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Original Article

The Clinical Outcomes of Acute Myocarditis in Pediatric Population: A Prospective Study

Zia Ur Rehman[1], Ijaz Hussain[2], Murad Ali[3], Aiman Maria Aziz[4], Zia ul Islam[5], Ijaz Hussain[6]*

[1]MMC Teaching Hospital, Peshawar.
[2]PIC, Peshawar.
[3]Mardan Medical Complex, Mardan.
[4]Northwest General Hospital, Peshawar.
[5]AWKUM, Mardan.
[6]Lady Reading Hospital, Peshawar.
*Corresponding Author: Ijaz Hussain, Professor and Incharge Pediatric Cardiology; Email: ijazpaeds@yahoo.com

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ABSTRACT

Background: Myocarditis, a serious complication of acute viral infections, is a significant concern in pediatric healthcare. Often underdiagnosed due to its subtle symptoms like cough and easy fatigability, myocarditis can lead to severe cardiac complications.

Objectives: The primary objective of this study was to examine the outcomes of acute myocarditis in children who received early diagnosis and management. The study focused on identifying factors influencing these outcomes, rather than comparing different treatment methods.

Methods: This prospective study involved 118 pediatric patients (age < 16 years) admitted with acute myocarditis to the Pediatric Cardiology Ward at Lady Reading Hospital. Data were collected using a specialized proforma with informed consent. Comprehensive monitoring included echocardiography for assessing left ventricular function, ECG for arrhythmia detection, and cardiac enzyme levels. Patients were treated with a standard management plan, including immunosuppressive therapy, diuretics, and inotropic support. Follow-up was conducted for an average of six months.

Results: The age distribution was as follows: 70 patients in Group-A (below 4 years), 35 in Group-B (5-10 years), and 13 in Group-C (10-16 years). The gender ratio was 53 males to 65 females. Ejection fractions were: 15-20% in 40 patients, 20-25% in 44 patients, and 26-35% in 34 patients. Left Ventricular End-Diastolic Diameter (LVEDD) showed 49 patients in Grade 1, 45 in Grade 2, and 24 in Grade 3. Improvements were observed in 37 patients (31.3%) with normal ventricular functions, 32 (27.1%) with mild dysfunction, and 29 (24.5%) with moderate dysfunction. 20 patients (16.9%) showed no improvement, and complications included LV clot (11%), stroke (2.5%), arrhythmias (1.7%), and mortality (5.9%).

Conclusion: Timely diagnosis and appropriate management are crucial for improving outcomes in children with acute myocarditis. Delayed management can lead to severe complications including dilated cardiomyopathy, cardiac thrombi, stroke, arrhythmias, and mortality.

Keywords: Myocarditis, Pediatric Cardiology, Echocardiography, Cardiac Enzymes, Acute Viral Infections, Treatment Outcomes.

INTRODUCTION

Myocarditis, an inflammation of the heart muscle, is a significant concern in children's health. This condition often results from a viral infection, leading to an immune response that causes harm to the heart (1). Symptoms can be severe, ranging from shock and irregular heartbeats to life-threatening cardiac arrest. In Pakistan, myocarditis is not uncommon among children. An alarming 55% of children diagnosed with myocarditis had this confirmed through autopsy (2).

While many children recover from acute myocarditis with appropriate treatment, some face long-term complications. Studies indicate that around 9% of these children might develop dilated cardiomyopathy, a condition that weakens and enlarges the heart, during a year or more of follow-up (3). Therefore, timely and effective treatment of acute myocarditis is vital.

The current treatment approach focuses on supporting the heart's function. Medications like inotrops, specifically Dobutamine ± Dopamine, are used for children with severe myocarditis (3). In extreme cases, mechanical support may be necessary. Additionally,

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recent studies have been exploring immune-modifying treatments. One such treatment is pulse steroid therapy, followed by a 4-6 week course of oral prednisolone, which some studies recommend (4,5,6,7). However, the effectiveness of steroid therapy on reducing the illness's impact or preventing death is still debated, as some studies show no significant benefits (8,9,10).

Another treatment under investigation is the use of immunoglobulins, which are meant to modulate the immune system. Despite their potential, a recent trial suggested that they might not improve outcomes in acute viral myocarditis (11). Our study aims to demonstrate the importance of early and accurate diagnosis of acute viral myocarditis. We will explore how combining supportive care with immunosuppressive therapy can positively influence the disease's prognosis and clinical outcomes.

MATERIAL AND METHODS

In this study, 118 children under the age of 16 were included. They were admitted to the Pediatric Cardiology Ward of Lady Reading Hospital for acute myocarditis treatment. Each child's history was meticulously recorded, with consent obtained from their guardians, focusing on any upper or lower respiratory tract infections as a possible precursor to myocarditis. The children typically stayed in the hospital for about 13 days, though this varied between 2 and 28 days.

For monitoring, each child underwent thorough assessments including regular checks of vital signs like temperature, blood pressure, respiratory rate, heart rate, and oxygen saturation. Standard laboratory tests such as complete blood count (CBC), renal function tests (RFTs), liver function tests (LFTs), serum electrolytes, electrocardiograms (ECG), and chest X-rays were performed for all. Echocardiography was also conducted in each case to evaluate left ventricular function, including ejection fraction and fractional shortening. It also assessed for structural heart defects (like aortic stenosis, coarctation of the aorta, and coronary artery anomalies) and the presence of clots in cardiac chambers. Right ventricular function was evaluated using the Tricuspid Annular Plane Systolic Excursion (TAPSE) method, while special attention was given to identifying mitral regurgitation, vegetations, and pericardial effusion.

Regarding treatment, all patients received a regimen of immunosuppressive therapy, diuretics, and inotropic support. In the hospital, 91.5% received Dobutamine, and 8.5% were treated with a combination of Dopamine and Dobutamine. Furosemide, potassium-sparing diuretics like Aldactone, ACE inhibitors like Captopril, and antiplatelets were administered to all patients. Corticosteroids were used as immuno-modulators for all, with an additional 7.6% receiving intravenous immunoglobulins combined with corticosteroids. Anticoagulants (Clexane and Warfarin) were given to 7.6% of the patients, Digoxin to 6.7%, and Adenosine to 1.7%. Post-discharge, home medication included Furosemide, Aldactone, Captopril, antiplatelets, and oral corticosteroids for all patients. Additionally, 15.2% were prescribed a beta-blocker (Carvedilol), and 6.7% continued with Digoxin.

The primary outcomes measured in this study were survival, improvement in left ventricular function, and the incidence of complications such as cardiomyopathy, clot formation, stroke, and arrhythmias. Statistical analysis involved presenting data as mean values with standard deviations, medians with ranges, and frequency distributions. Echocardiography findings were calculated relative to age and body surface area and expressed as Z-scores compared to a standard population. The mean Z-score was evaluated against a null hypothesis of population mean using a t-test. The Fisher Test was applied to assess correlations, calculating odds ratios (OR) at a 95% confidence interval. A probability (p) value of less than 0.05 was considered statistically significant.

RESULTS

The study involved a detailed analysis of 118 pediatric patients suffering from acute myocarditis, with the age distribution segmented into three groups: Group-A (below 4 years) included 70 patients, Group-B (5-10 years) comprised 35 patients, and Group-C (10-16 years) had 13 patients. The gender split showed 53 male and 65 female patients. The timing of their presentation to the hospital was also noted, with 57 presenting within 14 days of symptom onset and 61 presenting after 14 days.

In terms of cardiac function, the ejection fraction varied across the cohort: 40 patients had an ejection fraction between 15-20%, 44 patients between 20-25%, and 34 patients between 26-35%. When examining the Left Ventricular End-Diastolic Diameter (LVEDD), 49 patients were classified as Grade 1 ($1.6 \geq Z \leq 2.0$), 45 as Grade 2 ($2.1 \leq Z \leq 2.6$), and 24 as Grade 3 ($Z > 2.6$). The Left Ventricular Posterior Wall Thickness (LVPWT) measurements were 4-7 mm in 64 patients, 7.1-9 mm in 40 patients, and above 9.1 mm in 14 patients.

Electrocardiography (ECG) abnormalities were observed in 20 patients, with 12 showing low voltage QRS complexes, 6 with a Q wave in leads I, II, AVF, and 2 with Supraventricular Tachycardia (SVT). Regarding cardiac enzyme levels, 54 patients showed raised Troponin I, 19 had raised Creatinine Kinase-MB (CK-MB), 18 had both Troponin I and CK-MB raised, and 27 had normal levels of both enzymes.

The final outcomes of these patients with acute myocarditis were varied: 37 patients (31.3%) improved with normal ventricular functions, 32 patients (27.1%) improved with mild dysfunction remaining, and 29 patients (24.5%) improved with moderate dysfunction remaining. However, 20 patients (16.9%) showed no improvement. There were 13 cases (11%) of left ventricular (LV) clots, 3 cases (2.5%) of stroke, 2 cases (1.7%) of arrhythmias (SVT), and 7 deaths (5.9%). None of the patients were lost to follow-up.

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Further analysis revealed a significant correlation between the time of presentation and patient improvement. Of the 57 patients presenting within 14 days, 24 (42%) showed improvement, with an odds ratio of 5.50 (95% CI: 2.14-14.1) and a p-value of 0.0003. Among the 61 patients presenting after 14 days, only 13 (21%) showed improvement.

Table 1 Patient Data at Presentation

Variables	Number of Patients
Age Range in Years	
Group-A (below 4 yr)	70
Group-B (5-10 yr)	35
Group-C (10-16 yr)	13
Sex	
Male patients	53
Female patients	65
Time of Presentation	
Within 14 days of symptoms	57
After 14 days of symptoms	61
Ejection Fraction	
15-20%	40
20-25%	44
26-35%	34
LVED Dimension	
Grade 1 (1.6 ≥ Z ≤ 2.0)	49
Grade 2 (2.1≤ Z ≤ 2.6)	45
Grade 3 (Z > 2.6)	24
LVPWT mm	
4-7	64
7.1-9	40
9.1 and above	14
ECG Abnormalities	
Low voltage QRS complexes	12
Q wave in I, II, AVF	6
SVT	2
Cardiac Enzyme Level Raised	
Troponin I raised	54
CK-MB raised	19
Both Troponin I and CK-MB raised	18
Both Troponin I and CK-MB normal	27
LVEDD: Left Ventricular End-Diastolic Diameter LVPWT: Left Ventricular Posterior Wall Thickness ECG: Electrocardiography SVT: Supraventricular Tachycardia CK-MB: Creatinine Kinase-MB	

Table 2 Final Outcomes of All Patients with Acute Myocarditis

Outcome	Number of Patients	Percentage
Improved with normal ventricular functions	37	31.3%
Improved with mild dysfunction remaining	32	27.1%
Improved with moderate dysfunction remaining	29	24.5%

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Outcome	Number of Patients	Percentage
No Improvement	20	16.9%
LV clot	13	11%
Stroke	3	2.5%
Arrhythmias (SVT)	2	1.7%
Expired	7	5.9%
Lost to follow up	0	0%

Table 3 Correlation between Time of Presentation and Improvement

Presentation Time	Number of Patients	Number Improved (%)	Odd Ratio with 95% CI	P-value
Within 14 days	57	24 (42%)	5.50 (2.14-14.1)	0.0003
After 14 days	61	13 (21%)	-	-

Table 4 Correlation Between LVEDD and Improvement

LVEDD Grade	Number of Patients	Improved with Normal EF (%)	Not Improved (%)
Grade 1	49	20 (40.8%)	29 (59.1%)
Grade 2	45	13 (28.8%)	32 (71.2%)
Grade 3	24	4 (16.6%)	20 (83.3%)
LV: Left Ventricular SVT: Supraventricular Tachycardia LVEDD: Left Ventricular End-Diastolic Diameter EF: Ejection Fraction			

The correlation between LVEDD and improvement indicated that among the 49 patients with Grade 1 LVEDD, 20 (40.8%) improved with normal ejection fraction (EF), but 29 (59.1%) did not improve. In Grade 2 (45 patients), 13 (28.8%) improved, whereas 32 (71.2%) did not. Grade 3 had the lowest improvement rate, with only 4 out of 24 patients (16.6%) showing improvement and 20 (83.3%) not improving.

DISCUSSION

Myocarditis, a serious health concern particularly in pediatric cases, is often a consequence of acute viral infections and poses a substantial risk, sometimes leading to life-threatening complications as identified in pediatric medical literature (1). This study aimed to shed light on the outcomes of pediatric patients diagnosed with acute myocarditis, specifically focusing on the benefits of early diagnosis and standardized treatment. It's important to note that the study did not aim to compare different treatment methods, as all children involved were treated according to the same protocol. Rather, the study was oriented towards understanding various factors that could potentially influence patient outcomes.

The research involved a cohort of 118 children, all under the age of 16, who were admitted to the Pediatric Cardiology Ward at Lady Reading Hospital diagnosed with acute myocarditis. These patients were followed over an average period of six months. Data collection was meticulous, utilizing a specialized proforma and ensuring that informed consent was duly obtained from the patients' guardians. The diagnostic approach was comprehensive, encompassing various parameters to precisely assess the outcomes of acute myocardial infection and to formulate an effective management plan. Echocardiographic parameters, such as the dimensions of the left ventricle in both systole and diastole, left ventricular ejection fraction, and fractional shortening, were measured. The study also delved into the quantification of mitral regurgitation and the assessment of pulmonary artery hypertension. The left ventricular function was evaluated using Z-score grading, based on standard pediatric population parameters. This included detailed assessments of end-diastolic and end-systolic left ventricle dimensions, posterior wall thickness, and septal thickness. The study also focused on right ventricular functions assessed via the TAPSE method and sought to identify any structural heart anomalies, such as LVOT obstruction, Coarctation of the aorta, or coronary anomalies. Special attention was given to the detection and immediate management of clots in any cardiac chamber. Mean-end diastolic diameter of the left ventricle was categorized into three grades based on the Z-score (16). The measurement of Fractional Shortening, a crucial parameter, was taken into account as the percentage shortening of the left ventricular diameter between end-diastole and end-systole (13).

The primary outcome was gauged based on the improvement in the left ventricle's ejection fraction. The study classified the grades of left ventricular dysfunction from normal to severe, providing a comprehensive view of the range of heart function in the patients (13). An important aspect of the study was the role of Electrocardiography (ECG) in determining the severity of the disease. Arrhythmia was observed as a significant indicator of the disease's severity and was used to predict the prognosis in pediatric cases (14). The ECG was particularly useful in identifying arrhythmias like Supraventricular Tachycardia or Ventricular Tachycardia that may have contributed to LV dysfunction. Specific ECG changes, including deep Q waves and variations in the ST segment in left antero-lateral leads, were focused upon. Additionally, the measurement of QRS amplitude was instrumental in diagnosing low amplitude myocarditis.

The study also examined the correlation between steroid therapy and patient outcomes. Viral myocarditis, as the literature suggests, results not only from direct viral insult but also from activated host immunity causing cardiac damage (15). Hence, immunosuppressive drugs, including steroids, were hypothesized to play a significant role in suppressing adverse outcomes due to immunological insult. Some studies have indicated that steroids and other immune modulating treatments positively impact the improvement in left ventricular functions, thereby decreasing morbidity and mortality in a significant percentage of the affected pediatric population (16,17). However, contrasting findings from recent meta-analytical reviews suggested no significant impact of immunomodulating therapy on the morbidity and mortality of children with acute myocarditis (9,10).

The study further delved into outcomes related to Intravenous Immunoglobulin (IVIG) treatment. IVIG was noted to improve left ventricular systolic functions and prevent deleterious outcomes of myocarditis in several studies (18,19,20,13). However, conflicting evidence, such as that reported by Yu et al., indicated no significant difference in outcomes between groups that did and did not receive IVIG treatment (21).

The role of Beta Blockers, specifically Carvedilol, in the context of acute myocarditis was not directly assessed in this study. Nevertheless, other research has pointed to the positive impact of beta blockers on children with myocarditis and decreased ventricular function (1,22). The underlying mechanisms remain unclear, but the antioxidant effects of these medications are proposed as a potential contributing factor to patient improvement.

In diagnosing and prognosticating acute myocarditis, cardiac troponins and CK-MB played a pivotal role, demonstrating sensitivity and specificity. Elevated levels of these enzymes were detected in about 33 percent of children with myocardial injury (9). However, it was also noted that normal enzyme levels do not necessarily rule out acute viral myocarditis (10). Further studies have highlighted that elevated cardiac Troponin levels, coupled with left ventricular systolic dysfunction, are independent markers of mortality in myocarditis patients (14).

A particular aspect of concern in acute myocarditis is the formation of intra-cardiac thrombi. The study found that clot formation in the ventricular and atrial chambers was quite common, especially in cases of extreme grades of ventricular enlargement. Other predisposing factors, such as prothrombotic hematological status, rheumatological problems, and certain medications, were also considered. The study underscored a strong relationship between the end-diastolic dimension at the time of presentation and the development of a clot in the left ventricle. It was observed that all nine children who developed a left ventricular clot had a grade 3 end-diastolic diameter and an ejection fraction of less than 20%.

However, the study was not without limitations. The diagnosis of myocarditis was primarily based on the typical clinical history of upper or lower respiratory tract infections (URTI or LRTI). Detailed histories of recent viral illnesses were obtained, categorizing patients as early presenters (within two weeks before admission) and late presenters (more than two weeks before presentation). Due to the lack of more definitive diagnostic tools like endomyocardial biopsy, which is invasive and carries risks, the study relied on history, clinical signs, echocardiography, ECG, and levels of cardiac enzymes. The study did not establish a relationship between the outcome of acute myocarditis and the thickness of the interventricular septum or left ventricular posterior wall.

CONCLUSION

In conclusion, the study emphasizes the critical importance of timely diagnosis and appropriate management in improving outcomes for children with acute myocarditis. Delayed or inadequate management can escalate the condition, leading to complications like dilated cardiomyopathy, thrombus formation in cardiac chambers, stroke, arrhythmias, and, in severe cases, the death of the child. This study, through its comprehensive analysis, contributes valuable insights into the management and prognosis of acute myocarditis in the pediatric population.

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