Life Sciences Student Journal

2025 Vol.3 No.3, pp: 33-44

DOI:10.22034/LSSJ.2025.164

Post COVID-19 Cardio-Vascular Complications in Pediatric Cases: A Systematic Review

Shahla Afsharpayman[1], Farshad Kahrizirad[1], Hassan Abolghasemi[1], Mehdi Raei[2, 3], Sedigheh Madani[1*]

1. Department of Pediatrics, Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, I.R. Iran.
2. Health Research Center, Life Style Institute, Baqiyatallah University of Medical Sciences, Tehran, I.R. Iran.
3. Department of Epidemiology and Biostatistics, Faculty of Health, Baqiyatallah University of Medical Sciences, Tehran, I.R. Iran.

*Corresponding authors: Sedigheh Madani, Sedigheh_Madani@yahoo.com

Dr. Shahla Afsharpayman

Article type:

Systematic Review

Received: 26 Oct. 2025

Revised: 12 Nov. 2025

Accepted: 20 Nov. 2025

ePublished: 6 Dec. 2025

Abstract:

Respiratory failure is the primary cause of death in COVID-19 patients, with cardiac dysfunction identified as the second leading contributor. This manuscript provides an overview of cardiovascular implications in pediatric cases of COVID-19 infection. The study was conducted in compliance with PRISMA-NMA and the Declaration of Helsinki. Using the PICO framework, the population was children under 18 years, the exposure was COVID-19 infection, the comparison group was non-infected pediatrics, and the outcome was any cardiovascular complication. Literature published between January 1, 2020, and January 21, 2024, was searched in PubMed, Scopus, and Web of Science. Two reviewers screened titles and abstracts, assessed full texts, and performed data extraction and quality appraisal. Out of 2383 studies, 1795 underwent title/abstract screening, 157 were reviewed in full, and 26 met inclusion criteria. Altogether, 9023 participants were analyzed (mean age 9.5 years; 54.3% male). Comorbidities were present in 2022 (22.4%). Shock was reported in 667 patients, while ECG alterations, elevated cardiac troponin, and pro-BNP were observed in 382 (4.2%), 403 (4.5%), and 459 (5.1%) respectively. Myocardial dysfunction occurred in 14.5% of cases, and coronary artery involvement was noted in 815 (9%). Management included inotropes in 17.3% and extracorporeal membrane oxygenation in 9.5%. Mortality was documented in 61 (0.6%) patients, while 542 (6%) had persistent cardiac sequelae; 8419 (93.3%) recovered fully.In conclusion, critically ill pediatric COVID-19 patients require thorough cardiac evaluation during hospitalization and follow-up to detect and manage cardiovascular complications.

Introduction

COVID-19, an illness resulting from infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first observed in Wuhan, China, in December 2019, and quickly disseminated across the world (1). Severe cases of COVID-19 and the correlated mortality have been most pronounced in the elderly and individuals with comorbidities. Throughout the course of the pandemic, COVID-19 in children has predominantly exhibited an asymptomatic or mild nature, resulting in minimal pediatric hospitalizations and low mortality rates (2).

COVID-19 clinical presentations in children are similar to other pediatric viral infections. Frequently, children exhibit initial symptoms akin to a mild flu-like condition, which may advance to severe manifestations, including potentially life-threatening acute respiratory distress syndrome, fulminant pneumonia, fulminant meningitis, and multi-organ failure (3-7).

The main reported cause of death in COVID-19 patients is respiratory failure, with cardiac

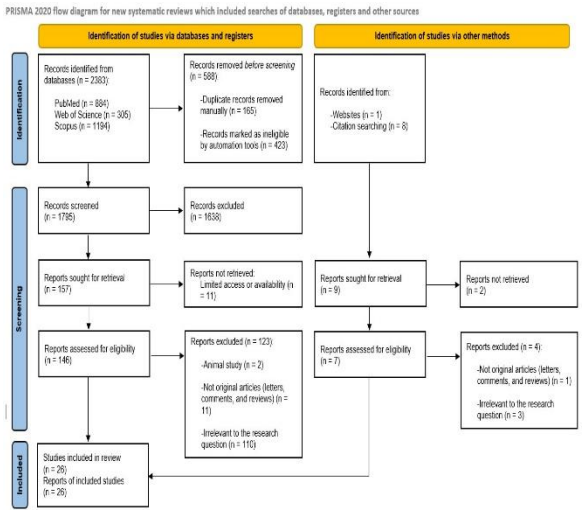

Figure 1. PRISMA Diagram of included studies

dysfunction identified as the subsequent leading cause of mortality. Cardiac injury, characterized by elevated troponin I and electro cardiac changes, is observed in 7–17% of hospitalized patients, particularly in more severe cases. Nonetheless, the cardiac manifestations of COVID-19in children are less frequently studied (8, 9).

In this manuscript, our objective is to provide a comprehensive overview of the existing knowledge regarding the potential cardiovascular implications in the pediatric cases of COVID-19 infection. The intention is to offer insights into the appropriate care for this demographic amidst the ongoing pandemic emergency.

Methods

Study design

The current investigation was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement (PRISMA-NMA). PRISMA diagram is illustrated as Figure 1. The study was performed in compliance with the international guidelines on clinical investigation of the World Medical Association's Declaration of Helsinki; the local ethics committee approved the study protocol. At first glance research question was formatted based on PICO: (P)opulation was pediatrics (age <18), (I)ntervention/Exposure was COVID-19 infection, (C)omparison was done with the group of pediatrics who didn't develop to COVID-19, and (O)utcome was considered as any cardiovascular complication including heart failure, stroke, cerebro-vascular disease, arrhythmia, cardiogenic shock, cardiovascular death, myocarditis, endocarditis, acute coronary syndrome, and thromboembolic events.

Search strategy

Literature searched to identify publications from January 1st, 2020 until January21st, 2024 was conducted using PubMed, Scopus, and Web of Science databases to identify potentially eligible articles. Mesh Terms-Key words in our search strategy included ("pediatrics*" OR "paediatric*" OR "child*") AND ("COVID-19" OR "novel coronavirus" OR "SARS-CoV-2" OR "2019-nCoV Infection" OR "SARS-CoV-2 Infection" OR "2019 Novel Coronavirus Disease" OR "COVID-19 Virus Infection" OR "Coronavirus Disease 2019" OR "Severe Acute Respiratory Syndrome Coronavirus 2 Infection" OR "COVID 19 Virus Disease" OR "SARS Coronavirus 2 Infection" OR "COVID 19 Pandemic") AND ("myocardial infarction" OR "heart attack" OR "arrhythmia" OR "cardiovascular involvement" OR "heart disease" OR "congenital heart disease" OR "pulmonary hypertension" OR "long QT" OR "cardiomyopathies" OR "channelopathies"). The comprehensive search strategy is provided in Table 1. In addition to reference lists of eligible studies and articles, key journals, conference proceedings, trial registers and internet resources were searched

to identify studies potentially missed by the database search. The chosen databases will be searched using keywords and subject header elements relevant to inclusion and exclusion criteria.

Inclusion criteria

We included research articles that report on significant cardiovascular outcomes in children with COVID-19, as well as interventional studies detailing the prevalence of cardiovascular outcomes. These studies utilized reverse transcription polymerase chain reaction (RT-PCR) for detecting SARS-CoV in children. The reference standard, comprising cohorts, clinical trials, and/or case series or reports, involves patients subjected to RT-PCR analysis for confirmation. Additionally, it encompasses patients without active disease but who manifested cardiovascular outcomes in the subsequent year (2020–2024).

Exclusion criteria

Adult-focused research will not be included. Additionally, studies published in languages other than English will be excluded. Also, the review will consider systematic reviews, ongoing trials, trial protocols, progress evaluations, research communications, correspondences, editorials, review articles, brief reports, journals, textbooks, or book chapters for exclusion.

Selection process

In our initial search, a total of 2383 studies were identified. To compile the relevant citations, a single endnote (version 21) library was employed, and duplicate articles were eliminated in two stages, initially through automated processes by the reference manager and subsequently through manual checks.

A total of 1020 papers were identified as duplicated and 588 of those were removed as extra versions and ultimately 1795 papers were selected for title/abstract screening. The identified articles were allocated between two reviewers(SM and FK). Each reviewer autonomously assessed their designated set of initially identified articles, after which they exchanged portions and cross-verified the screening conducted by the other reviewer. The review of titles and abstracts based on inclusion and exclusion criteria took place from January 21st, 2023, to January 31st, 2023. Any disparities were reconciled through consensus, and a senior review (SA) decision was sought whenever necessary.

Data extraction

After title and abstract screening, 157 articles were considered for full-text screening. The full-texts for shortlisted studies were retrieved and further assessed and perused carefully by SM and FK for inclusion criteria. Ultimately 26 papers were enrolled for data extraction and quality assessment. Three reviewers, SM, FK, and SA, were involved in the data extraction and quality assessment of included studies. The extracted data included information such as authors' names, study year and location, absolute population, mean age, male population size, treatment, clinical workups, and prevalence of each cardiovascular outcome, and, if not directly available, indirect estimation through percentages provided in the article. In cases where there was uncertainty about the relevance of a title, it was included for retrieval.

Qualitative Assessment

The assessment of the risk of bias was conducted using the New Castle Ottawa scale. For this stage relevant categories were considered: Representativeness of the exposed cohort, selection of non-exposed cohort, ascertainment of exposure, outcome not present at start of the study, comparability of cohorts on the basis of the design or analysis, assessment of outcome, follow-up long enough for outcomes to occur, adequacy of follow up.

Statistical Analysis

Categorical variables were presented in percentages and continuous variables were presented in mean and standard deviation or

median. Analysis was performed using SPSS (IBM, Version 26).

Results

The selection of studies, based on PRISMA guidelines, is shown in Figure 1. Among 2383 studies, 1795 were selected for title/abstract screening. Then, 157 of those were considered for full-text screening. Eleven papers were not open-accessed, and their authors neglected our request to send us the article's full text. Besides, 123 papers were omitted based on exclusion criteria, and 23 were considered for enrollment. Such a process was applied for manual search, and three papers were entered for final analysis. Ultimately, 26 papers underwent data extraction and quality analysis.

Most investigations (eight) were conducted in the USA; meanwhile, five, four, and two projects were accomplished in Britain, France, and Italy, respectively. Eventually, only a single original study was done in Bosnia and Herzegovina, Netherlands, Russia, Israel, Switzerland, and Spain. A summary of these papers illustrates that 9023 participants who were younger than 18 were considered and analyzed; their mean age was 9.5 years, and 54.33% were male.

Among these pediatric cases, 2022 (22.4%) had at least one sign, symptom, or laboratory value indicating any comorbidities, including respiratory, cardiac, neurological, gastrointestinal, endocrinological, and genitourinary disorders. Totally, 667 patients were referred by shock; meanwhile, ECG alterations, increased cardiac Troponin, and pro-BNP were detected in 382 (4.2%), 403 (4.46%), and 459 (5.08%) respectively. Most of the patients [1312(14.5%)] presented with myocardial dysfunction as the main cardiac complication; however, coronary artery involvement was noted within 815 (9%) children.

A small portion of these patients (3.26%) have required mechanical support; meanwhile, management with inotropic medication and extracorporeal membrane oxygenation was documented in 1567 (17.3%) and 201 (9.5%) pediatric cases. Among other medications which were used in a therapeutic course for these patients, IVIG, steroids, anti-platelet, and anti-coagulants were respectively applied in 1569 (17.3%), 3348 (37.1%), 140 (1.55%), and 258 (2.85%) cases. Pediatrics ICU admission was needed for 2689 (29.8%) children; at the end of the evaluation period, 61 (0.6%) patients ended up with death, and others were discharged. Among those 542 (6%) cases had cardiac sequel but 8419 (93.3%) patients were fully recovered.

Qualitative analysis and risk of bias assessment were conducted using the New Castle Otawwa instrument scale. All the papers owned proper quality scores; therefore, they can be considered for further prospective meta-analysis.

Discussion and conclusion

In this comprehensive review, we have compiled the current evidence concerning cardiovascular involvement in pediatric COVID-19. While respiratory symptoms prevail in COVID-19 clinical presentations, cardiovascular complications are evolving as a noteworthy complexity in SARS-CoV-2 infections among children. Notably, pre-existing cardiovascular conditions contributed to a poorer outcome associated with COVID-19. These findings underscore the poorer prognosis associated with impaired cardiovascular function during SARS-CoV-2 infection in children.

The investigators observe that acute coronary syndrome could represent an early presentation of COVID-19 infection, encompassing a spectrum from ST elevation myocardial infarction to cardiomyopathies. This phenomenon may occur either as a result of plaque rupture induced by a stress response or due to thrombosis, leading to ischemia and myocardial infarction. It is postulated that the cardiovascular system's impairment in COVID-19 patients stems from a systemic inflammatory response, involving ischemia and vasculitis alongside pre-existing coronary artery disease. Furthermore, the

cytokine storm and systemic inflammation induced by SARS-CoV-2 contribute to hypo-perfusion, excessive stimulation of β-adrenergic receptors, thrombosis, thromboembolism, and shock. Intense inflammatory cascades impacting the cardiovascular system result in the emergence of arrhythmias, myocarditis, cardiomyopathy, and acute heart failure. SARS-CoV-2, affecting vascular endothelial cells, interferes with their regular functioning and tone regulation. This disruption contributes to heightened blood clotting and clot formation, ultimately culminating in the development of cardiac pathologies. Considerably, a noteworthy proportion of previously healthy infected children have encountered severe acute cardiovascular events, including the newly identified Pediatric Multisystem Inflammatory Syndrome (PMIS), arrhythmias, pulmonary hypertension, heart failure, and even fulminant myocarditis. Common manifestations include cardiogenic shock, ECG alterations, myocardial dysfunction, and coronary artery dilation. The majority of cases necessitated admission to the Pediatric Intensive Care Unit (PICU) and inotropic support, with a rare requirement for extracorporeal membrane oxygenation. Nearly all these children achieved complete recovery within a few days, although isolated instances of fatalities have been reported. These observations emphasize that, despite being infrequent, the occurrence of cardiovascular events during SARS-CoV-2 infection is not exempt in any child. It is pivotal to diagnose and manage cardiac complications of COVID-19 in children to decrease the morbidity and mortality rate in them. Accordingly, we conclude that each child who requires hospitalization due to his critical condition in the context of COVID-19 needs to be evaluated for the presence of cardiac disorders during their hospitalization and in future follow ups. Moreover, each COVID-19 positive child, who has a preexisting cardiomyopathy or has been identified with a cardiac abnormality in the screening workups, should be visited by a pediatric cardiologist. When sufficient data are lacking, the management of identified cardiac complications should adhere to existing guidelines, local protocols, and the doctor's expertise tailored to each specific situation.

Statements and Declarations

Ethics approval and consent to participate: Not applicable. Study was conducted based on PRISMA guidelines.
Consent for publication: Not applicable.
Availability of data and materials: Data is available upon request to corresponding author.
Competing interests: No potential conflict of interest relevant to this article was reported.
Funding: Not applicable. No funding was received.
Acknowledgement: Not applicable.
Author contributions: Conception or design of the work: SA, SM, and FK; Initial search: FK and SM; Title/abstract screening: SM, FK, and SA; full text screening: SM, FK, and SA; Acquisition of data (data extraction): SM and FK; Descriptive Analysis or interpretation of data: SM, FK, SA, MR, and HA; Drafting the article: SM and FK; and critical revision of the article and final approval of the version to be published: SM, FK, SA, MR, and HA.

Table 1. Comprehensive Search Strategy

PubMed (N=884)	**Query:**(((Pediatrics) OR (paediatric) OR (child)) AND (("novel coronavirus") OR (SARS-CoV-2*) OR (2019-nCoV*) OR ("Novel Coronavirus Disease") OR ("COVID-19 Virus*")) AND (("Myocardial Infarction") OR (Arrhythmia) OR (Arryth*) OR ("Heart Failure") OR ("congenital heart disease") OR ("pulmonary hypertension") OR ("long QT") OR (cardiomyopathies) OR (cardiomyo*) OR ("channelopathies") OR ("myocarditis") OR ("fulminant myocarditis"))) **Expansion:**("paediatrics"[All Fields] OR "pediatrics"[MeSH Terms] OR "pediatrics"[All Fields] OR "paediatric"[All Fields] OR "pediatric"[All Fields] OR ("paediatrics"[All Fields] OR "pediatrics"[MeSH Terms] OR "pediatrics"[All Fields] OR "paediatric"[All Fields] OR "pediatric"[All Fields]) OR ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields] OR "child s"[All Fields] OR "children s"[All Fields] OR "childrens"[All Fields] OR "childs"[All Fields])) AND ("novel coronavirus"[All Fields] OR "sarscov 2*"[All Fields] OR "2019 ncov*"[All Fields] OR "Novel Coronavirus Disease"[All Fields] OR "covid 19 virus*"[All Fields]) AND ("Myocardial Infarction"[All Fields] OR ("arrhythmia s"[All Fields] OR "arrhythmias, cardiac"[MeSH Terms] OR ("arrhythmias"[All Fields] AND "cardiac"[All Fields]) OR "cardiac arrhythmias"[All Fields] OR "arrhythmia"[All Fields] OR "arrhythmias"[All Fields]) OR "arryth*"[All Fields] OR "Heart Failure"[All Fields] OR "congenital heart disease"[All Fields] OR "pulmonary hypertension"[All Fields] OR "long QT"[All Fields] OR ("cardiomyopathie"[All Fields] OR "cardiomyopathies"[MeSH Terms] OR "cardiomyopathies"[All Fields] OR "cardiomyopathy"[All Fields]) OR "cardiomyo*"[All Fields] OR "channelopathies"[All Fields] OR "myocarditis"[All Fields] OR "fulminant myocarditis"[All Fields])
SCOPUS (N=1194)	(TITLE-ABS-KEY (pediatrics OR paediatric OR child) AND TITLE-ABS-KEY ("novel coronavirus" OR sars-cov-2* OR 2019-ncov* OR "Novel Coronavirus Disease" OR "COVID-19 Virus*") AND TITLE-ABS-KEY ("Myocardial Infarction" OR arrhythmia OR arryth* OR "Heart Failure" OR "congenital heart disease" OR "pulmonary hypertension" OR "long QT" OR cardiomyopathies OR cardiomyo* OR "channelopathies" OR "myocarditis" OR "fulminant myocarditis"))
Web of Science (N=305)	(((Pediatrics) OR (paediatric) OR (child)) AND (("novel coronavirus") OR (SARS-CoV-2*) OR (2019-nCoV*) OR ("Novel Coronavirus Disease") OR ("COVID-19 Virus*")) AND (("Myocardial Infarction") OR (Arrhythmia) OR (Arryth*) OR ("Heart Failure") OR ("congenital heart disease") OR ("pulmonary hypertension") OR ("long QT") OR (cardiomyopathies) OR (cardiomyo*) OR ("channelopathies") OR ("myocarditis") OR ("fulminant myocarditis"))) **(Topic)** or (((Pediatrics) OR (paediatric) OR (child)) AND (("novel coronavirus") OR (SARS-CoV-2*) OR (2019-nCoV*) OR ("Novel Coronavirus Disease") OR ("COVID-19 Virus*")) AND (("Myocardial Infarction") OR (Arrhythmia) OR (Arryth*) OR ("Heart Failure") OR ("congenital heart disease") OR ("pulmonary hypertension") OR ("long QT") OR (cardiomyopathies) OR (cardiomyo*) OR ("channelopathies") OR ("myocarditis") OR ("fulminant myocarditis"))) **(Title)** and (((Pediatrics) OR (paediatric) OR (child)) AND (("novel coronavirus") OR (SARS-CoV-2*) OR (2019-nCoV*) OR ("Novel Coronavirus Disease") OR ("COVID-19 Virus*")) AND (("Myocardial Infarction") OR (Arrhythmia) OR (Arryth*) OR ("Heart Failure") OR ("congenital heart disease") OR ("pulmonary hypertension") OR ("long QT") OR (cardiomyopathies) OR (cardiomyo*) OR ("channelopathies") OR ("myocarditis") OR ("fulminant myocarditis"))) **(Keyword Plus ®)**

Table 2. Descriptive data about post-covid pediatric cardiovascular complications

Authors	Country	Size	Age (median or mean)	Male Sex	Comorbidity	Shock	ECG alterations	Increased cTn or median	Increased pro-BNP or median	Myocardial dysfunction	Coronary artery involvement
Mesihović-Dinarević (2023)(10)	Bosnia and Herzegovina	70	11-15y (30%) 16-18y (10%)	40 (57%)	NM	NM	25 (36%)	NM	NM	NM	NM
Son (2022)(11)	USA	518	8.7	301 (58%)	128 (25%)	93 (18%)	NM	0.11 (0.02–0.74)	04.0 (87.1–1062.9)	212 (41%)	NM
Belay (2022)(12)	USA	1733	0-4 y (40%)	994 (57.6%)	931(53%)	197 (11%)	NM	NM	NM	484 (31.0%)	258 (16.5%)
Buonsenso (2022)(13)	Italy	129	11 ± 4.4	67 (52%)	NM	NM	NM	NM	NM	NM	NM
Buonsenso (2021)(14)	USA, Great Britain	510	10.3	213 (42%)	287 (57%)	15 (3%)	NM	NM	NM	183 (35%)	NM
Brackel (2021)(15)	Netherlands	89	13	43 (49%)	NM	0 (0%)	NM	NM	NM	32 (28%)	NM
Theocharis (2021)(16)	Great Britain	20	11	15 (75%)	NM	NM	15 (75%)	NM	NM	10 (50%)	12 (60%)
Osmanov (2021)(17)	Russia	518	10.4	248 (48%)	113 (22%)	23 (4%)	73 (14%)	NM	NM	21 (4.5%)	8 (2%)
Liat Ashkenazi-Hoffnung (2021)(18)	Israel	90	12 ± 5	49 (55%)	10 (11%)	12 (13.3%)	2 (2.2%)	1 (1.3%)	11 (14.1%)	30 (33.3)	2 (2.2%)
Miller (2021)(19)	England and Wales	4678	11	2749 (47%)	382 (8%)	83 (1.7%)	123 (2.6%)	NM	NM	(529; 11.3%)	423 (9%)
Feldstein (2020)(20)	United States	186	8.3	115 (62%)	59 (31%)	NM	22 (12%)	77/153 (50%)	94/128 (74%)	70 (38%)	15 (8%)
Dufort (2020)(21)	United States	99	8.4	53 (53%)	35 (35%)	32 (32%)	59 (59%)	63/89 (71%)	74/82 (90%)	51 (52%)	9 (9%)
Miller (2020)(22)	United States	44	7.3	20 (45%)	16 (36%)	NM	22 (50%)	NM	NM	22 (50%)	0 (0%)
Capone (2020)(23)	United States	33	8.6	20 (60%)	4 (9%)	16 (48%)	NM	33 (100%)	33 (100%)	19 (58%)	16 (48%)
Kaushik (2020)(24)	United States	33	10	20 (60%)	16 (48%)	21 (63%)	NM	33 (100%)	33 (100%)	22 (63%)	0 (0%)
Cheung (2020)(25)	United States	17	8	8 (47%)	3 (17%)	13 (76%)	16 (94%)	14 (82%)	15 (88%)	6 (35%)	7 (41%)
Riollano-Cruz (2020)(26)	United States	15	12	11 (73%)	5 (33%)	13 (87%)	2 (13%)	13 (87%)	13 (87%)	7 (57%)	3 (20%)
Verdoni (2020)(27)	Italy	10	7.5	7 (70%)	0 (0%)	5 (50%)	NM	5/9 (55%)	10 (100%)	5 (50%)	2 (80%)
Whittaker (2020)(28)	United Kingdom	58	9	25 (43%)	7 (12%)	27 (46%)	4 (7%)	34/50 (68%)	24/29 (83%)	18 (31%)	8 (14%)
Ramcharan (2020)(29)	United Kingdom	15	8.8	11 (73%)	0 (0%)	10 (66%)	9 (60%)	15 (100%)	15 (100%)	12 (80%)	14 (93%)
Hameed (2020)(30)	United Kingdom	35	11	27 (77%)	0 (0%)	21 (60%)	NM	35 (100%)	35 (100%)	15 (43%)	6 (20%)
Toubiana (2020)(31)	France	21	8	9 (43%)	0 (0%)	12 (57%)	2 (10%)	17 (81%)	14/18 (78%)	16 (76%)	8 (38%)
Belhadjer (2020)(32)	France & Switzerland	35	10	18 (51%)	10 (28.5%)	28 (80%)	1 (3%)	35 (100%)	35 (100%)	35 (100%)	6 (17%)
Grimaud (2020)(33)	France	20	10	10 (50%)	0 (0%)	20 (100%)	NM	20 (100%)	15/15 (100%)	20 (100%)	0 (0%)
Pouletty (2020)(34)	France	16	10	8 (50%)	6 (37.5%)	11 (68%)	NM	11/11 (100%)	16 (100%)	7 (43%)	3 (18%)
Moraleda (2020)(35)	Spain	31	7.6	18 (58%)	10 (32%)	15 (48%)	7 (23%)	NM	22 (71%)	15 (48%)	3 (10%)

Abbreviations: NM, not mentioned; cTn: Cardiac Troponin; BNP: B-type natriuretic peptide.

Table 2 (continued). Descriptive data (Treatment and outcome) about post-covid pediatric cardiovascular complications

Authors	Mechanical ventilation	Inotropic support	ECMO support	IVIG	Steroids	Antiplatelet	Anticoagulation	Biologics	PICU admission	Full recovery	Cardiac sequelae	Death
Mesihović-Dinarević (2023)(10)	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Son (2022)(11)	91 (18%)	93 (18%)	16 (3%)	206 (40%)	103 (20%)	NM	NM	206 (40%)	385 (74%)	508 (98%)	NM	9 (2%)
Belay (2022)(12)	NM	NM	NM	NM	NM	NM	NM	NM	1009 (58.2%)	1709 (98.6%)	NM	24 (1.4%)
Buonsenso (2022)(13)	3 (2.3%)	3 (2.3%)	3 (2.3%)	3 (2.3%)	3 (2.3%)	NM	NM	NM	3 (2.3%)	54(42%)	75 (58%)	0 (0%)
Buonsenso (2021)(14)	NM	NM	NM	NM	NM	NM	NM	NM	22 (4.3%)	510 (100%)	76 (58%)	1 (0%)
Brackel (2021)(15)	NM	NM	NM	NM	NM	NM	NM	NM	26 (29%)	67 (64%)	32 (36%)	0 (0%)
Theocharis (2021)(16)	5 (25%)	2 (10%)	10 (50%)	3 (15%)	5 (25%)	3 (15%)	NM	NM	5 (25%)	15 (75%)	5 (25%)	0 (0%)
Osmanov (2021)(17)	NM	NM	NM	16 (4%)	84 (21%)	NM	NM	NM	50 (9%)	480 (92%)	39 (8%)	0 (0%)
Lisi Ashkenazi-Hoffnung (2021)(18)	NM	NM	NM	NM	NM	NM	NM	NM	11 (12.2%)	85 (95%)	5 (5%)	0 (0%)
Miller (2021)(19)	49 (1%)	1075 (23%)	143 (3%)	785 (16.7%)	2765 (59%)	53 (1.13%)	46 (1%)	153 (3.2%)	673 (14.3%)	4395 (93.8%)	273 (5.8%)	15 (0.3%)
Feldstein (2020)(20)	37 (20%)	90 (48%)	8 (4%)	144 (77%)	91 (49%)	0 (0%)	87 (47%)	38 (21%)	148 (80%)	182 (98%)	0 (0%)	4 (2%)
Dufort (2020)(21)	10 (10%)	61 (62%)	4 (4%)	69 (70%)	61 (62%)	0 (0%)	0 (0%)	0 (0%)	79 (80%)	97 (98%)	0 (0%)	2 (2%)
Miller (2020)(22)	1 (2%)	22 (50%)	0 (0%)	36 (81%)	42 (95%)	0 (0%)	40 (90%)	8 (18%)	22 (50%)	44 (97%)	0 (0%)	1 (2%)
Capone (2020)(23)	6 (18%)	25 (75%)	0 (0%)	33 (100%)	23 (70%)	29 (87%)	14 (42%)	7 (21%)	26 (79%)	24 (73%)	9 (27%)	0 (0%)
Kaushik (2020)(24)	5 (15%)	17 (51%)	1 (3%)	18 (54%)	17 (51%)	0 (0%)	32 (97%)	12 (36%)	33 (100%)	29 (88%)	2 (6%)	1 (3%)
Cheung (2020)(25)	0 (0%)	10 (59%)	0 (0%)	13 (76%)	15 (92%)	4 (24%)	11 (64%)	0 (0%)	15 (88%)	16 (94%)	1 (6%)	0 (0%)
Riollano-Cruz (2020)(26)	3 (20%)	8 (53%)	1 (6%)	12 (80%)	3 (20%)	2 (13%)	15 (100%)	14 (93%)	14 (93%)	13 (88%)	1 (6%)	1 (6%)
Verdoni (2020)(27)	0 (0%)	2 (20%)	0 (0%)	8 (80%)	10 (100%)	2 (20%)	0 (0%)	0 (0%)	5 (50%)	10 (100%)	0 (0%)	0 (0%)
Whittaker (2020)(28)	25 (43%)	29 (50%)	3 (5%)	41 (70%)	37 (64%)	0 (0%)	0 (0%)	11 (19%)	29 (50%)	56 (98%)	0 (0%)	1 (2%)
Ramcharan (2020)(29)	4 26%)	10 (67%)	0 (0%)	10 (66%)	5 (33%)	11 (73%)	0 (0%)	0 (0%)	10 (67%)	12 (80%)	3 (20%)	0 (0%)
Hameed (2020)(30)	7 (20%)	20 (57%)	2 (6%)	35 (100%)	35 (100%)	0 (0%)	0 (0%)	0 (0%)	25 (69%)	33 (97%)	0 (0%)	1 (3%)
Toubiana (2020)(31)	11 (52%)	15 (71%)	0 (0%)	21 (100%)	10 (48%)	21 (100%)	0 (0%)	0 (0%)	17 (81%)	21 (100%)	0 (0%)	0 (0%)
Belhadjer (2020)(32)	22 (62%)	28 (80%)	10 (28%)	25 (71%)	12 (35%)	0 (0%)	23 (65%)	3 (9%)	35 (100%)	25 (71%)	19 (29%)	0 (0%)
Grimaud (2020)(33)	8 (40%)	19 (95%)	0 (0%)	20 (100%)	2 (10%)	0 (0%)	0 (0%)	2 (10%)	20 (100%)	20 (100%)	0 (0%)	0 (0%)
Poulletty (2020)(34)	2 (12%)	6 (38%)	0 (0%)	15 (93%)	4 (25%)	15 (93%)	0 (0%)	2 (12%)	7 (44%)	14 (88%)	2 (12%)	0 (0%)
Moraleda (2020)(35)	6 (19%)	15 (48%)	0 (0%)	20 (65%)	21 (68%)	0 (0%)	0 (0%)	0 (0%)	20 (65%)	30 (97%)	0 (0%)	1 (3%)

Abbreviations: NM, not mentioned; ECMO: Extracorporeal membrane oxygenation; IVIG: Intravenous immunoglobulin; PICU: Pediatric intensive care unit.

343

Table 3. Quality assessment of included studies using Newcastle Ottawa scale

First Author, Year	Selection				Comparability	Outcome			Quality score
	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow up	
Mesihović-Dinarević (2023)(10)	*	*	*	*	*	*	*	*	**8**
Son (2022)(11)	*	*	*	*	*	*	*	*	**8**
Belay (2022)(12)	*	*	*	*	*	*	*	*	**9**
Buonsenso (2022)(13)	*	*	*	*	*	*	*	*	**9**
Brackel (2021)(15)	-	-	-	*	**	*	*	*	**6**
Theocharis (2021)(16)	*	*	*	*	**	*	*	-	**8**
Buonsenso (2021)(14)	*	*	*	*	**	*	*	*	**9**
Osmanov (2021)(17)	*	*	*	*	**	*	*	*	**9**
Liat Ashkenazi-Hoffnung (2021)(18)	*	*	*	*	**	*	*	*	**9**
Miller (2021)(19)	*	*	*	*	**	*	*	*	**9**
Feldstein (2020)(20)	*	*	*	*	**	*	*	*	**8**
Dufort (2020)(21)	*	*	*	*	**	*	*	*	**9**
Miller (2020)(22)	*	*	*	*	**	*	*	*	**9**
Capone (2020)(23)	*	*	*	*	**	*	*	*	**9**
Kaushik (2020)(24)	*	*	*	*	**	*	*	*	**9**
Cheung (2020)(25)	*	*	*	*	**	*	*	*	**9**
Riollano-Cruz (2020)(26)	*	*	*	-	**	*	*	*	**8**
Verdoni (2020)(27)	*	*	*	*	**	*	*	*	**9**
Whittaker (2020)(28)	-	-	*	*	**	*	*	*	**7**
Ramcharan (2020)(29)	-	-	-	*	**	*	*	*	**6**

Hameed (2020)(30)	*	*	*	*	*	*	*	*	**8**
Toubiana (2020)(31)	-	-	*	*	**	*	*	*	**7**
Belhadjer (2020)(32)	*	*	*	*	*	*	*	*	**8**
Grimaud (2020)(33)	-	-	*	*	**	*	*	*	**7**
Pouletty (2020)(34)	*	*	*	*	*	*	*	*	**8**
Moraleda (2020)(35)	-	*	*	*	**	*	*	-	**7**

Wells, G. A, Shea, B., O'Connel, D. et al. The Newcastle-Ottawa scale (NOS) for assessing the quailty of nonrandomised studies in meta-analyses. http://www ohri ca/programs/clinical_epidemiology/oxford htm 2009 Feb 1

References

1. Castiello T, Georgiopoulos G, Finocchiaro G, Claudia M, Gianatti A, Delialis D, et al. COVID-19 and myocarditis: a systematic review and overview of current challenges. Heart Fail Rev. 2022;27(1):251-61.
2. Hoste L, Van Paemel R, Haerynck F. Multisystem inflammatory syndrome in children related to COVID-19: a systematic review. Eur J Pediatr. 2021;180(7):2019-34.
3. Rodriguez-Gonzalez M, Castellano-Martinez A, Cascales-Poyatos HM, Perez-Reviriego AA. Cardiovascular impact of COVID-19 with a focus on children: A systematic review. World J Clin Cases. 2020;8(21):5250-83.
4. Afsharpayman S, Madani S, Amirsalari S, Momeni N, Torkaman M, Beiraghdar F, et al. Fulminant coronavirus disease 2019 meningitis in Iranian infants: a case series Journal of Medical Case Reports. 2024;18(1):121.
5. Madani S, Shahin S, Yoosefi M, Ahmadi N, Ghasemi E, Koolaji S, et al. Red flags of poor prognosis in pediatric cases of COVID-19: the first 6610 hospitalized children in Iran. BMC Pediatrics. 2021;21(1):563.
6. Madani S, Rezaei N, Farzadfar F. COVID-19 treatment of pediatric cases: Advantages vs Disadvantages. 2022.
7. Abdolsalehi MR, Madani S, Mahmoudi S, Navaeian A, Khodabandeh M, Hosseinpour Sadeghi R, et al. Association of body mass index with COVID-19 outcome in a pediatric tertiary referral hospital in Iran. Arch Pediatr. 2023;30(5):297-301.
8. Sanna G, Serrau G, Bassareo PP, Neroni P, Fanos V, Marcialis MA. Children's heart and COVID-19: Up-to-date evidence in the form of a systematic review. Eur J Pediatr. 2020;179(7):1079-87.
9. Vakhshoori M, Heidarpour M, Shafie D, Taheri M, Rezaei N, Sarrafzadegan N. Acute Cardiac Injury in COVID-19: A Systematic Review and Meta-analysis. Arch Iran Med. 2020;23(11):801-12.
10. Mesihović-Dinarević S, Lisičić-Konaković M, Prguda-Mujić J, Jogunčić A. COVID-19 Seroprevalence in Children during Pandemic Waves in Sarajevo, a Single Center Experience. Acta Med Acad. 2023;52(1):56-62.
11. Son MBF, Murray N, Friedman K, Young CC, Newhams MM, Feldstein LR, et al. Multisystem Inflammatory Syndrome in Children — Initial Therapy and Outcomes. New England Journal of Medicine. 2021;385(1):23-34.
12. Belay ED, Abrams J, Oster ME, Giovanni J, Pierce T, Meng L, et al. Trends in Geographic and Temporal Distribution of US Children With Multisystem Inflammatory Syndrome During the COVID-19 Pandemic. JAMA Pediatrics. 2021;175(8):837-45.
13. Buonsenso D, Pujol FE, Munblit D, Pata D, McFarland S, Simpson FK. Clinical characteristics, activity levels and mental health problems in children with long coronavirus disease: a survey of 510 children. Future Microbiology. 2022;17(8):577-88.
14. Buonsenso D, Munblit D, De Rose C, Sinatti D, Ricchiuto A, Carfi A, et al. Preliminary evidence on long COVID in children. Acta Paediatrica. 2021;110(7):2208-11.
15. Brackel CLH, Lap CR, Buddingh EP, van Houten MA, van der Sande LJTM, Langereis EJ, et al. Pediatric long-COVID: An overlooked phenomenon? Pediatric Pulmonology. 2021;56(8):2495-502.
16. Theocharis P, Wong J, Pushparajah K, Mathur SK, Simpson JM, Pascall E, et al. Multimodality cardiac evaluation in children and young adults with multisystem inflammation associated with COVID-19. European Heart Journal - Cardiovascular Imaging. 2020;22(8):896-903.
17. Osmanov IM, Spiridonova E, Bobkova P, Gamirova A, Shikhaleva A, Andreeva M, et al. Risk factors for post-COVID-19 condition in previously hospitalised children using the ISARIC Global follow-up protocol: a prospective cohort study. European Respiratory Journal. 2022;59(2):2101341.
18. Ashkenazi-Hoffnung L, Shmueli E, Ehrlich S, Ziv A, Bar-On O, Birk E, et al. Long COVID in Children: Observations From a Designated Pediatric Clinic. The Pediatric Infectious Disease Journal. 2021;40(12):e509-e11.

19. Miller F, Nguyen DV, Navaratnam AM, Shrotri M, Kovar J, Hayward AC, et al. Prevalence and Characteristics of Persistent Symptoms in Children During the COVID-19 Pandemic: Evidence From a Household Cohort Study in England and Wales. Pediatr Infect Dis J. 2022;41(12):979-84.
20. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. N Engl J Med. 2020;383(4):334-46.
21. Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, Rowlands J, et al. Multisystem Inflammatory Syndrome in Children in New York State. N Engl J Med. 2020;383(4):347-58.
22. Miller J, Cantor A, Zachariah P, Ahn D, Martinez M, Margolis KG. Gastrointestinal Symptoms as a Major Presentation Component of a Novel Multisystem Inflammatory Syndrome in Children That Is Related to Coronavirus Disease 2019: A Single Center Experience of 44 Cases. Gastroenterology. 2020;159(4):1571-4.e2.
23. Capone CA, Subramony A, Sweberg T, Schneider J, Shah S, Rubin L, et al. Characteristics, Cardiac Involvement, and Outcomes of Multisystem Inflammatory Syndrome of Childhood Associated with severe acute respiratory syndrome coronavirus 2 Infection. J Pediatr. 2020;224:141-5.
24. Kaushik S, Aydin SI, Derespina KR, Bansal PB, Kowalsky S, Trachtman R, et al. Multisystem Inflammatory Syndrome in Children Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection (MIS-C): A Multi-institutional Study from New York City. J Pediatr. 2020;224:24-9.
25. Cheung EW, Zachariah P, Gorelik M, Boneparth A, Kernie SG, Orange JS, et al. Multisystem Inflammatory Syndrome Related to COVID-19 in Previously Healthy Children and Adolescents in New York City. Jama. 2020;324(3):294-6.
26. 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.
27. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet. 2020;395(10239):1771-8.
28. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al. Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2. Jama. 2020;324(3):259-69.
29. Ramcharan T, Nolan O, Lai CY, Prabhu N, Krishnamurthy R, Richter AG, et al. Paediatric Inflammatory Multisystem Syndrome: Temporally Associated with SARS-CoV-2 (PIMS-TS): Cardiac Features, Management and Short-Term Outcomes at a UK Tertiary Paediatric Hospital. Pediatr Cardiol. 2020;41(7):1391-401.
30. Hameed S, Elbaaly H, Reid CEL, Santos RMF, Shivamurthy V, Wong J, et al. Spectrum of Imaging Findings at Chest Radiography, US, CT, and MRI in Multisystem Inflammatory Syndrome in Children Associated with COVID-19. Radiology. 2021;298(1):E1-e10.
31. Toubiana J, Poirault C, Corsia A, Bajolle F, Fourgeaud J, Angoulvant F, et al. Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study. Bmj. 2020;369:m2094.
32. Belhadjer Z, Méot M, Bajolle F, Khraiche D, Legendre A, Abakka S, et al. Acute Heart Failure in Multisystem Inflammatory Syndrome in Children in the Context of Global SARS-CoV-2 Pandemic. Circulation. 2020;142(5):429-36.
33. Grimaud M, Starck J, Levy M, Marais C, Chareyre J, Khraiche D, et al. Acute myocarditis and multisystem inflammatory emerging disease following SARS-CoV-2 infection in critically ill children. Ann Intensive Care. 2020;10(1):69.
34. Pouletty M, Borocco C, Ouldali N, Caseris M, Basmaci R, Lachaume N, et al. Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease (Kawa-COVID-19): a multicentre cohort. Ann Rheum Dis. 2020;79(8):999-1006.
35. Moraleda C, Serna-Pascual M, Soriano-Arandes A, Simó S, Epalza C, Santos M, et al. Multi-inflammatory Syndrome in Children Related to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Spain. Clin Infect Dis. 2021;72(9):e397-e401.