Original Research Article

Study of characteristic of pericardial effusion and to analyze pericardial fluid in various etiologies

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Abstract

Background: Pericardial effusion in clinical practice is commonly under diagnosed or missed especially minimal to moderate effusion.

Aim and objectives: To study the clinical and etiological profile of pericardial effusion and to recognize radiological, electrocardiographic and echocardiographic features that are characteristic of pericardial effusion and to analyze pericardial fluid in various etiologies.

Materials and methods: It was prospective study in patients presenting with pericardial effusion in department of Medicine and Cardiology. Total of 30 patients who presented with pericardial effusion based on clinical criteria and confirmed by echocardiography were included in the study.

Results: The causes of pericardial effusion in this study were Tuberculosis (33.33%), Uremia (20%), Viral /Idiopathic (16.67%), Bacterial (10%), Malignancy (10%), Hypothyroidism (3.33%), and post MI with ischemic cardiomyopathy (3.33%), SLE (3.33%). 3 cases (10%) were HIV positive among viral causes,1 patient had tuberculous pericarditis. ECG findings of low voltage complexes were present in 90% of patients and electrical alternans was seen mainly in tamponade cases. Chest X-ray finding of cardiomegaly was present in 90% patients with pleural effusion in 13.3% patients. ADA levels elevated in all 10 patients of tuberculous effusion with 100% sensitivity and among them smear for AFB was positive in 3 patients. Increased levels of ADA>60U/L was associated with increased incidence of effusive constrictive pericarditis in TB effusion. Pericardial fluid IFN-γ increased greater than 200 pg/L, tuberculous etiology showed 100% sensitivity and specificity. In all 10 patients of

2Dimensional echocardiographic findings of right atrial, right ventricular collapse and left atrial collapse was seen predominantly in tamponade cases. Pericardiocentesis showed hemorrhagic effusion in malignancy and uremia, serous and serofibrinous in tuberculosis and purulent in pyogenic effusion. In 3 cases of pyogenic effusion, culture revealed Staphylococcus aureus in 2 patients and Klebsiella pneumonia in 1 patient. Among 3 cases of HIV, one patient had ADA >40 and smear for AFB positive suggesting tuberculous etiology and other 2 cases were directly due to HIV. In HIV with tubercular effusion the patient presented with cardiac tamponade.

Conclusions: ADA>40U/L is diagnostic of tuberculous effusion which showed 100% sensitivity and specificity. Increase of ADA>60 U/L is associated with effusive constrictive pericarditis which has poor prognosis. IFN-γ is increased >200pg/l in all patients of tuberculous etiology showing 100% sensitivity and specificity.

Key words

Pericardial effusion, Pericardial fluid, Etiology.

Introduction

Pericardial effusion in clinical practice is commonly under diagnosed or missed especially minimal to moderate effusion. Any cause of pericarditis can lead to effusion. The available data show that it is more prevalent than what is clinically evident. High index of clinical suspicion is required which is confirmed by ECG, Chest X-Ray PA view, 2D-Echo and pericardiocentesis. Clinical features of pericardial effusion mimic Right ventricular infarction, Restrictive cardiomyopathy, Right heart failure and needs to be differentiated from these conditions because if not treated early pericardial effusion can lead to cardiac tamponade or constrictive pericarditis. If mistakenly treated with anticoagulants as for RVMI leads to hemorrhagic effusion. Hence early diagnosis and proper management is invaluable in better outcome.

In view of increasing prevalence of HIV/AIDS, incidence of pericardial effusion in them is increasing. Malignancy is common in developed countries whereas Tuberculosis and purulent effusion is common in developing world. Pericardial effusion is especially important clinically when it develops within a relatively short time as it may lead to cardiac tamponade. In addition to fatal out come if unrecognized, pericardial effusions have complication of constriction, which requires pericardiectomy [1].

Materials and methods

It was a Prospective study in patients presenting with pericardial effusion from September 2011 to October 2013 to Department of Medicine and Cardiology. Total of 30 patients were included in this study.

Inclusion criteria

Patients who presented with pericardial effusion based on clinical criteria and confirmed by echocardiography were included in the study.

Exclusion criteria

Patients with pericardial effusion resulting from cardio pulmonary surgery.

Patients with minimal effusion as a part of polyserositis with viral fever (Dengue).

In all 30 patients detailed history was taken and complete clinical examination was done. In addition to routine investigations the following investigations were done for all patients as X-Ray Chest PA view, Ultrasound abdomen, ECG and 2D echocardiogram was done for all patients, using 2D Echo machine, Pericardiocentesis was done under 2D Echo Guidance, Pericardial fluid was analyzed for protein, sugar, cell count, ADA levels, IFN-γ, Gram stain, smear for AFB and culture sensitivity and Miscellaneous investigations ELISA for HIV-I and II and computer

Tomogram of chest, Serum TSH and Serum T3 and T4, ANA were done in selected patients.

Results

Out of 30 patients pericardial effusion is seen mainly in the age group of 40-59 years and males were affected more than females.

26 (86.67%) patients had shortness of breath at presentation, 15 (50%) patients had symptoms suggestive of congestive heart failure, 18 patients (60%) had fever, 9 patients (30%) had chest pain and 12 patients (40%) had cough (**Figure – 1**).

Pulse rate was greater than 100/min in 26 (86.67%) patients. In 10 patients systolic blood pressure was less than 100 mm Hg and pulse paradoxus ranges from 8-16mm Hg this is present mainly in tamponade cases. Out of 10 cases 8-12mm Hg range in 8 patients and 12-16mm Hg range in 2 patients. Systolic blood pressure greater than 100 mm Hg was seen in all patients with chronic renal failure. Patients with pericardial effusion without tamponade there is no appreciable amount of systolic blood pressure variation with respiration (**Table – 1**).

Figure - 1: Distribution of symptoms.

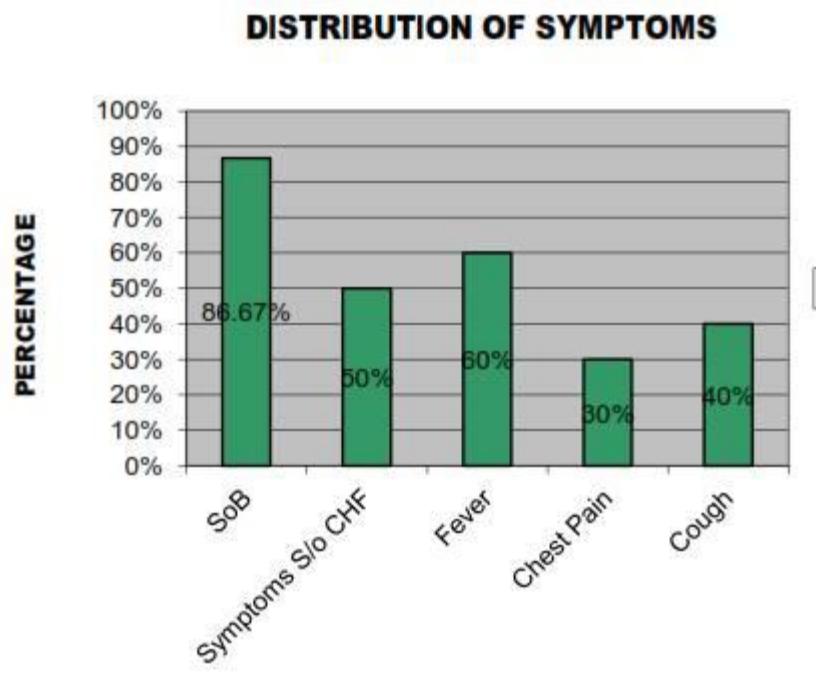


Table - 1: Distribution of vital data.

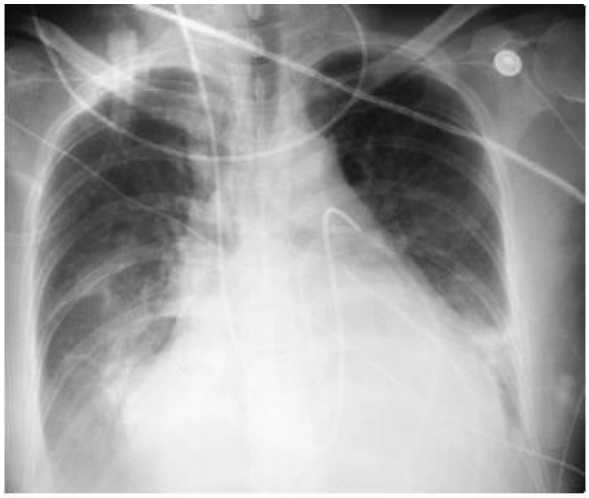
Vital Data	No. of Patients (%)
Pulse Rate	
> 100/min.	26 (86.67%)
< 100/min.	4 (13.33%)
Systolic Blood Pressure	
> 100mm Hg	20 (66.67%)
< 100mm Hg	10 (33.33%)
Pulsus Paradoxus mm Hg (tamponade cases)	
8-12mm Hg	8 (80%)
12-16mm Hg	2 (20%)

Table - 2: Investigation findings in study.

Cardiovascular Examination	**No. of Patients**	**%**
Heart sounds		
Normal in intensity	9	30%
Diminished in intensity	21	70%
pericardial friction RUB	2	6.70%
ECG changes		
Low voltage complexes	27	90
ST /T Changes	15	50
Electrical alternans	6	20
X- ray chest PA view		
Cardiomegaly	27	90
Findings S/0	2	6.7
Pulmonary KOCH s		
Pleural effusion	4	13.3
Protein		
> 3 gm/dl	27	90%
< 3 gm/dl	3	10%
Cell count		
<100	9	30%
>100	21	70%
Predomonant lymphocytosis	15	50%
Predomonant neutrophils	6	20%
ADA U/Lit		
> 40 U/Lit	10	33.30%
< 40 U/Lit	20	67%
INF- alpha		
200-240	6	20%
240-280	3	10%
>280	2	6.67%
Gram stain		
Gram+	2	6.67%
Gram -	1	3.33%
culture positive	3	10%
smear for AFB	3	10%

Diminished intensity of heart sounds was present in 21 patients. Pericardial friction Rub was heard in 2 patients. Electrocardiographic changes in order of frequency are low voltage complexes in 27 patients (90%). Electrical alternans is seen mainly in cardiac tamponade. Radiological changes in x-ray chest PA view showed predominantly cardiomegaly (ranging from 0.63 to 1 of cardio thoracic ratio) in 27 patients (90%). Protein <3g/ dl mainly in post MI patients and hypothyroidism patients. Cell count > 100 was seen in 21 patients (70%); predominant lymphocytosis. ADA Levels >40 U/Lit was seen in 10 patients (33.33%) out of 30 cases and was diagnostic of Tuberculous pericardial effusion. In all ten patients of suspected tuberculous etiology with clinical history, predominant lymphocytosis and raised ADA levels IFN-γ was also analysed and found to be greater than 200 pg/L which showed 100% sensitivity and specificity. In 3 cases of pyogenic pericardial effusion, 2 cases are gram stain positive and the culture shows staphylococci and 1 case was gram stain negative. Out of 30 cases in 3 cases smear for AFB was positive (**Table – 2**).

Figure - 2: Chest x-ray showing moderate tuberculous pericardial effusion with minimal pleural effusion.



Gross appearance was serous in 15 patients (50 %) serofibrinous in 6 patients (20%), haemorrhagic in 6 patients (20%) and purulent in 3 patients (10%). It was predominantly serous and serofibrinous in tuberculosis; purulent in pyogenic, hemorrhagic in malignancy and chronic renal failure (**Figure – 2, 3**).

Among 10 cases of tuberculous pericarditis levels of ADA >60U/L in pericardial fluid was found in patients with effusive-constrictive

pericarditis. Increased ADA levels were associated with increased risk of constriction which has poor outcome (**Table – 3**).

Large effusions are seen predominantly in tuberculosis and malignancy whereas hypothyroidism and viral etiology presents with mild effusion in majority of cases but HIV with tubercular superinfection presented with cardiac tamponade. In our study commonest etiology was tuberculosis (33.3%) followed by uremia (20%), viral/idiopathic including HIV 16.67%, Purulent in 10%, malignancy in 10%, hypothyroidism, SLE, post MI each 3.33% (**Table – 4**).

Figure - 3: Gross appearance of pleural fluid.

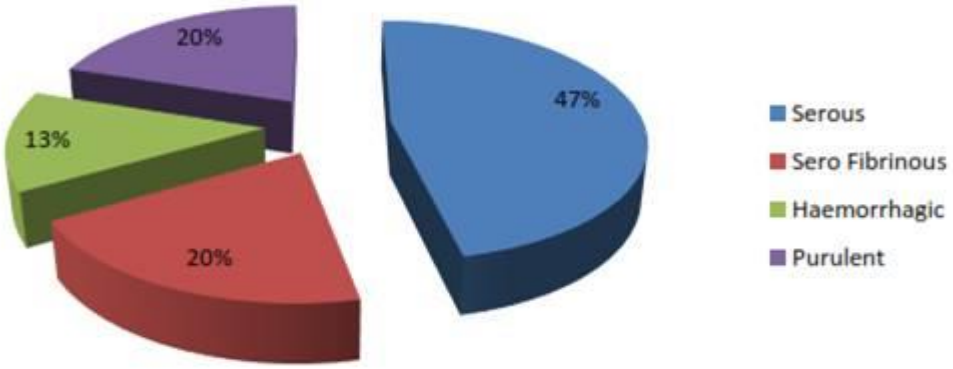


Table - 3: Pericardial fluid ADA levels in constrictive vs non-constrictive pericarditis.

ADA(U/l)	Number of Patients	2-D Echo findings
40-60	7	Effusive
>60	3	effusive- constrictive

Table - 4: Distribution of pericardial fluid volume in various etiological groups.

	MILD	MODERATE	LARGE
tuberculous pericardial effusion	1	4	5
uremic pericardial effusion	-	4	2
viral/idiopathic effusion	4	1	-
bacterial pericardial effusion	-	1	2
Malignant	-	1	2
Hypothyroidism	1	-	-
post ischemic	-	1	-
SLE	-	-	1

Discussion

Pericardial effusion is a clinical diagnosis mainly by raised jugular venous pressure, hypotension, pulsus paradoxus in combination with decreased intensity of heart sounds and clear lung fields. Roentgenographic examination reveals enlarged cardiac silhouette with clear lung fields, electrocardiographic changes include low voltage complexes and electrical alternans. Confirmation of diagnosis is by characteristic changes in 2Dimensional echocardiogram. Pericardiocentesis is the treatment of choice and analysis of pericardial fluid may provide etiological diagnosis.

In our study 26 patients (87%) presented predominantly with shortness of breath, 15 patients (50%) had symptoms suggestive of congestive heart failure, 18 patients (60%) had fever, 9 patients (30%) had chest pain and 12 patients (40%) had cough. Symptoms in order of frequency are shortness of breath, fever, symptoms suggestive of congestive heart failure, chest pain and cough. All patients with tuberculous, pyogenic and viral pericarditis had fever and cough was seen mainly in patients with tuberculous and pyogenic pericarditis. It was similar to the study [2] 36 conducted by Himalayan Institute of Medical Sciences, HIHT University, Dehradun in Uttarakhand (from 2002-2007 for 5 years in 90 cases). In that study Dyspnea in 75% of cases; cough in 30%; fever 30% cases and chest pain in 25% of cases.

On examination pulse rate was greater than 100/mt in 26 patients (87%) and systolic blood pressure was less than or equal to 100 mm Hg in 10 patients (33%). Systolic Blood pressure greater than 100 mm Hg was seen in 20 patients (67%). Pulsus paradoxus is seen mainly in patients with tamponade presentation. Pulsus paradoxus ranging from 8-12 mmHg in 8 patients and 12-16 mm Hg in 2 patients. There is no appreciable amount of systolic blood pressure variation with respiration in patients with pericardial effusion without tamponade. Raised jugular venous pressure was seen in 20 patients with characteristic ‘a’ wave, ‘v’ wave, prominent x descent and obliterated or absent Y descent. Heart sounds, first and second heart sound, were decreased in intensity in 21 patients (70%) and were of normal intensity in 9 patients (30%). Pericardial friction rub was heard in two patients. Presence of systolic blood pressure greater than 100mm Hg and normal intensity of heart sounds does not exclude a diagnosis of cardiac tamponade and pulse paradoxus and raised JVP provide valuable clue on examination in addition to imaging and Echocardiographic confirmation.

The presence of raised JVP, pulsus paradoxus, hypotension is seen mainly in pericardial effusion with tamponade. In our study out of 30 cases, 10 presented with cardiac tamponade findings. In these 10 cases findings of physical examination PR> 100/min (100%) raised jugular venous pressure (100%); SBP<100 mmHg, presence of pulsus paradoxus (100%) are consistent with the study done for 17 years by Guberman, et al. [3]. Presence of tamponade with SBP> 100mmHg is seen mainly in chronic renal failure patients. Erythrocyte sedimentation rate was raised > 50mm in 1 patients (70%) and was < 20 mm in 1in 24 patients (80%) hour in 21 hour in 9 patients (30%). Leucocytosis was seen Electrocardiographic changes in order of frequency are low voltage complexes in 27 patients (90%), ST/T changes in 15 patients (50%) and electrical alternans in 6 patients (20%).

X-Ray chest PA view showed cardiomegaly (ranging from 0.63 to 1 cardiothoracic ratio) in 27 patients (90%), pleural effusion in 4 patients (13.3%) and findings suggestive of pulmonary Kochs in 2 patients (6.67%). Absence of cardiomegaly does not exclude diagnosis of cardiac tamponade, as nearly 250ml of fluid is required before radiological changes appear and this happened in patients with traumatic tamponade. Out of 10 patients with tuberculous effusion, only 2 patients had radiological evidence of pulmonary Kochs.

Echocardiographic confirmation of tamponade as indicted by right atrial collapse, right ventricular diastolic collapse and abnormal increase in inspiratory tricuspid flow velocities and decrease in mitral flow velocities was noticed in 10 patients (33.3%). Left atrial collapse was seen in 5 patients (16.67%) especially in patients with large fluid collections as in tuberculosis. Fibrin strands were seen in 9 patients (30%) predominantly in tuberculous and uremic pericardial effusions. Based on amount of fluid accumulation on 2D Echo pericardial effusion was classified as mild Echo Free space (Anterior + posterior) <10 mm, moderate (10 mm-20 mm), (large >20 mm). It would be emphasized that these definitions may vary laboratory to laboratory. Amount of fluid was large in 12 patients (40%) especially in tuberculous, uremic pericardial effusions while in 12 patients (40%) moderate collection of fluid. Pericardial constriction was found in 4 patients of which three cases are TB and one case is of purulent effusion. Cardiac tamponade was mainly seen in cases of tuberculosis, malignancy and CRF. In our study out of 3 cases of malignancy both are known cases of bronchogenic carcinoma who presented with cardiac tamponade. The echocardiographic findings of tamponade found in the study are compatible with study done by Lorel, et al. [4].

Pericardial fluid analysis, on gross appearance was serous in 15 patients (50%) serofibrinous in 6 patients (20%). It was predominantly serous and serofibrinous in tuberculous, hemorrhagic in malignancy and uremic pericarditis and purulent in pyogenic effusion. In 27 patients pericardial fluid protein was greater than 3 mg/dl. 3 patients had pericardial fluid protein level < 3 g/dl which is present mainly in Hypothyroidism and Ischemic cardiomyopathy. Pericardial fluid cell count > 100 was seen in 21 patients predominant lymphocytosis in 15 patients (50%) mainly in tuberculous pericarditis and 6 patients (20%) had predominant neutrophils especially pyogenic (Bacterial) pericarditis.

Pericardial fluid ADA levels of greater than 40 U/lit were seen in 10 patients all of tuberculous etiology and less than 40 U/lit in 20 patients. ADA levels of > 40 U/lit is diagnostic of tuberculous pericardial effusion with sensitivity of 100% as compared to study done by Kopecky SL, et al. [5] where they found sensitivity of 93% and specificity of 97%. Further very high levels of ADA >60U/L shows increased incidence of effusive constrictive pericarditis. Pericardial fluid IFN-γ is increased in all 10 patients of tuberculous etiology showing 100% sensitivity and specificity. Smear for AFB was positive in 3 patients. In purulent effusion smear of pericardial fluid showed gram-positive cocci in 2 patients and Gram-negative bacillus in 1 patients. Culture was positive in 3 patients of bacterial pericarditis and organism isolated was staphylococcus aureus in 2 patients and klebisella pneumonia 1 patient.

Of 30 patients with pericardial effusion, in study period of 20 months, predominant cause was Tuberculous pericardial effusion in 10 patients (33.33%), Uremic pericarditis in 6 patients (20%), Viral / Idiopathic pericarditis in 5 patients (16.67%) with HIV in 3 patients out of which 1 patient had tuberculous effusion (smear for AFB positive), Pyogenic 3 patients (10%), Malignancy in 3 patients (10%) Hypothyroidism was responsible in 1 patient (3.33%), and post myocardial infarction with Ischemic 84 cardiomyopathy in 1 patient (3.33%), SLE in 1 patient (3.33%) The etiological diagnosis was based on clinical and laboratory data, radiological findings and pericardial fluid analysis.

The study done by Dhall, et al. [6] in Pune for etiological diagnosis for pericardial effusion were they found Tuberculosis (50%), connective tissue disorder (20%), Bacterial (10%), Hypothyroidism (10%), viral/Idiopathic (10%) in their study. The study36 conducted by HIHT University, Uttarakhand. In their study tuberculosis (42.2%) cases; malignancy (14.4%) cases; viral (14.4%) cases; collagen vascular disease (13.3%) cases; Uremia (3.3%) cases; purulent (3.3%) cases and Hypothyroidisim

(2.2%) cases. The study conducted by A.K. Bhattacharya [7] in Amrutha Institute of Gastro Enterology published in APICON 2002 in that study CRF (50%) cases; tuberculosis (20%) cases; collagen vascular disease (14%) cases; malignancy (6%) cases; hypothyroidism (6%) cases; viral (4%) cases.

A study conducted by T. Sand TS; Barnes ME, Gersh BJ [8] in 1,127 cases of pericardial effusion . They found latrogenic in (35%) cases; Malignancy in (33%) cases; Infection in (6%) cases; Idiopathic in (8%) cases; collagen vascular disease in (4%) cases; post MI in (3%) cases, other causes in (11%) cases and Tuberculosis in (0%) cases. They found malignancy is an important cause of pericardial effusion; where tuberculosis was rare.

A study conducted by Sagrista-Sauleda[9] in Spain in the year of 2000 in 322 number of patients. They found Idiopathic in (29%) cases; Malignancy (13%) cases; latrogenic (16%) cases; Post MI (8%) cases; Uremia (6%) cases; collagen vascular disease (5%) cases; and tuberculosis (0%) cases.

A study conducted by Corey [10] GR, comphell PT, van TP in 1993 in 75 cases. They found malignancy in (23%) cases; Infection (27%) cases; Uremia (12%) cases; collagen vascular disease in (12%) cases; Idiopathic in (7%) cases. So after review of the other studies, in developed countries, malignancy is the most common etiology of pericardial effusion while tuberculosis and uremia have been implicated in the pathogenesis in developing countries.

The present study demonstrated tuberculosis as the most common etiology of pericardial effusion. Infections like tuberculosis and uremic pericarditis are more common in our place where the study was conducted was not a referral centre for malignancies and the number of invasive diagonostic procedures done in our setting is less as compared. My study results are similar to the studies conducted in India like "Dhall" at Pune and HIHT University of Uttarakhand. But there was some difference compared to the study conducted by A.K. Bhattacharya and R.M. Mehta. These can be attributed to lesser duration of our study and small number of patients.

In our series out of 30 cases, 3 (15%) are HIV positive in that 1 case presented with tuberculous pericarditis etiology. An increase in prevalence of HIV infection is a threat for increasing tuberculous effusion.

Conclusion

In developing countries like India TB, uremia and purulent effusions are more common compared to malignancy and iatrogenic causes in developed world. ADA>40U/L is diagnostic of tuberculous effusion which showed 100% sensitivity and specificity. Increase of ADA>60 U/L is associated with effusive constrictive pericarditis which has poor prognosis.

IFN-γ is increased >200pg/l in all patients of tuberculous etiology showing 100% sensitivity and specificity. In pyogenic effusion the common organism isolated is Staphylococcus aureus. Mild to moderate effusion is seen in HIV but in HIV with tuberculous superinfection massive effusion leading to cardiac tamponade is seen.

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