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Covid-19 Affects Cardiovascular System 6 Months after Symptoms in Pediatric

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ORIGINAL ARTICLE

Coronavirus Disease 2019 Affects Cardiovascular System 6 Months After Symptoms in Pediatric

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Abstract

Background: **Coronavirus disease 2019 (COVID-19), which resulted in a global pandemic, is caused by severe acute respiratory syndrome coronavirus 2. We aimed to highlight the cardiovascular involvement in children after 6 months of COVID-19 recovery.**

Aim and objectives: **To highlight the cardiovascular involvement in children after 6 months of COVID-19 since this has the potential for morbidity and mortality in this age group.**

Patients and methods: **This observational cross-sectional descriptive study was conducted on 42 pediatrics aged less than 18 years old who recovered from COVID-19 after 6 months at hospitals from January 2022 to February 2023. All patients were subjected to full history taking, clinical examination, laboratory investigations as N-terminal pro-brain natriuretic peptide (NT-proBNP), troponin I, creatinine kinase MB (CK-MB) and lipoprotein profile were assessed in each child and imaging examinations, such as transthoracic echocardiography and 12 -lead ECG.**

Results: **Regarding the findings of imaging examination, the mean ejection fraction was 57.67 ± 4.69%, two (4.76%) patients had ST-wave change, two (4.76%) patients had prolonged PR interval, five (11.9%) patients had diastolic dysfunction and none of the studied patients had either abnormal systolic function or left ventricular dysfunction.**

Conclusions: **Abnormalities in the cardiovascular system in children with COVID-19 are of various nature, from mild changes in the echocardiographic image, to severe changes in heart according to the severity of infection. Even though most of these changes are withdrawn after the implementation of appropriate treatment.**

Keywords: Cardiovascular system, Coronavirus disease 2019, Mortality, Pediatrics

1. Introduction

Coronavirus disease 2019 (COVID-19), which resulted in a global pandemic, is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease presents acutely as cough, fever, and chills with ensuing shortness of breath and hypoxia.[1]

COVID-19 is rare in pediatric patients, with an incidence of less than 1% in children and adolescents aged less than 10 years. However, it can become a serious disease in 2.5% of this population, especially in those aged under 5 years as the hospital admission rate is up to 20% in this population.[2,3]

Cardiovascular complications from this infection in adults include myocardial injury, arrhythmias, acute coronary syndrome, and venous thromboembolism. Pre-existing cardiovascular diseases are associated with increased morbidity and mortality in adults with SARS-CoV-2 infection.[4] In contrast,

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most pediatric and adolescent patients infected with SARS-CoV-2 are asymptomatic or have mild disease.[5]

The involvement of the cardiovascular system in this viral infection can be explained in a multifactorial manner.[6] Cardiotoxicity, the primary mechanism of injury to cardiac tissue, results from the entry of the virus into cells, hypoxia resulting from this disease, and adverse events of drugs used in the treatment of COVID-19.[7]

Also, the main serious complication in children affected by the disease is multisystemic inflammatory syndrome (MIS-C). This syndrome had a cardiovascular involvement in 80–100% of cases, with mortalities occurring in 67% of patients.[8,9] However, it is a rare but severe post inflammatory complication of SARS-CoV-2 infection that can cause acute myocardial dysfunction, arrhythmias or conduction abnormalities, and coronary artery dilation.[10] Although adults with COVID-19 and cardiac disorders have an undoubtedly higher mortality rate, mortality may also occur in children and adolescents.[11]

We aimed to highlight the cardiovascular involvement in children after 6 months of COVID-19 since this has the potential for morbidity and mortality in this age group.

2. Patients and methods

This observational cross-sectional descriptive study was conducted on 42 paediatrics aged less than 18 years old who recovered from COVID-19 after 6 months. An informed written consent was obtained from the patients. The study was done after approval from the Ethical Committee of Faculty of Medicine- Hospitals from January 2022 to February 2023.

Exclusion criteria were children with neoplasm or any cardiovascular complication, congenital heart disease, children who tested positive for SARS-CoV-2 but had no symptoms or presented with minor symptoms (without fever, breathing difficulty or GIT distress).

2.1. Laboratory investigations

Diagnosis was done by Multiplex polymerase chain reaction (PCR), respiratory panel film array (Biomerieux film array, Biomerieux Company). D-dimer was evaluated by Stago. Complete blood count investigations was performed using Sysmex xn1000. Ferritin, vit D, high sensitivity troponin T (hs-TnT) and pro brain natriuretic peptide (BNP) was analyzed by Cobas e411 electrochemiluminescence, ROCHE company. Beckman DXC 700 AU was utilized for analysis of C-reactive protein, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) and Westergren method was used for evaluation of erythrocyte sedimentation rate.[12]

2.1.1. Sample size calculation

The sample size calculation was performed using G. power 3.1.9.2 (Universität Kiel, Germany). The sample size was calculated based on the following considerations: 0.05 α error and 90% power of the study and the mean of LVEDV was 83.1 ± 14.2 in case groups compared to 98.5 ± 14.2 in control group according to a previous study.[13] Four cases were added to overcome dropout. Therefore, 42 patients were allocated.

2.2. Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Armonk, NY, USA). Quantitative variables were presented as mean and standard deviation (SD). Qualitative variables were presented as frequency and percentage (%).

3. Results

Our study included 42 pediatric children, their mean age 12.43 ± 3.89 years, 24 (57.14%) males and 18 (42.86%) females and their mean BMI was 21.56 ± 5.15 kg/m^2 Table 1.

Among the studied patients, six (14.29%) were diabetic patients, three (7.14%) patients were hypertensive, five (11.9%) patients had chronic obstructive pulmonary disease and 10 (23.8%) patients had sleep disorders. All the included patients had negative PCR Table 2.

The median NT-pro BNP was 11.4 (10.25–14) pg/mL. 3 (7.14%) patients had elevated NT-pro BNP, five (11.9%) patients had elevated Troponin (hs-TnT) and 14 (33.33%) patients had vit D deficiency Table 3.

Table 1. Patient characteristics of the studied patients.

	Patients (N = 42) [n (%)]
Age (y)	12.43 ± 3.89
Sex	
Male	24 (57.14)
Female	18 (42.86)
Weight (Kg)	43.88 ± 9.48
Height (m)	1.43 ± 0.07
BMI (kg/m^2)	21.56 ± 5.15

Data are presented as mean ± SD or frequency (%).
BMI, Body mass index.

Table 2. Patient comorbidities of the studied patients.

	Patients ($N = 42$) [n (%)]
DM	6 (14.29)
HTN	3 (7.14)
COPD	5 (11.9)
Sleep disorders	10 (23.8)
PCR	
Positive	0
Negative	42 (100)

COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HTN, hypertension; PCR, polymerase chain reaction.

As shown in Table 4, the mean HR of the studied patients was 80.26 ± 6.84 beat/min, the mean SBP was 128.57 ± 8.43 mmHg, the mean DBP was 85.95 ± 9.39 mmHg and the mean temperature was 36.91 ± 0.33 °C.

Regarding the findings of imaging examination, the mean ejection fraction (EF) was 57.67 ± 4.69%, 2 (4.76%) patients had ST -wave change, 2 (4.76%) patients had prolonged PR interval, 5 (11.9%) patients had diastolic dysfunction and none of the studied patients had either abnormal systolic function or left ventricular dysfunction Table 5.

Table 3. Laboratory investigations of the studied patients.

	Patients ($N = 42$) [n (%)]
Hb (gm/dL)	11.41 ± 1.07
WBCs (*10^3 cells/all)	7.78 ± 3.92
Platelet count (*10^3 cells/all)	326.62 ± 67.36
CRP (mg/L)	87.38 ± 29.78
ESR (mm/hr)	6.76 ± 1.78
D-dimer (mg/L)	36.91 ± 0.33
Serum albumin (g/dL)	4.46 ± 0.56
Ferritin (ng/mL)	70.23 ± 31.62
Lipid profile	
Cholesterol (mg/dL)	158.48 ± 20.4
HDL (mg/dL)	51.76 ± 7.2
LDL (mg/dL)	110.6 ± 10.93
TG (mg/dL)	79.45 ± 24.57
Liver function test	
ALT (U/L)	22.98 ± 7.96
AST (U/L)	23.67 ± 8.29
Kidney function tests	
Serum creatinine (mg/dL)	0.9 ± 0.18
Urea (mg/dL)	29.6 ± 5.85
BUN (mg/dL)	11.38 ± 3.98
NT-pro BNP (pg/mL)	11.4 (10.25–14)
NT-pro BNP	
High	3 (7.14)
Normal	39 (92.86)
Troponin (hs-TnT)	
High	5 (11.9)
Normal	37 (88.1)
Vit D deficiency	14 (33.33)

Data are presented as mean ± SD, median (IQR) or frequency (%).
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NT-pro BNP, N-terminal pro B-Type Natriuretic Peptide; TLC, total leucocytic count.

Table 4. Vital signs of the studied patients ($n = 42$).

	Patients (n = 42)
HR (beat/min)	80.26 ± 6.84
SBP (mmHg)	128.57 ± 8.43
DBP (mmHg)	85.95 ± 9.39
Temperature (°C)	36.91 ± 0.33

Data are presented as mean ± SD or frequency (%).
DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure.

4. Discussion

Our results showed that among the studied patients, six (14.29%) were diabetic patients, three (7.14%) patients were hypertensive, five (11.9%) patients had chronic obstructive pulmonary disease and 10 (23.8%) patients had sleep disorders. All the included patients had negative PCR.

In agreement with our findings, a systematic review of the pediatric literature demonstrated that 108 of 5686 children (1.9%) required intensive care and mechanical ventilation because of acute SARS-CoV-2 infection. In this review, of those with severe illness and mechanical ventilation for whom detailed medical information was available, 75% had comorbidities, including various forms of congenital heart disease or cardiomyopathy (21%), obesity (15%), neurological disorders (10%), asthma (10%), and hypertension (2%).[14]

In the present study, the median NT-pro BNP was 11.4 (10.25–14) pg/mL, three (7.14%) patients had elevated NT-pro BNP, five (11.9%) patients had elevated Troponin and 14 (33.33%) patients had vit D deficiency.

The present study in line with Stasiak *et al.*[15] who observed that children with higher NT-pro-BNP, troponin I, triglycerides, C-reactive protein, PCT, D-dimers, ferritin, and creatinine and lower lymphocytes, PLT, haematocrit and EF more often presented with circulatory failure, hypotension, and

Table 5. Imaging examination findings of the studied patients.

	Patients ($N = 42$) [n (%)]
EF %	57.67 ± 4.69
ST -wave change	2 (4.76)
Prolonged PR interval	2 (4.76)
Diastolic dysfunction	5 (11.9)
Abnormal systolic function	0
Left ventricular dysfunction	0

Data are presented as mean ± SD or frequency (%).
EF, ejection fraction.

required hospitalization in the intensive care unit (ICU) and appliance of catecholamines. A higher concentration of troponin I and creatinine, a lower concentration of leukocytes and lymphocytes.

Our findings revealed that the mean EF was 57.67 ± 4.69%, 2 (4.76%) patients had ST -wave change, 2 (4.76%) patients had prolonged PR interval, 5 (11.9%) patients had diastolic dysfunction and none of the studied patients had either abnormal systolic function or left ventricular dysfunction.

Also, our results in consistent with Tsuji *et al.*[16] who revealed that the most frequently observed abnormalities in ECG recordings in patients with PIMS-TS were repolarization disorders, prolongation of the QTc interval, or arrhythmias in the form of premature supraventricular/ventricular beats, as well as more complex arrhythmias such as atrial fibrillation. The present study in line with a study conducted in the United States on a large group of patients, arrhythmia was found in 12% of children with PIMSTS.[17] Exact data on the incidence of arrhythmias in children with PIMS and their follow-up are unknown.[17]

As regards 6-week follow-up, our findings in agreement with Stasiak *et al.*[15] who stated that Only 2/51 children (3.9%) had persistent repolarization disorders in ECG. Echocardiography showed persistent trace regurgitation of the heart valves in 25/51 patients (49%) (mitral regurgitation in 21 patients, tricuspid regurgitation in seven patients, atrial regurgitation in four patients, and pulmonary regurgitation in 5 patients). Pericardial fluid persisted in 24/51 patients (47%). Coronary artery lesions were found in 10/51 children (19.6%), who required further administration of acetylsalicylic acid. Borderline EF was found in 2/51 patients (3.9%). Completely normal echocardiographic and electrocardiographic images were found in 13/51 patients (25.5%)

This underscores the importance of obtaining the first echocardiogram, within 24 h of admission but also illustrates that subsequent echocardiogram are useful to follow any abnormal LVEF and the need and frequency can be dictated by this first echocardiogram. At the time of discharge mild dysfunction persisted in 11.3% of the patient, similar to contemporary literature which describes persistence of ventricular dysfunction in 6–14%.[18,19] The natural history of this persistent systolic dysfunction is available in only a handful of studies.

In agreement with our results, Penner *et al.*[20] in a large single centre study from UK, described resolution of LV dysfunction in all patients by 6 months. Similar inferences were drawn from studies by Capone *et al.*,[21] Aziz *et al.*[13] and Dove *et al.*[22] Most of the other studies describe near complete resolution of myocardial dysfunction with 4–18 days at the time of discharge.[23,24]

4.1. Conclusion

Abnormalities in the cardiovascular system in children with COVID-19 are of various nature, from mild changes in the echocardiographic image, to severe changes. Even though most of these changes are withdrawn after the implementation of appropriate treatment, close cardiac supervision over these patients is necessary.

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Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

Conflicts of interest

There are no conflicts of interest.

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