ORIGINAL ARTICLE

ÖZGÜN ARAŞTIRMA

Patterns of Myocardial Involvement During COVID-19 Pandemic; From Newborn to Adolescents

Yenidoğandan Adolesana COVID-19 Pandemisinde Çocuklarda Kardiyak Tutulum Şekilleri

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Abstract

Introduction: Coronavirus 2 (SARS-CoV-2) has infected people of all ages all across the world, with children accounting for 1.7 percent of cases. Despite the fact that over 90% of children with COVID-19 had asymptomatic, mild, or moderate disease, new worries about hyperinflammatory states or Kawasaki-like disease have surfaced.

Materials and Methods: We would like to present 17 patients with different patterns of myocardial involvement. They were selected from our database of 214 patients (19 newborns) hospitalized for SARS-CoV-2 infection treatment in our pediatrics clinic from March 2020 to October 2020. Selection criteria involved cardiac involvement in terms of positive laboratory findings (elevated troponin I) electrocardiographic and echocardiographic findings.

Results: Cardiac involvement was detected in only 17 (7.9%) of the 214 hospitalized patients. Patients were grouped into three categories according to their hospitalization units which were neonatal intensive care, pediatric intensive care and pediatric inpatient clinic. Most of our patients (88.2%) had elevated troponin I levels whereas 12 patients (70.5%) had abnormal electrocardiograms and echocardiographic exams. Fourteen (82.3%) of patients with high troponin I levels had also abnormal electrocardiograms whereas 13 (76.4%) of them had abnormal echocardiographic exams.

Conclusion: Although we did not observe cardiac involvement in most of the patients (92.1%) hospitalized for SARS-CoV-2 infection treatment in our pediatrics clinic, subjects with involvement had quite diverse patterns ranging from only troponin I elevation to the multisystem inflammatory syndrome in children needing arteriovenous extracorporeal membrane oxygenation therapy.

Öz

Giriş: COVID-19 çocuklarda hafif seyirli bir hastalık olmakla beraber, Kawasaki benzeri hastalık ya da hiperinflamatuar durumlar ile kendini gösterebilmektedir. Biz çalışmamızda COVID-19 pandemisinde çocuklarda kardiyak tutulum sıklığı ve şekillerini ortaya koymayı amaçladık.

Gereç ve Yöntem: Mart 2020 ile Ekim 2020 arasında SARS-CoV-2 enfeksiyonu nedeni ile pediatri kliniğimizde tedavi gören 214 hastamızdan değişik şekillerde kardiyak tutulum gözlediğimiz 17 hastayı sunmak istiyoruz. Hastaların seçilme kriterleri laboratuar (artmış troponin I), elektrokardiyografik ve ekokardiyografik bulgulara dayanmaktadır. Hastalar tedavi gördükleri birimler olan pediatri servisi, yenidoğan yoğun bakım ünitesi ve cocuk yoğun bakım ünitesi olarak üc ayrı gruba ayrılmışlardır.

Bulgular: Kardiyak tutulum 214 hastanın %7,9'unda gözlenmiş olup bunların %88.2'sinde troponin I yüksekliği, %70,5'inde anormal elektrokardiyografi bulguları saptadık. Troponin I yüksekliği saptanan hastaların %82.3'ünde beraberinde anormal elektrokardiyografi bulguları saptanırken, yine bu hastaların %76.4'ünde anormal ekokardiyografi bulguları saptadık. Yedi hasta çoklu sistem inflamatuar sendromu olarak değerlendirildi.

Sonuç: SARS-CoV-2 enfeksiyonu tedavisi alan hastalarımızın büyük bir kısmında kardiyak tutulum tespit etmedik. Tutulum saptadığımız hastalarda ise tutulum şekli oldukça değişkenlik göstermekte idi. Lakin bu yelpazenin bir ucunda sadece troponin I yüksekliği olan hastalarımız var iken diğer ucunda ekstrakorporeal membran oksijenizasyonu tedavisine ihtiyaç duyan sol ventrikül sistolik fonksiyon bozukluğu olan hastalarımız mevcuttu.

Introduction

Coronavirus 2 (SARS-CoV-2) has infected people of all ages all across the world, with children accounting for 1.7 percent of cases (1). Despite the fact that over 90% of children with COVID-19 had asymptomatic, mild, or moderate disease, new worries about hyperinflammatory states or Kawasakilike disease have surfaced (2,3) COVID-19 patients, including those who were previously healthy and had no cardiac problems, show signs of cardiac muscle inflammation (4). We would like to present 17 patients with different patterns of myocardial involvement which were selected from our database of 214 pediatric patients (19 newborns) hospitalized for SARS-CoV-2 infection treatment in our pediatrics inpatient clinic. Patients of all ages from newborns to adolescents were included in the study and that they all had symptoms and signs of cardiac involvement as well as laboratory, electrocardiographic and echocardiographic findings. However, we observed that disease course and duration of troponin level normalization were highly variable in subjects. Although newborns had high levels of troponin levels and some subjects had a prolonged course of elevated troponins for more than two months, none of them had any serious complications and they were just followed up and recovered well. On the opposite end of the spectrum, we had adolescents with the multisystem inflammatory syndrome in children (MIS-C) who needed arteriovenous extracorporeal membrane oxygenation therapy (ECMO) and fortunately recovered and discharged.

Materials and Methods

Seventeen patients were included in this retrospective study. They were selected from our database of 214 pediatric patients who were hospitalized for SARS-CoV-2 infection in our pediatrics inpatient clinic from March 2020 to October 2020. COVID-19 was diagnosed based on a history of infection, nasal polymerase chain reaction testing, and/or SARS-CoV-2 serology, as well as chest X-ray and computed tomography. One hundred sixty patients (74.7%) tested positive with nasal polymerase-chain-reaction testing, and/or SARS-CoV-2 serology. Clinical evaluation included physical examination, signs, electrocardiogram, chest X-ray, and echocardiographic examination. Selection criteria involved cardiac involvement in terms of positive laboratory findings (elevated high-sensitivity troponin I). electrocardiographic and echocardiographic findings. Selected patients were divided into three groups regarding their hospitalization clinics which were neonatal intensive care unit (group A), pediatric intensive care unit (group B) and, pediatric inpatient clinic (group C). Usual etiologies of acute myocarditis were systematically screened including the testing of a large panel of non-SARS-CoV-2 viruses in blood, feces, and nasopharyngeal swabs in all groups.

As the study was retrospective and also the patients' routine data was obtained from the hospital records we did not get informed consent from the subjects.

Statistical Analysis

Proportions were used to describe nominal data. Means and medians were used to depict normally distributed discrete data, whereas minimums and maximums were employed to represent data that were not normally distributed. SPSS version 25.0 was used for statistical analysis (IBM, Armonk, New York, USA).

Results

Group A had four newborns, three (75%) of which were female. The median age of the newborns was 15.8 days (max: 20, min: 10). All the newborns were tested positive for SARS-CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR) and were interned in the neonatal intensive care unit. The parents of the newborns either one or both were tested positive before the newborns. Case four had bradycardia and the other three of the newborns had tachycardia at admission. Whole blood count, C - reactive protein and procalcitonine values were unremarkable in all cases as well as liver enzymes and serum electrolytes. However, cases one and two had very high troponin I levels, 2500 picogram/mL (The 99th percentile for Troponin I is 117 picogram/mL for newborns after vaginal delivery) and 2410 picogram/mL respectively. The one with the highest troponin level had minimal pericardial effusion (6 mm at the apex of the heart) detected by echocardiographic examination that did not need any intervention. The Troponin level of this baby dropped to normal with a fluctuating pattern after 70 days. The other newborn's troponin level dropped to normal with a fluctuating pattern after 30 days. Echocardiographic examination revealed minimal aortic insufficiency in case three. Case four in this group had a slightly elevated troponin I value of 500 picogram/mL returning to normal in a week but she had also negative T waves in precordial leads of V5 and V6. Chest X-rays of group A did not reveal any kind of involvement regarding SARS-CoV-2 infection. Echocardiographic examinations of the group revealed nothing special apart from the aforementioned findings. Ejection fractions were all in normal ranges in all patients of group A as well as coronary arteries' calibrations. Group A was monitored in isolation for a week and no specific treatment for COVID-19 was given. They were all nursed by their mothers, did not have a worsening course, on the contrary, full recovery was achieved. They all tested negative for SARS-CoV-2 after an average of ten days (min: 5, max: 22) after the first positive result.

Group B consisted of nine patients five (55%) of which were male. The median age of patients was 142 months (max: 212, min: 9). All the subjects had documented fever >38.0°C (100.4°F) for ≥24 hours with/without other symptoms. Symptoms, signs, initial laboratory values, echocardiographic findings,

and special treatment modalities of the patients are depicted in Table 1. Electrocardiograms revealed low voltage in Case 1, 4, and 7, first-degree atrioventricular block in case 6, and ST-segment elevation in precordial leads of V3 and V4 in case nine. Ground-glass opacifications were detected on chest X-rays and chest computed tomography images of all patients of group B. Bilateral, predominantly peripheral, somewhat asymmetrical consolidation with air bronchograms were also detected on chest X-rays of patients who needed extracorporeal membrane oxygenation support. Except for cases three and seven, all the cases of this group were regarded as MIS-C. Case 3, 4, and 7 had concomitant diseases of epilepsy, Crohn's disease, and chronic kidney disease respectively. Subjects' systolic function returned to normal at an average of 6.4 days. Patients of this group were transferred from the pediatric intensive care unit to the pediatric inpatient clinic and were all discharged without any residual cardiac damage except for mild mitral regurgitation in cases one and four.

Group C had four patients, three (75%) of which were male. The median ages of patients were 182 months (max 195, min: 147). They were all tested positive for SARS-CoV-2 RT-PCR. Whole blood count, C - reactive protein and procalcitonine values were unremarkable in all cases as well as liver enzymes and serum electrolytes. Case one of this group was 180 months old and had fever and chest pain at admission. He had a troponin I value of 178 picogram/mL. His electrocardiogram had few monomorphic ventricular extrasystoles. Case two of this group was 184 months old and had chest pain, abdominal pain, and vomiting at admission. His troponin I was 27778 picogram / mL. Case three was 195 months old. He had chest pain at admission and had a troponin I value of 1878 picogram/mL. Case four was 147 months old female. She had fever and cough at admission and her troponin I value was in normal ranges. Electrocardiograms of cases two and four had negative T waves in precordial leads of V5 and V6 whereas electrocardiogram of case three revealed T segment elevation in precordial leads of V3 and V4. Echocardiographic exam of case three revealed mild mitral regurgitation. Except for case one, all other cases' X-ray and chest computed tomography images revealed ground-glass opacifications. The standard treatment regimen of this group was 400 mg of hydroxychloroquine twice on day 1, then 400 mg

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Symptoms	Fever, vomiting, diarrhea	Fever	Fever	Fever, vomiting, diarrhea	Fever, vomiting, diarrhea	Fever, vomiting, abdominal pain	Fever, Vomiting, fatigue	Fever, fatigue	Fever, cough
Signs at admission	Hypotension	Tachycardia+ tachypnea	tachypnea	Shock	Thrombocytopenia + Hypotension	Hypotension	Tachycardia+ tachypnea	Hypotension	Hypotension
SARS-CoV-2 testing	Positive Ig G for SARS-CoV-2	Positive RT-PCR	Positive RT-PCR	Negative Ig G and Ig M for SARS-CoV-2	Negative Ig G and Ig M for SARS-CoV-2	Negative RT-PCR	Negative Ig G and Ig M for SARS-CoV-2	Positive Ig G for SARS- CoV-2	Negative RT-PCR
White blood cells	9650	7600	6190	31100	6200	7700	4800	6900	10600
Neutrophil ratio %	94	88	39	81.7	84.8	80	88	65	90
Hemoglobin (g/dl)	11.4	11.9	15.4	9.6	11.8	8.8	7	10.1	11.6
Platelets (μ /L)	80000	231000	249000	73000	239000	374000	144000	428000	405000
C-reactive protein (mg/dl) (0-0.5)	31	14	1.5	10	25	16	5.9	12.6	25
ALT (U/L) (0-55)	22	10	63	381	14	17	20	38	31
Albumin (g/L) (38 - 54)	28,7	40	48	11	32	28	30	29	29
Procalcitonin (ng/ml) (0- 0.05)	38	0.24	0.01	16.8	13.5	7.61	0.1	0.29	2.59
Ferritin (ng/ml) (4 - 207)	2504	229	44	721	454	1143	1022	194	1031
IL-6 (pg/ml) (0- 5.9)	356	12	14.6	663	222	620	8.6	2.46	10
Fibrinogen (mg/dl) (200 - 400)	432	657	178	177	522	568	585	594	658

Table 1. Symptoms, signs, laboratory values, echocardiographic findings and special treatment modalities of the patients of group B

D-Dimer (µg/ml) (0 - 0.5)	2.3	1.8	0.59	2	2.8	2.7	2.02	3.2	2.01
Troponin (pg/ml) (0 - 13.8)	1218	146	1404	106695	308	46	86	761	143
Antibiotic and antiviral treatment	Ceftriaxone, azithromycin, oseltamivir	Cefotaxime, teicoplanin, lopinavir	Amphicillin, cefotaxime, azithromycin	Vancomycin meropenem favipiravir, azithromycin	Vancomycin meropenem favipiravir	Meropenem, teicoplanin, amikacin, lopinavir	Teicoplanin, meropenem, favipiravir	Vancomycin, cefotaxime, lopinavir	Cefotaxime, teicoplanin, favipiravir
IVIG	+	-	+	+	+	+	-	+	+
IL-6R	+	-	-	+	-	-	-	-	-
Corticosteroids	+	-	-	+	+	+	+	-	+
Plasmapheresis	+	-	-	+	-	+	-	-	+
IL-1Ra	-	-	-	+	-	-	-	-	-
ECMO support	+	-	-	+	-	-	-	-	-
Lowest LVEF (%)	31			20	37			54	56
Inotropic support	+	-	_	+	÷	+	-	+	+
Echocardiographic findings	Mild to moderate mitral regurgitation + increased perivascular echogenicity in the left coronary artery	Mild mitral regurgitation	normal	Mild to modrate mitral regurgitation+ increased perivascular echogenicity in the left coronary artery	Mild mitral regurgitation	Mild mitral regurgitation+ increased perivascular echogenicity in the right coronary artery	Pericardial effusion	Mild mitral regurgitation + increased perivascular echogenicity in the left coronary artery	Mild mitral regurgitation + increased perivascular echogenicity in the left coronary artery
Echocardiographic	Mild to moderate mitral regurgitation + increased perivascular echogenicity in the left coronary		normal	modrate mitral regurgitation+ increased perivascular echogenicity in the left coronary		regurgitation+ increased perivascular echogenicity in the right coronary		regurgitation + increased perivascular echogenicity in the left coronary	regurgitation + increased perivascular echogenicity in the left coronary
Echocardiographic findings Systolic function normalization	Mild to moderate mitral regurgitation + increased perivascular echogenicity in the left coronary artery		normal	modrate mitral regurgitation+ increased perivascular echogenicity in the left coronary artery	regurgitation	regurgitation+ increased perivascular echogenicity in the right coronary		regurgitation + increased perivascular echogenicity in the left coronary artery	regurgitation + increased perivascular echogenicity in the left coronary artery
Echocardiographic findings Systolic function normalization (days) Non-invasive	Mild to moderate mitral regurgitation + increased perivascular echogenicity in the left coronary artery 15	regurgitation		modrate mitral regurgitation+ increased perivascular echogenicity in the left coronary artery 8	regurgitation	regurgitation+ increased perivascular echogenicity in the right coronary artery		regurgitation + increased perivascular echogenicity in the left coronary artery 3	regurgitation + increased perivascular echogenicity in the left coronary artery
Echocardiographic findings Systolic function normalization (days) Non-invasive ventilation	Mild to moderate mitral regurgitation + increased perivascular echogenicity in the left coronary artery 15	regurgitation		modrate mitral regurgitation+ increased perivascular echogenicity in the left coronary artery 8	regurgitation	regurgitation+ increased perivascular echogenicity in the right coronary artery	effusion -	regurgitation + increased perivascular echogenicity in the left coronary artery 3	regurgitation + increased perivascular echogenicity in the left coronary artery

RT-PCR: Reverse transcriptase polymerase chain reaction, IL-6R: Anti-interleukin-6 receptor monoclonal antibody, IL-1Ra: Interleukin-1 receptor antagonist, IVIG: Intravenous immunoglobulin, Plasmapheresis therapeutic plasma exchange, PICU: Pediatric intensive care

daily on days 2 through 5. Azithromycin was given once 500 mg on the first day and 250 mg once a daily for the other four days. Patients of group C were all discharged without any residual cardiac damage.

We did not detect typical clinical features of the COVID-19-linked myocarditis with Kawasaki clinical features in our cohort.

To summarize, cardiac involvement was detected in only 17 (7.9%) of the entire hospitalized patients. Most of our patients (88.2%) had elevated troponin I levels whereas 12 patients (70.5%) had abnormal electrocardiograms and echocardiographic exams. Fourteen (82.3%) of patients with high troponin I levels had also abnormal electrocardiograms whereas 13 (76.4%) of them had abnormal echocardiographic exams.

Discussion

Troponin levels that are elevated may be a significant prognostic factor in COVID-19. Those with cardiovascular disease and elevated troponins have the highest mortality, followed by those with elevated troponins but no cardiovascular disease (4). Because few research have been conducted on this topic, the role of troponin in children is significantly less defined than in adults. However, data on a troponin I rise as a marker of myocardial damage in children is being gathered as well (5-7). We found that most of our patients (88.2%) had elevated troponin levels albeit 11.7% were slightly high. We attributed this to the myocardial injury inflicted by the SARS-CoV-2 infection. We assumed that cardiac involvement may manifest itself as myocarditis ranging from mild to severe. Myocarditis diagnosis has mainly become clinical in the current era, with supportive ancillary tests. D'Ambrosio et al. (8) underlined that this condition has a positive prognosis because in around 80% of the patients, complete healing is seen. This fact is supported by our findings that mild forms of myocarditis of our group A and C patients albeit having high troponin levels, recovered completely without any complications. However, it is also evident that for some of our patients with normal electrocardiograms and normal echocardiographic examination, we as the authors need to acknowledge that this can be "possible myocarditis" at the best. However, there is also another fact in this conundrum. Although abnormal electrocardiograms have been detected in 93 percent

to 100 percent of pediatric patients with myocarditis in retrospective studies, a normal ECG does not rule out the potential of myocarditis (9-11) An ECG has a sensitivity of just 47% for diagnosing myocarditis in patients, despite its widespread usage as a screening tool (12,13) We would also like to point out that the troponin level of our patients did not correlate with the severity of the disease process as some of the group B patients with hyperinflammatory states or Kawasakilike disease did not have very high values compared to other patients with the same clinical status. Case four, one, eight, five, and nine of group B had all diminished left ventricular function as well as mild to moderate mitral regurgitation plus perivascular echo brightness of coronary arteries. Case one and four also needed ECMO support. However their troponin I values were 106695, 1218, 761, 308, 143 picogram/mL respectively presenting a large gap and inconsistency between them. Another gap exists between the two cases who needed ECMO support in terms of their troponin I values which are 1218 and 106695 picogram/mL respectively.

In terms electrocardiographic of findings of our study, four (23.5%) patients had normal electrocardiograms although they had elevated troponin I levels and various abnormal echocardiographic findings. Our finding is in line with Xia et al. (14) as they also reported that supraventricular tachycardia, premature atrial and ventricular complexes, firstdegree atrioventricular blocks, and incomplete right bundle branch blocks are less common in children with COVID-19. The echocardiography is crucial for myocarditis diagnosis and monitoring. Myocardial function is assessed at the time of diagnosis and serves as a baseline for evaluating disease progression and therapy response in the future (15). Echocardiographic examinations of our study did not include an analysis performed like Speckle tracking echocardiography that has been proven to be a valuable method in detecting subclinical contractility abnormalities in various clinical situations like myocarditis. This shortcoming of our study may explain the discrepancy between high troponin I levels and normal echocardiographic exams as well as normal electrocardiograms. There is another shortfall in our study as we did not perform cardiac resonance imaging in our patients which is the most comprehensive and accurate diagnostic tool in patients with suspected myocarditis. In the quantitative

assessment of systolic ventricular function, cardiac resonance imaging is regarded the gold standard. In addition, cardiac resonance imaging is the only imaging modality that can detect myocardial edema, a common sign of inflammation. Verification of myocarditis in patients with acute cardiac syndromes but normal coronary arteries or with atypical symptoms is one of its major capabilities in clinical practice (16).

None of the group B patients had the findings related with the complete Kawasaki disease based on the American Heart Association criteria which are bilateral non-exudative conjunctival injection, unilateral cervical lymphadenopathy, changes within the lips and oral cavity, skin rash, and changes in extremities, including indurative angioedema and desquamation. However, most of the patients (77.7%) in this group meet the criteria for multisystem inflammatory syndrome in children (MIS-C). The criteria used for the case definition of MIS-C change slightly between different health agencies (17-19). The case definitions indicated by the United States Centers for Disease Control and Prevention (CDC) and also the World Health Organization (WHO) need fever (though they differ with regard to duration), elevated inflammatory markers, a minimum of two signs of multisystem involvement, evidence of SARS-CoV-2 infection or exposure, and exclusion of other potential causes. All of the patients in this group had documented fever, at least two organ systems involved and laboratory evidence of inflammation. Though we failed to detect Ig G and Ig M for SARS-CoV-2 in three patients of this group, two of them admitted with hypotension and shock respectively and had diminished left ventricular function, one of them needing ECMO support. All of those three children had findings compatible with SARS-CoV-2 infection on their chest X-rays and chest computed tomography images. There also are three other patients in this group who tested negative RT-PCR for SARS-CoV-2. Both of those patients were also admitted with hypotension, had positive chest X-rays and chest computed tomography findings related to SARS-CoV-2 as well as positive cardiac findings. There were 783 children in the known case series of MIS-C in the literature who had both PCR and serology conducted (20-25) Of those, 60 percent had positive serology with negative PCR, 34 percent were positive on both tests, and 5 percent were negative on both tests which can explain our negative serology and

PCR testing results in group B of our study. Natasha et al. (26) made a review about MIS-C following SARS-CoV-2 Infection. 26 In their review of case series from three countries including total 70 children, the majority of patients had reduced cardiac ventricular function on echocardiography, but they were less likely to have valvular regurgitation or dilated coronary arteries (11/70 = 16%). Troponin levels were elevated in many patients (57/70, 81%). The majority of recorded patients have had positive serologic tests for SARS-CoV-2, indicating that this illness could be postinfectious rather than related to acute early infection (60/69, 87%) and fewer commonly positive RT-PCR testing from nasopharyngeal testing (23/70, 32%). Following SARS-CoV-2 infection, Grimaud et al. (27) reported 20 children with acute myocarditis and multisystem inflammatory after the illness. Although the patients' coronary arteries were not dilated, they showed acute myocardial systolic dysfunction. None of the individuals fit the classic Kawasaki illness profile. Nineteen of the 20 patients had tested positive for SARS-CoV-2 infection on PCR and/or by serology. Data revealed in these aforementioned two works of literature are compatible with our findings in terms of cardiac involvement which show the variety of types of involvement as well as SARS-CoV-2 infection detection rates.

Another issue to address is ongoing controversy about the normal serum troponin levels in newborns. The cut-off value for serum troponin levels in newborns is somehow troublesome. Troponin T and Troponin I reference ranges for term and preterm newborns have been issued by several authors (28). The largest study to date was published by Baum et al. (29) who examined both Troponin T and Troponin I values in cord blood samples of 869 healthy term infants. We accepted 117 picogram/mL for the cut-off value of Troponin I according to the data published by Baum et al. (29). According to the research, the top limit of serum troponin levels in children is significantly higher than in adults (30,31). COVID-19 is anticipated to be less dangerous to newborns and children due to factors such as the reduced function of angiotensin converting enzyme type 2 receptors (32). This fact may explain the benign course of the disease in our newborn patients though they had prolonged high troponin levels. The patients of group C had also mild symptoms and signs as well as benign findings.

Another significant element to consider is patient critical care management. Early recognition of shock (vasoplegic vs. cardiogenic), proper and judicious fluid resuscitation, early establishment of invasive monitoring, intubation and mechanical ventilation, oxygen delivery optimization, oxygen consumption minimization, and appropriate initiation of inotropes and vasopressors are all important factors in achieving a successful and favorable outcome (33). We suppose that the explanation for the favorable outcome for children in group B is related to the special treatments like anti-interleukin-6 receptor monoclonal antibody, interleukin-1 receptor antagonist, plasmapheresis (therapeutic plasma exchange), and ECMO. A study conducted by Belhadjer et al. (24) supports our findings. They described the experience of thirtyfive critically ill children with MIS-C presenting with cardiogenic shock, left ventricular dysfunction, and severe inflammatory state. All of the patients lived, and those who were given extracorporeal membrane oxygenation were weaned satisfactorily. Our study consists of 17 patients which limits its ability to indicate the extent of cardiac involvement during this pandemic. However, they were selected from our database of 214 patients (19 newborns) and they only constitute 7.9% of all the patients. This factor may show that degree of cardiac involvement is not high in children. As most of our patients (88.2%) had elevated troponin I levels and 70.5% had abnormal electrocardiograms and echocardiographic exams, we may state that from newborn to adolescents regardless of clinical status there are different patterns of cardiac involvement during the COVID-19 pandemic.

Conclusion

Newborns seem to have a mild disease process with possible myocarditis or clinically suspected myocarditis lingering on without any complications and recovering well. On the opposite hand, children may experience a devastating course with diminished cardiac function but fortunately recovering with appropriate treatment modalities and complete recovery may also be observed. Some of the children can cope with the disease very well with mild symptoms and signs as well as mild involvement of the heart only detected by diagnostic tools like laboratory, electrocardiographic and echocardiographic exams. Our results confirm the low morbi-mortality of COVID-19 in children as all of

Ethics

Ethics Committee Approval: The local ethical committee of Saglik Bilimleri University Prof. Dr. Ilhan Varank Training and Research Hospital approved this retrospective study on 16.12.2020 with a 2020/52 report number. As the study was retrospective and the patients' routine data was obtained from the hospital records we did not get informed consent from the subjects.

Conflict of Interest: No conflict of interest was declared by the authors.

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