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CLINICAL AND LABORATORY PROFILE OF ADULT PATIENTS WITH PERICARDIAL EFFUSION AT DR GEORGE MUKHARI ACADEMIC HOSPITAL, PRETORIA, SOUTH AFRICA

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Abstract

OBJECTIVE: Pericardial effusion has become a common clinical condition and consequent to human immunodeficiency virus pandemic, the condition has been on the increase. Its effects on the heart often present as an emergency requiring early recognition and interventions to prevent disability and death. This study evaluated the clinical, laboratory profile of patients and clinical outcomes of treatment of this condition.

METHODS: A cross-sectional study based on retrospective review of medical records of patients admitted for pericardial effusion, over an eleven-year period was undertaken. Outcome variables analysed were: demographics, percentage with cardiac, renal or liver failure and the

percentage of those with abnormal ECG and echo findings. Correlation between biochemical results of pericardial fluid and final aetiology of pericardial effusion was determined.

RESULTS: 204 medical records of patients, aged between 25 and 55 years, with 50.7% males and 49.3% females, were reviewed. Cardiac, renal and liver failure were noted in 36.8%, 26.0% and 17.2% patients, respectively. Cardiogenic shock was found in 5.9%, and 96.5% had cardiomegaly on chest X-ray. From records of ECG, 22.8% had normal findings, 26.5% had small-QRS complexes and 57.4% presented with mild pericardial effusion based on echo findings. There was poor correlation (*r = 0.44)* between the biochemistry results of pericardial fluid and the aetiology of pericardial effusion.

CONCLUSION: Curative outcome was achieved in 78.9% of the patients and mortality rate among the patients was 88 deaths/1000 patients. Cardiomegaly was the most accurate investigation related to pericardial effusion but biochemical results were poorly correlated with the disease.

Keywords: Clinical/Laboratory features; Adult patients; pericardial effusion

Introduction

Pericardial effusion (PE) is a frequent clinical diagnosis at Dr George Mukhari Academic Hospital. Pericardial ailment has expanded in the sub-Saharan Africa on account of the human immunodeficiency virus infection pandemic. A multicenter study in Germany show that PE was reported in up to 11% of HIV-infected patients before the introduction of antiretroviral drugs [Lind et al; 2011]. In the United States, the prevalence of PE has been reported to be 20% [Sampat et al; 2010] and Lazaros et al reported a high PE prevalence of 60% [Lazaros et al; 2019]. Such high prevalence of PE raises legitimate concerns because of associated medical conditions such as human immunodeficiency viral infection pulmonary arterial hypertension (PAH) [Sahay & Tonelli; 2013], acute lymphatic leukemia (ALL) [Sampat et al 2010], Perimyocarditis (PMY) [Buiatti et al; 2013] and end-stage renal disease (ESRD) [Hwang et al; 2012].

The heart is becoming the most affected structure in the context of the HIV pandemic and PE is one of the chief manifestations. The impacts of PE on the heart regularly present as a medical crisis requiring early identification and intervention to restore wellbeing and counteract possible disabilities and death. PE is a negative predictive association in patients with malignancy as was reported by Kim and his co-workers [Kim et al; 2010] who showed PE, in association with malignancy, in only 2.7% of 8.1% of patients. Besides its association with malignancy, PE in immune compromised patients carries a negative outcome, especially when it is superimposed with tuberculosis [Cherian; 2004]. Mayosi and his colleagues reported on their study in Cape Town, a high mortality from 26% to 40% at 6 months in a group of patients with PE [Mayosi et al; 2014].

The management of PE is a challenge due to absence of standard guidelines and management protocol. At the onset of the disease, the diagnosis of PE may be difficult to ascertain because of lack of sensitivity of initial general investigations [Peebles et al; 2011]. This assertion is true for radiologists, but clinicians are required to exercise more clinical acumen when confronted with this medical condition. In that case, indirect findings may help in assessing the aetiology of PE, such as the absence of cardiac tamponade or only the existence of inflammatory signs that comprehend chest pain, pericardial friction rub, and pyrexia with limited echocardiographic changes [Peebles et al; 2011]. Such indirect findings can help in the timely intervention and stratification of the risks to patients, hence the need for Dr George Mukhari Hospital to establish a clinical profile of patients with PE. It is against this backdrop of information that this study was conceptualized to determine the profile of pericardial effusion among adult patients admitted at Dr George Mukhari Academic Hospital.

Materials and Methods

Design: This study was a cross-sectional study, with data collection based on retrospective document review. We retrieved and studied the clinical records of patients diagnosed with pericardial effusion in the departments of internal medicine, cardiology and cardiothoracic unit. The files of patients who were admitted and followed up after diagnosis of pericardial effusion at Dr George Mukhari Academic Hospital were retrieved dating between 1st January 2004 and 31st December 2014.

Sample and sampling method: Total population sampling technique, as outlined by Leedy and Ormrod, was used to select medical records from1st January 2004 to 31st December 2014 [Leedy and Ormrod; 2005]. Two hundred and four medical records of patients diagnosed with pericardial effusion were reviewed. The selected samples were of patients over the age of 18 years and an exhaustive retrieval of medical files was done to include all the files of patients admitted and managed during the specified study period.

Data collection: Data was collected using a data collection sheet. Since the study was retrospective, there was no need to obtain consent from the patients. However, personal identifiers were de-linked from the collected data to maintain patient confidentiality. Ethical clearance was requested and obtained from Sefako Makgatho Health Sciences University, Research and Ethics Committee (Certificate Number: *SMUREC/M/38/2015:PG*). In addition, permission to perform the study was also requested and obtained from the hospital management of Dr. George Mukhari Academic Hospital.

Clinical, radiological and laboratory data were captured on the data collection sheet. Patient demographics, clinical symptoms and signs were also recorded on the data collection sheet. Findings of chest X-Ray, ECG and laboratory reports from the patients' files were reviewed and recorded. The type of treatment the patients received and the treatment outcomes were recorded.

Data analysis: Descriptive and inferential statistics were used to analyse the collected data. Frequency distribution, cross tabulations and charts were used to describe the data while regression analysis and one-way ANOVA test were done for inferential analysis. P-values of $\leq$ 0.05 were noted to be statistically significant. All data analysis was done in STATA version 12 (Stata Corp, TX) and SPSS version 22 (IBM Corp, Illinios, USA).

Results

The study included 204 records of patients with pericardial effusion. The demographic data showed that 67.1% of the records reviewed were for patients between the ages of 25 and 55 years and female patients were 49.3%.

Table 1: Age and gender characteristics of patients from the reviewed records

Item	Frequency	Percentage
Age		
< 25	34	16.7
26 – 35	55	27.0
36 – 45	47	23.0
46 – 55	35	17.2
56 – 65	16	7.8
66 – 75	14	6.9
76 – 85	2	1.0
>85	1	0.5
Total	204	100
Gender		
Male	104	50.7
Female	100	49.3
Total	204	100

Data on system failures and cardiogenic shock showed that cardiac failure occurred in 36.8%, renal failure in 26.0%, liver failure in 17.2% and cardiogenic shock in 5.9% of the patients.

Table 2: System Failures and Cardiac Shock Results for Patients in the Reviewed Records

	Frequency	Percentage

Cardiac Failure		
Yes	75	36.8
No	129	63.2
Renal Failure		
Yes	53	26.0
No	151	74.0
Liver Failure		
Yes	35	17.2
No	169	82.8
Cardiogenic Shock		
Yes	12	5.9
No	192	94.1

Radiological data showed that 96.5% of patients had cardiomegaly on chest X-ray (Table 3). Patients, for whom ECG was done (N= 138), ECG findings showed that 26.5% had small QRS complexes and 22.8% were normal (Table 3). Echo findings showed that 57.4% of patients had mild pericardial effusion. Other chest X-ray results, ECG findings, and Echo findings occurred with small frequencies.

Table 3: Radiological, ECG and Echo Findings for Patients in the Reviewed Records

Item	Frequency	Percentage
Chest-X-Ray		
Cardiomegaly	192	96.48
Bilateral pleural effusion	3	1.51
Normal	2	1.01
Right pleural effusion	2	1.01
ECG Findings		

tachycardia	9	4.76
Global flat T-waves	1	0.53
Normal	43	22.75
Small QRS complexes	50	26.46
Inverted T-waves	9	4.76
Not done	66	34.92
Q-waves	1	0.53
Left ventricular strain	1	0.53
Atrial fibrillation	7	3.70
Ischaemic heart disease	2	1.06
Echo findings		
Mild pericardial effusion	117	57.35
Moderate pericardial effusion	32	15.69
Massive pericardial effusion	55	26.96

Pericardial effusion tap was done in 32.8% of the patients (Figure 1) while biochemistry results showed that 31.9% had exudative effusion (Figure 2). Aetiology data showed that 57.5% of patients had TB pericardial effusion while 27.5% had heart disease (Figure 3).

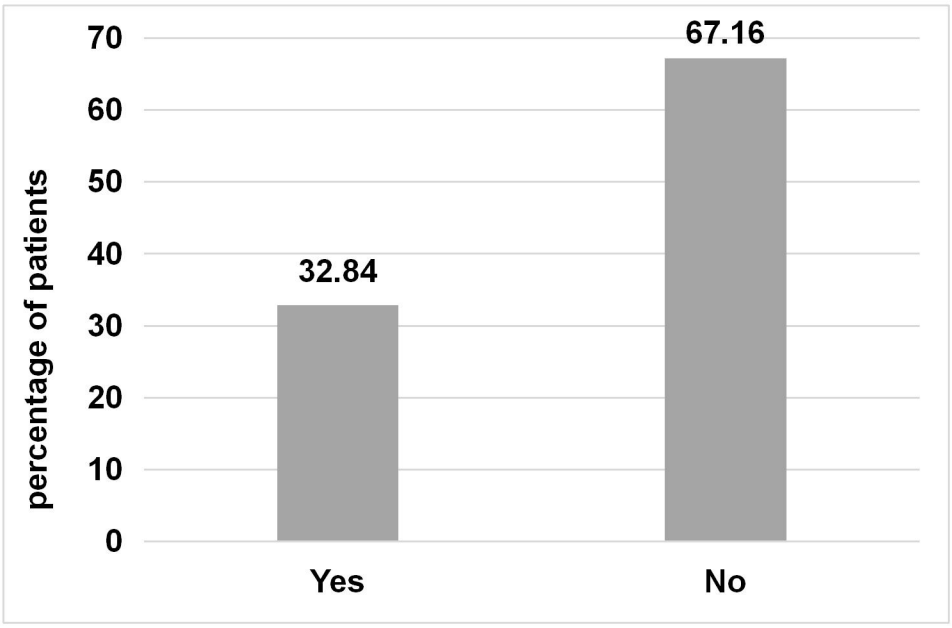

Figure 1: Pericardial tap done.

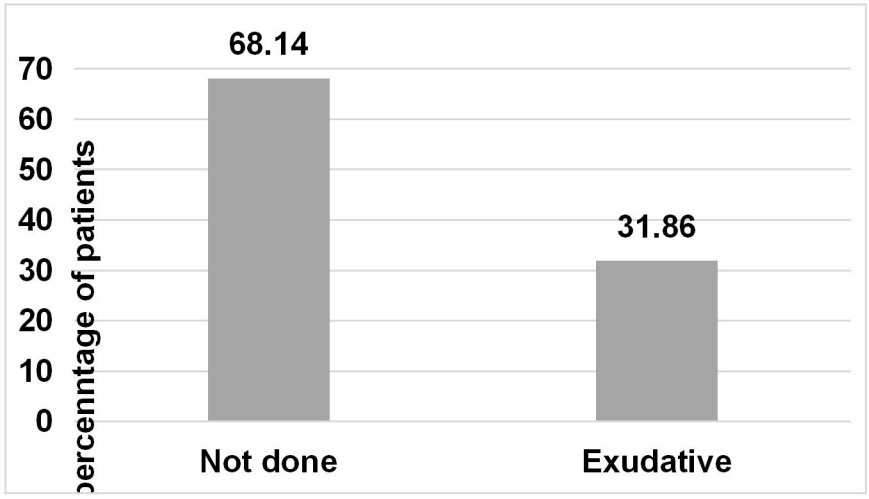

Figure 2: Biochemistry results of the pericardial effusion.

The results are the proportions of the outcomes of biochemistry examination. Biochemistry not done for the majority of PE but for those that were done, exudative effusion was found in 32.0%.

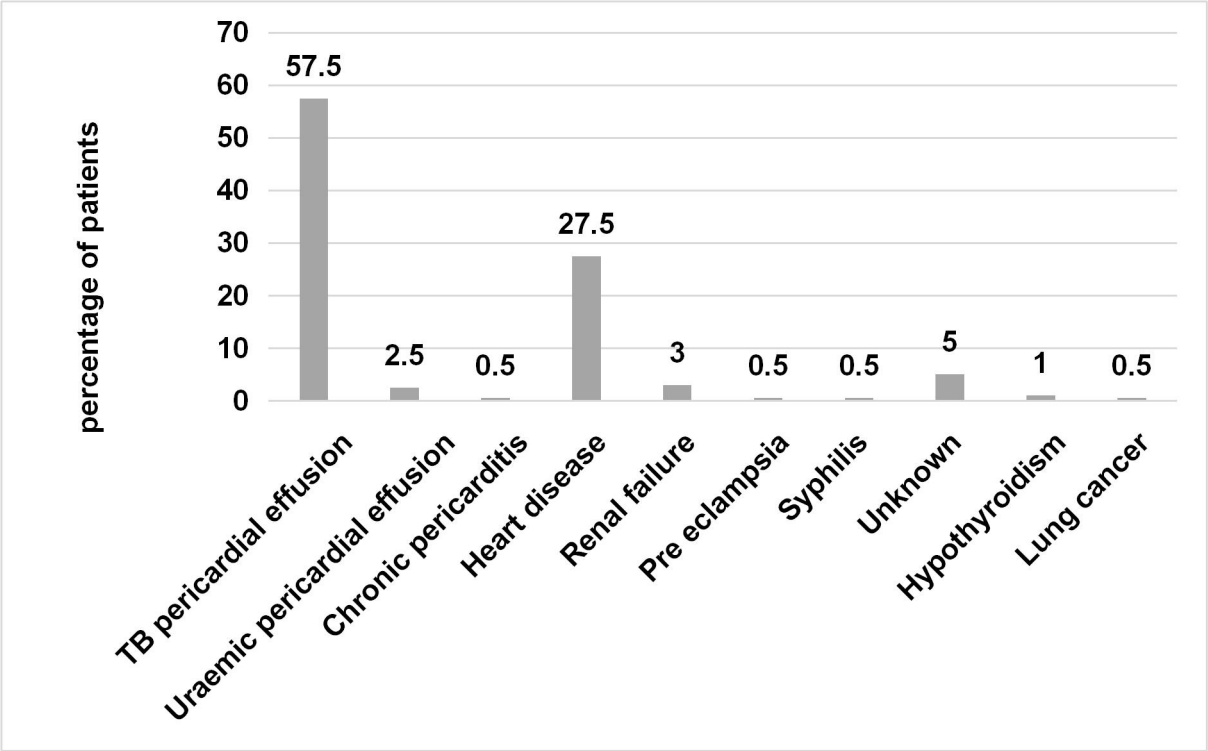

Figure 3: Aetiology of Pericardial effusion.

Shown in this figure are the various final aetiology of pericardial effusion. TB pericardial effusion and heart disease are the two significant aetiological factors.

For co-morbidities of PE, 48.4% of the patients had retroviral disease (Figure 4) and the treatment outcomes showed that 78.9% were cured of the pericardial effusion (Figure 5).

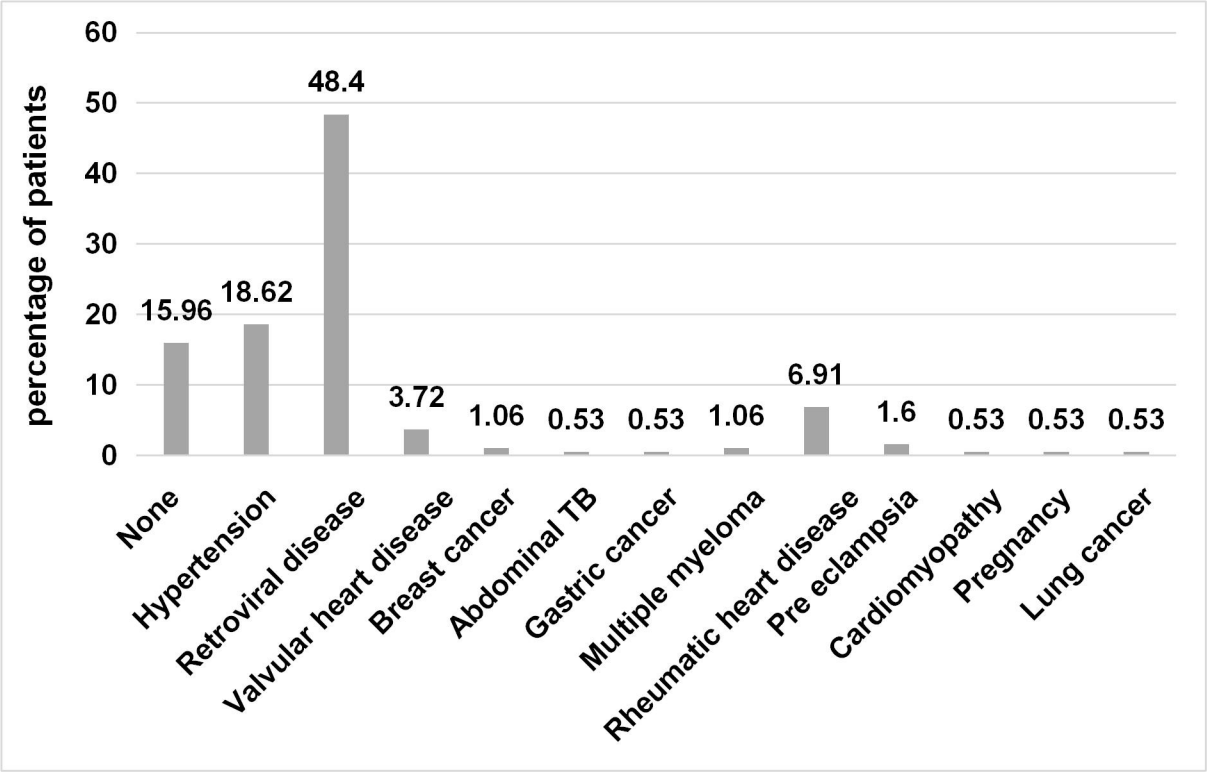

Figure 4: Co-morbidities of pericardial effusion.

Shown are the co-morbidities of patients with PE. Retroviral disease was the most significant co-morbidity, followed by hypertension. Rheumatic heart disease (N = 8 patients) and valvular heat disease (N = 14 patients) also occurred in significant numbers.

Figure 5 shows the proportions for the treatment outcomes of PE. Although the vast majority of the patients recovered (78.9%), there was a sizeable proportion of patients (8.8%) who demised. proportion died (8.8%).

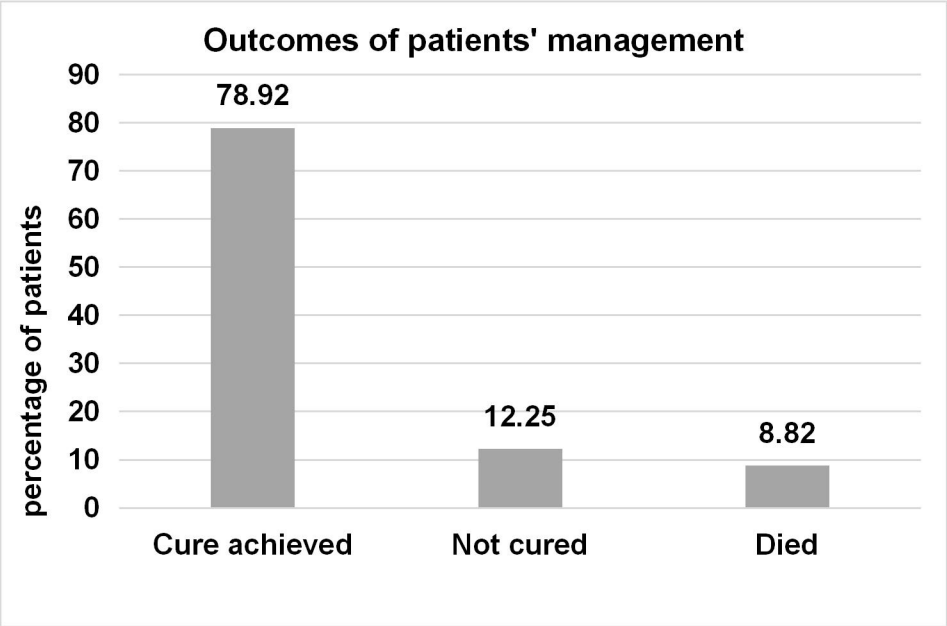

Figure 5: Outcome of pericardial effusion.

Regression analysis revealed that biochemistry outcomes of pericardial fluid were poorly correlated to the final aetiology of pericardial effusion (R = 0.4430; Table 4). Adjusted R^2 showed that only 19.2% of biochemistry results explained final aetiology of pericardial effusion (Table 4).

Table 4: Regression Analysis of the Biochemistry Results of Pericardial Fluid in relation to Aetiology.

Regression Statistics	
Multiple R	0.44302
R Square (R^2)	0.196267
Adjusted R Square	0.192288
Standard Error	0.419787
Observations	204

The results for ANOVA showed that biochemistry results for the pericardial fluid were significantly different from the final aetiology of the pericardial effusion (correlation coefficient = 2.632); with 95% CI: [2.53 - 2.74] and $p < 0.05$ (Table 5).

Table 5: The ANOVA Test of the Pericardial Fluid Biochemistry and Aetiology of Pericardial Effusion

	df	SS	MS	F	Significance F	
Regression	1	8.692501249	8.692501	49.32717	3.24E-11	
Residual	202	35.59671444	0.176221			
Total	203	44.28921569				
	Coefficients	**Standard Error**	**t-Stat**	**P-value**	**Lower 95% CI**	**Upper 95% CI**
Intercept	2.631511	0.053370971	49.30604	1.4E-114	2.526275	2.736747
X Variable 1	-0.08756	0.01246644	-7.02333	3.24E-11	-0.11214	-0.06297

Discussion

This 11-year retrospective document review examined the clinical and laboratory profile of patients who had presented with pericardial effusion (PE) at Dr George Mukhari Academic Hospital - a tertiary institution in Pretoria, (South Africa). Previous studies have defined PE as the abnormal accumulation of fluids in the pericardial space beyond 15 - 35ml [Peebles et al, 2011; Leedy et al, 2005; Imazio et al, 2009]. In developing countries, PE is a common manifestation in many pathological conditions, but is more often associated with inflammatory diseases, like tuberculous pericarditis or viral infections [Mayosi et al, 2014; Peebles et al, 2011; Leedy et al, 2005; Imazio et al, 2009; Shahbaz Sarwa et al, 2019].

In this present study, out of 204 eligible patients, there were 104 males (51.0%) and 100 females (49.0%), with a calculated prevalence of 32.8%. The value of the prevalence in this study is different from the prevalence reported in a study conducted in Tanzania and published in 2011 by Kabangila and his co-workers [Kabangila et al; 2011]. However, a similar prevalence was previously reported in a study from Cape Town, South Africa [Mayosi et al; 2014]. In this study, gender for patients with PE was evenly distributed unlike in other studies [Shahbaz Sarwar et al, 2019; Reuter et al, 2005]. In terms of age, majority of patients presenting with PE were between

25 and 55 years, representing the socially and economically active stage of life. This means that there is a high likelihood of exposure to health issues.

Radiological analysis which is an important key for PE assessment was found to be massively used at our institution (Dr George Mukhari Academic Hospital). Chest X-ray, which is a conventional technique, was found to be useful. Almost all patients underwent this procedure and it revealed the presence of cardiomegaly. These findings are consistent with the report by Peebles and colleagues [Peebles et al; 2011] on the importance of chest X-ray in showing the presence of cardiomegaly with or without indications on the mediastinal abnormalities.

Echocardiography was also frequently performed for the PE patients at Dr George Mukhari Academic Hospital. Its use shows that Dr George Mukhari Academic Hospital agrees with previous studies that echocardiography is the gold standard for PE patients and helps confirm diagnosis as well as follow-up treatment [Lind et al, 2011; Ntsekhe et al, 2012; Jung, 2012; Dunne et al, 2011]. The results of echocardiography show that most patients have mild PE, which corresponds to less than 50% of the cases of pericardial tap done in this study population.

Pericardial tap is not necessary for patient with mild PE. Only patients with moderate or large PE require pericardial tap to obtain fluid necessary for biochemistry and histological examinations. At our institution, there was a low rate of pericardial tap, which corresponds to less than 50% of the cases. These findings contradict previous studies that exudate effusion is the most common type of pericardial effusion [Hwang et al, 2012; Kabangila et al, 2011; Mayosi et al, 2019]. However, the reason of less than 50% cases of exudate in our study is that the majority of cases had a mild effusion (57.4%) and that made it too precarious to tap them because pericardial tap procedure also increases the risk of complications.

Neither chest CT scan nor MRI were performed at Dr George Mukhari Academic Hospital. It was assumed that since chest X-ray and echocardiography confirmed the presence of PE, a CT scan and MRI could have been a costly exercise with no significant diagnostic purposes. The ECG was, however, performed with clinical suspicion of PE. Its usefulness was recognized because it identified low voltage QRS, inverted T-wave, tachycardia, atrial fibrillation, ischemic heart disease, global flat T-wave, W-wave, and left ventricular strain. These findings are consistent with previous reports which showed that small QRS complex and T-wave abnormalities are common in PE [Buiatti et al, 2013; Jung, 2012; Eisenberg et al, 1996]. ECG

findings have no specific, diagnostic importance but they are important indicators as disease markers.

The findings of biochemistry on the exudate samples showed that tuberculosis was the most prominent finding in the fluid tapped from the pericardial space, followed by unspecified heart disease and uremic pericardial effusion, respectively. Other biochemistry findings were chronic pancreatitis, lung cancer, syphilis, and hypothyroidism. The findings of high TB related pericardial effusion were in line with the report of a study done in Tanzania [Kabangila et al, 2011], and studies by [Shahbaz Sarwa et al, 2019; Reuter et al, 2005]. However, the present audit shows that biochemistry data and etiological causes, were weakly correlated and the two variables were significantly different.

This report also reflects on important comorbidities, including retroviral disease, arterial hypertension, rheumatic heart disease, valvular heart disease, breast cancer, pre-eclampsia, abdominal tuberculosis, lung cancer, gastric cancer, and cardiomyopathy. The findings are consistent with previous studies that PE is generally associated with these comorbidities. In our study, PE with HIV-infection was at least 3-fold higher than any other comorbidity, just as Kabangila and his colleagues in Tanzania [Kabangila et al, 2011] and Mayosi and co-workers in South Africa [Mayosi et al, 2019] had reported that the pandemic of human immune deficiency viral infection, justifies this high prevalence of PE among the African population.

At Dr George Mukhari Academic Hospital, where this review was undertaken, there were no histological reports probably because the histology of the pericardial membranes was not so regularly requested in patients with PE, unless there was serious doubt on the aetiology. It is only when the nature, the aetiology and the location of the PE have been properly worked out that an appropriate management can be done. Santas and Nunez reporting on the prognostic implications of pericardial effusion, stressed once more, the importance of identifying the exact cause, in dealing with patients with PE [Santas et al, 2016]. They rightfully remarked that if PE is present in patients with heart failure, the mechanism still needs to be fully elucidated. Therefore, one should constantly consider the fact that the aetiology of PE is multifactorial and if not thoroughly investigated, it can have a negative impact on the management outcomes [Santas et al, 2016].

Pericardiocentesis was used to drain the fluid collection and majority of the patients obtained complete resorption. Malignancies were seen in less than 5% for breast cancer, lung cancer and

lymphoma; the findings of which contradict the report by Maisch et al who found that 68 out of 357 patients (19.0%) had a cancer-related PE [Maisch et al, 2010]. Our findings also did not show recurrence, six months post specific treatment for the cause of PE - another contradiction to a previous reports by Kim and his colleagues [Kim et al, 2010]; and by Sampat and co-workers [Sampat et al, 2010].

The survival rate of PE patients in our study was high, which can be attributed to most patients having mild PE. The survival rate of PE patients reduces, if the patients, concurrently have non-idiopathic Pulmonary Arterial Hypertension (PAH) [Sahay et al, 2013; Eysmann et al, 2019; Raymond et al, 2002; Zhang et al, 2011] and malignant PE [Kim et al, 2010]. In our study, only six patients had malignant PE as reflected by breast, lungs, multiple myeloma and gastric cancers.

Conclusions

In conclusion, pericardial effusion is encountered in any pathological condition in which there is an excessive production of pericardial fluid above a physiologic threshold of 25 - 35 ml. Its content can be an exudate or a transudate according to the underlying aetiology. It can present with one of the following aspects: serous, sero-haemorrhagic, pure haemorrhagic, chylous or in extremely rare cases, filled with air or pus [Imazio et al, 2019].

The incidence of PE increases in any environment where infectious diseases are more prominent and there is presence of malignancies or connective tissue damage. The HIV pandemic and tuberculosis are presently the major contributory factors of pericardial effusion. Therefore, one should expect to have a high prevalence of PE in a setting where HIV and Tuberculosis are present. In our 11-year retrospective study from Pretoria (South Africa), the authors found a prevalence of 32.8% of PE. The chest X-ray with all the findings on the cardiac silhouette and the mediastinum configurations was a source of the invaluable information to PE physician. 12-lead ECG was also an important procedure in the clinical examination of PE. The chest X-ray together with the ECG could provide good screening tests for patients with PE.

Physicians at Dr George Mukhari Academic Hospital rely on these conventional investigations to diagnose more than a third of the patients. With proper diagnosis, the curative outcome was achieved for most of the patients with low mortality rate at this healthcare institution.

Notwithstanding the fact that PE is a serious medical condition, it is the gravity of this condition that motivated the authors to study its clinical and laboratory profile which have never been reported on from this institution. We further emphasize the need for an early diagnosis and the choice of appropriate management modalities. From the information derived from this study at Dr George Mukhari Academic Hospital, we recommend further research to focus on expanding this area of knowledge in other health settings.

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