	24 (53%)	21 (47%)
Eghbali 2020[18]	Case series retrospective	Tehran	4	1	11	4 (100%)	-
Shahbaznejad[13]	Cross-sectional	Mazandaran	100	4	104.63 ± 79.14 months (8.6)	57 (57%)	43 (43%)
Soltani 2020[10]	Cross-sectional	Hamadan and Kurdistan	30	1	5.8	14 (46.7%)	16 (53.3%)
Esmaeeli 2020[19]	Case series	Mashhad, Tehran, Gorgan	7 (4 infants)	2 (9M, 14Y)	9 months	5 (71%)	2(29%)
Rahimzadeh 2020[20]	Case Series	Sari, Gonabad, Mazandaran, Tehran, Mashhad	9	0	4.9	6	3
Mehrvar 2021[21]	Cross-sectional	Tehran	17	3	9.17 ± 1.5	10	7

Table 2. Comorbidities: Summary of Articles Identified in this Systematic Review and Meta-Analysis

Study	Study Aim	No comorbidities (n)	Comorbidities (n)	Kind of comorbidities in death patients (n)	Kind of comorbidities overall
Mamishi 2020[17]	Evaluate the epidemiological, clinical, and radiological and laboratory findings	24	-	3	Is not mentioned
Mamishi 2020[12]	Definition for MIS-C	39	6	0	acute lymphocytic leucaemia, chronic kidney disease, underlying seizur disorder, cerebral palsy, cardiovascular disease and Budd–Chiari syndrome were present in six (13%) patients
Eghbali 2020[18]		2	2	Aplastic Anemia 1	Aplastic Anemia 1 cyanotic congenital heart disease 1
Shahbaznejad [13]	Clinical Characteristics and Outcomes of COVID-19	96	4	Chronic renal failure 2 Down syndrome with cerebral palsy 1 Obesity 1	Underlying Diseases. Among 4 died patients, 2 children had chronic renal failure, another one was a Down syndrome with cerebral palsy, and the last one suffered from morbid obesity (16 years, weight 95 kg),
Soltani 2020[10]	The clinical, laboratory, and radiological	23	7	Fulminant pneumonia 1	Among all the cases, 23 (76.6%) cases did not have any underlying predisposing conditions, and 7 cases had a Underlying Diseases include: Chronic kidney disease 1 immunocompromised condition 4 Cerebral palsy 2
Esmaeeli 2020[19]		0	7	2	All children with Congenital Heart Diseases
Rahimzadeh 2020[20]	The incidence, severity, and prognosis of this disease are likely to be different in children compared with adults	9	0	-	-
Mehrvar 2021[20]		0	17	Burkitt lymphoma 1 Osteosarcoma 1 Acute lymphoblastic leukemia 1	All pediatric patients with cancer

utilized to calculate the mortality rate of infected pediatrics with COVID-19, and binomial distribution to calculate standard error in each study. A random effects model was chosen due to the probable variation in study samples resulting in outcomes differences due to comorbidities.

Heterogeneity in the results of various investigations was analyzed using a Chi-squared-based Q-test with a significance level of $P < 0.1$ and I2 statistics with values > 75% as significant heterogeneity. Moreover, the effects of factors affecting possible heterogeneity and comorbidities in the mortality rate of children infected with COVID-19 were evaluated by a moment-based meta-regression model. A visual inspection of the funnel plot helped assess potential publication bias. Moreover, Egger's test was done to evaluate the statistical publication bias, in which $P < 0.05$ was considered statistically significant. If the publication bias tests showed bias existed, the Duval and Tweedie ''trim and fill'' method was used to adjust for the bias.

Results

Study Patient Characteristics and mortality rate: Our search recognized eight articles published from January 1st, 2020 to April 30th, 2021. After removing duplicates and filtering from the titles and abstracts, 34 studies were assessed for eligibility. The full texts of the remaining 34 articles were reviewed for the presence of pediatric study sample who had SARS-CoV-2 disease with evident outcomes. Articles without reported patient outcomes were excluded from our study. Finally, eight articles were included in this review with a total sample size of 238 pediatric patients with laboratory-confirmed SARS-CoV-2 infection. Among these studies, about 43 cases had at least one underlying comorbidity (Table 2). Also, one article included in this review was on children with MIS-C total sample size of 45 participants (Figure 1) A PRISMA flow diagram demonstrating the systematic search is illustrated (Figure 1). The results focused on demographics, clinical data, and outcomes. Based on gender, 105 (44.5%) were female and 131 (55.5%) were male of 238 SARS-CoV-2 infected children with a mean age of 6.7 years. About 14 of the 236 patients included in this meta-analysis died while being infected with SARS-CoV-2. We obtained a total mortality ratio of 9% (95% CI 0.055-0.146) (Figure 1) recruiting a random-effects model to examine the mortality rate of COVID-19 among children with or without comorbidities.

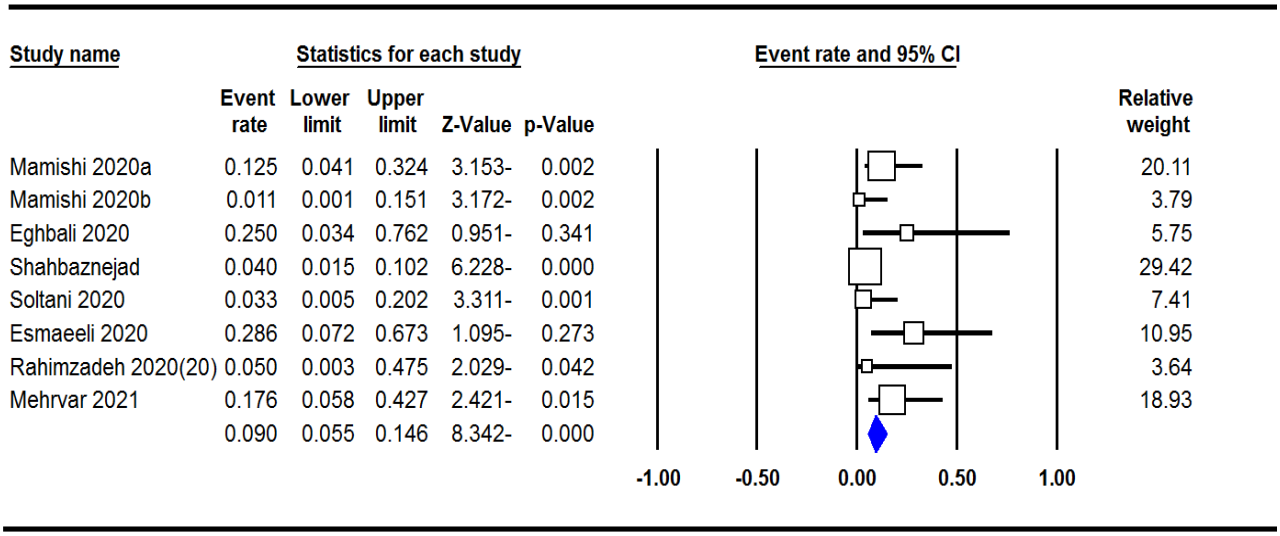

Figure 1. Forest Plot for Mortality Rate of Pediatric Patients Infected with COVID-19

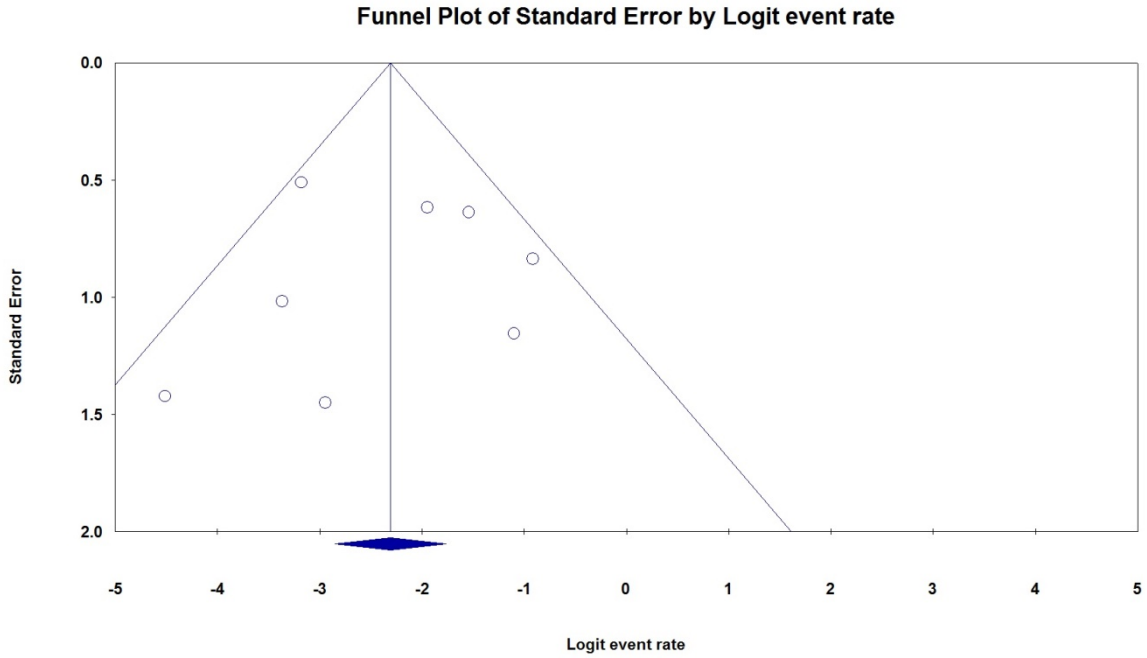

Figure 2. The Funnel Plots of Publication Bias for Mortality Rate of Pediatric Patients Infected with COVID-19

Evaluation of effects of comorbidities on mortality of COVID-19 Infection in pediatrics: Among the 236 pediatric patients with COVID-19 infection about 43 pediatrics with severe COVID-19 associated mortality had comorbidities. Also, 11 of these patients with comorbidities died. It is important to note that only 8 studies examined COVID-19-associated deaths. Typically, children who died from severe COVID-19 had comorbidities such as aplastic anemia, chronic renal failure, down syndrome with cerebral palsy, obesity, pulmonary hemorrhage, electrolyte pneumonia, congenital heart diseases, and cancer including burkitt lymphoma, osteosarcoma, acute lymphoblastic leukemia. In two of the studies all patients were found to have comorbidities. Another study reported heart disease in all 7 cases with two incidents of deaths. A study included 17 cancer patients with 3 deaths. We intended to examine the likely association between specific comorbidities and the risk of severe SARS-CoV-2 manifestations. We found different comorbidities accounting for the death in pediatric patients and no specific comorbidity was found to increase the mortality risk among COVID-19 infected patients although we found that CHD had a more prominent role in raising the mortality risk. However, more case-controlled, well-defined investigations are required to examine the link between other comorbidities on the severity of COVID-19 manifestations (Table 2).

Publication Bias: The Begg‟s and Egger‟s linear regression tests were applied to test the potential publication bias for literature on mortality rate of COVID-19 infected pediatrics. As shown in figure 2, the shapes of the Begg‟s funnel plot did not show any evidence of publication bias in the current meta-analysis. Moreover, the Egger‟s tests did not show an evidence of publication bias on a statistical level (PBegg‟s = 0.058; PEgger‟s = 0.698), indicating that our pooled data were statistically robust and reliable.

Discussion

COVID-19 infection is seldom fatal in pediatric population (< 18 years old), but quantifying the risk of deaths related to COVID-19 can be difficult because they are usually asymptomatic or portray mild signs and symptoms.

These values are imperative for making decisions on vaccinations and prevention

strategies for the pediatric population. Determining the children at risk of severe disease and deaths from COVID-19 infection is essential in guiding clinicians, families, and policy-makers in terms of future prevention, school attendance, novel medicinal agents and, vaccine prioritization.[22]

In our study, we found a mortality rate of 9% among the pediatric population with COVID-19 infection in Iran. However, our sample size was small and consisted of symptomatic children who were hospitalized. In the study led by Karimi et al. which assessed pediatric mortality rate since the outbreak of COVID-19 in Iran until March 05, 2020 revealed a total of more than 3500 confirmed cases and approximately 3.3% deaths.[23]

Studies so far have reported varying degrees of pediatric mortality associated with COVID-19. Smith et al., in his study evaluated deaths in children and young people in England during the first round of the pandemy. His study reported a very low rate of mortality, stating that 99.995% of the children with a positive SARS-CoV-2 test survived. The study explained that COVID-19-related deaths in children older than 10 years, Asian and Black ethnicities and with comorbidities were over-represented in general. Their findings did highlight the significance of underlying comorbidities as a major risk factor of mortality.[22] Bhopal et al., reported 80 deaths in children aged 0-14 years in a population of 137,047,945, resulting in a mortality rate of 0.06 per 100,000 populations.[24] American Academy of Pediatrics assessed COVID-19 case fatality rate in 42 states of USA, reporting mortality rates at 0-0.23% as of 22 October 2020.[25] Ahmed et al., in a systematic review evaluated MIS-C in COVID-19 infected children demonstrating that only 11 deaths (1.7%) were reported among 662 patients who fulfilled the MIS-C criteria. Pudjiadi et al., reported as of December 21, 2020, there were 35,506 suspected cases of children with SARS-CoV-2 in Indonesia. In total, there were 522 deaths, with a case fatality ratio (CFR) of 1.4.[27]

On the other hand, the study by Dewi et al. reported a high mortality among pediatrics with a positive COVID-19 PCR test. Their study showed that 40% of children with COVID-19 had fatal outcomes. The proportion of COVID-19-associated deaths in their study is significantly higher compared to other studies. Also, they observed a higher proportion of deaths in patients aged >10 years with severe symptoms on admission.[28] In our study patients often presented with one or more pre-existing underlying chronic diseases that influencing their prognoses and mortality.

It seems that the children who died of SARS-CoV-2 were more likely to be older children, indicating the increasing trend in terms of risk with age. Usually, neonates infected with COVID-19 had a favorable outcome.[29]

In addition, our investigation is subject to a high grade of study heterogeneity due to the small sample size in the studies included. Furthermore, given the vast amount of literature published SARS-CoV-2 infection in a short time, some studies may have incorporated data from the same participants. Thus, we cannot be sure that patient data were not copied in our study.[8]

Various therapy regimens including antivirals, interferon, and hydroxychloroquine therapies have been tested on the pediatric population but at present, there exists no single study demonstrating the superiority of one regimen over the other. Besides, the virus is presumed to have milder effects on the pediatric population. As the management of SARS-CoV-2 has advanced, information on the use of steroids, intravenous immunoglobulin, and low-molecular-weight heparin for prophylaxis of thrombosis was not very common in the early stages of the pandemic, meaning there was no specified treatment for SARS-CoV-2. This mandates strategies for infection prevention and control, particularly in the pediatric with chronic illnesses who may require multiple hospitalizations.[28] In contrast, some studies

have reported good health status in children with chronic underlying diseases and in people undergoing immunosuppressive therapy30, which may be due to more care services.[30] Another reason for the high mortality rate in our study can be attributed to ethnicity. Previous studies have shown that a higher proportion of Asian and black children died from causes other than COVID-19 although deaths were still very rare. Ethnic differences may be due to biological talent and / or access to care.[31,32]

In our manuscript, children with underlying diseases are at higher risk for severe COVID-19 infection and related deaths. In particular, child deaths resulting from severe COVID-19 also had comorbidities such as aplastic anemia, thrombocytopenia, pulmonary hemorrhage, renal failure, electrolyte imbalance, obesity, and so on. Further studies are needed to improve the estimation of the mortality rate and investigate common comorbidities leading to death in children with COVID-19.

Conclusion

To our knowledge, this is the first systematic review and meta-analysis estimating the mortality rate of COVID-19 infection among pediatric patients with comorbidities or without comorbidities in Iran.

Most children with SARS-CoV-2 infection were asymptomatic and undiagnosed, but the data in our study assessed symptomatic children, and most had an underlying illness. Our study highlights the high mortality rate in pediatric patients with positive SARS-CoV-2 PCR tests in Iran. These results could be attributed to having comorbidities alongside SARS-CoV-2 infection. However, more studies are needed to estimate the mortality rate and also investigate the effects of comorbidities on the mortality rate in pediatrics infected with SARS-CoV-2.

Conflict of Interests

Authors have no conflict of interests.

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References

1. Bahrami R, Ekraminasab S, Asadian F. A survey on cardiac complications of COVID-19 in infants. World J Peri & Neonatol 2021; 4(1): 50-9.
2. Javaheri A, Noorishadkam M, Mazaheri M, Dadbinpour A, Dastgheib SA, Bahrami R, et al. Current state of knowledge about transplacental transmission of SARS-CoV-2 infection. World J Peri & Neonatol 2021; 3(2): 50-5.
3. Baghalsafa F, Neamatzadeh H, Ekraminasab S. Death of a 3 month-old infected infant with dilated cardiomyopathy after COVID-19 infection: A case report. World J Peri & Neonatol 2021; 4(1): 60-4.
4. Noorishadkam M, Lookzadeh MH, Mazaheri M, Mirjalili SR, Bahrami R, Asadian F, et al. Coronavirus disease 2019 (COVID-19) and late pregnancy loss in infected pregnant women: A mini review. World J Peri & Neonatol 2020; 2(2): 67-70.
5. Patel NA. Pediatric COVID-19: Systematic review of the literature. Am J Otolaryngol 2020; 41(5): 102573.
6. Bahrami R, Neamatzadeh H, Akbarian E. COVID-19 and renal complications in neonates and pediatrics. World J Peri & Neonatol 2020; 3(2): 48-9.
7. Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: A systematic review. JAMA Pediatr 2020; 174(9): 882-9.
8. Tsankov BK, Allaire JM, Irvine MA, Lopez AA, Sauvé LJ, Vallance BA, et al. International Severe COVID-19 infection and pediatric comorbidities : A systematic review and meta-analysis. Int J Infect Dis 2021; 103: 246-56.

9. Raoult D, Zumla A, Locatelli F, Ippolito G, Kroemer G. Coronavirus infections: Epidemiological, clinical and immunological features and hypotheses. Cell Stress 2020; 4(4): 66-75.
10. Soltani J, Sedighi I, Shalchi Z, Sami G, Moradveisi B, Nahidi S. Pediatric coronavirus disease 2019 (COVID-19): An insight from west of Iran. North Clin Istanb 2020; 7(3): 284-91.
11. Riollano-Cruz M, Akkoyun E, Briceno-Brito E, Kowalsky S, Reed J, Posada R, et al. Multisystem inflammatory syndrome in children related to COVID-19: A New York City experience. J Med Virol 2021; 93(1): 424-33.
12. Mamishi S, Movahedi Z, Mohammadi M, Ziaee V, Khodabandeh M, Abdolsalehi MR, et al. Multisystem inflammatory syndrome associated with SARS-CoV-2 infection in 45 children : a first report from Iran. Epidemiol Infect 2020; 148: e196.
13. Shahbaznejad L, Rouhanizadeh H, Navaeifar MR, Hosseinzadeh F, Movahedi FS, Rezai MS. Clinical characteristics and outcomes of COVID-19 in children in Northern Iran. Int J Pediatr 2021; 2021: 5558287.
14. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020; 395(10229): 1054-62.
15. Caussy C, Wallet F, Laville M, Disse E. Obesity is associated with severe forms of COVID-19. Obesity (Silver Spring) 2020; 28(7): 1175.
16. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J 2020; 55(5): 2000547.
17. Mamishi S, Heydari H, Aziz-Ahari A, Shokrollahi MR, Pourakbari B, Mahmoudi S, et al. Novel coronavirus disease 2019 (COVID-19) outbreak in children in Iran: Atypical CT manifestations and mortality risk of severe COVID-19 infection. J Microbiol Immunol Infect 2021; 54(5): 839-44.
18. Eghbali A, Shokrollahi S, Mahdavi NS, Mahdavi SA, Dabbagh A. COVID-19 in pediatric patients: A case series. J Cell Mol Anesth 2020; 5(1): 3-5.
19. Esmaeeli H, Ghaderian M, Sayadpour Zanjani K, Ghalibafan SF, Mahdizadeh M, Aelami MH. COVID-19 in children with congenital heart diseases: A multicenter case series from Iran. Case Rep Pediatr 2021; 2021: 6690695.
20. Rahimzadeh G, Ekrami Noghabi M, Kadkhodaei Elyaderani F, Navaeifar MR, Enayati AA, Manafi A, et al. COVID-19 infection in Iranian children: A case series of 9 patients. J Pediatr Rev 2020; 8(2): 139-44.
21. Mehrvar A, Qaddoumi I, Tashvighi M, Naderi A, Mousakhani H, Alasvand R, et al. Treatment and outcomes of pediatric patients with cancer and COVID-19 at MAHAK pediatric cancer treatment and research center, Tehran, Iran. Semin Oncol 2021; 48(4-6): 295-303.
22. Smith C, Odd D, Harwood R, Ward J, Linney M, Clark M, et al. Deaths in children and young people in England after SARS-CoV-2 infection during the first pandemic year. Nat Med 2022; 28(1): 185-92.
23. Karimi A, Rafiei Tabatabaei S, Rajabnejad M, Pourmoghaddas Z, Rahimi H, Armin S, et al. An algorithmic approach to diagnosis and treatment of coronavirus disease 2019 (COVID-19) in children: Iranian expert's consensus statement. Arch Pediatr Infect Dis 2020; 8(2): e102400.
24. Bhopal SS, Bagaria J, Olabi B, Bhopal R. COVID-19 deaths in children: comparison with all- and other causes and trends in incidence of mortality. Public Health 2020; 188: 32-4.
25. Pediatric AA of. Children and COVID-19: State data report 4 February 2021. Child Hosp Assoc 2021; 1-26.
26. Ahmed M, Advani S, Moreira A, Zoretic S, Martinez J, Chorath K, et al. Multisystem inflammatory syndrome in children: A systematic review. EClinicalMedicine 2020; 26: 100527.
27. Pudjiadi AH, Putri ND, Sjakti HA, Yanuarso PB, Gunardi H, Roeslani RD, et al. Pediatric COVID-19: Report from indonesian pediatric society data registry. Front Pediatr 2021; 9: 716898.
28. Dewi R, Kaswandani N, Karyanti MR, Setyanto DB, Pudjiadi AH, Hendarto A, et al. Mortality in children with positive SARS-CoV-2 polymerase chain reaction test : Lessons learned from a tertiary referral

hospital in Indonesia. Int J Infect Dis 2021; 107: 78-85.
29. Lookzadeh MH, Ekraminasab S, Baghalsafa F. Outcome of a neonate born to a mother with COVID-19: A case report of vertical transmission. World J Peri & Neonatol 2022; 4(2): 124-9.
30. Di Giorgio A, Nicastro E, Arnaboldi S, Montini O, Di Stasio F, D'Antiga L, et al. Health status of children with chronic liver disease during the SARS-CoV-2 outbreak: results from a multicentre study. Clin Res Hepatol Gastroenterol 2021; 45(2): 101610.
31. Clift AK, Coupland CAC, Keogh RH, Diaz-Ordaz K, Williamson E, Harrison EM, et al. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. BMJ 2020; 371: m3731.
32. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature 2020; 584(7821): 430-6.