

ORIGINAL ARTICLE

Clinical Presentation of Myocarditis in Children Visiting Dr Ruth KM PFAU, Civil Hospital, Karachi. A Cross-Sectional Study

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ABSTRACT

Objective: To determine the frequency of various clinical presentations of myocarditis in children visiting to Dr Ruth KM PFAU, Civil Hospital Karachi.

Study design: Cross-Sectional Study.

Place and duration: Department of Pediatric Medicine, Dr Ruth K.M PFAU Civil Hospital, Karachi, Pakistan from September, 2020, to March, 2021

Methodology: The study covered all patients who visited Karachi's Civil Hospital and met the inclusion criteria. After describing the study's process, hazards, and benefits, informed consent was obtained. The initial ECG, echocardiography, and cardiac enzyme readings were all documented. Stroke, congenital heart disease, sepsis, asthma, pulmonary embolism, cardiomyopathy, gastroenteritis, diabetes mellitus, and renal failure were among the clinical presentations that were noted. The proforma that is supplied at the end was filled out with all the acquired data and used electronically for research.

Results: Age was 6.8 ± 2.1 years on average. A total of 238 (67.6%) of the 352 patients were male, and 114 (32.4%) were female. In patients with myocarditis who presented clinically, renal disease was found in 46 (13.1%), cardiomyopathy in 30, congenital heart disease in 56 (15.9%), stroke in 41 (11.5%), gastroenteritis in 65 (18.5%), diabetes mellitus in 19 (5.4%), sepsis in 32 (9.2%), and asthma in 48 (13.6%) patients, while pulmonary embolism was found in 15 (4.3%) patients.

Practical implication

There is growing evidence to support the use of tests such as cardiac magnetic resonance imaging and serum N-terminal B-type natriuretic peptide measurements as supplements to clinical diagnosis. These could eventually lessen the need for invasive procedures like endomyocardial biopsy, which is still the gold standard.

Conclusion: The most frequent clinical manifestation of myocarditis was gastroenteritis, which was followed by congenital heart disease and asthma. For the purpose of validating the results so far, additional extensive research is advised.

Keywords: Clinical Presentation, Myocarditis, Epidemiology, Asthma, Gastroenteritis

INTRODUCTION

In the absence of predominant acute or chronic ischemia, myocarditis is a non-familial form of inflammatory heart muscle disease that can affect both children and adults.^{1,2} Other infections, poisons, hypersensitivity reactions, and various autoimmune and systemic processes constitute additional etiologies, though they are far less frequent.³

Nearly half of all occurrences of dilated cardiomyopathy in children are caused by myocarditis, an uncommon, potentially fatal inflammatory condition of the heart.⁴⁻⁵ Due to clinical overlap with more prevalent conditions including gastroenteritis and asthma, myocarditis may be challenging to diagnose.⁶⁻⁸ Infant and child mortality rates from myocarditis may be as high as 75% and 25%, respectively,⁹ making early treatment initiation and fast identification essential [10].

The diagnosis might be difficult, especially in young children and newborns. Accurate assessments of the epidemiology and natural history of myocarditis have been limited by the lack of easily accessible sensitive and precise clinical diagnostic tests, substantial variance in diagnostic criteria, and selected patient populations among published research.¹

Depending on the level of myocardial inflammation and ventricular dysfunction, cardiac symptoms in myocarditis can vary and lack specificity, making the disease difficult to diagnose. ECG signs, such as all varieties of "idiopathic" atrial or ventricular tachyarrhythmias or bradyarrhythmias, P-Q segment depression, and/or repolarization abnormalities, are likewise neither specific nor sensitive for myocarditis.¹¹⁻¹² The established histological, immunological, and immunohistochemical results in cardiac tissue samples acquired during endomyocardial biopsy (EMB) provide the final diagnosis.¹³⁻¹⁴

There hasn't been a clear health and social policy to control myocarditis among the younger population despite the fact that Pakistan's population is largely young, like that of the majority of developing nations. Furthermore, our under-resourced health delivery system will be further taxed by the double burden of disease caused by the increasing trend of myocarditis, especially in developing nations.

Therefore, research on the prevalence of myocarditis and its clinical manifestation in children is necessary in order to put in place effective preventive measures. Therefore, the purpose of this study was to determine various clinical manifestations of myocarditis in young patients. Data generation could be used to focus efforts on their control, especially in resource-poor nations where treatment options might not be readily available. Additionally, the findings of this study will be disseminated to neighbourhood pediatricians and utilised to develop recommendations, on the standard of care we offer to these infants who already have myocarditis.

METHODOLOGY

This cross-sectional study was conducted at Dr Ruth K.M PFAU Civil Hospital, Karachi from September 2020, to March 2021. By using the WHO sample size calculator using the frequency of cardiomyopathy (2.4%) [1] in pediatric patients with myocarditis, Marginal of Error (d)=1.6%, Confidence Level (C.I) =95% then the estimated sample size came out to be 352 children. Children between the age group 1 month to 12 years of either gender who presented with myocarditis as per operational definition were included in this study. Those patients who were already diagnosed as having a cardiac problem on Echocardiography different from myocarditis were excluded from the study.

On the basis of symptoms, all of the included patients had a general and systemic examination as well as laboratory tests. After gaining informed written consent, the caregivers provided a thorough history. Every medical record was examined. The patient's demographic information, medical background, vital signs, outcomes of the physical examination, and findings of laboratory testing were noted. The initial ECG, echocardiography, and cardiac enzyme readings were all documented. The principal investigator collected the outcome variables, such as the patient's clinical presentation, which included stroke, congenital heart disease, sepsis, asthma, pulmonary embolism, cardiomyopathy, gastroenteritis, diabetes mellitus, and renal failure. By closely upholding the inclusion criteria, bias and confounding variables were managed.

Data about the patient were gathered and examined using SPSS 23.0, the statistical software for social sciences. Age and disease duration were determined using mean and SD. For gender, clinical presentation, such as stroke, congenital heart disease, sepsis, asthma, pulmonary embolism, cardiomyopathy, gastroenteritis, diabetes mellitus, and renal failure, frequency and percentages were calculated. To see how they affected the results, effect modifiers were managed by stratification of age, gender, and disease duration. Following stratification, the appropriate Chi-square or Fisher's Exact test was used, with two-sided P 0.05 being used as the threshold for statistical significance.

RESULTS

The mean ± SD of age was 6.8±2.1 with CI (6.57-7.02) years. The mean ± SD of the duration of the disease was 2.8±0.34 with CI (2.76-2.83) months. Out of 352 patients, 238 (67.6%) were male while 114 (32.4%) were female.

Table 1: Frequency of Clinical Presentation of Myocarditis n=352

CLINICAL PRESENTATION	FREQUENCY	PERCENTAGE
Renal Disease	46	13.1%
Cardiomyopathy	30	8.5%
Congenital Heart Disease	56	15.9%
Stroke	41	11.5%
Gastroenteritis	65	18.5%
Diabetes Mellitus	19	5.4%
Sepsis	32	9.2%
Asthma	48	13.6%
Pulmonary Embolism	15	4.3%

Table 2: Stratification of Age Group with Clinical Presentation of Myocarditis n=352

CLINICAL PRESENTATION	AGE (in Years)		P-VALUE
	0.1 - 6	>6	
Renal Disease	21 (6.0%)	25 (7.1%)	0.599
Cardiomyopathy	17 (4.8%)	13 (3.7%)	
Congenital Heart Disease	30 (8.5%)	26 (7.4%)	
Stroke	17 (4.8%)	24 (6.8%)	
Gastroenteritis	30 (8.5%)	35 (9.9%)	
Diabetes Mellitus	12 (3.4%)	7 (2.0%)	
Sepsis	20 (5.7%)	12 (3.4%)	
Asthma	24 (6.8%)	24 (6.8%)	
Pulmonary Embolism	9 (2.6%)	6 (1.7%)	

In the clinical presentation of myocarditis renal disease was noted in 46 (13.1%) patients, cardiomyopathy in 30 (8.5%), congenital heart disease in 56 (15.9%), stroke in 41 (11.5%), gastroenteritis in 65 (18.5%), diabetes mellitus in 19 (5.4%), sepsis in 32 (9.2%), asthma in 48 (13.6%) while 15 (4.3%) patients had pulmonary embolism as shown in TABLE 1. Stratification of age group, gender and duration of disease was done with respect to the clinical presentation of myocarditis in order to find a significant difference from TABLE 2-4.

Asthma was equally present in below and above the 6 years of age group, while congenital heart disease was most common 30 (8.5%) in less than 6 years age group. Asthma was most common in males 33 (9.4%) as compared to females 15 (4.3%) while the congenital heart disease was also common in males 43 (12.2%) as compared to females 13 (3.7%)

Table 3: Stratification of Gender with Clinical Presentation of Myocarditis n=352

CLINICAL PRESENTATION	GENDER		P-VALUE
	Male	Female	
Renal Disease	31 (8.8%)	15 (4.3%)	0.080
Cardiomyopathy	21 (6.0%)	9 (2.6%)	
Congenital Heart Disease	43 (12.2%)	13 (3.7%)	
Stroke	24 (6.8%)	17 (4.8%)	
Gastroenteritis	42 (11.9%)	23 (6.5%)	
Diabetes Mellitus	14 (4.0%)	5 (1.4%)	
Sepsis	25 (7.1%)	7 (2.0%)	
Asthma	33 (9.4%)	15 (4.3%)	
Pulmonary Embolism	9 (2.6%)	6 (1.7%)	

Table 4: Stratification for Duration of Disease with Clinical Presentation of Myocarditis n=352

CLINICAL PRESENTATION	DURATION (in Months)		P-VALUE
	0.5 - 3	>3	
Renal Disease	26 (8.2%)	17 (4.8%)	0.576
Cardiomyopathy	18 (5.1%)	12 (3.4%)	
Congenital Heart Disease	40 (11.4%)	16 (4.5%)	
Stroke	22 (6.2%)	19 (5.4%)	
Gastroenteritis	44 (12.5%)	21 (6.0%)	
Diabetes Mellitus	10 (2.8%)	9 (2.6%)	
Sepsis	21 (6.0%)	11 (3.1%)	
Asthma	30 (8.5%)	18 (5.1%)	
Pulmonary Embolism	7 (2.0%)	8 (2.3%)	

DISCUSSION

Because symptoms and clinical findings are typically ambiguous, diagnosing myocarditis in children is difficult [15]. Smaller children frequently exhibit respiratory or gastrointestinal symptoms, while infants frequently exhibit restlessness, poor feeding, or symptoms that resemble a severe bacterial infection [16]. Teenagers, on the other hand, may have chest pain, palpitations, and rhythm problems. Only 17% of cases of paediatric myocarditis were diagnosed upon initial presentation, according to Durani et al. [17].

The main reason why myocarditis is difficult to diagnose is that it lacks a pathognomonic clinical manifestation and can show a number of different non-inflammatory cardiac illnesses. As a result, the disease is described histologically as an inflammatory disease of the myocardium diagnosed on endomyocardial biopsy (EMB), based on histological, immunological,

immunohistochemical, and molecular findings the detection of the disease is done.

The average age in our study was 6.8 ±2.1 years. According to Arola A, et al.¹, the age was 10.6± 4.9 years. The mean illness duration in this study was 2.8 ±0.34 months. Out of 352 patients in the current study, 238 (67.6%) were male and 114 (32.4%) were female. In addition, Arola A, et al. reported 50 (23%) females and 163 (77%) males. According to Sarda L. et al.¹⁸, there were 16 (35.56%) females and 29 (64.44%) males. A total of 80.6% of the participants in another study conducted by Ammirati E, et al.¹⁹ were male, whereas 19.4% were female. A total of 18 (86%) male and 3 (14%) female patients were listed in Francone M, et al's study²⁰.

In the current study, renal disease was one of the most common clinical manifestations of myocarditis, occurring in 46 (13.1%) patients, cardiomyopathy in 30, congenital heart disease in 56 (15.9%), stroke in 41 (11.5%), gastroenteritis in 65 (18.5%), diabetes mellitus in 19 (5.4%), sepsis in 32 (9.2%), and asthma in 48 (13.6%) patients, while pulmonary embolism occurred in 15 (4.3%) patients. In the study by Arola A, et al.¹, 10 patients (4.7%) had renal disease, 05 (2.4%) had cardiomyopathy, 02 (0.9%) had congenital heart disease, 02 (0.9%) had strokes, 02 (0.9%) had gastroenteritis, 02 (0.9%) had diabetes mellitus, 01 (0.5%) had sepsis, 01 (0.5%) had asthma, and 01 (0.5%) had a pulmonary embolism.

In an international study, the most prevalent particular cardiac symptom was chest discomfort (40%) in 40% of cases. The most frequent non-cardiac first complaints were respiratory tract symptoms (cough, apnea, rhinorrhea) (38%), shortness of breath (35%), gastrointestinal tract symptoms (vomiting, abdominal discomfort, diarrhoea) (33%), and fever (31%). On the initial physical exam, tachycardia (57%) and tachypnea (52%) were the most prevalent symptoms, followed by nonspecific respiratory tract infection symptoms (44%) and respiratory distress symptoms (35%)²¹. In another study, congestive heart failure, refractory arrhythmia, and syncope were the three main cardiovascular symptoms at the time of commencement in 70, 37, and 17 patients, respectively.

Age group, gender, and disease duration were not significantly different in this study's stratification of confounders and impact modifiers with regard to the clinical presentation of myocarditis (P=0.593, 0.080, and 0.576, respectively) [22]. In a local study, there were 161 patients enrolled in all. The median age for 66.4% of males and 33.5% of females was 5.01± 3.38 years. The average length of symptoms was 8.35± 3.49 days. Infection in the upper respiratory tract was detected in 84 (52.2%) and 8 (5%) participants with had diarrhoea. A total of 153 (96.27%) participants reported losing their appetite, while 148 participants reported being irritable. Tachycardia was present in 148 (91.9%), vomiting in 132 (82%) and abdominal pain in 112 (69.6%), as well as pallor in 143 (88.8%)²³.

CONCLUSION

The most frequent clinical manifestation of myocarditis was discovered to be gastroenteritis, which was followed by congenital heart disease and asthma. For the purpose of validating the results so far, additional extensive research is advised. The results of the current study need to be validated by more research, which should be conducted in different study locations throughout Pakistan with a larger sample size and more criteria.

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Conflict of interest: None

REFERENCES

- Arola A, Pikkariainen E, Sipilä JO, Pykärä J, Rautava P, Kytö V. Occurrence and features of childhood myocarditis: a nationwide study in Finland. *J Am Heart Assoc.* 2017; 18; 6(11): 1-7.
- Merlo M, Cannata A, Gobbo M, Stolfo D, Elliott PM, Sinagra G. Evolving concepts in dilated cardiomyopathy. *European journal of heart failure.* 2018 Feb; 20(2):228-39.
- Rroku A, Kottwitz J, Heidecker B. Update on myocarditis—what we know so far and where we may be heading. *European Heart Journal Acute Cardiovascular Care.* 2021 Apr; 10(4):455-67.
- Bejiqi R, Retkoceri R, Maloku A, Mustafa A, Bejiqi H, Bejiqi R. The diagnostic and clinical approach to pediatric myocarditis: a review of the current literature. *Open access Macedonian journal of medical sciences.* 2019 Jan 1; 7(1):162.
- Heidecker B, Dagan N, Balicer R, Eriksson U, Rosano G, Coats A, Tschöpe C, Kelle S, Poland GA, Frustaci A, Klingel K. Myocarditis following COVID-19 vaccine: incidence, presentation, diagnosis, pathophysiology, therapy, and outcomes put into perspective. A clinical consensus document supported by the Heart Failure Association of the European Society of Cardiology (ESC) and the ESC Working Group on Myocardial and Pericardial Diseases. *European Journal of Heart Failure.* 2022 Sep 6.
- Romer AJ, Rajagopal SK, Kameny RJ. Initial presentation and management of pediatric heart failure. *Current Opinion in Pediatrics.* 2018 Jun 1; 30(3):319-25.
- Allan CK, Fulton DR, Kaplan SL. Clinical manifestations and diagnosis of myocarditis in children. *UpToDate.* 2019.
- Caforio AL, Marcolongo R, Baritussio A, Leoni L, Cheng CY, Iliceto S. Myocarditis in Systemic Immune-Mediated Diseases. In *Myocarditis 2020* (pp. 195-221). Springer, Cham.
- Chang YJ, Hsiao HJ, Hsia SH, Lin JJ, Hwang MS, Chung HT, Chen CL, Huang YC, Tsai MH. Analysis of clinical parameters and echocardiography as predictors of fatal pediatric myocarditis. *PLoS One.* 2019 Mar 20; 14(3):e0214087.
- Fadl S, Wähländer H, Fall K, Cao Y, Sunnegårdh J. The highest mortality rates in childhood dilated cardiomyopathy occur during the first year after diagnosis. *Acta Paediatrica.* 2018 Apr; 107(4):672-7.
- Siripanthong B, Nazarian S, Muser D, Deo R, Santangeli P, Khanji MY, Cooper Jr LT, Chahal CA. Recognizing COVID-19-related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management. *Heart rhythm.* 2020 Sep 1; 17(9):1463-71.
- Gannon MP, Schaub E, Grines CL, Saba SG. State of the art: evaluation and prognostication of myocarditis using cardiac MRI. *Journal of Magnetic Resonance Imaging.* 2019 Jun; 49(7):e122-31.
- De Gaspari M, Larsen BT, d'Amati G, Kreutz K, Basso C, Michaud K, Halushka MK, Lin CY. Diagnosing myocarditis in endomyocardial biopsies: survey of current practice. *Cardiovascular Pathology.* 2022 Oct 29:107494.
- Ammirati E, Buono A, Moroni F, Gigli L, Power JR, Ciabatti M, Garascia A, Adler ED, Pieroni M. State-of-the-Art of Endomyocardial Biopsy on Acute Myocarditis and Chronic Inflammatory Cardiomyopathy. *Current Cardiology Reports.* 2022 Feb 24:1-3.
- Alamri AS, Khayat LT, Alzahrani AJ, Kurdi LK, Alkhamsees NF, Bahaidarah SA. Clinical Presentation of Myocarditis in the Pediatric Age Group and Predictors of Poor Early and Late Outcomes: Academic Hospital Experience. *Cureus.* 2022 Nov 18; 14(11).
- El-Radhi AS. Fever in common infectious diseases. In *Clinical Manual of Fever in Children 2018* (pp. 85-140). Springer, Cham.
- Durani Y, Giordano K, Goudie BW. Myocarditis and pericarditis in children. *Pediatric Clinics.* 2010 Dec 1; 57(6):1281-303.
- Sarda L, Colin P, Boccarda F, Daou D, Lebtahi R, Faraggi M, Nguyen C, Cohen A, Slama MS, Steg PG, Le Guludec D. Myocarditis in patients with clinical presentation of myocardial infarction and normal coronary angiograms. *Journal of the American College of Cardiology.* 2001 Mar; 37(3):786-92.
- Ammirati E, Frigerio M, Adler ED, Basso C, Birnie DH, Brambatti M, Friedrich MG, Klingel K, Lehtonen J, Moslehi JJ, Pedrotti P. Management of acute myocarditis and chronic inflammatory cardiomyopathy: an expert consensus document. *Circulation: Heart Failure.* 2020 Nov; 13(11):e007405.
- Francone M. Role of cardiac magnetic resonance in the evaluation of dilated cardiomyopathy: diagnostic contribution and prognostic significance. *International Scholarly Research Notices.* 2014; 2014.
- 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 Journal of Clinical Cases.* 2019 Mar 6; 7(5):548.
- Saji T, Matsuura H, Hasegawa K, Nishikawa T, Yamamoto E, Ohki H, Yasukochi S, Arakaki Y, Joo K, Nakazawa M. Comparison of the clinical presentation, treatment, and outcome of fulminant and acute myocarditis in children. *Circulation Journal.* 2012; 76(5):1222-8.
- Khalid A, Kamran A, Rafiq N, Kumari V, Sheikh AS, Patel N. Clinical Presentation, Complications and Early Predictors for Poor Outcomes in Pediatric Myocarditis in a Tertiary Care Hospital. *Pakistan Armed Forces Medical Journal.* 2022 Jun 1; 72(3).