ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.5336/medsci.2022-89203

Retrospective Evaluation of the Cases Presenting to the Pediatric Intensive Care Unit with Cardiogenic Shock in Terms of Etiology, Treatment and Long-Term Prognosis

Pediatrik Yoğun Bakım Ünitesine Kardiyojenik Şok Tablosunda Başvuran Olguların Etiyoloji, Tedavi ve Uzun Dönem Prognoz Açısından Retrospektif Değerlendirilmesi

Ebru AZAPAĞASI[a], Selman KESİCİ[b], Bilge AKKAYA[c], Tamer YOLDAŞ[d], Mutlu UYSAL YAZICI[a], Zeynelabidin ÖZTÜRK[e], Mehmet TAŞAR[f], Utku Arman ÖRÜN[d]

[a]Division of Pediatric Intensive Care, Gazi University Faculty of Medicine, Ankara, Türkiye
[b]Division of Pediatric Intensive Care, Hacettepe University Faculty of Medicine, Ankara, Türkiye
[c]Department of Pediatrics, University of Health Sciences Dr. Sami Ulus Maternity and Children's Training and Research Hospital, Ankara, Türkiye
[d]Division of Pediatric Cardiology, University of Health Sciences Dr. Sami Ulus Maternity and Children's Training and Research Hospital, Ankara, Türkiye
[e]Division of Pediatric Intensive Care, University of Health Sciences Dr. Sami Ulus Maternity and Children's Training and Research Hospital, Ankara Türkiye
[f]Division of Cardiovascular Surgery, University of Health Sciences Dr. Sami Ulus Maternity and Children's Training and Research Hospital, Ankara, Türkiye

ABSTRACT Objective: Cardiogenic shock is acute circulation failure emerging with a linkage to disrupted myocardial contraction. The aim of this study is to identify the underlying etiology, assess the treatment methods, and the long-term prognoses of survivors among the patients admitted to intensive care with cardiogenic shock for the first time and without a previous heart disease history. **Material and Methods:** This study included patients admitted to the intensive care unit in our hospital for the first time with cardiogenic shock from March 2016 to March 2020. The age interval was 1 month to 18 years. The demographic, clinical, laboratory, and radiological findings for patients were recorded. All patients were evaluated with echocardiography at admission and 12 months after discharge. **Results:** Of the 24 patients included in this study, 50% were girls (n=12). Nineteen (79.1%) of the 24 patients had acute myocarditis as the underlying cause. Three (12.5%) patients had hypocalcaemia linked to vitamin D deficiency, 1 (4.2%) patient had anomalous left coronary artery from the pulmonary artery syndrome, and 1 (4.2%) patient had cardiac tamponade linked to purulent pericarditis. In echocardiographic examinations performed at a 12-month interval, left ventricle ejection fraction increased from 32.45±9.26% to 49.18±15.53%, and left ventricle end-diastolic diameter Z score decreased from 5.65 (4.4) to 2.02 (4.76). **Conclusion:** With appropriate fluids, diuretic treatment, inotrope management, and extracorporeal support, the prognosis for these patients has clearly improved in recent years.

Keywords: Pediatric intensive care; cardiogenic shock; myocarditis; dilated cardiomyopathy

ÖZET Amaç: Kardiyojenik şok, miyokardiyal kontraksiyonun bozulmasına bağlı akut dolaşım yetersizliğidir. Bu çalışmanın amacı, yoğun bakıma kardiyojenik şok kliniği ile ilk kez yatırılan ve bilinen kalp hastalığı olmayan hastalarda, altta yatan etiyolojiyi saptamak, uygulanan tedavi yöntemlerini ve yaşayan hastalarda uzun dönem prognozu değerlendirmektir. **Gereç ve Yöntemler:** Bu çalışmaya, Mart 2016-Mart 2020 tarihleri arasında kardiyojenik şok kliniği ile ilk kez hastanemiz yoğun bakım ünitesine yatırılan hastalar dâhil edildi. Yaş aralığı 1 ay-18 yaş idi. Hastaların demografik, klinik, laboratuvar ve radyolojik bulguları kaydedildi. Tüm hastalar, yatışta ve taburcu olduktan 12 ay sonra ekokardiyografi ile değerlendirildi. **Bulgular:** Çalışmaya 24 hasta dâhil edildi, %50'si kız (n=12) idi. Yirmi dört hastanın 19'unda (%79,1) altta yatan neden akut miyokardit, 3 (%12,5) hastada D vitamini eksikliğine bağlı hipokalsemi, 1 (%4,2) hastada sol koroner arterin pulmoner arterden çıkış anomalisi, 1 (4,2%) hastada pürülan perikardite bağlı kardiyak tamponad idi. On iki ay arayla yapılan ekokardiyografik incelemelerde sol ventrikül ejeksiyon fraksiyonunun %32,45±9,26'dan %49,18±15,53'e yükseldiği; sol ventrikül diyastol sonu çapı Z skorunun 5,65'ten (4,4) 2,02'ye (4,76) düştüğü bulundu. **Sonuç:** Uygun sıvı, uygun diüretik tedavi, doğru inotrop yönetimi ve uygun ekstrakorporeal destek tedavileri ile son yıllarda bu hastaların prognozlarında belirgin düzelme izlenmektedir.

Anahtar Kelimeler: Çocuk yoğun bakım; kardiyojenik şok; miyokardit; dilate kardiyomiyopati

Correspondence: Ebru AZAPAĞASI
Division of Pediatric Intensive Care, Gazi University Faculty of Medicine, Ankara, Türkiye
E-mail: ebruazapagasi@hotmail.com

Peer review under responsibility of Turkiye Klinikleri Journal of Medical Sciences.

Received: 24 Feb 2022 ***Accepted:*** 31 Mar 2022 ***Available online:*** 31 Mar 2022

Cardiogenic shock is an acute state of circulatory failure due to impairment of myocardial contractility. In children, the clinical signs of cardiac failure are tachycardia, dyspnea, and hepatomegaly, together with global signs correlated with a decrease of cardiac output.[1] When shock progresses, mental status impairment develops.[2] Among cases of shock treated in pediatric emergency departments, 5-13% are cardiogenic shock cases.[1]

Cardiac causes of cardiogenic shock include primary and secondary dilated cardiomyopathy (DCM), acute or fulminant myocarditis, arrhythmia, congenital heart disease, cardiac surgery, drugs, toxic substances, Kawasaki disease, endocarditis, rheumatic fever, and cord rupture. Non-cardiac causes include sepsis-related myocardial failure, pulmonary embolism, pneumothorax, and tamponade.[1]

Mortality is related to the underlying disease. The mortality in cases of congenital heart disease, rhythm disorders, acquired heart diseases, and cardiomyopathies has been reported to be 4.7%, 23%, 8.7%, and 25%, respectively.[3,4] Mortality increases five fold in the presence of signs such as sepsis, acute renal failure, or liver failure.[1]

The aim of this study is to identify the underlying etiology, assess the treatment methods applied, and determine the mortality rates and long-term prognosis for survivors among patients admitted to intensive care with cardiogenic shock for the first time and without known heart disease.

MATERIAL AND METHODS

This study included 24 patients admitted to the intensive care unit for the first time with cardiogenic shock between March 2016 and March 2020.

Ethics committee approval was obtained for this study from the University of Health Sciences, Sami Ulus Maternity and Children's Training and Research Hospital Clinical Research Ethics Committee (date: December 1, 2021, number: 2020-KAEK-141/265) and it was in accordance with the Declaration of Helsinki.

Cardiogenic shock was defined as circulatory disorder caused by systolic and/or diastolic dysfunction of the heart.

All patients had echocardiography (ECHO) performed with left ventricle ejection fraction (LVEF) and left ventricle end-diastolic diameter (LVEDD) Z score recorded at the first admission and 12 months after discharge.

The study was retrospective. The age interval of the patients was between 1 month and 18 years. Data on patients' age, gender, cause of cardiogenic shock, reason for hospitalization in the intensive care unit, time from the onset of symptoms to diagnosis, findings on admission, urine output at first hospitalization and during follow-up, duration of hospitalization in the intensive care unit, duration of hospitalization in the ward, degree and velocity of entry-exit tricuspid regurgitation, degree and velocity of entry-exit mitral regurgitation, inotrope score at admission to the intensive care unit, whether levosimendan was used, whether arrhythmia developed, admission pH, lactate and bicarbonate values, admission troponin, kinase isoenzyme (creatinine kinase-myocardial band), C-reactive protein level, and prohormone B-type natriuretic peptide (pro-BNP) level were recorded. Viral panels were analyzed for all patients. Telecardiography was performed and the cardiothoracic ratio was recorded. Electrocardiography (ECG) findings were recorded. The following were also noted: whether patients were connected to mechanical ventilation and for how many days, whether they needed non-invasive supportive therapy or extracorporeal support therapy [extracorporeal membrane oxygenation (ECMO)], whether therapeutic plasma exchange or continuous renal replacement therapy was applied, which drugs were used, the Pediatric Risk of Mortality (PRISM) score, laboratory parameters, development of multiple organ failure, results of metabolic tests, and survival. Organ failures were determined according to the International Pediatric Sepsis Consensus Conference criteria published in 2005.[5]

Patients with DCM as identified by ECHO were noted. DCM was defined as the presence of left ventricular systolic dysfunction, LVEDD Z score above +2 for age by ECHO, left ventricular dilatation, and LVEF of <50% and cardiothoracic ratio of >0.60 by telecardiography. Patients with LVEF of <55% identified by ECHO at 12 months after discharge were considered to have chronic DCM.

Patients with structural heart disease, ongoing follow-up for arrhythmia or recent diagnosis of arrhythmia, metabolic diseases, dysmorphic findings, previous diagnosis of DCM, or coronavirus disease-2019-related hyperinflammation syndrome (multisystem inflammatory syndrome in children) were not included in the study. Patients whose files could not be accessed were also excluded.

STATISTICAL ANALYSIS

Statistical analysis was performed with IBM SPSS statistics version 22.0 (IBM Co, Armonk, NY, ABD). In the evaluation of data, frequencies and percentages were given for qualitative data. For quantitative data, descriptive statistical methods were applied to obtain an arithmetic mean for those with normal distribution and a median [interquartile range (IQR)] for those without standard deviation. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to identify normally distributed data. The chi-square test or Fisher's exact test was used to compare qualitative data between groups. In comparisons between two dependent groups, paired sample tests were used for data with normal distribution and the Wilcoxon test was used for data with non-normal distribution. All statistical calculations were evaluated at 95% confidence intervals and at a significance level of $p<0.05$.

RESULTS

This study included 24 patients, half of whom (n=12) were female. The median age of patients was 9 months (IQR: 10). The mean admission weight of the patients was 9.39±3.63 kg and the mean duration to diagnosis was 9.45±5.34 days. The PRISM score was 16±6.6.

The underlying cause was acute myocarditis in 19 (79.1%) of 24 cases. The cause was hypocalcemia due to vitamin D deficiency in 3 (12.5%) cases, anomalous left coronary artery from the pulmonary artery (ALCAPA) syndrome in 1 (4.2%) case, and cardiac tamponade due to purulent pericarditis in 1 (4.2%) case. One-fourth (25%, n=6) of the patients were from migrant families. At the time of admission, 54.1% of the patients (n=13) had grade 3-4 mitral regurgitation. Pulmonary hypertension was detected in 8 (33.3%) cases at admission. The initial symptoms of 18 (75%) patients were cough and wheezing. Fifteen (62.5%) patients had a history of fever. Eighteen (75%) patients had a pro-BNP value of >35,000 pg/mL at first admission. Ten (41.6%) patients had severe arrhythmia requiring the use of antiarrhythmics and/or cardioversion and defibrillation. Three patients had amiodarone used alone due to arrhythmia. Other patients required cardioversion and/or defibrillation in addition to amiodarone treatment. Two patients additionally started lidocaine. Eighteen (75%) patients needed mechanical ventilation. All patients (100%) had inotrope treatment administered. Ten (41.6%) patients had 2 or more signs of multiple organ failure (cardiovascular dysfunction, respiratory, neurologic, hematologic, hepatic, renal). Eighteen (75%) patients were administered levosimendan infusion, while 4 (16.6%) patients were administered intravenous immunoglobulin. The mortality rate was 8.3%. One (4.1%) patient was treated with continuous renal replacement therapy. Enteral feeding was started on the first or second day for 91.6% (n=22) of the patients. Congenital metabolic disease was not detected in any cases. All patients needed diuretic therapy. Furosemide 1 mg/kg push dose and then 0.1 mg/kg/hr infusion dose was begun. The dose was titrated according to urine output. Viral agents were detected in 5 (26.3%) patients. Three patients had influenza A (H1N1), 1 patient had respiratory syncytial virus, and 1 patient tested positive for parainfluenza virus.

Three (15.7%) of 19 patients diagnosed with myocarditis underwent ECMO. Indications for treatment by ECMO were the need for high-dose inotropic/vasoactive agents, deep metabolic acidosis, uncontrollable arrhythmia, and/or cardiac arrest. One (4.1%) of the patients undergoing ECMO was treated with therapeutic plasma exchange due to multiple organ failure. The surviving patient was admitted to the intensive care unit with LVEF of 15%, while the 2 patients who died were admitted to the intensive care unit with LVEF of 18% and 25%, respectively. The first of these patients was transported to the heart transplant center with ECMO administration to be included in the national emergency list. The cardiac functions of this patient, who was followed for 33 days with ECMO, recovered during this period and

the patient was discharged with complete neurological recovery. The other 2 patients who underwent ECMO died. While 2 of these patients were H1N1-positive, parainfluenza virus positivity was found for 1 patient. Therapeutic plasma exchange treatment via ECMO was applied for 1 of the patients who died due to multiple organ failure.

Inotropes were prescribed for all patients, which included adrenaline, milrinone, noradrenaline, dopamine, dobutamine, and levosimendan. Inotrope strategy was in the form of dobutamine if there was no hypotension; first adrenaline if there was hypotension followed by milrinone when hypotension resolved; and if hypotension continued in spite of adrenaline, patients were given noradrenalin and rarely additional dopamine. When appropriate, patients began levosimendan treatment in addition to inotrope in the early period. Inotrope dosages were determined according to the condition of the patients and titrated; additional inotropes were added as necessary.

Beta-blockers and angiotensin receptor blockers were added to the treatment of hemodynamically stable patients. Angiotensin receptor blockers were begun in the early period for patients. Patients with heart functions returning to normal stopped these after 6 months, while those whose heart functions did not return to normal continued to use them. Selected patients were given beta blockers for a short period.

Demographic data, hospital details, and clinical, laboratory, and radiological characteristics of the patients are shown in Table 1 and Table 2. Figure 1 shows characteristics of the patients.

The LVEF of these patients was mean 32.45±9.26% at admission and mean 49.18±15.53% at the 12th month. While the median (IQR) LVEDD Z score at admission was 5.65 (4.4), the same score at the 12th month after discharge was 2.02 (4.76). It was determined that the LVEF value after discharge was statistically significantly increased compared to LVEF at admission ($p<0.05$). On the other hand, the LVEDD Z score after discharge was found to be statistically significantly lower than the admission LVEDD Z score ($p<0.05$) (Table 3). The correlation between levosimendan infusion and survival was not statistically significant ($p>0.05$).

Five patients with a diagnosis of acute myocarditis had LVEF of <55% after discharge and these patients were accepted as having chronic DCM.

TABLE 1: Demographic, clinical, radiological, and laboratory characteristics of the patients.

Parameters	n	%
Number of patients (n=24)		
Female gender	12	50
Age at diagnosis, mean (IQR)	9 (10)	
Age at present, mean (IQR)	35 (32)	
Migrant	6	25
Primary diagnosis		
Acute myocarditis	19	79.1
DCM		
Hypocalcemia	3	12.5
ALCAPA	1	4.2
Purulent pericarditis (cardiac tamponade)	1	4.2
Clinical details		
Inotropic/vasoactive agent	24	100
Levosimendan	17	70.8
Organ failure-2 or more signs	10	41.6
Arrhythmia	10	41.6
3rd or 4th degree MR	13	54.1
Pulmonary HT	8	33.3
Mechanical ventilation	18	75
IVIG	4	16.6
Mortality	2	8.3
ECHO-radiology and laboratory		
LVEF<50	24	100
CTO>0.60	14	58.3
Pro-BNP>35,000 pg/mL	18	75
Troponin >0.09 ng/mL	24	100
CRP>0.5 mg/dL	10	41.6
CK-MB>0.5 U/L	24	100
Extracorporeal treatments		
ECMO	3	12.5
Continuous renal replacement therapy	1	4.1
Therapeutic plasma exchange	1	4.1

IQR: Interquartile range; DCM: Dilated cardiomyopathy; ALCAPA: Anomalous left coronary artery from the pulmonary artery; MR: Mitral regurgitation; HT: Hypertension; IVIG: Intravenous immunoglobulin; ECHO: Echocardiography; LVEF: Left ventricular ejection fraction; CTO: Cardiothoracic ratio; BNP: B-type natriuretic peptide; CRP: C-reactive protein; CK-MB: Creatinine kinase-myocardial band; ECMO: Extracorporeal membrane oxygenation.

TABLE 2: Clinic, laboratory, and hospital data.

	All cases (n=24)
Duration to diagnosis, day, mean±SD	9.45±5.34
Admission weight, kg, mean±SD	9.39±3.63
Admission pH, mean±SD	7.15±0.21
Admission bicarbonate, mmol/L, mean±SD	14.55±6.16
Admission lactate, mg/dL, median (IQR)	31.5 (61)
Urine, cc/kg/h median (IQR)	4 (3)
Inotrope score, µg/kg/min, median (IQR)	37 (70)
Troponin, ng/mL, median (IQR)	1.56 (4.15)
Duration of MV, day, median (IQR)	6.5 (12)
PICU admission, day, median (IQR)	9.5 (5)
Ward admission, day, median (IQR)	7.5 (8)
Duration of hospitalization, day, median (IQR)	18.5 (12)

SD: Standard deviation; IQR: Interquartile range; MV: Mechanical ventilation; PICU: Pediatric intensive care unit.

Laboratory parameters, QTc values, and LVEF values of the three patients who developed DCM due to vitamin D deficiency are shown in Table 4.

The tamponade fluid of one patient with a diagnosis of purulent pericarditis was found to have exuded, but the agent could not be produced.

DISCUSSION

Cardiogenic shock occurs when heart and circulation are no longer able to adapt to the situation and is characterized by severely impaired myocardial contractility.[1] In our study, it was observed that among patients admitted to the intensive care unit due to cardiogenic shock, the most common underlying cause was acute myocarditis. Less common causes included hypocalcaemia, ALCAPA syndrome, and cardiac tamponade.

Acute myocarditis is the inflammation of the heart muscle. In a study using the Pediatric Health Care Information System database, it was reported that it is a rare diagnosis that accounts for 0.05% of pediatric referrals.[6] Acute fulminant myocarditis (AFM) is a clinical disorder that occurs with sudden-onset cardiogenic shock, severe arrhythmia, and heart failure and can cause sudden death in both children and adults.[7] In our study, there were 19 patients hospitalized in the intensive care unit due to myocarditis. It has been reported in the literature that myocarditis peaks in 2 different age groups. The age group with

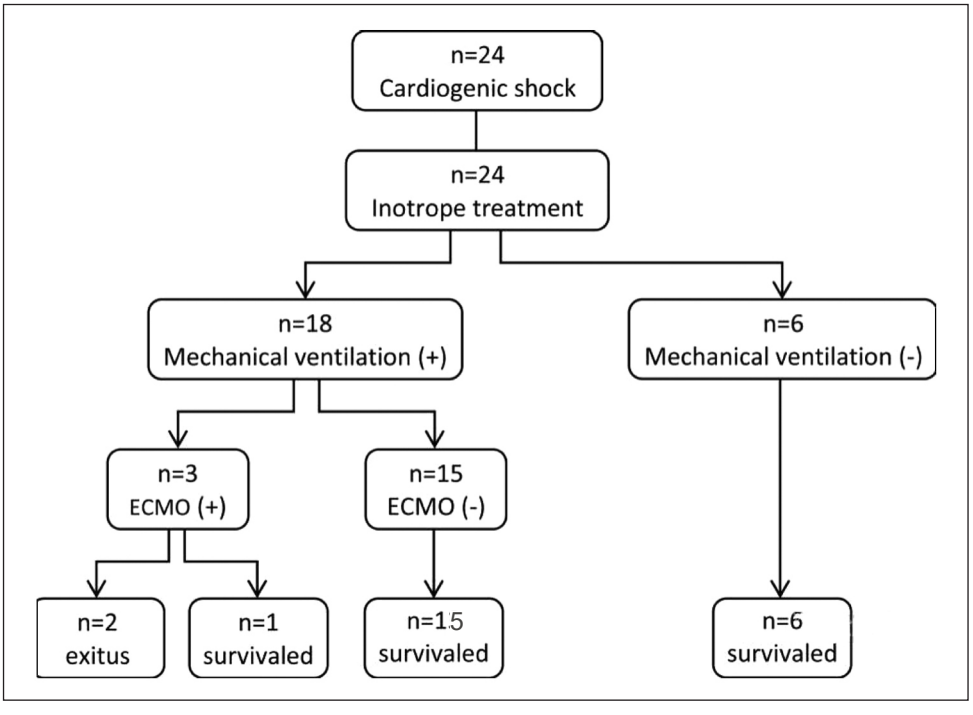

FIGURE 1: Clinical characteristics of the patients. ECMO: Extracorporeal membrane oxygenation.

TABLE 3: Z scores for LVEF and LVEDD.

		p value
Admission LVEF, mean±SD	32.45±9.26	<0.001*
Discharge LVEF, mean±SD	49.18±15.53	
Admission LVEDD Z score, median (IQR)	5.65 (4.4)	0.001**
Discharge LVEDD Z score, median (IQR)	2.02 (4.76)	

*Paired sample t-test; **Wilcoxon test; SD: Standard deviation; LVEF: Left ventricle ejection fraction; LVEDD: Left ventricle end-diastolic diameter.

the first peak is the infantile group of <1 year, while the second peak occurs in the adolescent age group.[8] The median age of the patients in our study was 9 months, representing the peak in the infantile group.

Three (15.7%) of 19 patients needed ECMO due to AFM. In the literature, the need for ECMO among patients with AFM was reported as 15.4% in one study, while this rate was 17% in another group of patients hospitalized for myocarditis.[9,10] Indications were reported to be severe arrhythmia, end-organ failure and circulation failure.[11,12] In our patients, these were among ECMO indications in addition to cardiac arrest. Al-Biltagi et al. established a relationship between low LVEF levels and poor prognosis in patients with myocarditis.[13] In another study, compared factors that affected mortality in patients with myocarditis and presented the following results; patients who survived had a mean LVEF of 30%, whereas patients who did not survive had a mean LVEF of 19%.[14] Three of our patients had LVEF below 30% and only one patient survived.

The diagnosis of myocarditis is difficult, especially in young children. This is because symptoms and clinical findings are usually non-specific. Patients may apply to the hospital with respiratory or gastrointestinal findings.[8] Durani et al. reported in their pediatric patients with myocarditis that 83% were not diagnosed at the first visit to a clinician and required two or more clinician examinations before myocarditis was suspected.[15] In the literature, an important portion of these patients were stated to have initial finding of respiratory distress, similar to our patients. In Freedman et al.'s retrospective study of 31 pediatric patients, the most frequently presenting symptoms were respiratory (32%), Rady and Zekri also report that the most frequently presenting symptom was respiratory (62.5%) in their prospective cohort of 63 children in the pediatric intensive care unit.[15] The majority of our patients were treated for bronchiolitis in external centers. There was nearly 10-day duration between the onset of first symptoms in these patients and receiving diagnosis. Probably the most important factor making diagnosis difficult for these patients was respiratory distress. It has also been reported in the literature that the diagnosis of AFM can be overlooked. In particular, patients initially thought to have sepsis and who underwent high-volume fluid replacement may rapidly decompensate due to cardiovascular collapse.[6] The reason

TABLE 4: Laboratory parameters of hypocalcemic DCM patients.

Laboratory	Normal values	Infant 1	Infant 2	Infant 3
Calcium				
Total (mg/dL)	8.8-10.8	6.4	6.7	5.7
Ionized (mmol/L)	1.12-1.23	0.7	0.6	0.6
Magnesium (mg/dL)	1.6-2.6	1	0.63	1.55
Phosphate (mg/dL)	4-7	6.7	4.2	13.4
Alkaline phosphatase (U/L)	132-315	525	687	271
25-OH vitamin D (ng/mL)	24-45	4	5	3.1
Parathormone (pg/mL)	11-67	1,969	320	568.4
POCR (CTO %)	<55	65	62	62
ECG: QTc (s)	<0.45	0.52	0.55	0.52
LVEF (%)	>55	38	30	20

DCM: Dilated cardiomyopathy; POCR: Posterior-anterior chest radiograph; CTO: Cardiothoracic ratio; ECG: Electrocardiography; LVEF: Left ventricular ejection fraction.

for decompensation in 5 (26.3%) of our cases was the high volume of fluid administered in the form of a bolus in an external center, as stated in the literature. For this reason, while one reason for patients being decompensated and admitted to the intensive care unit with cardiogenic shock was the delay in diagnosis, another reason was the aggressive fluid volume. Chong et al. reported that there was increased respiratory distress, hypotension, ECG abnormality or cardiomegaly, pulmonary congestion or pleural effusion on chest radiography for patients with delayed diagnosis, as in our patients.[16]

Life-threatening bradyarrhythmia and tachyarrhythmia may occur at any stage during the clinical course of patients diagnosed with myocarditis and sudden cardiac death may also occur.[17] Severe arrhythmia was observed in 47.3% (n=9) of our patients diagnosed with myocarditis. However, sudden death due to arrhythmia was not recorded in any cases. In addition to amiodarone and/or lidocaine infusions, these patients required cardioversion and defibrillation depending on their conditions.

Heart biopsy is one of the most important methods in the diagnosis of acute myocarditis.[18] However, it has some risks as it is an invasive procedure. While cardiac complications were reported at rates of 1-2% in some centers, this rate increased to 8.9% in other centers.[18] Cardiac magnetic resonance imaging is a more valuable non-invasive examination for these patients. It shows the volume of the ventricles, the ejection fraction, and the cardiac volume.[18,19] We did not perform cardiac biopsy for our patients due to complications. Moreover, cardiac magnetic resonance imaging was not performed because the patients were unstable and were receiving multiple inotropic treatments. On the other hand, the facts that the patients were healthy at the beginning, troponin I levels were high at admission, patients had a history of upper respiratory tract infection (URTI) and fever was accompanied by URTI, the causative agent was detected for 26% of the patients, metabolic test results were normal, and most patients were admitted in a fulminant state all suggest acute myocarditis.

Five (26%) of the patients in our patient group had LVEF of <55% in follow-up and these patients were considered to have chronic DCM. Although some patients were initially diagnosed with DCM, they were later determined to have AFM due to the recovery from DCM without sequelae in follow-up. The DCM frequency in our patient group is similar to the literature. In one study, this rate was given as 10-34%, while other studies reported the incidence of DCM was 27-46%.[20-24]

DCM is the most widespread form of cardiomyopathy. It is characterized by enlargement of the left ventricle and deterioration of systolic functions.[25] Its etiology is diverse. While one of the most important correctable causes of DCM is hypocalcaemia due to vitamin D deficiency, another cause is ALCAPA syndrome.[26,27]

Hypocalcaemia is a less known but treatable cause of DCM, which causes severe heart failure in children. Cardiogenic shock due to hypocalcaemic cardiomyopathy is a rare event.[28] Calcium ions play a fundamental role in regulating the contraction of the myocardium.[29] Vitamin D deficiency is the most important cause of DCM due to hypocalcaemia in infants and older children.[26] In our study, there were 3 patients who developed DCM due to vitamin D deficiency. These patients presented with cardiogenic shock. Inotropic and intensive care support, high-dose vitamin D and calcium therapy is recommended for treatment.[30] We initially applied high-dose vitamin D and high-dose calcium infusion treatment for our patients. Afterwards, we continued both supplements orally. In the literature, it has been reported that patients with DCM due to vitamin D deficiency respond dramatically to vitamin D and calcium treatment and recover within months.[28,30] The response of our patients to treatment was also very good. Cardiac functions had returned to normal at follow-up visits 3 months later. Neurological findings were good in all 3 cases and the patients recovered without any sequelae.

ALCAPA syndrome is defined as the congenital anomaly of the left coronary artery from the pulmonary artery. It is extremely rare; its incidence has been reported as 1/300,000.[31] The infant type of this syndrome is usually symptomatic in the second month of life. Its incidence among all congenital

heart diseases is 0.25-0.5% and its mortality is considerably high. In the event that treatment is delayed, approximately 90% of these patients die within the first year.[32] In our study, 1 patient was diagnosed with ALCAPA syndrome. As described in the literature, our patient became symptomatic in the second month of life.[32] The patient presented with cardiogenic shock, was intubated, and was connected to mechanical respiratory support. The definitive treatment of ALCAPA syndrome is surgery. Early diagnosis and prompt surgical intervention have excellent results and provide gradual myocardial recovery.[32] Our patient was diagnosed with angiography on the fifth day of hospitalization and a corrective surgery was performed with the reimplantation method shortly thereafter. The patient was discharged from the hospital on day 76, having recovered completely after surgical treatment.

Purulent pericarditis is a rare disease in developed countries. It usually manifests as sepsis or with signs of acute heart failure.[33] It can cause rapid deterioration of the patient and death. If clinical diagnosis is delayed, symptoms may worsen and cardiac tamponade may occur.[33,34] In our study, there was only one case. It has been reported that good results can be achieved with the combined application of surgical and medical treatment.[34,35] The case fully recovered as a result of administering medical and surgical treatment together. Figure 2 shows ECG images of patients, and Figure 3 shows chest X-rays.

The survival rate of our study group, which consisted of 24 patients hospitalized in the intensive care unit with cardiogenic shock, was 91.7%. Considering the long-term prognosis of surviving patients, the differences between patients' LVEF values at admission and after discharge and between LVEDD Z scores at admission and after discharge were statistically significant. Therefore, the long-term prognosis of the patients was good. The most frequent cause of cardiogenic shock in our patients was acute myocarditis. The second most common cause we encountered was DCM linked to vitamin D deficiency. In these patients, in addition to inotrope and support treatment, high-dose vitamin D and calcium treatment is stated to have perfect effects on prognosis.[28,30] In our study, the least common 2 causes were ALCAPA syndrome and cardiac tamponade linked to purulent pericarditis. Both patients were treated appropriately. This patient group requires emergency treatment and rapid management. The reason for better prognosis in this patient group according to us is early diagnosis, correct fluid and inotrope management, appropriate diuretic, appropriate medical and surgical treatments and extracorporeal support treatments.

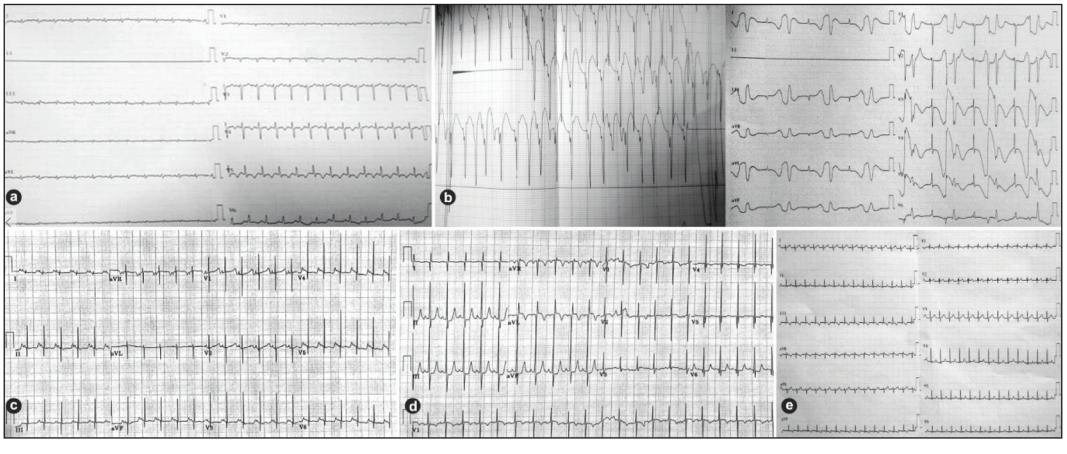

FIGURE 2: Electrocardiography images. **a)** Wide QRS voltage suppression, T wave negativity in V5-V6; **b)** Non-sustained ventricular tachycardia and bigeminy ventricular extrasystoles; **c)** Prolongation of the QT interval due to hypocalcemia; **d)** Pathological Q waves in DI and aVL (associated with ALCAPA syndrome); **e)** Wide QRS voltage suppression and T wave negativity in the inferior leads.

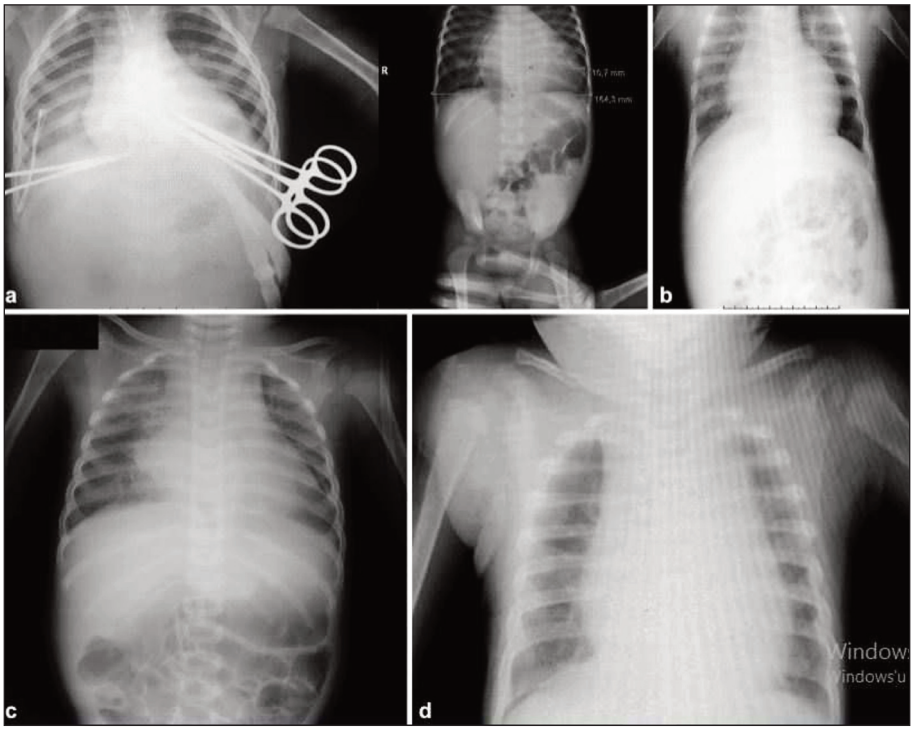

FIGURE 3: Chest X-ray. **a)** Acute myocarditis; **b)** Hypocalcaemia, DCM; **c)** ALCAPA syndrome; **d)** Purulent pericarditis, cardiac tamponade. DCM: Dilated cardiomyopathy; ALCAPA: Anomalous left coronary artery from the pulmonary artery.

LIMITATIONS OF THE STUDY

This study was a retrospective study. It was conducted in a single center and a limited number of patients could be included.

CONCLUSION

In conclusion, within the context of this study, it should be kept in mind that acute myocarditis is one of the most important causes among patients hospitalized with cardiogenic shock, especially among patients under 2 years of age, and that vitamin D deficiency, ALCAPA syndrome, and purulent pericarditis with delayed treatment may also be among the causes of cardiogenic shock. It should be remembered that prognosis may be positive in these patients with early diagnosis and appropriate treatment.

Acknowledgment

We would like to thank Prof. Dr. Tanıl KENDİRLİ, the Head of the Pediatric Intensive Care Department of the Ankara University Faculty of Medicine, and his team for their assistance with the patient transported under ECMO.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Ebru Azapağası, Tamer Yoldaş, Zeynelabidin Öztürk;* ***Design:*** *Ebru Azapağası, Tamer Yoldaş,Utku Arman Örün;* ***Control/Supervision:*** *Tamer Yoldaş, Zeynelabidin Öztürk, Utku Arman Örün;* ***Data Collection and/or Processing:*** *Ebru Azapağası, Bilge Akkaya, Mutlu Uysal Yazıcı;* ***Analysis and/or Interpretation:*** *Selman Kesici, Mehmet Taşar, Utku Arman Örün;* ***Literature Review:*** *Ebru Azapağası, Bilge Akkaya;* ***Writing the Article:*** *Ebru Azapağası, Zeynelabidin Öztürk, Tamer Yoldaş;* ***Critical Review:*** *Ebru Azapağası, Selman Kesici, Bilge Akkaya, Mehmet Taşar, Utku Arman Örün, Mutlu Uysal Yazıcı, Tamer Yoldaş, Zeynelabidin Öztürk.*

REFERENCES

1. Brissaud O, Botte A, Cambonie G, Dauger S, de Saint Blanquat L, Durand P, et al. Experts' recommendations for the management of cardiogenic shock in children. Ann Intensive Care. 2016;6(1):14. [Crossref] [PubMed] [PMC]
2. Subramaniam S, Rutman M. Cardiogenic shock. Pediatr Rev. 2015;36(5):225-6. [Crossref] [PubMed]
3. Massin MM, Astadicko I, Dessy H. Epidemiology of heart failure in a tertiary pediatric center. Clin Cardiol. 2008;31(8):388-91. [Crossref] [PubMed] [PMC]
4. Biarent D, Bingham R, Eich C, López-Herce J, Maconochie I, Rodríguez-Nú-ez A, et al. European Resuscitation Council Guidelines for Resuscitation 2010 Section 6. Paediatric life support. Resuscitation. 2010;81(10):1364-88. [Crossref] [PubMed]
5. Goldstein B, Giroir B, Randolph A; International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. Pediatr Crit Care Med. 2005;6(1):2-8. [Crossref] [PubMed]
6. Tunuguntla H, Jeewa A, Denfield SW. Acute myocarditis and pericarditis in children. Pediatr Rev. 2019;40(1):14-25. [Crossref] [PubMed]
7. Huang X, Sun Y, Su G, Li Y, Shuai X. Intravenous immunoglobulin therapy for acute myocarditis in children and adults. Int Heart J. 2019;60(2):359-65. [Crossref] [PubMed]
8. Arola A, Pikkarainen E, Sipilä JO, Pykäri J, Rautava P, Kytö V. Occurrence and features of childhood myocarditis: a nationwide study in Finland. J Am Heart Assoc. 2017;6(11):e005306. [Crossref] [PubMed] [PMC]
9. Kim J, Cho MJ. Acute myocarditis in children: a 10-year nationwide study (2007-2016) based on the health insurance review and assessment service database in Korea. Korean Circ J. 2020;50(11):1013-22. [Crossref] [PubMed] [PMC]
10. Wu HP, Lin MJ, Yang WC, Wu KH, Chen CY. Predictors of extracorporeal membrane oxygenation support for children with acute myocarditis. Biomed Res Int. 2017;2017:2510695. [Crossref] [PubMed] [PMC]
11. Duncan BW, Bohn DJ, Atz AM, French JW, Laussen PC, Wessel DL. Mechanical circulatory support for the treatment of children with acute fulminant myocarditis. J Thorac Cardiovasc Surg. 2001;122(3):440-8. [Crossref] [PubMed]
12. Kato S, Morimoto S, Hiramitsu S, Uemura A, Ohtsuki M, Kato Y, et al. Risk factors for patients developing a fulminant course with acute myocarditis. Circ J. 2004;68(8):734-9. [Crossref] [PubMed]
13. Al-Biltagi M, Issa M, Hagar HA, Abdel-Hafez M, Aziz NA. Circulating cardiac troponins levels and cardiac dysfunction in children with acute and fulminant viral myocarditis. Acta Paediatr. 2010;99(10):1510-6. [Crossref] [PubMed]
14. Lee EY, Lee HL, Kim HT, Lee HD, Park JA. Clinical features and short-term outcomes of pediatric acute fulminant myocarditis in a single center. Korean J Pediatr. 2014;57(11):489-95. [Crossref] [PubMed] [PMC]
15. Howard A, Hasan A, Brownlee J, Mehmood N, Ali M, Mehta S, et al. Pediatric myocarditis protocol: an algorithm for early identification and management with retrospective analysis for validation. Pediatr Cardiol. 2020;41(2):316-26. [Crossref] [PubMed]
16. Chong SL, Bautista D, Ang AS. Diagnosing paediatric myocarditis: what really matters. Emerg Med J. 2015;32(2):138-43. [Crossref] [PubMed]
17. Tschöpe C, Ammirati E, Bozkurt B, Caforio ALP, Cooper LT, Felix SB, et al. Myocarditis and inflammatory cardiomyopathy: current evidence and future directions. Nat Rev Cardiol. 2021;18(3):169-93. [Crossref] [PubMed] [PMC]
18. Ammirati E, Frigerio M, Adler ED, Basso C, Birnie DH, Brambatti M, et al. Management of acute myocarditis and chronic inflammatory cardiomyopathy: an expert consensus document. Circ Heart Fail. 2020;13(11):e007405. [PubMed] [PMC]
19. Rodriguez-Gonzalez M, Sanchez-Codez MI, Lubian-Gutierrez M, Castellano-Martinez A. Clinical presentation and early predictors for poor outcomes in pediatric myocarditis: a retrospective study. World J Clin Cases. 2019;7(5):548-61. [Crossref] [PubMed] [PMC]
20. Feldman AM, McNamara D. Myocarditis. N Engl J Med. 2000;343(19):1388-98. [Crossref] [PubMed]
21. Cooper LT Jr. Myocarditis. N Engl J Med. 2009;360(15):1526-38. [Crossref] [PubMed] [PMC]
22. Daubeney PE, Nugent AW, Chondros P, Carlin JB, Colan SD, Cheung M, et al; National Australian Childhood Cardiomyopathy Study. Clinical features and outcomes of childhood dilated cardiomyopathy: results from a national population-based study. Circulation. 2006;114(24):2671-8. [Crossref] [PubMed]
23. Lipshultz SE, Sleeper LA, Towbin JA, Lowe AM, Orav EJ, Cox GF, et al. The incidence of pediatric cardiomyopathy in two regions of the United States. N Engl J Med. 2003;348(17):1647-55. [Crossref] [PubMed]
24. Towbin JA, Lowe AM, Colan SD, Sleeper LA, Orav EJ, Clunie S, et al. Incidence, causes, and outcomes of dilated cardiomyopathy in children. JAMA. 2006;296(15):1867-76. [Crossref] [PubMed]
25. Weintraub RG, Semsarian C, Macdonald P. Dilated cardiomyopathy. Lancet. 2017;390(10092):400-14. [Crossref] [PubMed]
26. Sanyal D, Raychaudhuri M. Infants with dilated cardiomyopathy and hypocalcemia. Indian J Endocrinol Metab. 2013;17(Suppl 1):S221-3. [Crossref] [PubMed] [PMC]
27. Krishna MR. ALCAPA-A reversible cause of dilated cardiomyopathy in infants. Indian J Pediatr. 2022;89(2):197. [Crossref] [PubMed]
28. Gupta P, Tomar M, Radhakrishnan S, Shrivastava S. Hypocalcemic cardiomyopathy presenting as cardiogenic shock. Ann Pediatr Cardiol. 2011;4(2):152-5. [Crossref] [PubMed] [PMC]
29. Calaghan SC, White E. The role of calcium in the response of cardiac muscle to stretch. Prog Biophys Mol Biol. 1999;71(1):59-90. [Crossref] [PubMed]
30. Tomar M, Radhakrishnan S, Shrivastava S. Myocardial dysfunction due to hypocalcemia. Indian Pediatr. 2010;47(9):781-3. [Crossref] [PubMed]
31. Dodge-Khatami A, Mavroudis C, Backer CL. Anomalous origin of the left coronary artery from the pulmonary artery: collective review of surgical therapy. Ann Thorac Surg. 2002;74(3):946-55. [Crossref] [PubMed]
32. Pe-a E, Nguyen ET, Merchant N, Dennie C. ALCAPA syndrome: not just a pediatric disease. Radiographics. 2009;29(2):553-65. [Crossref] [PubMed]
33. Bhaduri-McIntosh S, Prasad M, Moltedo J, Vázquez M. Purulent pericarditis caused by group a streptococcus. Tex Heart Inst J. 2006;33(4):519-22. [PubMed] [PMC]
34. Cakir O, Gurkan F, Balci AE, Eren N, Dikici B. Purulent pericarditis in childhood: ten years of experience. J Pediatr Surg. 2002;37(10):1404-8. [Crossref] [PubMed]
35. Majid AA, Omar A. Diagnosis and management of purulent pericarditis. Experience with pericardiectomy. J Thorac Cardiovasc Surg. 1991;102(3):413-7. [Crossref] [PubMed]