Original Article

Clinical and Etiological Profile of an Exudative Pleural Effusion in a Tertiary Care Center

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Abstract

Background: Pleural effusion is common clinical entity in day-to-day clinical practice. There are various etiologies for pleural effusion. Among those tubercular pleural effusion, parapneumonic effusion, malignant effusion, and congestive heart failure were the most common causes of pleural effusion. Here, we have done a retrospective study to see the etiology of pleural effusion in our tertiary care center. **Patients and Methods:** This retrospective study conducted in a tertiary care center over 1 year period. A total of 63 patients were included in this study after verifying in patient records of all patients who were admitted with exudative pleural effusion. The demographic data collected and complete history was obtained. Investigations such as complete hemogram, random blood sugar; renal function tests, serum proteins, chest x-ray, and pleural fluid analysis and investigations such as ultrasonogram of the chest and abdomen, echocardiogram, computed tomography scan of chest, fine-needle aspiration cytology, and pleural biopsy reports (if done) were collected. **Results:** Among the study participants, 40 were male and 23 were female patients with male-to-female ratio of 1.7:1. Mean age of the study population was 48.8 ± 18.7 years. The most common presenting symptom was dyspnea (84%) followed by cough (80%), fever (65%), and chest pain (43%). The most frequent cause of pleural effusion was tuberculosis in 38% of patients, followed by parapneumonic effusion (28.5%) and malignant pleural effusion (22.2%). Three patients had chylothorax, two patients had pancreatic pleural effusion and the diagnosis was unknown in two patients. Mean ± standard deviation (SD) adenosine deaminase (ADA) value of the study population was 45.3 ± 28.1. Mean ± SD of ADA values in tuberculous, parapneumonic, and malignant pleural effusion was 54.5 ± 16.8, 65.2 ± 30.7, and 18.2 ± 11.0, respectively. **Conclusions:** Tuberculosis is one of the common causes of exudative effusions along with parapneumonic effusions and malignancy. Pleural fluid ADA levels are highly sensitive with good specificity for the diagnosis of etiology of tubercular effusions. However in view of high levels of ADA in pleural fluid in parapneumonic effusions also, other measures such as clinical evaluation, lymphocyte to neutrophil ratio, and glucose levels are necessary to separate both these entities.

Keywords: Adenosine deaminase, pleural effusion, tuberculosis

Introduction

Pleural effusion results from either excess fluid accumulation in pleural space or decreased absorption by pleural lymphatics.[1] Normally, 0.13 mL/kg of body weight of fluid is present in pleural space. This small amount of fluid acts as a lubricant to allow the smooth sliding of parietal and visceral pleura during respiration.[2] Normal amount of fluid is maintained by the balance between hydrostatic, oncotic pressure of pleural capillaries and intrapleural pressure, oncotic pressure of pleural fluid. Any imbalance of the above mechanism will lead to excess fluid accumulation in pleural space.[3] Pleural effusions were either transudative or exudative, Light's criteria[4] are commonly used to differentiate exudative effusion from transudative effusion. Pleural fluid is exudative if it meets any one of the following criteria-pleural fluid protein/serum protein ratio >0.5 or pleural fluid lactate dehydrogenase (LDH)/serum LDH ratio >0.6 or pleural fluid LDH level greater than two-thirds the upper limit. Congestive heart failure is the most common condition that produce transudative pleural effusion followed by hepatic hydrothorax. Nephrotic syndrome, hypoproteinemia are some other common causes.[5] Common causes of exudative effusion include tuberculosis, parapneumonic effusion, viral infections, and malignancy.[6] Other causes include hypothyroidism,

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pulmonary embolism with infarction, connective tissue disorders, pancreatitis, esophageal rupture (Boerhaave's syndrome), collagen vascular disorders, chylothorax, and hemothorax.

On chest radiograph, pleural effusion is usually seen as an area of homogeneous opacity with ill-defined margins with tracking along the lateral chest wall. If the fluid is small (up to 50 mL) lateral chest radiograph is better than posteroanterior chest X-ray.[7] Computed tomography (CT) is usually required to quantify the fluid and to identify loculations along with the presence of parenchymal and mediastinal abnormalities which may be missed on the standard radiograph. Ultrasonography chest recently gained more importance in diagnosis of pleural effusion and it is more sensitive than chest radiograph. It is safe, there is no radiation and has the benefit of repeatability.[8] It can be used to identify the loculations and septations in pleural cavity. It can also be used to guide aspiration and choose site of insertion of intercostal tube.

A provisional diagnosis is usually made in over 90% of patients based on clinical features and pleural fluid analysis.[9] However, definitive diagnosis is usually made by either identification of malignant cells, pleural biopsy or identification of a specific organism in pleural fluid. Thoracentesis is indicated in all patients with suspicion of exudative pleural effusion with thickness >10 mm in lateral chest radiograph, ultrasound, or in CT scan. The first step is to differentiate between transudative from exudative pleural effusion. All the exudative effusions should be observed for color and odor. Laboratory tests that are performed to analyze the pleural fluid include total leucocyte count, differential count, and biochemical tests such as proteins, glucose, LDH, amylase, microbiological examinations such as AFB stain, Gram stain, culture sensitivity, adenosine deaminase (ADA) levels, and cytopathology. Additional investigations such as triglycerides and chylomicrons are requested depending on the clinical dilemma. Closed pleural biopsy is indicated if there is suspicion of tuberculosis and ADA levels were low. Thoracoscopy is a highly sensitive tool for evaluation of undiagnosed exudative pleural effusions.[10] Two diagnoses that commonly obtained with thoracoscopic pleural biopsy are tuberculosis and malignancy.

This is a retrospective study conducted to look at the etiology of exudative pleural effusion in a tertiary care center.

Patients and Methods

This study was performed in the Department of Pulmonary Medicine, Nizam's Institute of Medical Sciences, a tertiary care center in Hyderabad, Telangana. The main aim of this study was to assess the clinical and etiological profile of exudative pleural effusions. This was a retrospective study which included all in-patients admitted with exudative pleural effusion from January 2017 to December 2017. Totally 63 patients with exudative pleural effusion were recruited for this study. All patients with transudative pleural effusions were excluded.

The demographic data collected included age, sex, and address. A detailed history including chief complaints, history of presenting illness, significant history including comorbidities was obtained. Investigations obtained included complete hemogram, random blood sugar; renal function tests, thyroid function tests, serum proteins, chest X-ray, and pleural fluid analysis, ultrasonogram of the chest and abdomen, echocardiogram, CT scan of chest, fine-needle aspiration cytology and pleural biopsy reports (if done).

All the data were entered into Microsoft Excel and Statistical Package for the Social Sciences (SPSS, Chicago, U.S) version 20.0 was used to analyze the data. All data were analyzed for frequency distribution, and results were given in mean and standard deviation (SD). Analysis of variance and *t*-test were used to test the significance in between group variables. $P < 0.05$ was considered as statistically significant.

Results

This retrospective study was conducted in a tertiary care hospital in Hyderabad. Totally 63 patients were recruited during 1 year period.

Among the study participants, 40 were male and 23 were female with male-to-female ratio of 1.7:1.

Age ranged from 14 to 85 years. Mean age of the study population was 48.8 ± 18.7 years. Majority of the study population (63.4%) were between 20 and 60 years of age. Only five patients were below 20 years.

The most common presenting symptom was dyspnea (84%) followed by cough (80%), fever (65%), and chest pain (43%). Loss of weight and loss of appetite were present in 27% of the patients. Hoarseness of voice was present in two patients and jaundice, hemoptysis, and pedal edema; were present in one patient each.

Majority of the study population had 3–4 weeks duration of symptoms before coming to our institution. Mean ± SD duration of symptoms was 3.82 ± 2.8 weeks. Very few participants had symptoms of <1 week duration.

The most frequent etiology of pleural effusion was tuberculosis in 38% of patients, followed by parapneumonic effusion (28.5%), malignant pleural effusion (22.2%). Three patients had chylothorax, two patients had pancreatic pleural effusion, and the diagnosis was unknown in two patients.

All the patients with tuberculous pleural effusion had ADA levels above the cut-off value (30 U/L) with mean ± SD value of 54.50 ± 16.8 whereas, 88% of patients with malignant effusion had ADA levels below the cut-off value (30 U/L). Only two patients with malignant effusion had ADA value above cut-off value ($P < 0.01$).

Discussion

This retrospective study was conducted in a tertiary care hospital in Hyderabad. Totally 63 patients were included during 1 year period. Among the study participants, 40 were male

and 23 were female patients with a male-to-female ratio was 1.7:1 [Figure 1]. Age is ranged between 14 and 85 years. Mean age of the study population was 48.8 ± 18.7. Majority of the study population (63.4%) was between 20 and 60 years of age because people of this age group were physically active and are exposed to occupation hazards, smoking, and infections. Only five patients were below 20 years [Table 1]. A study in Qatar by Khan *et al*.[11] showed that the mean age of the study population was 47.4 ± 18.2 years and male-to-female ratio was 3:1. Similarly in a study by Arya Shashikant and Archana[12] from India showed that the mean age of their 100 study population was 38.10 years with most of the study population were between 21 and 60 years of age and male-to-female ratio was 2.3:1. Another study from India by Raghavan *et al*.[13] included 100 patients of which majority of male patients with an age group of 30–60 years with a mean of 46.49 ± 13.5 years.

In our study, most common presenting symptom was dyspnea (84%) followed by cough (80%), fever (65%), chest pain (43%). Loss of weight and loss of appetite was present in 27% of the patients. Hoarseness of voice was present in two patients and jaundice, hemoptysis; pedal edema was present each in one patient [Table 2]. Similar study by Al-Alusi[14] included 100 patients in their study, of which the most common symptoms were dyspnea (87%), cough (86%), fever (79%) followed by chest pain (67%). In a similar study done by Mbata Godwin *et al*.,[15] the major symptoms were cough in 156 (78.4%) patients followed by chest pain in 142 (71.4%) and dyspnea in 130 (65.3%). Desalew *et al*.[16] in their study of 110 patients, cough fever, and weight loss were present in 90%, 77.3%, and 77.3% of cases, respectively. Majority of the study population had 3–4 weeks duration of symptoms before coming to our institution. Mean ± SD duration of symptoms 3.82 ± 2.8 weeks. Very few participants had symptoms of <1 week duration [Figure 2].

Table 1: Age wise distribution of study population

Age group	Number	Percentage
<20	5	8.0%
20-39	16	25.0%
40-60	24	38.0%
>60	18	29.0%

Table 2: Symptomology of study population

Symptom	Frequency	Percentage
Dyspnea	53	84.0%
Cough	51	80.0%
Fever	41	65.0%
Chest pain	27	43.0%
Loss of appetite	17	27.0%
Loss of weight	17	27.0%
Hoarseness of voice	2	3.0%
Jaundice	1	1.50%
Hemoptysis	1	1.50%
Pedal edema	1	1.50%

The most frequent cause of pleural effusion was tuberculosis in 38% of patients, followed by parapneumonic effusion (28.5%), malignant pleural effusion (22.2%). Three patients had chylothorax, two patients had pancreatic pleural effusion and the diagnosis was unknown in 2 patients [Figure 3]. In a similar study done by Adeoye *et al*.,[17] the most common cause of pleural effusion was tuberculosis in 32.9% of patients, followed by malignancy (29.1%) and pneumonia (15%). Mbata Godwin *et al*.[15] in a 5-year retrospective study, the most common etiology was tuberculosis in 42.2% of patients followed by parapneumonic effusion in 14.07% of patients. A study from Qatar by Khan *et al*.[11] showed that the most common cause of pleural effusion was tuberculosis in 32.5% of patients, followed by parapneumonic effusion, malignant effusion, and cardiac failure in 19%, 15.5%, 13%, respectively.

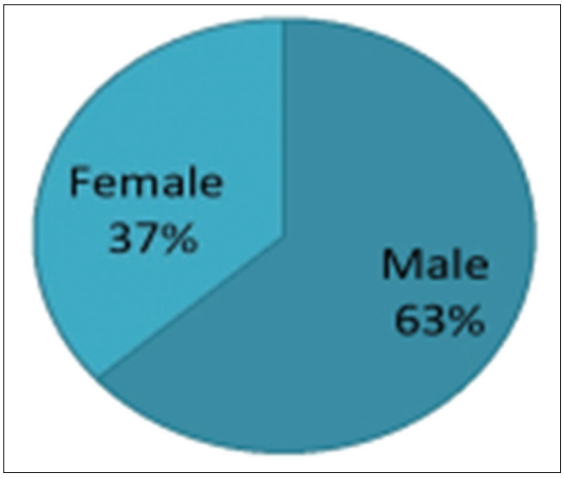

Figure 1: Gender distribution of the study population

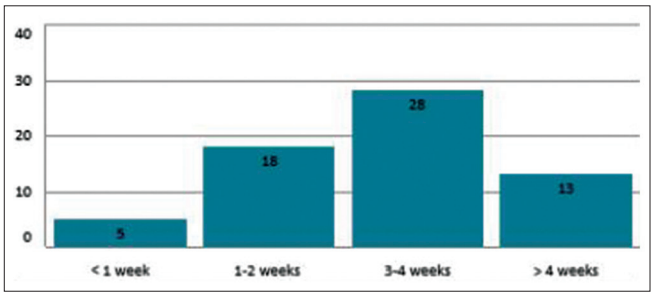

Figure 2: Duration of symptoms of the study population

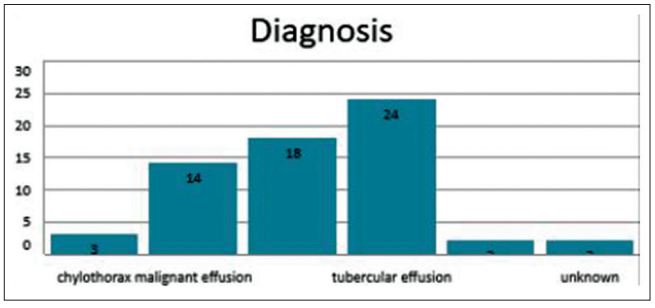

Figure 3: Etiology of pleural effusion of the study population

In 1.5% of cases, the etiology of pleural effusion was not found. Al-Alusi[14] included 100 patients in their study which showed that the most frequent cause of pleural effusion was tuberculosis, which occurred in 38% of patients and malignant disease accounted for 34% of cases.

In our study, mean ± SD of age in tuberculous, parapneumonic, and malignant pleural effusion was 51.8 ± 16.5, 45.7 ± 21.6, and 44.6 ± 19.9, respectively. Mean ± SD of duration of symptoms was 4.22 ± 3.2, 3.59 ± 3.2, and 3.94 ± 2.3 weeks in tuberculous, parapneumonic, and malignant pleural effusions, respectively. Similar study by the Desalew *et al*.[16] showed that the mean duration of the clinical symptoms was 66 days prior to hospital visit with a range of 3–365 days which was high when compared to our study, this may be due to better availability of health-care facilities in India compared to Ethiopia where above study was conducted. Pleural fluid glucose ranged between 3 and 290 mg/dl and mean ± SD value was 67.7 ± 48.2. Mean ± SD of glucose in tuberculous group was 82.7 ± 34.3, in malignant group, it was 72.7 ± 43.6. In parapneumonic effusion group, it was 31.2 ± 24.6. Pleural fluid lymphocyte (%) ranged from 0 to 100%. Mean ± SD value of study population was 47.9 ± 33.3 (%). Mean ± SD of lymphocyte (%) of tuberculous, parapneumonic, and malignant pleural effusion was 74.5 ± 23.7, 43.9 ± 29.4, and 16.3 ± 14.9 (%), respectively [Table 3].

In our study, ADA value ranged between 1.7 and 130U/L. Mean ± SD ADA value of the study population was 45.3 ± 28.1. Mean ± SD of ADA values in tuberculous, parapneumonic, and malignant pleural effusion was 54.5 ± 16.8, 65.2 ± 30.7, and 18.2 ± 11.0, respectively [Table 3]. Gupta *et al*.[18] in their study showed that in tuberculous group the mean ± SD ADA was 67.34 ± 22.85, while in nontuberculous group, it was 18.60 ± 9.12. In our study, the mean ADA value in parapneumonic effusion group was higher than tuberculous effusion group and this can be explained by the fact that differentiation between parapneumonic effusions and empyema was not done leading to high ADA levels. In a similar study by Valdés *et al*.,[19] the mean ADA concentration in the patients with tuberculous effusion was 111.1 U/I and in empyema it was 139.7 U/I. Hence, pleural ADA carries high diagnostic importance for tuberculosis and it should be done wherever possible. ADA levels were elevated not only in lymphocytic effusions but also in neutrophilic effusions. Extremely high ADA levels were seen in lymphoma and empyema.[20] Shenoy *et al*.[21] conducted a retrospective study on patients who were diagnosed to have tuberculous pleural effusion and empyema of nontubercular origin. Among 46 patients, 25 patients with tuberculous pleural effusion and 21 patients with empyema were diagnosed, respectively. Pleural fluid ADA levels among tuberculous pleural effusion and empyema were 109.38 ± 53.83 U/L and 141.20 ± 71.69 U/L respectively. They concluded that apart from ADA, other parameters like lymphocyte to neutrophil ratio and glucose levels should be used to diagnose tubercular pleural effusion.

In our study, ADA level in all 24 patients of tuberculous pleural effusion was above diagnostic cut-off (30 U/L), whereas out of 14 malignant effusion patients, only two patients had above the cut-off value and 12 patients had ADA value below the cut-off (30 U/L) and it was statistically significant ($P < 0.05$) [Table 4]. Helmy *et al*.[22] did a retrospective study with 30 patients. There was a statistically significant difference according to the levels of pleural fluid ADA between tuberculous pleural effusion and malignant pleural effusion groups and confirmed that ADA is a very useful parameter for the differential diagnosis of tuberculous and malignant pleural effusion. In review article by Goto *et al*.,[23] the sensitivity of ADA reported in ranged from 47.1% to 100% and the specificity from 50% to 100%. In our study, ADA (cut-off 30 U/L) had 92% sensitivity, 100% specificity and positive and negative predictive values were 1.00 and 0.85 for diagnosis of tuberculosis. In a similar study by Bandrés Gimeno *et al*.,[24] the cut-off value of ADA >23 U/L had sensitivity, specificity, positive, and negative predictive values were 96%, 100%, 1.0%, and 0.94%, respectively, for differentiating tuberculous pleuritis or neoplasia with lymphocytic exudate. Therefore, ADA value is sensitive and specific test for the diagnosis of tuberculous pleurisy. The results of ADA levels should be interpreted in parallel with clinical findings and other pleural fluid parameters such as lymphocyte to polymorphs ratio, glucose levels, and cytopathology to differentiate between tuberculous effusion and parapneumonic effusion.

Table 3: Pleural fluid characteristics of major types of effusions

	Tuberculous effusion (24)	Malignant effusion (14)	Parapneumonic effusion (18)	*P*
Male	15 (62.5%)	8 (57%)	11 (61%)	0.950
Female	9 (37.5%)	6 (45%)	7 (39%)	
Age	51.8±16.53	45.7±21.6	44.6±19.29	0.420
Symptoms duration (weeks)	4.22±3.26	3.59±3.38	3.94±2.26	0.819
TLC	1442.8±1144	425.3±304.2	3172.2±2654.5	0.00004*
Lymphocytes (%)	75.58±23.7	49.3±29.4	16.39±14.8	0.0000*
LDH	1363.5±1083	1002.9±949.5	2309.6±2018	0.025*
Amylase	61.63±54.9	177.2±156.4	58.5±38.6	0.0085*
ADA	54.50±16.8	18.2±11.0	65.2±30.2	0.0000*

Table 4: Pleural fluid Adenosine deaminase (ADA) levels with their significance

Group	ADA levels	Frequency	Mean±SD	*P*
Tuberculous effusion (*n*=24)	<30	0 (0%)	54.50±16.8	<0.05*
	>30	24 (100%)		
Malignant effusion (*n*=14)	<30	12 (88%)	18.2±11.0	
	>30	2 (12%)		

Conclusions

Pleural effusion is common clinical entity in day-to-day practice in India. Tuberculosis is one of the common causes of exudative effusions along with parapneumonic effusions and malignancy. Pleural fluid ADA levels highly sensitive with good specificity for the diagnosis of etiology of tubercular effusions. However, in view of high levels of ADA in parapneumonic effusions also, other measures such as clinical evaluation, lymphocyte to neutrophil ratio, and glucose levels are necessary to separate both these entities.

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Conflicts of interest

There are no conflicts of interest.

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