

Pediatric Heart Complications of COVID-19 During Recent Six Months In Kurdistan / Iran: A Case Series Study

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Abstract

Introduction: SARS-CoV-2 can infect host cells through ACE2 with possible damage to the myocardium. Likewise, cytokine storm in later stages of COVID-19 infection may cause progressive inflammatory phenomenon. We reported 12 pediatric patients having different severity of cardiac complications with history of COVID-19 in themselves or their older family members. In all of these pediatric cases there was a family history of positive laboratory reports for SARS-CoV-2 infection in older family members.

Methods: This is a case series study. We were being randomly consulted for possible cardiovascular involvement of pediatric COVID-19 patients in corona intensive care unit. During the past six months, we confronted twelve children from corona intensive care unit with various findings of myocarditis and/or Kawasaki-like disease on echocardiographic evaluation. These patients were treated appropriately depending on their cardiovascular disorders. We followed these pediatric patients with intermittent echocardiographic evaluation for the following 2 to 6 months.

Results: In spite of preceding optimistic attitude regarding COVID-19 in children, we found a series of recent pediatric cases with treatable cardiac complications. Myocardial and coronary artery involvement were the main problems in these young patients. Fortunately, on follow up, all of these cardiac complications were appropriately managed by our therapeutic protocol with satisfying outcomes.

Conclusion: We emphasize on especial concern about cardiac involvement in children and adolescents with recent COVID-19 in their family. This can be achieved by echocardiographic evaluation in suspicious younger individuals during one to two months of SARS-CoV-2 infection in the older family members.

Keywords: SARS-CoV-2 • Children • Myocarditis • Kawasaki Disease

Introduction

Severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] a member of the genus Beta-corona-virus is supposed to infect human cells probably through angiotensin converting enzyme 2 [ACE2] to cause COVID-19. ACE2 deterioration by SARS-CoV-2 infection is considered to be the possible cause of cardiovascular complications. Furthermore, an inflammatory cascade so called cytokine storm emerge during progressive stages of COVID-19 with subsequent end organ damage [1,2]. Comparing with adults, in children SARS-CoV-2 transmission rate and incubation period is lower and longer respectively [3]. Generally, COVID-19 has lower clinical manifestation in children than adults [4]. Multi-systemic inflammatory syndrome [MIS] is a severe clinical presentation of COVID-19 in both adults and children with multi-organ complications [5,6]. Cardiovascular complications associated with COVID-19 is relatively well experienced in adult patients with a broad spectrum of cardiac presentations including heart failure, cardiogenic shock, right heart failure, myocarditis, arrhythmia and sudden cardiac arrest [7]. However, in children and adolescents there are relatively fewer reports about cardiovascular involvement associated with COVID-19.

We reported 12 pediatric patients with different cardiac complications with history of COVID-19 in themselves or their older family members. In all of these

children there were positive laboratory reports for SARS-CoV-2 infection in older family members during the past one to two months ago. These younger family members usually were referred to emergency room due to respiratory distress or severe fatigue. On echocardiographic assessment we frequently realized different presentations of myocarditis and/or Kawasaki-like disease. The prominent echocardiographic data were including mild to severe left ventricular dilatation, mild to moderate mitral regurgitation, different degrees of left ventricular dysfunction and some evidences of coronary artery disorders. These patients were treated through appropriate medications depending on present of heart failure and/or Kawasaki-like coronary artery disease.

Methodology

This was a case series study conducted on pediatric heart complications in COVID-19; during recent six months in Kurdistan/Iran. We were consulted for patients referred from pediatric Corona intensive care unit for cardiac evaluation since 2020/08/25 to 2021/02/25. On the first cardiac evaluation a complete standard echocardiography was performed [by Samsung HS70A]. Left ventricular ejection fraction [LVEF] and cardiac output of more than 57% and 3.9 L/M/M2 were considered normal. Left ventricular dilatation was supposed with left ventricular end diastolic dimension [LVEDD] of more than 45 mm/m². Standard echocardiographic values were used for the aforementioned echocardiographic measurements [8]. In cases with heart complications, appropriate medications were started according to the definite clinical and para-clinical findings. Intravenous immuno-globulin [IVIG] and aspirin were administered to those patients with coronary artery involvement detected by echocardiography. Methylprednisolone was considered for those cases unresponsive to previous medications. Inotrope drugs including Milrinone and Dopamine were administered for those cases with heart failure. We followed these pediatric patients with intermittent echocardiographic

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evaluation for the following 2 to 6 months depending on their early and ongoing cardiac issues. Laboratory tests including complete blood cell count [CBC], erythrocyte sedimentation rate [ESR], C reactive protein [CRP], COVID 19 reverse transcription polymerase chain reaction [rt-PCR] and antibody and troponin 1 were performed for all complicated patients at the beginning and later during follow up. Chest X ray and computed tomography [lung-CT] were routinely ordered for all COVID-19 patients. All findings are summarized using descriptive statistics in SPSS software version 22.

Results

Twelve cases between 2 to 11 years with cardiac complications after family history of COVID-19 were evaluated during the past 6 months since 2020/08/25 to 2021/02/25. The mean age was 6 years old. Table 1 shows symptoms of the patients before and during admission. Almost all the cases had typical or atypical symptoms of Kawasaki disease. Symptoms and signs related to cardiovascular dysfunction were fatigue 100%, tachycardia, 66% and respiratory distress, 41% (Table 1).

COVID-19 rt-PCR was positive only in 16%, comparing with serologic test [immunoglobulin G antibody, IgG Ab] that was positive in 75%, however family rt-PCR was positive in all cases Table 2. Acute phase reactants including ESR and CRP were increased in most, %83, but troponin 1 in only two patients Table 2. In chest X-ray and lung-CT, there were usually some degrees of

increased CT ratio [50%] and/or pulmonary vascular marking [PVM] [41%]. However, pulmonary involvement indicated by mild patchy infiltration was present in only two patients [16%] (Table 2).

Different echocardiographic findings of the children with COVID-19 were shown in Table 3. Fifteen percent of all cases had prominent echocardiographic findings of left ventricular dysfunction with decreased both cardiac output [CO] and left ventricular ejection fraction [LVEF] and also increased left ventricular end diastolic dimension [LVEDD]. All patients had different levels of mitral and tricuspid valve regurgitation. Different kinds of Kawasaki-like echocardiographic changes including coronary artery brightness, ectasia and aneurysm were present in most of the cases [91%] with coronary artery brightness was the most common finding [66%] followed by ectasia [50%] and aneurysm [16%] respectively (Figures 1-3).

Different therapeutic medications were shown in Table 4. Intravenous immunoglobulin [IVIg] and aspirin were administered for all cases with possible coronary artery involvement [91%]. Methylprednisolone was infused for those cases that were not responsive to previous medications after 1 week [16%].

The minimum and maximum duration of hospitalization were 4 and 15 days respectively Table 2. Minimum and maximum duration of prominent improvement in echocardiographic findings were 18 to 54 respectively (Table 2).

Table 1. Early and late symptoms of 12 patients with COVID-19.

Patient number	Age (y)	Sex	Fever	Skin Rash	°Eyes redness	°Lymph nodes	° scaling	Fatigue	£RD	° High HR
1	8	f	+	+	-	+	-	+	-	+
2	5	m	+	-	-	+	-	+	-	-
3	11	f	+	+	+	+	-	+	+	-
4	2.5	m	-	-	+	+	+	+	+	+
5	7	f	+	-	-	+	-	+	-	+
6	9	f	+	+	+	-	+	+	-	-
7	5	m	-	-	-	+	+	+	+	+
8	3.5	m	+	-	-	-	+	+	+	+
9	8	m	-	+	+	-	-	+	-	+
10	5	m	+	-	-	-	+	+	+	+
11	3	m	+	+	-	-	-	+	-	+
12	6	f	+	-	-	-	+	+	-	-

Fever of more than 5 days, skin rashes including erythematous or maculopapular, Eye redness means non-exudative conjunctivitis, Acute unilateral cervical lymphadenopathy, scaling around the upper and lower limb nails and anus, £ RD means respiratory distress, High HR means tachycardia

Table 2. Para clinic findings and clinical progress of 12 pediatric cases with COVID-19.

Patient number	£iPVM	°CT ratio	¥Patchy	rtPCR in family member	rt PCR in Patient	° duration after COVID onset (days)	Duration of Hospital (days)	° Ab test in patient	° OC	° NEF T (days)
1	+	+	-	+	-	35	10	+	+	28
2	-	-	-	+	-	43	7	+	+	25
3	+	+	-	+	+	25	14	-	+	45
4	+	+	+	+	-	28	12	+	+	54
5	-	-	-	+	-	39	5	+	+	18
6	-	-	-	+	-	41	5	+	+	21
7	+	+	+	+	-	34	11	-	+	33
8	+	+	-	+	+	27	15	-	+	46
9	-	-	-	+	-	31	6	+	+	21
10	-	+	-	+	-	40	6	+	+	35
11	-	-	-	+	-	30	4	+	+	24
12	-	-	-	+	-	46	5	+	+	38

£ iPVM or increased pulmonary vascular marking recorded by Computed tomography or chest X ray, ° increased cardio-thoracic index, ¥ Patchy density of the lung tissue recorded by Computed tomography or chest X ray, ° Duration after COVID onset means the period between starting early COVID 19 symptoms in the patient or family and cardiac complication ° Ab test means IgG or IgM antibody against COVID 19 in patient, ° OC is Outcome ° NEFT is Normal (or relatively normal) echo finding time which means the duration between the first abnormal echocardiography and the final normal or near normal echo

Table 3. * Echocardiographic results of 12 podiatric cases with COVID-19

	LVEF%	CO L/m/m ²	MR Degree	TR Degree	LVEDD Cm/m ²	LV Mass gr/m ²	CA Bright	CA Ectasia	CA Aneurysm
1	52	3.5	2	3	5	86	+	+	-
2	60	5.2	1	2	4	90	+	-	-
3	48	2.9	2	2	5.5	76	+	+	+
4	32	1.8	3	3	6	91	+	+	-
5	65	6.1	0	1	3.8	98	-	+	-
6	58	4.6	1	1	4.2	79	-	-	-
7	45	3	2	2	5.3	81	+	-	-
8	30	1.5	2	3	5.9	93	+	-	-
9	56	4	1	2	4.1	76	-	+	-
10	54	3.9	2	2	4.4	94	-	+	+
11	62	4.7	0	1	4	90	+	-	-
12	59	4.7	2	2	3.9	75	+	-	-

* This is the first time Echocardiographic findings

MR, mitral regurgitation, and TR, tricuspid regurgitation, degrees are between 0 to 4 with 0 means no MR and 1 to 4 are equal to trivial, mild, moderate and severe respectively Ectasia is referred to main coronary artery trunks diameter of more than 4 mm/m² but less than 8 mm/m² and Aneurysm indicating dilatation of more than 8 mm/m²

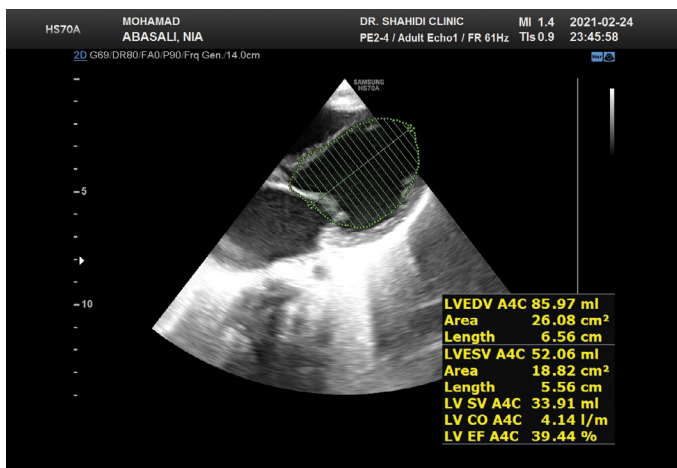


Figure 1. Left ventricular dysfunction of an 11-year-old COVID-19 patient.

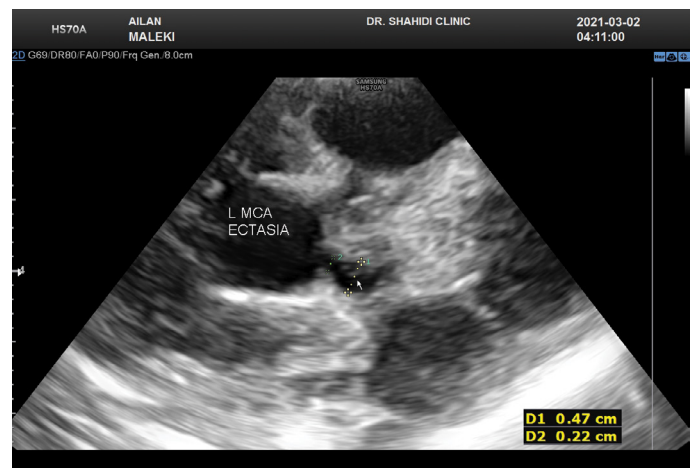


Figure 3. Left main coronary artery ectasia of an 8-year-old COVID-19 patient.

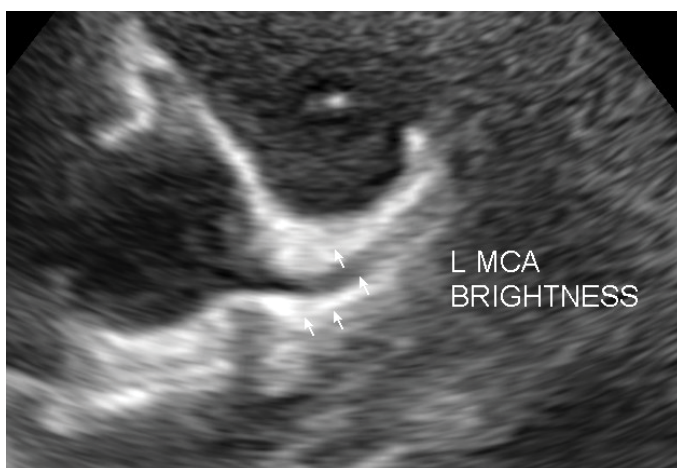


Figure 2. Left main coronary artery brightness of a 7-year-old COVID-19 patient.

Discussion

COVID-19 is a systemic disease with early and late clinical presentations including cardiovascular complications that better known in adult and older ages [2]. We confronted children with recent history of COVID-19 and unexpected heart complications including myocardial and coronary artery involvement. The triad of left ventricular dilatation and/or dysfunction, different degrees of mitral regurgitation accompanied with various stages of Kawasaki-like

coronary artery disease, was found almost in all of these patients. Relatively delayed heart issues were a matter of concern which was accompanied by a negative rt-PCR in most cases but positive serologic tests in all. The late onset of cardiac involvement may demonstrate an inflammatory phenomenon [1]. In this report there was a short period between systemic symptoms and myocarditis with negative rt-PCR but positive serologic tests. In one study, cardiac complications of COVID-19 were divided into primary and secondary types depending on direct myocardial injury or an inflammatory process respectively [5]. Indirect mechanism of myocardial involvement seems to be the result of cytokine storm; micro-angiopathy and myocardial oxygen supply mismatch [9]. Cardiac complications in children and adolescents reported in some articles. Some medical centers reported Multi-systemic inflammatory syndrome in children [MIS-C] including shock-like syndrome and Kawasaki-like disease prominently with more priority in older kids [10,11]. In our case report the mean age was 6 years old with Kawasaki-like coronary artery complications were usually more prominent in older ages. Approximately all the patients had some degrees of echocardiographic changes in both left and right main coronary arteries including; coronary artery brightness, ectasia and aneurysm. However, left main coronary artery involvement was either more common or more prominent. Pericardial effusion was indicated in none of the cases but different evidences of myocardial injury or myocarditis including left ventricular dilatation and/or dysfunction and mitral regurgitation were detected. We did not find any primary risk factors in our patients. Previously healthy children and adults with systemic COVID-19 were reported in other centers [5].

Prompt therapy with IVIG in all patients due to their Kawasaki-like disease accompanied by other medications depending on their especial issues supposed to have satisfactory results. Aspirin was administered to all

Table 4. Treatment of 12 pediatric cases with COVID-19.

Patient number	Dopamine	Milrinone	IVIg	M-Pred	ASA
1	+	+	+		+
2	-	-	+	-	+
3	+	+	+	+	+
4	+	+	+	+	+
5	-	-	+	-	+
6	-	-	-	-	+
7	+	+	+	-	+
8	+	+	+	-	+
9	-	-	-	-	+
10	+	-	+		+
11	-	-	-	-	+
12	-	-	+	-	+

IVIg intravenous immunoglobulin

M-pred is Methyl prednisolone

ASA is Aspirin started with anti-inflammatory dose at the beginning and change to anti-coagulant dose according to the laboratory and Echo findings

patients because of the coronary artery involvement with the known protocols of Kawasaki disease. Methylprednisolone was started for those patients who were not responsive to IVIg indicated by echocardiographic evaluation of left ventricular dysfunction and/or coronary artery disease. Milrinone and Dopamine were started for patients with heart failure accompanied with different degrees of respiratory support depending on the patient's condition. Beta blockers, digoxin and diuretics were not administered at the acute phase of the disease. Administration of angiotensin converting enzyme inhibitor [ACE inhibitors] or angiotensin receptor blockers [ARBs] during COVID-19 is not well known with equivocal concepts [12,13]. ACE inhibitors and ARBs were not part of our primary therapeutic protocol because of suspected harmful adverse effects.

All of our patients were discharged from the hospital with follow up echocardiographic evaluation. Cardiac complications were improved in most of the cases during their hospitalization or a couple of weeks after discharge. One of our patients with cardiomegaly and heart failure is still under outpatient therapy. Two more patients still have some degrees of left main coronary artery ectasia but with progressive improvement.

Conclusion

There are relatively fewer reports regarding cardiac complications in children after COVID-19. Our recent evaluation of pediatric heart complications due to COVID-19 indicated a triad of left ventricular dysfunction, mitral regurgitation and Kawasaki-like disease. Though, we suppose more caution about the younger members of family with COVID-19 and early echocardiographic evaluation.

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' Contributions

Mohsen Shahidi: Study design, manuscript writing and editing of

manuscript. Abdorrahim Afkhamzadeh: statistical analysis and editing of manuscript. Both of authors critically reviewed the manuscript and approved the final version submitted for publication.

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