

# Myocarditis in childhood report of 67 patients

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## Abstract

**Aim:** The aim of this study is to evaluate the clinical findings, sociodemographic characteristics and follow -up of the myocarditis cases and to investigate factors affecting the mortality.

**Materials and Methods:** Patients who diagnosed myocarditis from January 2009 to December 2017 were included in this study. Sex, date of admission, age at the time of admission, presence of previous infection, physical examination findings, serum cardiac biomarkers, whole blood count, C reactive protein and viral serology results, electrocardiographic findings, telecardiography and echocardiographical findings and the medical records about complications and mortality during follow-up were analysed. Statistical analyzes performed with IBM SPSS 22.0. Pearson chi-square and continuity corrected chi-square tests were used. Numerical data were summarized with median, minimum and maximum values. Univariate Kaplan - Meier and Cox regression analyzes were used in comparisons. The significance level was accepted as 0.05 in all tests.

**Results:** From January 2007 to December 2017, 67 patients with myocarditis were retrospectively analyzed. 31 (46.2%) patients were recovered. 21 patients (31.3%) developed dilate cardiomyopathy. Six patients were died in acute phase. 7 of 21 patients with dilate cardiomyopathy were died at follow-up period. Nine patients were referred to a cardiovascular surgery center for VAD, ECMO or cardiac transplantation. Among them seven patients were died under ECMO. 2 patients were implanted VAD.

**Conclusion:** Myocarditis is an inflammatory disease of the myocardium. Diagnosis of myocarditis may be difficult to subtle clinical findings. The clinical picture may be varying from a mild subclinical period to congestive heart failure. The prognosis varies from recovery to complicated chronic disease and death. In our study, increased cardiothoracic index and pulmonary congestion findings in telecardiography, increased serum myoglobin level and decreased echocardiographic shortening fraction were factors associated with increased mortality. The using the cardiac support devices in patients with myocarditis may decrease mortality.

**Keywords:** Dilated cardiomyopathy; heart failure; myocarditis

## INTRODUCTION

Myocarditis is an inflammatory disease of myocardium. In children, viral agents are often responsible for etiology. Coxsackie B virus was more common in previous decades, recently Adenovirus and Parvovirus B 19 have been found the most frequent pathogens in virally myocarditis (1). Clinical presentation of myocarditis may be asymptomatic, nonspecific systemic symptoms and some cases may have congestive heart failure and cardiogenic shock due to fulminant myocarditis. Although the myocardial biopsy is gold standard for diagnosis, it's not useful due to its complications and low sensitivity (2). Nonspecific tests such as telecardiogram, electrocardiogram, cardiac enzymes, cardiac magnetic resonance imaging and viral serology are performed for diagnosis (3). Clinical suspicion is important for diagnosis of myocarditis. The aim of this study is to evaluate the clinical findings,

sociodemographic characteristics and follow -up of the myocarditis cases who followed-up in our clinic from January 2009 -December 2017 and to investigate factors affecting the mortality.

## MATERIALS and METHODS

Patients who diagnosed myocarditis from January 2009 to December 2017 were included in this study. The medical records of patients were reviewed and sex, date of admission, age at the time of admission, presence of previous infection, physical examination findings, serum cardiac biomarkers, whole blood count, C reactive protein and viral serology results, electrocardiographic findings, telecardiography and echocardiographical findings and the medical records about complications and mortality during follow-up were analysed. Statistical analyzes performed with IBM SPSS 22.0. Pearson chi-square and continuity corrected chi-square tests were used.

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Numerical data were summarized with median, minimum and maximum values. Univariate Kaplan - Meier and Cox regression analyzes were used in comparisons. The significance level was accepted as 0.05 in all tests.

## RESULTS

From January 2007 to December 2017, 67 patients with myocarditis were retrospectively analyzed who were followed up in the Pediatric Cardiology department in Our University Hospital. Patient complaints were; shortness of breath (28.3%), scorpion insertion (11.9%), fever (8.9%), cough (7.5%), chest pain (7.5%), palpitation (5.9%), malaise (4.5%), rash and swelling in the body (2.9%), fainting (2.9%), abdominal pain (2.9%), vomiting/diarrhea (2.9%), restlessness (1.5%) and fatigue (1.5%). Physical examination findings revealed as tachypnea (25.3%), systolic murmur (22.3%), tachycardia (17.8%), crepitantrales in pulmonary auscultation (8.9%), gallop rhythm (7.4%), edema (4,5%) and hepatomegaly (10.3%). Symptoms and clinical findings of patients are shown in Table 1.

In the laboratory, C reactive protein was elevated in 14 patients (20.8%) and normal in 53 patients (79.2%). Myoglobin was found as normal in 43 patients (64.2%) and it was high in 24 patients (35.8%). CK-MB was found normal in 32 patients (47.8%) and it was high in 35 patients (52.2%). Troponin was found as normal in 40 patients (59.8%) and it was high in 27 patients (40.2%).

**Table 1. Symptoms and clinical findings of patients**

Symptom	Number of patients	%
Shortness of breath	19	28.3%
Scorpion insertion	8	11.9%
Fever	6	8.9%
Cough	5	7.5%
Chest pain	5	7.5%
Palpitation	4	5.9%
Malaise	3	4.5%
Fainting	2	2.9%
Abdominal pain	2	2.9%
Vomiting/ diarrhea	2	2.9%
Rash	2	2.9%
Restlessness	1	1.5%
Fatigue	1	1.5%
<b>Clinical findings</b>		
Tachypnea	17	25.3%
Murmur	15	22.3%
Tachycardia	12	17.8%
Hepatomegaly	7	10.3%
Crepitant rales	6	8.9%
Gallop rythm	5	7.4%
Edema	3	4.5%

**Table 2. Electrocardiographic, telecardiographic, echocardiographic and laboratory findings of patients**

	Number of patients	Percent
<b>Electrocardiographic</b>		
Voltage suppression	21	31.4%
Sinus tachycardia	14	20.8%
Supraventricular tachycardia	3	4.46%
<b>Telecardiography</b>		
Cardiomegaly	13	19.4%
Pulmonary congestion with cardiomegaly	13	19.4%
<b>Echocardiographic examination</b>		
	<b>Mean</b>	
LVIDD	43.8 (23-82) ± 12.2	
LVIDS	34.6 (18-60) ±10.1	
EF	42.3 (13-78) ± 14.1	
SF	21.3 (9-45) ± 8.1	
<b>Laboratory findings</b>		
Myoglobin (ng/ ml)	87.7 (6-945) ± 151.6	
CK – MB (ng/ ml)	6.08 (0.3-19) ± 5.3	
Troponin I (ng/ ml)	2.12 (0.06-14) ± 3	
Pro-BNP (pg/ ml)	20271 (44-7288) ± 19752	

LVIDD: Left ventricular diastolic diameter, LVIDS: Left ventricular systolic diameter, EF: Ejection fraction, SF: Shortening fraction

Electrocardiography showed voltage suppression 31.4% patients, 20.89% sinus tachycardia and 4.47% supraventricular tachycardia. Telecardiography showed pulmonary congestion with increase of cardiothoracic ratio in 19.4% of patients and increase of cardiothoracic ratio in 19.4% of patients.

On echocardiographic examination mean ejection fraction was 42.35% (13- 78% ± 14,1) and the mean shortening fraction was 21.36% (9- 45% ± 8.1). Electrocardiographic, telecardiographic, echocardiographic and laboratory findings of are shown in Table 2.

The etiological factors were scorpion insertion in 8 patients (11.9%) previous viral infections in 46 patients (68.6%) which were 4.5% Parvovirus, 2.9% EBV, 1.5% Rotavirus, 1.5% Rhinovirus, 1.5% HSV and Mycoplasma infections were detected in 1.5% patients. Etiological factors of the disease are shown in Table 3.

Table 3. Etiology

Etiology	Number of patients	Percent
Gastroenteritis	2	2.9%
Upper respiratory tract infection	18	26.8%
Bronchiolitis	4	5.9%
Pneumonia	2	2.9%
Scorpion insertion	8	11.9%
Parvovirus	3	4.5%
EBV	2	2.9%
Mycoplasma	1	1.5%
HSV	1	1.5%
Rotavirus	1	1.5%
Rhinovirus	1	1.5%

EBV: Ebstein Barr Virus, HSV: Herpes Simplex virus

In medical treatment, 79.1% patients receive diuretics, 73.1% ACE inhibitors, 19.4% aspirin, 56.7% dopamine and dobutamine, 62.6% digoxin and 13.4% milrinon. 28.3% patients also received IVIG treatment when consider to viral infection. There was left ventricular thrombus at 3 patients and they received heparin. Medical treatments of the patients are shown in Table 4.

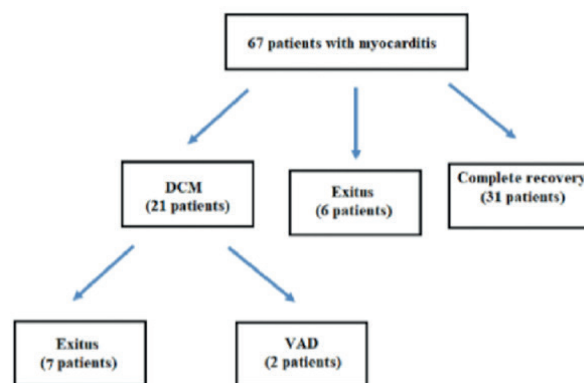
Of the 67 patients, 31 (46.2%) were fully recovered. There was developed dilate cardiomyopathy in 21 patients (31.3%). Six patients were died in acute phase. 7 of 21 patients with dilate cardiomyopathy were died at follow-up period. Seven patients were referred to an cardiovascular surgery center for VAD, ECMO or cardiac transplantation. Prognosis is shown in Figure 1.

Of the 67 patients, 31 (46.2%) were fully recovered. There was developed dilate cardiomyopathy in 21 patients (31.3%). Six patients were died in acute phase of myocarditis. 7 of 21 patients with dilate cardiomyopathy were died at follow-up period. Nine patients were referred

to an heart transplant center for VAD, ECMO or cardiac transplantation. Among them 7 seven patients were died under ECMO, VAD implanted in 2 patients and they are still waiting for heart transplantation.

Table 4. Medical treatment

Drugs	Number of patients	Percent
Diuretic	53	79.1%
ACE inhibitors	49	73.1%
Dopamine	38	56.7%
Dobutamine	38	56.7%
Digoxin	42	62.6%
Milrinon	9	13.4%
IVIG	19	28.3%
Aspirin	13	19.4%
Heparin	3	4.47%



DCM: Dilated cardiomyopathy, VAD: Ventricular assist device

Figure 1. Prognosis

## DISCUSSION

Myocarditis is an important cause of morbidity and mortality in children and young adults. In this study, we reviewed 67 patients who were followed in our clinic between January 2009 and December 2017, ages ranged from 0-18 years; as clinical presentation, treatment and prognostically. The average age of our patients was 4.4 years. In our study we couldn't find statistical significance between the age and mortality ( $p = 0.135$ ). Klugman et al. showed a bimodal age distribution with a peak in infancy and a similar peak in mid-teenage years (4). Our study also showed that the frequency of myocarditis in infancy was consistent with the literature. In our study the duration of hospitalization was at least 1 day, at most 28 days, a mean of 6.64 days. In Klugman et al. study the mean duration of hospitalization time was 7 days. It is similar to our study (4).

Many factors are mentioned in the etiology of myocarditis. Viruses are the most cause of myocarditis. Enteroviruses, influenza virus, adenovirus, parvovirus B19, Epstein-Barr virus, human herpesvirus 6 and cytomegalovirus are the main ones (5). In our study, 46 patients (68.6%) were

examined for viral serology. In serology 4.5% parvovirus, 2.9% EBV, 1.5% rotavirus, 1.5% rhinovirus, 1.5% HSV. Mycoplasma also detected in 1.5% of patients. Haider et al. noted a seasonal variation of myocarditis and found a peak during April 19% (12 patient) and maximum incidence to be from March to May 45% (28 patient) (6). We found a peak during December 14.9% (10 patient) and the second was April 10.4% (7 patient), November 10.4% (7 patient), August 10.4% (7 patient).

The clinical presentation of myocarditis is very wide ranging from mild viral illness to severe circulatory and cardiac failure (7). Haider et al. showed that patients with myocarditis presented with (73%) irritability, (65%) lethargy, (60%) anorexia/poor feeding, (58%) fever, (42%) vomiting, (29%) diarrhea, (23%) abdominal pain, (68%) tachypnea/difficulty in breathing and (60%) cough (6). In this study, %65 of patients has history of preceding upper respiratory tract infection. In our study patient complaints were; shortness of breath (28.3%), fever (8.9%), cough (7.5%), chest pain (7.5%), palpitation (5.9%), malaise (4.5%), rash and swelling in the body (3%), fainting (2.9%), abdominal pain (2.9%), vomiting - diarrhea (2.9%), restlessness (1.5%) and rapid fatigue (1.5%). In Durani et al. study the most common symptoms of myocarditis were shortness of breath (69%), vomiting (48%) and poor feeding (40%) (8). % 11.9 patients have preceding study scorpion insertion.

The clinical features can vary from a mild subclinical period to an acute cardiac insufficiency. Tachypnea, tachycardia, subcostal retractions and wheezing are usually seen in patients (9). Haider et al. noted that clinical examination findings were 90% tachycardia, 87% poor capillary refill, 84% cold extremities, 58% hepatomegaly, 50% hypotension and 57% basal crepitations (6). Butts et al. noted that physical examination revealed that 21.3% hepatomegaly 20.1% gallop rhythm, 21.3% respiratory distress, 16.4% diminished extremity pulses and 49.3% no significant findings (10). In our study, physical examination revealed tachypnea (25.3%), systolic murmur (22.3%), tachycardia (17.8%), crepitant rales in pulmonary auscultation (8.9%), gallop rhythm (7.4%), edema (4.5%) and hepatomegaly (10.3%).

Mogyorosy et al. found that voltage suppression, sinus tachycardia and ST-T abnormalities were most common ECG abnormalities (11). In our study 31.4% voltage suppression, 20.8% sinus tachycardia and 4.46% supraventricular tachycardia were detected in the patients. 43.3% patients' electrocardiogram were normal.

In Molina et al. study telecardiogram findings demonstrated cardiomegaly in 17 patients (89%) (12). In our study, abnormalities telecardiogram was found in 38.8% patients. Among them 19.4% of patients have cardiomegaly, 19.4% of patients have cardiomegaly with pulmonary congestion. In our study patients with increased cardiothoracic index was found 5,134-fold higher risk of death than patients without pathologic telecardiogram (Hazard ratio: 5.134 confidence interval:

1.165-22.625). Patients with increased cardiothoracic index and pulmonary congestion had a 3.805 times higher risk of death than patients without pathological telecardiogram findings (Hazard ratio: 3.805 confidence interval: 1.014-14.284).

In our study myoglobin level was high in 35.8% of patients. We found that patients whose myoglobin levels were determined at normal limits had a longer survival time ( $p=0.004$ ). In our study CK-MB was found high in 35 patients (52.2%). Han-Ping Wu et al. compared CK-MB levels in the ECMO and non-ECMO group of patients. The mean value of CK-MB was 122.73 ng / ml in ECMO group and 32.68 ng / ml in non-ECMO patients (13). Troponin was found high in 27 patients (40.2%) in our study. Han-Ping Wu et al. noted that the mean value of troponin was 25.48 ng / ml in ECMO group and 4.88 ng / ml in non-ECMO group (13).

Echocardiography is more useful in the evaluation diagnosis of myocarditis and response to treatment (14). Echocardiogram allows assessment of chamber size, valvular regurgitation, ventricular function, ventricular hypertrophy, ventricular dilatation, shortening fraction, ejection fraction and the presence of pericardial fluid (15). In our study, the ejection fraction was found to be lowest 13%, highest 78%, and average 42.35 ( $\pm 14.173$ ). The mortality effect of the ejection fraction was examined by Cox regression analysis and no statistically significant difference was found ( $p = 0.053$ ). But we found that 1-unit reduction in the shortening fraction increases the mortality risk by 1.109-fold (Hazard ratio: 1,109, confidence interval: 1,007-1,222).

Treatment strategies include activity restriction, supportive medical heart failure therapies and advanced life support. Medical therapies are; diuretics, vasodilators, inotropes, ACE inhibitors, beta-blockers, aldosterone antagonists, intravenous immunoglobulin, etc. Patients with acute myocarditis presenting with clinical features of shock or progressive low cardiac output syndrome may need advanced life support such as ECMO or VAD (16). Regarding treatment strategies Klugman et al. noted that patients received 69.8% IVIG, 36.1% dopamine, 15.9% dobutamine and 57% milrinone in their study (4). In our study patients receive 79.1% diuretic, 73.1% ACE inhibitors, 56.7% dopamine and dobutamine, 62.6% digoxin and 13.4% milrinone. 28.3% patients received IVIG treatment due to viral etiology. VAD has been applied to two patients at the heart transplantation center and follow-ups are continuing at our center.

In our study 31 patients (46.2%) were completely recovered. There was developed dilate cardiomyopathy in 21 patients (31.3%).

Six patients were died in acute phase. 7 of 21 patients with dilate cardiomyopathy were died at follow-up period. The mortality rate is 19.4%. Seven patients were referred to an cardiac transplantation center for VAD, ECMO or cardiac transplantation.

## CONCLUSION

Myocarditis is an inflammatory disease of the myocardium. Diagnosis of myocarditis may be difficult to subtle clinical findings. The clinical picture may be varying from a mild subclinical period to congestive heart failure. The prognosis varies from recovery to complicated chronic disease and death. In our study, increased cardiothoracic index and pulmonary congestion findings in telecardiography, increased serum myoglobin level and decreased echocardiographic shortening fraction were factors associated with increased mortality. The using the short- and long-term cardiac support devices in patients with myocarditis may decrease mortality. In our country, heart transplantation remains a major problem. The awareness of people about organ donation is the most important step in the survival of patients with dilated cardiomyopathy due to myocarditis.

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