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ORIGINAL ARTICLE

ASSESSMENT OF DIFFERENT PRESENTATIONS OF MYOCARDITIS IN PEDIATRIC INTENSIVE CARE UNITS: (A MULTI-CENTER STUDY IN AL-SHARQIA GOVERNORATE).

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ABSTRACT

Background: Myocarditis can be presented with various clinical manifestations that may be wrongfully diagnosed and managed as other illness. Early suspicion and detection would specify the management and improve outcome of such disease. **Objectives:** To determine the different clinical presentation and findings of acute myocarditis in pediatric patients admitted to PICU and clinical, radiological and laboratory factors that may affect the diagnosis and the outcome. **Methods:** This cross sectional study included twenty four cases taken as a comprehensive sample due to the relatively rare presentation, all of them are Egyptian children aged between: 1.2 month to 9 years (108 months) old, diagnosed as acute myocarditis during the period from November 2017 till November 2018. **Results** In our study, the patients were 13 males (54.2%) and 11 females (45.8%). Their age mean was 27.82 ± 30.47 months. Acute heart failure, respiratory distress, cerebral hypoperfusion and epigastric pain were the main clinical presentations of myocarditis. **Conclusion:** In this study, it was concluded that myocarditis has wide range of clinical presentations that might be missed for other system affection than the heart, and high clinical suspicion is mandatory for early diagnosis and management, and hence, better prognosis would be achieved. **Key words:** Acute heart failure, myocarditis, hypoperfusion, respiratory distress.

List of abbreviations: (ECG) Electrocardiogram.

INTRODUCTION

Myocarditis is an inflammatory disease of myocardium with both infectious (viruses, bacteria, parasites) and noninfectious (drugs) etiologies with predominance of the post viral infection type and it is frequently missed by medical personnel. It often masquerades as more common pediatric illnesses such as respiratory distress or gastrointestinal disease. The suspicion of this illness in the differential diagnosis of children presenting with nonspecific symptomatology and disease progression can be life saving. The incidence of myocarditis is difficult to calculate because of its nonspecific presentation and

definitive diagnostic test not routinely done being invasive⁽¹⁾⁽²⁾.

The prognosis varies from recovery to progression to chronic disease or even death. But improvement in long term and short term prognosis can be achieved by development of new targeted therapeutic approaches and diagnostic technique⁽³⁾⁽⁴⁾.

Making the diagnosis of myocarditis can be challenging due to its subtle clinical signs and symptoms. The diagnosis of myocarditis should be suspected whenever a child presents with unexplained shortness of breath or fatigue, a new arrhythmia, or acute cardiac failure just following a viral illness⁽⁵⁾.

PATIENTS AND METHODS

This study was a cross sectional study and conducted in the Pediatric Intensive Care Units (PICUs) of: Children's Hospital of Zagazig University, Al-Ahrar Teaching Hospital in Zagazig and Zagazig General Hospital. **The Sample size was** A comprehensive sample of 24 cases included in this study. **The Inclusion criteria included:** Pediatric age group from 28 day till 13 years old with at least one clinical presentation suggestive of acute myocarditis ⁽⁶⁾: Cardiac symptoms: of central hypo perfusion (syncope, confusion, lethargy & seizures). Respiratory symptoms: dyspnea and/or cyanosis. Abdominal symptoms: abdominal pain, vomiting & diarrhea. Viral prodroma in the preceding two weeks. Clinical picture suggestive of acute myocarditis as acute heart failure (tachycardia, tachypnea & enlarged tender liver) and Cardiac dysfunction requiring inotropic support to maintain cardiac output and perfusion. Radiological findings included Chest X-ray showing cardiomegaly (cardiothoracic ratio > 0.5). Echocardiography study to detect Impaired cardiac contractility functions (fraction shortening <25% & ejection fraction < 55%) and abnormal left ventricular end diastolic diameter (LVED). At least one laboratory finding: elevated cardiac enzymes: Troponin I or CK-MB or both, elevated liver enzymes: ALT & AST & presence of metabolic acidosis and positive CRP. **The Exclusion criteria included** Children with known cardiac lesions, either congenital or acquired, and presenting with heart failure and Children with inborn error of metabolism. The studied group was subjected to: full history taking with stress on viral prodroma, clinical examination including general and systemic examination, laboratory investigations including troponin I and creatinine kinase muscle brain, aspartate aminotransferase, c reactive protein and arterial

blood gases, radiological examination with chest X-ray, twelve lead Electrocardiogram (ECG) and echocardiographic examination to detect left side dimension and function. Written informed consent was obtained from all participants' parents and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University, Al-Ahrar Teaching Hospital, Zagazig and Zagazig General Hospital. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

RESULT

This study included 24 patients with myocarditis aged between 1.2- 108 months, with a mean age of 27.82 ± 30.47 months, recruited from the emergency department Zagazig University pediatric Hospital, Al-Ahrar Teaching Hospital and Zagazig General Hospital. We examined the different demographic (table 1), clinical (table 2& 5), laboratory (table 7) & radiological factors that may affect the diagnosis and outcome of myocarditis. Our result showed that younger age is the significant demographic factor related to death. Tachycardia, hypoperfusion, fever prodroma, restlessness, disturbed conscious level and presentation with respiratory complaints are the significant clinical data related to myocarditis. Elevated Trop. I, CK-MB, rising CRP and high AST are the significant laboratory data related to diagnosis of myocarditis. Abnormal left side function in form of low EF & FS percentages revealed by echocardiography was a leading diagnostic tool to myocarditis (table 6). Acute heart failure, respiratory distress, cerebral hypoperfusion and epigastric pain were the main clinical presentations of myocarditis (table 3). Cases treated with IVIG has been correlated to better outcome (table 8).

Table (1): Demographic data of the studied cross-section (N=24).

Demographic data	All studied patients (N=24)	
	No.	%
<u>Sex</u>		
Male	13	54.2%
Female	11	45.8%
<u>Age (months)</u>		
Mean \pm SD	27.82 \pm 30.47	
Median(Range)	18.50(1.20 – 108)	
<u>Residence</u>		
Urban	11	45.8%
Rural	13	54.2%

Table (2): Clinical presentation of the studied cross-section (N=24).

Clinical presentation	All studied patients (N=24)	
	No.	%
<u>Symptoms duration (days)</u>		
Mean \pm SD	7.33 \pm 6.45	
Median (Range)	5 (1 – 30)	
<u>Shortness of breath</u>		
Absent	5	20.8%
Present	19	79.2%
<u>Vomiting</u>		
Absent	13	54.2%
Present	11	45.8%
<u>Poor feeding</u>		
Absent	5	20.8%
Present	19	79.2%
<u>URT symptoms</u>		
Absent	10	41.7%
Present	14	58.3%
<u>Convulsions</u>		
Absent	20	83.3%
Present	4	16.7%
<u>Lethargy</u>		
Absent	8	33.3%
Present	16	66.7%
<u>Tachypnea</u>		
Absent	3	12.5%
Present	21	87.5%
<u>Hepatomegally</u>		
Absent	12	50%
Present	12	50%
<u>Fever</u>		
Absent	11	45.8%
Present	13	54.2%
<u>Abnormal lung findings</u>		
Absent	15	62.5%
Present	9	37.5%

Clinical presentation	All studied patients (N=24)	
	No.	%
<u>Dysproportionate tachycardia</u>		
Absent	0	0%
Present	24	100%

Table (3): Main presentation of myocarditis among all studied cases (N=24):

Main Presentation	No.	Percentage
Acute Heart Failure (dysproportionate tachycardia, hypotension, hepatomegaly and poor perfusion)	10	41.7%
Cerebral Hypoperfusion (lethargy, confusion or seizures)	4	16.7%
Respiratory Distress (with no chest abnormality)	6	24.9%
Epigastric pain (not consistent with GIT abnormality)	4	16.7%
Total	24	100%

Table (4): Initial diagnosis according to primary survey of studied cases (N=24):

Initial diagnosis by system affection	No.	Percentage
GIT	5	20.8%
Respiratory	6	25%
CVS	6	25%
CNS	4	16.7%
Other:		
Metabolic	1	4.2%
Immune	2	8.3%
Total	24	100%

Table (5): Clinical findings of the studied cross-section (N=24).

Clinical findings	All studied patients (N=24)	
	Mean \pm SD	Median (Range)
Weight (kg)	11.60 \pm 6.33	11 (3.60 – 28)
Temprature (°C)	37.97 \pm 0.50	38 (36.90 – 39)
Hert rate (b/min)	178 \pm 24.74	177.50 (130 – 240)
Respiratory rate (b/min)	51.66 \pm 11.18	53 (22 – 75)
Systolic Pressure (mmHg)	76.12 \pm 16.65	80 (40 – 110)
Diastolic pressure (mmHg)	40.95 \pm 11.53	39 (30 – 60)
Capillary refill time (sec.)	3.70 \pm 0.69	4 (3 – 5)
Glsgow Coma Scale (score of 15)	10.04 \pm 2.21	9.50 (7 – 15)
Oxygen saturation in arterial blood (%)	73.33 \pm 12.28	72 (53 – 91)

Table (6): Echocardiography findings of the studied cross-section (N=24).

Echo-cardiography findings	All studied patients (N=24)	
	No.	%
<u>Abnormal Functions</u>		
Absent	4	16.7%
Present	20	83.3%
<u>EF (%)</u>		
Mean \pm SD	43 \pm 8.22	
Median (Range)	42.50(29 – 58)	
<u>FS (%)</u>		
Mean \pm SD	18.08 \pm 3.85	
Median (Range)	18(11 – 26)	

Table (7): Laboratory findings of the studied cross-section (N=24).

Laboratory findings	All studied patients (N=24)	
	Mean \pm SD	Median (Range)
Hb (g/dl)	10.07 \pm 1.45	9.90 (8 – 14)
HCT (%)	29.43 \pm 4.60	28.55 (24 – 41)
WBC ($\times 10^3$)	13.70 \pm 7.43	11.65 (4 – 39)
Lymphocytes ($\times 10^3$)	5.45 \pm 3.50	4.81 (0.80 – 13.54)
Granulocytes ($\times 10^3$)	6.88 \pm 5.35	4.55 (1.28 – 21.60)
Plt count ($\times 10^3$)	229 \pm 151.54	180 (55 – 680)
CRP (mg/dl)	23.79 \pm 24.93	18 (1 – 96)
<u>CRP level:</u>		
Negative	11	45.8%
Positive	13	54.2%
AST (U/L)	220.45 \pm 188.92	204 (30 – 891)
<u>AST level:</u>		
Not Elevated	3	12.5%
Elevated	21	87.5%
Troponin I (ug/L)	0.40 \pm 0.29	0.30 (0.05 – 1.07)
<u>Troponin level:</u>		
Not Elevated	1	4.2%
Elevated	23	95.8%
CKMB (ng/ml)	19.16 \pm 12.22	22.50 (4 – 41)
<u>CKMB level:</u>		
Not Elevated	5	20.8%
Elevated	19	79.2%

Table (8): PICU course (PICU stay, MV requirement & outcome) of the studied cross-section (N=24).

Outcome	All studied patients (N=24)	
	No.	%
<u>Mortality</u>		
Alive	16	66.7%
Died	8	33.3%
<u>MV requirement</u>		
Yes	20	83.3%
No	4	16.7%
<u>MV duration (days)</u>		
Mean \pm SD	4.83 \pm 5.70	
Median (Range)	3 (1 – 23)	
<u>PICU stay (days)</u>		
Mean \pm SD	9.95 \pm 8.26	
Median (Range)	7.50(1 – 42)	

	Patient Survived (n=16)		Patients Died (n=8)		Test	P
PICU stay (days)					t	0.395
Mean \pm SD	11 \pm 8.78		7.87 \pm 7.2		-0.869	
MV requirement					0.999	
No	3	18.75%	1	12.5%		
Yes	13	81.25%	7	87.5%		
IVIG treatment					0.0047	
No	2	12.5%	6	75%	(S)	
Yes	14	87.5%	2	25%		

DISCUSSION

Myocarditis is the inflammation of the muscular walls of the heart ⁽⁶⁾.

The initial diagnosis of myocarditis is highly dependent on clinical suspicion because a diagnosis based on an endomyocardial biopsy has many immanent risks; consequently, biopsies are not performed routinely ⁽⁷⁾.

Clinical and experimental data suggest that, in myocarditis, elevated cardiac enzymes levels especially troponin-I levels, reflecting myocardial injury precede the occurrence of inflammation, and cardiac enzymes are frequently measured whenever myocarditis is considered clinically ⁽³⁾⁽⁸⁾.

Myocarditis as a cause of sudden death has been reported in up to 16% of youth. Recently, it is also suggested that myocarditis is

corresponding to approximately 2% of pediatric deaths ⁽⁹⁾⁽¹⁰⁾.

However, population based study from Finland documented that the incidence of fatal myocarditis (1.59 per 100000) was highest in infants under one year of age and incidence was lowest in young adults (5-24 years, 0.12-0.17/100000) ⁽¹¹⁾.

Diagnostic evaluation of a series of 1.278 patients (mean age: 50 years, range=15-87 years) with cardiomyopathy revealed that 9.8% of cases were diagnosed with myocarditis ⁽¹²⁾.

In a pediatric study assessing the incidence of cardiomyopathy, viral myocarditis was found to be responsible for 27% of cases with dilated cardiomyopathy. Moreover, in a prospective cohort study, it has been shown that

most common known cause of dilated cardiomyopathy is myocarditis (46%)⁽¹²⁾⁽¹³⁾.

The present study was planned and performed with the aim of the characterizing demographic, clinical manifestations, main different presentations, diagnostic parameters and outcomes of patients with acute myocarditis.

Our study examined a series of 24 critically ill children admitted to the PICUs of Zagazig University pediatric hospital, Al-Ahrar Teaching Hospital and Zagazig General Hospital over a period of one year they were screened through CXR, echo-cardiography, ECG, cardiac enzymes (Tn-I and CKMB).

In our study, the patients were 13 males (54.2%) and 11 females (45.8%). Their age at presentation ranged from 1.2 to 108 months, with a mean of 27.82 ± 30.47 months. Our patients were older than that reported by Rady and Zekri in 2014, with a median age for myocarditis patients of 5.5 months (range of 3.25-21mo) and younger than that observed by Hsiao et al. who found mean age of 5.1years (range: 0.08-7.9years) and Teele et al. who detected acute myocarditis among patients with mean age of 12.7years (6days-17.4years)⁽¹⁴⁾⁽¹⁵⁾.

Their mean weight was 11.60 ± 6.33 kg (ranged from 3.6-28 kg). Although there was a difference in the number of females (45.8%) versus males (54.2%) with myocarditis, this difference was statistically insignificant ($p=0.885$). In the study performed by Hsiao and his team they found no significant relation between sex and mortality⁽¹⁵⁾.

The most frequent presenting symptoms in our study were respiratory complaints. This was in agreement with Durani et al. and Freedman et al. who found that most patients present with complaints of shortness of breath and having tachypnea at presentation⁽³⁾⁽⁷⁾. On contrast, Hsiao and his team found that the gastro-intestinal symptoms are the commonest presenting symptoms, they found also that gastrointestinal symptoms had a poor prognosis⁽¹⁵⁾.

This difference may be explained by different age distribution of cases; their older

age group in comparison to our younger age group. The older children and adolescents with heart failure may have primarily abdominal symptoms and a surprising lack of respiratory complaints as well as they are able to verbalize their symptoms unlike younger children⁽¹⁵⁾.

On physical examination, the most frequent sign was sinus tachycardia; 23 (95.8%) of patients had sinus tachycardia which was inproportionate to their age or fever. This was in agreement with Hsiao and his team in 2012 who reported that 63% of their cases had sinus tachycardia as their most frequent presenting sign⁽¹⁵⁾.

While Kuhn and his team in, found that only 39% of their cases had tachycardia and their most frequent sign was hepatomegaly in 57% of cases. This may be explained by that Kuhn and his team had other non-cardiac causes of hepatomegaly like sepsis⁽⁵⁾.

Aspartate amino transferase was high in 21 cases (87.5%) in our study, in the same line, Hsiao and his team in 2012 had aspartate amino transferase (AST) as the most sensitive laboratory test in prognosis of the outcome of myocarditis with a sensitivity of 59%⁽¹⁵⁾.

Sixteen of our cases (66.7%) had IVIG as part of their management, while Hisao and his team in 2012, reported that IVIG was prescribed in 18 children (67% of their cases)⁽¹⁵⁾.

Multisystem organ failure (MOSF): in our study we found that cases with multi system organ failure had higher mortality rates than other cases. Tele and his team in agreement to our results proved that mortality is higher with multisystem failure. In contrast Rady& Zekri found no significant relation to mortality⁽¹⁴⁾⁽¹⁶⁾.

This may be explained by the low incidence of MOSF in their cases as they had 25% of their patients with either diabetic ketoacidosis, Enterocolitis, Guillain-Barré syndrome, septicemia, or multisystem organ failure as the diagnosis at admission.

The mean duration of PICU stay in our study was 9.95 ± 8.26 days which is shorter than that reported by Hisao and his team who

found mean hospitalization duration of 18.52 ± 13.47 days in their study⁽¹⁵⁾.

This may be explained by the extreme presentation we faced in our cases, either by late presentation with fulminant course accompanied with high morbidity rates and consequently longer PICU stay need, on the contrary, early presentation with early diagnosis and management leading to rapid recovery and consequently early discharge from PICU.

In our study, 8 (33.3%) cases died, 16 (66.7%) cases survived. We have similar mortality rate to Radi& Zekri who reported mortality rate of 6 cases (35%)⁽²⁾. But our mortality rate is high in comparison to Hsiao et al. who reported that 6 (22.2%) patients died and Teele et al. who reported death of 3 cases (15%)⁽¹⁴⁾⁽¹⁵⁾⁽¹⁶⁾. This high mortality rate may be due to the fact of the late fulminant presentation as explained earlier and also that hospitals issued in our study are tertiary centers with admission of the most severe complicated cases with unavailable cardiac transplantation treatment option and high cost of assisted devices. The mortality rate among myocarditis cases in our study was (33.3%), this percentage comes in line with previous reports that ranged from 13 to 38%⁽¹⁶⁾.

Persistent metabolic acidosis: in our study we found that cases with persistent metabolic acidosis had higher mortality rates than other cases. In 2011 Teele et al. proved that intractable metabolic acidosis is associated with higher mortality rates⁽¹⁶⁾.

Rising C- reactive protein (CRP) levels: in our study we found that cases with rising CRP had higher mortality rates than other cases. In 2012 Izumi and Nishii proved that high CRP is related to mortality. This difference may be related to the lower age of their cases than our cases⁽¹⁷⁾.

Regarding the use of IVIG in management, 66.7% of our patients received IVIG 400mg/kg/day for three to five days, our results revealed statistical significance between IVIG administration and survival of patients.

Similarly, Kishimoto and his team found a statistically significant difference between the

survival curves of the patients treated with IVIG and the survival curves of those who were not treated with IVIG with a lower mortality rate in the IVIG-treated patients⁽²¹⁾.

On the other side, Saji, et al. found that in patients with acute myocarditis, the survival rate at 1 month did not differ between those who received IVIG and those who did not receive it. Also Teele and her team in and Klugman and his team found no impact of IVIG use on survival⁽¹⁶⁾⁽²²⁾⁽²³⁾.

Oxygen saturation mean detected primarily in arterial blood gases in the whole study cases was 73.33 ± 12.28 ranging from 53% to 91%. In survived group was the mean saturation was 79.12 ± 10.92 which was higher than that of died group 63.0 ± 6.50 and that difference showed statistically significant value.

Similarly, Chong Shu-Ling and his team in a study published in 2013 found that ten of his confirmed diagnosis with myocarditis had showed low oxygen saturation <95% with a better prognosis for higher saturation patients⁽¹⁸⁾.

Our study had some limitations. First, the lack of unequivocal diagnostic criteria allows one to question the diagnosis of myocarditis; this is not unique to this study. Second, we wanted to investigate the period from when the first symptom appeared to the start of management and the relationship between this interval and outcome. However, most children and parents could not clearly state when their symptoms began. This is because myocarditis progresses through stages with distinctly different mechanisms and manifestations. Third, because our series of patients was collected from the same geographic distribution, the findings may not be completely representative of the general population. A population-based study is needed.

CONCLUSION

In this study, we concluded that myocarditis has wide range of clinical presentations that might be missed for other system affection than the heart, and high clinical suspicion is mandatory for early

diagnosis and management, and hence, better prognosis would be achieved.

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