Clinical audit of the management of pericarditis in children in a Tertiary Referral University Hospital in Egypt

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Background
Globally, pericarditis is the commonest form of pericardial disease. Pediatric pericarditis has diverse etiologies and its available epidemiological data and management guidelines are sparse.

Objective
To evaluate the management of children with pericarditis attending Assiut University Children Hospital according to the European Society of Cardiology (ESC) guidelines (2015).

Patients and methods
This descriptive study was conducted at Assiut University Children Hospital, Assiut, Egypt, during the period of 1 year (from June 2017 to June 2018). During the study period, 30 children with pericarditis (due to different causes) were included (14 males and 16 females). Full history, cause of pericarditis, symptoms, and signs were taken. Some investigations, including laboratory and radiological were recorded. Therapy and medication and the outcome measures were assessed. In addition, the approach of doctors toward the application of the ESC guidelines was investigated.

Results
Idiopathic pericarditis was the most common cause of pericarditis (43.3%) followed by renal (20.0%), autoimmune (16.7%), tuberculosis (10.0%), and malignant (10.0%) causes. Chest pain (61–100%) followed by dyspnea (40.0%) was the most common presenting symptom. Tachycardia was a common sign in all cases, followed by muffled heart sound (in approximately two-thirds of cases), friction rub, jugular vein distention, and pulsus paradoxus, successively. Of the 30 included cases, 14 (46.6%) cases improved, nine (30.0%) cases got recurrent pericarditis, and seven (23.3%) cases died.

Conclusion
The ESC guidelines (2015) help improve the management of pediatric pericarditis. It was followed by a reasonable percentage of our cases. It is strongly recommended for doctors to be trained to apply these guidelines. Future multicenter, long-term prospective studies are needed to develop therapeutic recommendations for pericarditis in pediatric patients in addition to understanding the pathophysiology for improving the outcome.

Keywords:
management, pediatric, pericarditis

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Introduction

Globally, pericarditis is the commonest form of pericardial disease. It is an inflammatory condition of the pericardium and proximal great vessels, and it has diverse etiologies, including infectious and noninfectious causes [1]. Pediatric pericarditis has sparse epidemiological data. It has an estimated incidence varying from 0.1 to 0.2% [2]. Moreover, an incidence of 27.7/1 00 000 population per year was reported [3]; besides, it accounts for approximately 5% of cases experiencing chest pain in emergency departments [4].

Nowadays, the awareness of pericarditis has increased owing to the development of noninvasive diagnostic techniques, including echocardiography, computed tomography (CT), and cardiac magnetic resonance (CMR) imaging [5]. Diagnosis of pericarditis depends on clinical criteria, which include chest pain, pericardial rub, raised temperature, echocardiography, and ECG changes and pericardial effusion, whereas clinical recognition in children was strongly related to the type and intensity of the pericardial reaction [6]. As the symptoms may be nonspecific, high suspicion is mandatory for the diagnosis of pericarditis in children [7].

Related etiologies and complications in addition to management protocols for pediatric pericarditis are poorly characterized compared with adults [8]. Management of pediatric pericarditis is correlated with the cause of the pericarditis. It may include supportive care, pain control in addition to the antibiotic therapy, pericardiocentesis, open pericardial drainage, or pericardiectomy as needed [9]. The 2015 ESC guidelines are an update of the previous edition (2004) on the diagnosis and management of pericardial diseases [4]. The objective of this study was to evaluate the management of children with pericarditis attending Assiut University Children Hospital according to the 2015 ESC guidelines.

Patients and methods

This is a clinical audit descriptive study that was conducted at Assiut University Children Hospital, Assiut, Egypt, during the period of 1 year (from June 2017 to June 2018).

Its IRB number is 17100094. During the study period, 30 children with pericarditis (with different causes) were included (14 males and 16 females). We included all children with pericarditis and/or pericardial effusion above 1 year of age detected clinically and by echocardiography, whereas children younger than 1 year were excluded. Ethical permission was sought from the Faculty of Medicine Research Ethics Committee before beginning of the study.

A full history was taken, including personal history in terms of name, age, sex, and history of admission and discharge. Causes of pericarditis, symptoms, and signs were recorded. Laboratory investigations, including complete blood count (CBC), renal function (urea/creatinine), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and myocardial lesion test (CK and troponin), were done. All children were subjected to chest radiograph, echocardiography, and ECG. Therapy and medication of pericarditis were recorded. The outcome measures were recorded according to the evidence of improvement (resolution of symptoms, normalization of raised inflammatory markers, and echocardiographic findings), length of hospital stay, recurrence, and mortality. We investigated the approach of doctors toward the application of the ESC guidelines (2015) for history, clinical signs, and investigations on the included patients. All patients signed an informed consent form.

Data entry and all statistical analyses were performed using SPSS, version 21 (version 20; IBM, Armonk, New York, USA), with the Windows 7 operating system. Results are expressed as means ± SD for quantitative data and by n (%) for qualitative data. Analyses were done for qualitative data by the χ^2 test or Fisher exact when appropriate. *P* value was assumed significant if less than 0.05 and highly significant if *P* value was less than 0.01. *P* value was considered nonsignificant if greater than or equal to 0.05.

Results

This study included 30 children (14 males '46.6%' and 16 females '53.4%'). The mean ± SD age of them was 9.6 ± 9.6 years, ranged between 3 and 18 years, and the mean weight was 15.4 kg, with a range of 15–44 kg.

Table 1 shows the causes of pericarditis of the studied patients. Pericarditis was idiopathic in 13 (43.3%) cases, renal in six (20.0%) cases, autoimmune in five (16.7%) cases, tuberculosis in three (10.0%) cases, and malignancy in three (10.0%) cases.

Table 2 shows the symptoms and signs of the studied patients regarding their main etiology. Chest pain was found in 23 (76.6%) cases, dyspnea in 27 (90%) cases, and nonspecific symptoms in 29 (96.6%) cases. No significant differences were observed among groups of different causes of pericarditis except dyspnea (lower incidence was noticed in the autoimmune group). Regarding signs, tachycardia, muffled heart sounds, friction rub, jugular venous congestion, and pulsus paradoxus were present in 30 (100%) cases, 17 (56.6%) cases, 11 (36.6%) cases, seven (23.3%) cases, four (13.3%) cases, respectively, with no significant differences among groups of different causes of pericarditis.

Table 3 shows the investigations done on the studied patients. The results showed that all patients had positive findings regarding CBC, kidney function tests (urea and creatinine), CRP, and ESR, with no significant differences among the different causes of pericarditis. Myocardial lesion test was positive in four (13.3%) cases, and chest radiograph and ECO findings were positive in almost all included cases, also with no significant differences. Overall, 9 (30%) cases had positive results in both ECG and CT/CMR.

Table 4 shows the therapy used in the treatment of different etiologies of pericarditis in the studied

Table 1 Cause of pericarditis of the studied patients

Cause of pericarditis	Description (30 cases) [*n* (%)]
Idiopathic	13 (43.3)
Renal	6 (20.0)
Autoimmune	5 (16.7)
Tuberculosis	3 ((10.0)
Malignant	3 (10.0)

Table 2 Symptoms and signs among studied patients

Variables		Idiopathic (*n*=13)	Cause of pericarditis [*n* (%)]				*P* (significance)
			Renal (*n*=6)	Autoimmune (*n*=5)	Tuberculosis (*n*=3)	Malignant (*n*=3)	
Symptoms Positive	Chest pain	8 (61.5)	5 (83.3)	5 (100.0)	2 (66.7)	3 (100.0)	0.352^{NS}
	Dyspnea	13 (100.0)	6 (100.0)	2 (40.0)	3 (100.0)	3 (100.0)	0.002**
	Nonspecific Symptoms	13 (100.0)	5 (83.3)	5 (100.0)	3 (100.0)	3 (100.0)	0.388^{NS}
Signs Positive	Muffled hear	9 (69.2)	4 (66.7)	0	2 (66.7)	2 (66.7)	0.097^{NS}
	t sound	4 (30.8)	1 (16.7)	3 (60.0)	1 (33.3)	2 (66.7)	0.466^{NS}
	Friction rub						
	Tachycardia	13 (100.0)	6 (100.0)	5 (100.0)	3 (100.0)	3 (100.0)	–0.503^{NS}
	Jugular vein Distention	4 (30.8)	2 (33.3)	0	1 (33.3)	0	0.667^{NS}
	Pulsus Paradoxus	2 (15.4)	1 (16.7)	0	1 (33.3)	0	

A χ^2 test was used. NS, not significant. **Significant ($P \leq 0.01$).

Table 3 Investigation results of studied patients

Investigation (+ve)	Idiopathic (*n*=13)	Cause of pericarditis autoimmune [*n* (%)]				*P* (significance)
		Renal (*n*=6)	Autoimmune (*n*=5)	Tuberculosis (*n*=3)	Malignant (*n*=3)	
CBC	13 (100.0)	6 (100.0)	5 (100.0)	3 (100.0)	3 (100.0)	–
Urea/creatinine	13 (100.0)	6 (100.0)	5 (100.0)	3 (100.0)	3 (100.0)	–
CRP	13 (100.0)	6 (100.0)	5 (100.0)	3 (100.0)	3 (100.0)	–
ESR	11 (84.6)	6 (100.0)	5 (100.0)	3 (100.0)	3 (100.0)	0.591^{NS}
Myocardial lesion test	2 (15.4)	1 (16.7)	0	0	1 (33.3)	0.667^{NS}
Chest radiograph	13 (100.0)	6 (100.0)	5 (100.0)	3 (100.0)	3 (100.0)	–
Echo	13 (100.0)	6 (100.0)	4 (80.0)	3 (100.0)	3 (100.0)	0.270^{NS}
ECG	4 (30.8)	1 (16.7)	2 (40.0)	0	2 (66.7)	0.412^{NS}
CT/CMR	4 (30.8)	2 (33.3)	0	0	3 (100.0)	0.033*

χ^2 test was used. CBC, complete blood count; CMR, cardiac magnetic resonance; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; NS, not significant. *Significant ($P \leq 0.05$).

Table 4 Therapy used for the treatment of the different causes of pericarditis of the studied patients

Therapy used in the different cause of		Description pericarditis [*n* (%)]
Idiopathic (*n*=13)	NSAIDs	5 (38.5)
	Colchicine	1 (7.7)
	Corticosteroids (prednisone)	3 (23.1)
	Immunosuppressant (biological drugs)	0
	International techniques	3 (23.1)
	Good AB therapy	13 (100.0)
Renal (*n*=6)	NSAIDS	2 (33.3)
	Steroids	6 (100.0)
	Dialysis	3 (50.0)
	Intensifying dialysis	2 (33.3)
	Pericardial drainage	0
Autoimmune (*n*=5)	Steroids	5 (100.0)
	Immunosuppressant (Cyclophosphamide)	2 (40.0)
Tuberculosis (*n*=3)	Antituberculosis therapy	3 (100.0)
	Prednisolone (steroids)	1 (33.3)
	Pericardiocentesis	1 (33.3)
Malignant (*n*=3)	Antibiotics	3 (100.0)
	Pericardiocentesis	1 (33.3)
	Pericardiotomy	1 (33.3)
	Treatment of the original cause (chemotherapy or radiotherapy)	3 (100.0)

patients. Regarding the cases due to idiopathic causes, antibiotics were prescribed in 13 (100%) cases, and NSAIDs, steroids, colchicine, and interventional techniques were used in five (38.4%) cases, three (23%) cases, one (7.6%) case, and three (23.1%) cases, respectively. Regarding therapy used in renal cases, NSAIDs, steroids, dialysis, intensifying dialysis, and pericardial drainage were used in two (33.3%) cases,

six (100%) cases, three (50%) cases, and two (33.3%) cases, respectively. In cases owing to autoimmune etiology, steroids were used in five (100%) cases and immune suppressants in two (40%) cases. In tuberculosis pericarditis, antituberculosis therapy was used in three (100%) cases, and steroids and pericardiocentesis were used in one (33.3%) case for each. However, in malignant pericarditis, symptomatic treatment in the form of antibiotics was used in three (100%) cases, pericardiocentesis in one (33.3%) case, and pericardiotomy in one (33.3%) case, and treatment of malignancy itself either by chemotherapy and/or radiotherapy was used in all three (100%) cases. From the 30 cases, 14 (46.6%) cases improved or were healed, nine (30.0%) cases were recurrent, and seven (23.3%) cases died owing to complications from the original etiology, not from pericarditis as a sole cause (Table 5).

Discussion

Pericarditis is the common form of the pericardial disease with diverse etiologies including infectious and noninfectious causes [1]. The present results revealed that the common cause of pericarditis in the included patients was idiopathic in 13 (43.3%) cases, followed by renal causes in six (20.0%) cases, autoimmune in five (16.7%) cases, and both tuberculosis and malignant causes in three (10.0%) cases. Similar to our findings, Kuhn *et al*.[10] and Ratnapalan *et al*.[11] reported that pericarditis owing to idiopathic causes in children accounts for 37–68%. Moreover, the proportion of patients with idiopathic pericarditis in our study was consistent with previous reports [12,13]. On the contrary, Imazio and Gaita[3] reported that idiopathic causes are responsible for 80 : 90% of pericarditis. In a study by Lin *et al*. [14], they reported that uremic pericarditis may occur in 6 : 10% of patients with pericardial effusions. Tuberculous pericarditis is the commonest cause of pericarditis in areas where Mycobacteria tuberculosis is widespread. M. tuberculosis causes up to 70% of pericarditis in Africa (this was higher than our findings) [15]. However, tuberculosis accounts for approximately 4.0% of pericarditis in developed countries. Cremer *et al*. and Imazio *et al* [16,17] found that malignancy accounts for 33% of cases with pericarditis (the majority of them had known malignant disease). Similar to our findings, it was reported that autoimmune pericarditis contributed to 2 : 24% [17]. In a recent study conducted in France, Gouriet *et al*.[18] reported that the etiologies of acute pericarditis were idiopathic in 55% of patients, autoimmune in 24%, neoplastic in 9%, bacterial 3.1%, and tuberculosis in only 0.5% of the patients.

In the current study, the most common presenting symptom was chest pain in 61–100% of cases of different types of pericarditis, followed by dyspnea,

Table 5 Attitude of doctors toward the application of the checklist for history, clinical signs, and investigations

History did you ask about	Yes [*n* (%)]	No [*n* (%)]
Chest pain	26 (86.7)	4 (13.3)
Radiating or not		
Aggravated by movement or not		
Dyspnea	30 (100.0)	0
Nonspecific symptoms as		
Cough, fever, abdominal pain and vomiting	30 (100.0)	0
Clinical signs did you examine?		
Muffled or distant heart sounds	23 (76.7)	7 (23.3)
Pericardial friction rub	20 (66.7)	10 (33.3)
Tachycardia	30 (100.0)	0
Jugular venous congestion	10 (33.3)	20 (66.7)
Pulsus paradoxus (with cardiac tamponade)	12 (40.0)	18 (60.0)
Investigations did you ask for?		
Laboratory		
Complete blood count	30 (100.0)	0
Serum urea and creatinine	30 (100.0)	0
C-reactive protein	30 (100.0)	0
Erythrocyte sedimentation rate	29 (96.7)	1 (3.3)
Myocardial lesion tests (CK and troponins)	5 (16.6)	25 (83.4)
Radiologically		
Chest radiograph	30 (100.0)	0
Echocardiography	30 (100.0)	0
ECG	15 (50.0)	15 (50.0)
CT or CMR	10 (33.3)	20 (66.7)

CMR, cardiac magnetic resonance; CT, computed tomography.

which was presented in all cases of different types of pericarditis, except in autoimmune pericarditis (40.0%). Nonspecific symptoms were presented in almost all cases of different types of pericarditis, with nonsignificant differences among them. These findings agreed with Imazio and Gaita[3] who reported that pericarditis is relatively commonly presented with chest pain. Moreover, Ratnapalan *et al.*[11] reported that the most common presenting symptom of pericarditis is chest pain, which was noticed in almost all children in their study. They added that pericardial chest pain may be felt over the entire precordium, to the left side over the trapezius ridge, and the scapula. Imazio *et al.*[17] reported that chest pain is frequently common in acute infectious pericarditis compared with the chronic type. Common pericarditis is associated with some symptoms in children, including dyspnea, cough, fever, abdominal pain, and vomiting [12]. However, Imazio *et al.*[19] reported that symptoms of pericarditis in children include fever in addition to respiratory and gastrointestinal complaints.

Regarding signs of pericarditis in our studied patients, the common sign was tachycardia in all of the 30 cases, followed by muffled heart sound (in about two-thirds of cases), friction rub, jugular vein distention, and pulsus paradoxus, successively, with no significant differences among the different types. It has been reported that pericardial effusion causes reveal tachycardia and muffled heart sounds and a pericardial friction rub may be noticed especially in small effusion [20]. Moreover, Imazio and Gaita[3] reported that friction rub is one of the reported signs in acute pericarditis. In a recent study, Brucato *et al.*[21] found that the signs of pericarditis include pericardial friction rub, narrow pulse pressures, muffled heart sounds, tachycardia, and pulsus paradoxus. However, Assolar *et al.*[12] reported that the presenting symptoms of pericardial effusion were breathlessness in 90% of cases, followed by chest pain in 74%, cough in 70%, abdominal pain in 61%, and fever in 28% of them. On the contrary, Miranda[15] reported that pulsus paradoxus was 100% specific for pericardial effusion.

The results of our study revealed that all cases of the different causes of pericarditis had positive findings in CBC, kidney/function, ESR, and CRP. Similar to our findings, Thompson *et al.*[22] reported that pericardial disease is associated with abnormal white blood cell, CRP, and ESR. In a retrospective review by Ratnapalan *et al.* [11], it was reported that CRP, ESR, and white blood cell were elevated in 100, 61, and 27% of children with pericarditis, respectively. Moreover, the present results demonstrated that all included patients had positive echo and chest radiograph findings. Similarly, Khandaker *et al.*[23] reported that pericarditis is strongly correlated with positive ultrasound findings, and ultrasound should be done on all patients to evaluate pericardial effusion. Besides, Assolar *et al.*[12] reported that echocardiography was considered as a principal diagnostic tool of pericardial effusions in the pediatrics. Abnormal ECG findings were found in four (30.8%) cases in idiopathic pericarditis, two cases in both autoimmune and malignant causes. In contrast, Ratnapalan *et al.*[11] found that 90-94 % of patients of patients had abnormal ECG findings. Imazio *et al.*[17] reported that most ECG results return toward normal with the resolution of disease. The present results demonstrated that CT or CMR findings were abnormal in four (30.8%) cases in idiopathic pericarditis, two (33.3%) cases in renal pericarditis, and all cases of malignant pericarditis. It has been reported that cardiac CT and cardiac MRI are adjunctive imaging modalities when the echocardiogram findings are inconclusive or nondiagnostic [17]. Moreover, Khandaker *et al.*[23] reported that cardiac CT and MRI are useful in differentiating pericarditis with a small effusion, restrictive cardiomyopathy, and constrictive pericarditis.

Regarding therapy used in the treatment of patients in the current study, in cases with idiopathic pericarditis, nonsteroidal anti-inflammatory was used in five (38.5%) cases, colchicine in only one (7.7%) case, corticosteroids (prednisone) in three (23.1%) cases, and international techniques in three (23.1%) cases. However, the used therapy in cases with pericarditis due to renal causes was steroids in all cases (100.0%) and NSAIDs in one-third of cases (33.3%), and half of the cases (three cases, 50%) had dialysis. In cases with autoimmune pericarditis, steroids were used in all cases (five cases, 100%); however, immunosuppressants (Cyclophosphamide) were used in two (40.0%) cases. In cases with tuberculosis, antituberculosis therapy was used in all cases, however, both steroids (prednisolone) and pericardiocentesis were used in only one case. The used therapy in cases of malignant pericarditis was chemotherapy or radiotherapy in all cases, antibiotics in all cases, and both pericardiocentesis or pericardiotomy in only one case.

The initial treatment in patients with pericarditis should be aimed to reduce the pericardial inflammation and the related chest pain [24]. Moreover, Bergmann *et al.*[7] reported that the initial treatment measures should focus on identifying and managing pericardial effusion and tamponade. NSAIDs are broadly accepted as first-line treatment in idiopathic pericarditis, although their use is based on a professional opinion from the 2015 ESC guidelines and some previous studies in children [7]. In a retrospective study by

Ratnapalan *et al*. [11], it was reported that 68% of children who had idiopathic pericarditis improved with NSAIDs. Khandaker *et al*.[23] demonstrated that low-dose corticosteroids should be reserved for patients with symptoms that are refractory to NSAIDs, uremic pericarditis, and autoimmune pericarditis. Significant evidence encourages the use of colchicine as an adjunct to NSAIDs to improve remission rates at 7 days and reduce recurrence rates in both acute and recurrent pericarditis compared with NSAIDs alone. Some studies [17,25–27] have reported that combined therapy was significantly better than any other treatment; therefore, pericardiocentesis and intrapericardial chemotherapy should be used if possible in lung cancer neoplastic pericardial disease (not only in case of tamponade). Bergmann *et al*.[7] reported that pericardiectomy did not give beneficial results in some patients; this may be owing to myocardial compliance abnormalities, residual constriction, or other myocardial processes.

Regarding the outcome of patients in our study, 14 (46.6%) cases improved or were healed, nine (30.0%) cases were recurrent, and seven (23.3%) cases died from the complications of original etiology, not from pericarditis as a sole cause. Similar findings were reported by Diamond *et al*.[28] and Schaefer *et al*. [29], who reported that the overall mortality owing to pericarditis was 6%. Few studies have investigated the relation of etiology, management, and outcomes of pericarditis in children. On the contrary, Cremer *et al*.[16] reported that mortality from purulent pericarditis has reduced in pediatric patients, and the readmission was associated with idiopathic etiology. However, Imazio and Gaita[3] stated that recurrent pericardial effusion was correlated to autoimmune inflammatory disorders. Our study did not classify a relationship between exact etiology and recurrence, perhaps because of the difference in design and study population. Finally, this study has some limitations; of these, the statistical power was limited because of the small number of included patients. Moreover, we could not study the predictors of pericarditis.

According to the guidelines, 26 (86.7%) of the doctors asked the patients about chest pain, whereas all of them asked about dyspnea and nonspecific symptoms. Regarding clinical signs, 23 (76.7%) of the doctors examined the patients about muffled or distant heart sounds, 20 (66.7%) of them examined patients about pericardial friction rub, all of them examined patients about tachycardia, 10 (33.3%) of them examined patients about Jugular venous congestion, and 12 (40.0%) of them examined patients about pulsus paradoxus. Regarding investigations, all of the doctors asked all patients for CBC, serum urea and creatinine, and CRP; however, 29 of them asked for ESR and only five (16.6%) of them asked for myocardial lesion tests (CK and troponins). All doctors asked patients for chest radiograph and echocardiography; however, half of them asked for ECG, and only one-third of them asked for CT or CMR.

Conclusion

Idiopathic pericarditis is the common type of pericarditis in our study (43.3%) followed by renal (20.0%), autoimmune (16.7%), tuberculosis (10.0%), and malignant (10.0%). Of the 30 cases included, 14 (46.6%) cases improved, nine (30.0%) cases were recurrent, and seven (23.3%) cases died. The initial management of pericarditis must focus on screening for exact causes which will help in choosing suitable therapy. The ESC guidelines help improve the management of pediatric pericarditis. So, it is strongly recommended that all doctors must be trained to use these guidelines. Future multicenter, long-term prospective studies are needed to develop therapeutic recommendations for pericarditis in pediatric patients in addition to understanding the pathophysiology of specific etiologies of pericarditis for improving the outcome.

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Conflicts of interest

There are no conflicts of interest.

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