

Clinical Presentation, Complications and Early Predictors for Poor Outcomes in Pediatric Myocarditis in a Tertiary Care Hospital

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ABSTRACT

Objective: To evaluate common clinical presentation, complications and poor prognostic outcomes in children with acute myocarditis.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Pediatric Cardiology Department, National Institute of Cardiovascular Disease Karachi Pakistan, from Feb to Aug 2020.

Methodology: The children aged one month to 16 years were included in the study. Clinical, demographic features, Electrocardiogram, Echocardiography, management, complications, and immediate outcomes were recorded.

Results: The total number of patients enrolled was 161. The median age was 5.01 ± 3.38 years for 66.4% of males and 33.5% females, mean Duration of symptoms was 8.35 ± 3.49 days. Upper respiratory tract infection was present in 84 (52.2%) and diarrhea in 8 (5%) in the preceding illness. Symptoms and signs include loss of appetite in 153 (96.27%), irritability in 148 (91.9%), vomiting in 132 (82%) and abdominal pain in 112 (69.6%), tachycardia in 148 (91.9%) and pallor in 143 (88.8%). Low voltage ECG was present in 125 (77.6%), arrhythmias in 12 (7.45%) and heart block in 6 (3.7%). Left ventricle end-diastolic dimensions (LVIDD) $>4SD$ were present in 30.2% and LV end-systolic dimensions (LVIDS) $>4SD$ in 19.5%, Left ventricular ejection fraction (LVEF) mean was 21.13 ± 5.07 vs 23.45 ± 3.31 at discharge. 9.21% of patients expired, out of which 78.5% had Left bundle branch block (LBBB), mean LVEF was 16.24 ± 3.16 , LVID d $>4SD$ in 78%, and LVIDs $>4SD$ in 30%.

Conclusion: The most frequent presentations were loss of appetite, difficulty breathing, irritability and abdominal pain. Tachycardia and pallor were the commonest clinical signs. LBBB pattern, LVID d and LVIDs $>4SD$, and LVEF $<20\%$ carries poor prognosis.

Keywords: ECG in myocarditis, ECHO in myocarditis, LBBB, LV dimensions in myocarditis, Outcomes in myocarditis, Poor prognostic markers.

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INTRODUCTION

Myocarditis is an inflammatory disease of the myocardium, defined pathologically as a process characterized by inflammatory infiltration of the myocardium with necrosis and/or degeneration of adjacent myocytes not typical of the ischemic damage associated with coronary artery disease. Myocarditis accounts for approximately 9-50% of all cases of dilated cardiomyopathy in pediatric patients.¹ It is the result of both myocardial infection and autoimmunity that results in active inflammatory destruction of cardiac myocytes. Viruses are the predominant cause of myocarditis.² The true incidence is difficult to calculate because many have mild symptoms and go unnoticed, while those with severe forms die before the definitive diagnosis is made, but roughly, the incidence in some

reports is 1.95 per 100,000.³

Manifestations of myocarditis range from asymptomatic or non-specific generalized illness to acute cardiogenic shock and sudden death. In a study, respiratory symptoms were present in 61.3% of the patients. Therefore, they were wrongly labelled as having sepsis/pneumonia/asthma.⁴ Alternatively, nausea and vomiting may be the primary symptom of myocarditis, so they can be misdiagnosed as gastroenteritis. Abdominal pain in myocarditis can be so severe that it can be misdiagnosed as acute abdomen. Patients even have undergone exploratory laparotomies for it.⁵ Morbidity and mortality of myocarditis in the paediatric population remain high.

Non-specific laboratory findings are present in myocarditis. Cardiac biomarkers have low sensitivity. Viral serology, Cardiac MRI, and endomyocardial biopsy are very helpful in making the definitive diagnosis of myocarditis. However, unfortunately, these

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investigations are not readily available in most of the centres in Pakistan. So, diagnosis is dependent on the clinical index of suspicion, ECG, Chest X-ray and echocardiography findings.

The treatment options for myocarditis are mainly supportive. Many children make a complete recovery from myocarditis. Children with lower ejection fraction at presentation have a poor outcome.⁶

This study aimed to find out clinical indicators of poor outcomes and to look for common clinical presentations, ECG and ECHO findings in children with myocarditis in our population, which can help in early diagnosis and initiation of supportive treatment so that mortality and morbidity can be minimized.

METHODOLOGY

This prospective longitudinal study was conducted at the Paediatric cardiology department of the National Institute of Cardiovascular Disease Karachi from Febuary 2020 to August 2020 (6 months). This study included one hundred sixty-one children.

Inclusion Criteria: Children of age range 1 month to 16 years, admitted with the diagnosis of acute myocarditis were included the study.

Exclusion Criteria: Patients with obstructive and regurgitant causes of Left ventricular dysfunction and other causes of Left ventricular dysfunction like non-compaction Myocardium, Endocardial fibroelastosis and ALCAPA were excluded.

Formal permission was taken from the Institutional Ethical Review Committee (ERC-08/2020). Written informed consent was also taken from parents or legal caretakers.

A minimum required sample size of 151 patients was calculated using WHO sample size calculator version 2.0 by taking a 95% confidence level, 5% margin of error and taking the percentage of mortality rate among children presented with acute myocarditis at 11%, as reported in a study conducted by Haider *et al.*⁷

The diagnosis of acute myocarditis was suspected clinically by a history of short illness of Duration 1-21 days, fever, acute upper respiratory infection, respiratory distress, oedema, diarrhoea, sweating, cough, palpitation, fatigue, irritability, loss of appetite, vomiting and abdominal pain and confirmed on reduced LVEF in Echocardiography.

All patients were subjected to entire history taking to identify the symptoms of myocarditis. First, the history of preceding illness, fever, diarrhoea, or other viral infection was obtained. This was followed

by a complete physical examination and 12 lead electrocardiogram (ECG). 12 lead ECG was done at the 10 mm=1 mV voltage standard and 25 mm/sec paper speed. Abnormal ECGs consistent with myocarditis were labelled if: axis deviation, low voltage QRS, ST or T wave abnormalities, LBBB, ventricular hypertrophy, heart block or arrhythmias were present. Finally, a chest x-ray was done to look for cardiomegaly and signs of pulmonary oedema.

All patients had a detailed ECHO study by an independent operator to analyze at the time of admission, at discharge, or in between if required. Echocardiographic findings consistent with myocarditis included reduced ejection fractions without any structural lesion. Other parameters obtained include ventricular endsystolic or enddiastolic dimensions, standardized for age, & secondary atrioventricular valve regurgitation.

Findings of the 2-D Echo, along with other information like name, age, gender, weight, signs and symptoms, ECG, and Chest X-ray, were recorded in a pre-designed proforma by a designated Paediatric cardiology fellow.

The data was entered and analyzed using Statistical Package for the Social Sciences (SPSS version 24). Qualitative variables like gender, signs and symptoms were measured in percentages and frequencies. Mean and standard deviations were calculated for data like weight, Duration of symptoms and mean Duration of hospitalization.

Post-stratification of data, the chi-square test was used. ECG and echocardiography findings at the time of presentation and discharge were compared by performing a Chi-square test for categorical response variables and a t-test for continuous response variables. The p -value ≤ 0.05 was regarded as statistically significant.

RESULTS

The total number of patients admitted with a diagnosis of myocarditis was 161. The demographic and clinical features of the study group were mentioned in Table-I and Table-II, respectively.

Table-I: Demographic features of the patients.

Characteristics	Values
Number of Patients	161
Gender	
Male	107 (66.4%)
Female	54 (33.5%)
Age (Years)	5.01 ± 3.38
≤5 Years	88 (54.7%)
>5 Years	73 (45.3%)
Weight (kg)	13.21 ± 6.59

The mean age of patients was 5.01 ± 3.38 years. There was male predominance with 107 (66.4%) males and 54 (33.5%) females. Preceding illnesses include upper respiratory tract infection in 84 (52.2%) and diarrhoea in 8 (5%) patients. Among clinical features, shortness of breath was present in 153 (95%), irritability in 148 (91.9%), cough in 133 (82.6%), lethargy in 131 (81.4%) and fever was present in 106 (65.8%). In gastrointestinal symptoms, anorexia was present in 155 (96.27%), vomiting in 132(82.0%), and abdominal pain in 112 (69.6%). General physical examination revealed that tachycardia was present in 148 (91.9%), pallor in 143 (88.8%), hepatomegaly in 36 (22.4%), and raised JVP in 34 (21.1%) and oedema in 32 (19.9%) at the time of presentation.

Table-II: Clinical presentation of the patients.

Characteristics	Values
Duration of symptoms (days)	8.35 \pm 3.49
Mean duration of hospitalization (days)	24.47 \pm 6.94
Number of patients	161
Loss of appetite	155 (96.27%)
Shortness of breath	153 (95%)
Irritability	148 (91.9%)
Fatigue	131 (81.4%)
Vomiting	132 (82%)
Cough	133 (82.6%)
Palpitation	124 (77%)
Abdominal pain	112 (69.6%)
Fever	106 (65.8%)
Edema	32 (19.9%)
Sweating	32 (19.9%)
Cerebrovascular accident (CVA)	4 (2.5%)
Preceding Illness	
Respiratory infection	84 (52.2%)
Common cold	52 (32.3%)
Diarrhea	8 (5%)
Signs	
Tachycardia	148 (91.9%)
Pallor	143 (88.8%)
Gallop	146 (90.7%)
Basal crepitations	131 (81.3%)
Edema	32 (19.9%)
Liver (cm)	2.37 \pm 0.74
2	125 (77.6%)
>2	36 (22.4%)
JVP raised	34 (21.1%)
Pulmonary Edema	42 (26.1%)
Systolic Blood Pressure (mmHg)	94.15 \pm 9.25
Diastolic Blood Pressure (mmHg)	57.73 \pm 5.09
Chest-ray	
Increased Cardiothoracic ratio (cm)	74 (46%)
Large Left Atrium (eyeball)	2 (1.2%)
Signs of Pulmonary Edema	132 (82%)
Upper Lobe Shunting	129 (97.7%)
Fluid in Fissure	34 (25.8%)
Bat wing Appearance	7 (5.3%)
Pleural Effusion	2 (1.5%)

On auscultation, gallop rhythm was found in 146 (90.7%) and basal crepitations in 131 (81.3%). Mean systolic and diastolic blood pressures were 94.15 ± 9.25 mmHg and 57.73 ± 5.09 mmHg, respectively.

In Chest X-ray, cardiomegaly was seen in 74 (46.0%). In addition, signs of pulmonary oedema on chest x-ray were present in 132 (82.0%) patients, which include upper lobe shunting in 97.7% (129/132), fluid in fissures in 25.8% (34/132), bat wing appearance in 5.3% (7/132), and pleural effusion in 1.5% (2/132).

All patients were given inotropes, i.e., Dopamine and Dobutamine infusion, Angiotensin-converting enzyme inhibitors and diuretics. In 8.7% (14), Digoxin was given, and antiarrhythmic drugs in 7.45% (12). Anticoagulation was required in 55.9% (90) of patients.

The mean duration of hospitalization was 24.47 ± 6.94 days. 147 (91.3%) of children improved with no complications, while 14 (8.7%) patients expired, as mentioned in Table-IV.

The ECG and ECHO findings of the included patients were summarized in Table-III. A normal ECG axis was present in 131 (81.3%) patients and LVH in 49 (30.4%). Low voltages were found in 125 (77.6%) vs 12 (8.1%) on discharge ECG with p -value of <0.001 , LBBB in 11 (6.8%). Arrhythmias were seen in 12 (7.45%), mostly had atrial tachycardia 6 (3.7%), decreased to 1 (0.62%) with a p -value of 0.056 on discharge. Atrial fibrillation was present in 1 (0.62%) and persisted. SVT was present in 5 (3.1%), non-seen on discharge with a p -value of 0.024. Ventricular Tachycardia (VT) was present in 3/12 (25%) as a terminal event. Varying types of heart block in 6(3.7%), which includes Mobitz Type II in 3/6(50%), Complete Heart block in 2/6 (33.3%), and Sick sinus syndrome in 1/6 (16.6%).

Out of 14 patients who expired, 11/14 (78.5%) had LBBB, 6/14 (42.8%) had low voltage ECG, and 1/14 (7.14%) had atrial fibrillation, while ventricular tachycardia being the terminal event in 3/14 (21.4%).

In ECHO assessment, we found mean LVIDd 39.86 ± 9.36 vs 38.52 ± 6.71 with p -value <0.001 , LVIDs 30.07 ± 8.43 vs 28.63 ± 6.21 with p -value <0.001 , LVEF 21.04 ± 5.1 vs 23.54 ± 3.22 with p -value of <0.001 on discharge. LVIDD $>4SD$ was present in 49 (30.4%) and LVIDS $>4SD$ in 32 (19.8%) of patients. Moderate tricuspid regurgitation (TR) was present in 13% (21) on presentation while severe TR in 6.8% (11) and non on discharge with a p -value <0.001 . Moderate to severe mitral regurgitation (MR) was present in 15(9.3%) on

presentation, while nil in subsequent echo *p*-value <0.001. Smoke was seen in LV in 72 (44.7%) patients and 4 (2.7%) in echo on discharge *p*-value 0.473.

Thrombus was seen in 18 (11%) and 1 (0.7%) on subsequent echo. On presentation, pulmonary artery pressures were 27.6 ± 8.51 and on discharge, 20 ± 8.8, *p*-

Table-III: Electrocardiography (ECG) and echocardiography (ECHO) findings.

Characteristics	At the time of admission	At the time of discharge	<i>p</i> -value
Number of patients	161	147	-
ECG			
LVH (SV1 + RV6)	49 (30.4%)	43 (29.3%)	0.821
RVH (Rv1 + SV6)	7 (4.3%)	6 (3.7%)	0.777
T wave inverted (V4 - V6)	15 (9.3%)	14 (9.5%)	0.95
Low voltage	125 (77.6%)	12 (8.1%)	<0.001*
LBBB#	11 (6.8%)	-	
Axis (left)	30 (18.6%)	30 (18.6%)	>0.99
Arrhythmia	12 (7.45%)	5 (3.10%)	0.069
Atrial tachycardia	6 (3.7%)	4 (2.70 %)	0.599
Atrial fibrillation	1 (0.62%)	1 (0.62%)	>0.99
Supraventricular tachycardia (SVT)	5 (3.10%)	0	0.024*
Heart block	6 (3.7%)	6 (4.0%)	0.96
Mobitz Type 2	3 (n=6) 50%	3 (n=6) 50%	>0.99
Complete Heart block	2 (n=6) 33.3 %	2 (n=6) 33.3 %	>0.99
Sick sinus syndrome	1 (n=6) 16.6%	1 (n=6) 16.6%	>0.99
ECHO			
LVIDd	39.86 ± 9.36	38.52 ± 6.71	<0.001*
LVIDs	30.07 ± 8.43	28.63 ± 6.21	<0.001*
EF (%)	21.04 ± 5.1	23.54 ± 3.22	<0.001*
LVIDd (Z score >4)	49 (30.4%)	47 (28.8%)	0.59
LVIDs (Z score >4)	32 (19.8%)	31 (18.2%)	0.95
Tricuspid Regurgitation (TR)			
Mild	127 (78.9%)	119 (81%)	<0.001*
Moderate	21 (13%)	14 (9.5%)	
Moderate to severe	2 (1.2%)	14 (9.5%)	
Severe	11 (6.8%)	0 (0%)	
Mitral Regurgitation (MR)			
Mild	100 (62.1%)	96 (65.3%)	<0.001*
Moderate	46 (28.6%)	51 (34.7%)	
Moderate to severe	15 (9.3%)	0 (0%)	
Severe	0 (0%)	0 (0%)	
Clot			
Smoke	72 (44.7%)	4 (2.7%)	0.473
Thrombus	18 (11%)	1 (0.7%)	<0.001*
PA pressure	27.6 ± 8.51	20 ± 8.8	<0.001*

Table-IV: Outcomes and poor prognostic parameters.

Outcomes	Total number of patients discharged	Number of patients expired	<i>p</i> -value
	91.3% (147)	8.7% (14)	
Comparison of various parameters in expired vs total number of patients			
	Findings in total patients n=161	Findings in expired patients n=14	
ECG			
Low voltage	125 (77.6%)	6 (42.8%)	<0.004*
LBBB	11 (6.8%)	11 (78.5%)	<0.001*
Atrial fibrillation	1 (0.6%)	1 (7.1%)	0.028*
ECHO			
LVIDd (Mean)	39.86 ± 9.36	44.54 ± 10.33	0.077
LVIDs (Mean)	30.07 ± 8.43	34.61 ± 9.53	<0.001*
LVEF (Mean)	21.04 ± 5.1	16.24 ± 3.16	<0.001*
LVIDd >4 SD	49 (30.4%)	12 (85.7 %)	<0.001*
LVIDs >4 SD	32 (19.8%)	5 (35.7%)	0.164
LVEF ≤20%	66 (41%)	11 (78.6%)	<0.007*
Thrombus	11 (6.8%)	3 (21.4%)	0.05

value <0.001.

In patients who expired, the mean LVIDd was 44.54 ± 10.33 , vs LVIDd 39.74 ± 9.33 in all patients p -value 0.070, mean LVIDs was 34.61 ± 9.53 in expired compared to LVIDs 29.91 ± 8.39 in all patients, p -value 0.049, LVIDd >4SD was present in 12 (85.7%), LVIDs >4SD in 5/14 (35.7%), mean LVEF 16.24 ± 3.16 in expired vs LVEF 21.13 ± 5.07 in all patients with significant p value <0.001, and thrombus was seen in 3/14 (21.4%).

DISCUSSION

Myocarditis is a rare disease and is due to inflammation of the myocardium. A high index of suspicion is required for diagnosing myocarditis, as there are variable signs and symptoms, clinical examination findings and limited supporting investigations. Myocarditis has vast symptoms, ranging from a mild flu-like illness to heart failure and cardiogenic shock. Because of these variable clinical presentations, the diagnosis of pediatric myocarditis is especially challenging.⁸ Shortness of breath (69%), vomiting (48%), and poor feeding (40%) were described by Durani *et al.*, as the most frequently occurring symptoms.⁹ A study done in Taiwan illustrates gastrointestinal manifestations as frequently occurring symptoms associated with grave outcomes.¹⁰ In our study, the main clinical presentation was the loss of appetite 155 (96.27%) and irritability 148 (91.9%).

Abdominal pain was present in (69.6%) of patients, similar to a study demonstrated by Zhu *et al.*¹¹ The older children and adolescents with heart failure presented with abdominal symptoms compared to respiratory.¹² Our study's most common clinical examination finding was tachycardia 148 (91.9%) and pallor 143 (88.8%). In comparison, the least common was oedema 32 (19.9%), in contrast to a study in which tachycardia (57%) and tachypnea (52%) were the most common clinical sign.¹³ Gallop rhythm (20%) and hepatomegaly (20%) were less prevalent in this study. In our study, however, gallop rhythm was present in 146 (90.7%) and hepatomegaly in 36 (22.4%).¹³

Electrocardiograms in our study showed LVH in 49 (30.4%) and arrhythmias in 12 (7.45%), with which atrial tachycardia 6 (3.7%) and SVT 5 (3.1%) were most common. Low voltage ECG in 125 (77.6%), LBBB 6.8% (11), and heart block in 6 (3.7%). Different types of arrhythmias can occur in myocarditis at any stage of the disease.¹⁴ Scheffold *et al.*, mentioned in their study that the commonest bradyarrhythmias in myocarditis are sinus arrest, sinoatrial blocks, and atrioventricular

(AV) blocks,¹⁵ compared to our study in which Mobitz Type II was present in 3/6 (50%), complete Heart block in 2/6 (33.3%), and sick sinus syndrome in 1/6 (16.6%) respectively. In corresponding with studies done previously,¹⁶ decreased LV function was strongly correlated with poor outcomes. On ECHO assessment, LVIDD of >4SD was present in 49 (30.4%) whereas LVIDS >4SD in 32 (19.8%), LVEF mean was 21.04 ± 5.1 , as compared to 23.54 ± 3.22 at the time of discharge with p -value 0.001. This is comparable to the study done by Toma *et al.*, severely impaired LV ejection fraction of <30% was present in 33.33% of cases.¹⁷ According to this study, significant MR was found in only 33.33%, while in our study, mild MR was seen in 100 (62.1%) and moderate to severe MR in 15 (9.3%) patients.

Smoke (a risk factor for thrombus) in the LV cavity was present in 72 (44.7%) and thrombus in 18 (11%), which was reduced to 4 (2.7%) and 1 (0.7%) respectively at the time of discharge. 4 (2.5%) of patients presented with cerebrovascular stroke. Regarding the outcome, 147 (91.3%) of patients improved while 14 (8.6%) expired. A study performed in the United States showed 80.5% ICU admissions and even using the best possible resources like LVAD, ECMO, and cardiac transplantation, there was 7.2% mortality.¹⁸

All the patients who had LBBB in our study expired, indicating a high likelihood of mortality in this sub-group. 11/14 (78.5%) of patients who expired had LBBB pattern on ECG and VT being the terminal arrhythmia, present in 3/12 (25%). Aleksova *et al.* also mentioned that LBBB is an independent predictor of long-term mortality in patients with idiopathic dilated cardiomyopathy.¹⁹ Mean LVEF in the expiry group was 16.24 ± 3.16 as compared to 21.13 ± 5.07 in all study populations with a p value <0.001.

LIMITATIONS OF STUDY

The definitive diagnostic test, i.e. an Endomyocardial biopsy and Cardiac MRI, was not performed on our patients due to a shortage of resources.

CONCLUSION

Paediatric patients with acute myocarditis may present with loss of appetite, abdominal pain and irritability, so for such patients, prompt clinical examination is very important to rule out this grave disease. LBBB pattern, atrial fibrillation, LVIDd and LVIDs>4SD, and LVEF <20% carries poor prognosis. The mainstay of treatment is supportive care. Mortality, despite limitations, is not very different in developed countries.

Conflict of Interest: None.

Authors' Contribution

AK: Conception and design of work, drafting the article, AK: Data collection, NR: Data analysis, VK: Literature review, ASS: Interpretation of data, NP: Revised it critically.

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