Original Article

Spectrum and outcome in patients with unilateral pleural effusion admitted in a tertiary care hospital

Neeraj Saini[1], Saumya Ahluwalia[1], Srishti Ahluwalia[1], Pavneet Kaur Selhi[2], Akashdeep Singh[3]

Departments of [1]Medicine, [2]Pathology, [3]Pulmonary Medicine, Dayanand Medical College and Hospital, Ludhiana, Punjab, India

Abstract

Background: Unilateral pleural effusion is a challenge for a physician as the differential diagnosis is varied; sparse epidemiological data are available from India on this subject.

Methods: We prospectively studied consecutive adult patients (aged >18 years) presenting with unilateral pleural effusion who underwent thoracocentesis with or without radiological guidance for diagnostic workup.

Results: Over a period of 1 year, 116 patients admitted with unilateral pleural effusion were included, majority (63.8%) were in the age group of 20–60 years. Most common presenting symptoms were shortness of breath (56%), fever (53.4%), cough (52.5%), chest pain (35.3%), anorexia (34.5%) and weight loss (18.9%). Ninety-nine patients (85.3%) had exudative and 17 patients (14.6%) had transudative pleural effusion. Amongst exudative, tuberculosis (TB) pleural effusion was the most common cause (45.7%) followed by para-pneumonic (12.9%), malignant (10.3%), among others. TB (44.8%) and malignancy (10.3%) were common aetiologies among the lymphocyte-predominant effusions, whereas para-pneumonic effusion (11.2%) and empyema (4.3%) were common aetiologies amongst the neutrophil-predominant effusions. Pleural fluid lymphocyte-to-neutrophil ratio >0.75 increased the sensitivity and specificity to diagnose TB pleural effusion.

Conclusions: Patients with TB pleural effusion were comparatively younger as compared to patients with malignant and para-pneumonic pleural effusion. Most pleural effusions resolved with treatment of underlying cause.

Keywords: Admitted patients, aetiology, unilateral pleural effusion

Address for correspondence: Dr Akashdeep Singh, Professor and Head, Department of Pulmonary Medicine, Dayanand Medical College and Hospital, Ludhiana 141 001, Punjab, India.
E-mail: drsinghakash@gmail.com

Submitted: 21-Sep-2021 **Revised:** 22-Oct-2021 **Accepted:** 25-Oct-2021 **Published:** 14-Apr-2022

INTRODUCTION

Pleural effusions are a common medical problem with more than fifty recognised causes, including disease local to the pleura or underlying lung, systemic conditions, organ dysfunction and drugs.[1] Unilateral pleural effusion is a challenge for a physician as the differential diagnosis is varied. Evidence-based decision needs robust information about the aetiology and epidemiology of a disease in a particular region. The aetiology can vary according to the geographical area, outpatient or inpatient healthcare setting, patient age and advances in the diagnostic methods among other factors.

Access this article online	
Quick Response Code:	Website: www.jcsr.co.in
	DOI: 10.4103/jcsr.jcsr_57_21

How to cite this article: Saini N, Ahluwalia S, Ahluwalia S, Selhi PK, Singh A. Spectrum and outcome in patients with unilateral pleural effusion admitted in a tertiary care hospital. J Clin Sci Res 2022;11:58-71.

In fact, over the years with increasing prevalence of human immunodeficiency virus (HIV) and malignancies, the pattern of unilateral pleural effusion is also evolving with a shift from classical presentations of disease to atypical presentation. The scenario is further compounded by confounding interpretation of laboratory investigations requiring hospitalisation to establish a correct diagnosis.

In our country, there is a paucity of epidemiological data about unilateral pleural effusions, especially in admitted patients. In this study, an attempt has been made to study unilateral pleural effusion to delineate aetiology, clinical spectrum and outcome in patients admitted in a tertiary care teaching hospital.

MATERIAL AND METHODS

All adult patients aged more than 18 years admitted with unilateral pleural effusion in Department of Medicine and Allied Specialties of Dayanand Medical College and Hospital (DMCH), Ludhiana, were prospectively studied from 1st January to 31st December 2019. The study was initiated after obtaining Institutional Ethics Committee clearance. Written informed consent was obtained from all the participants.

All patients who underwent thoracocentesis for diagnostic workup with or without radiological guidance were included. Patients aged <18 years, those with bilateral pleural effusion and those not giving consent for enrolment in the study were excluded. Laboratory investigations considered necessary by the treating clinicians were performed. These included complete haemogram, serum biochemistry, urinalysis, chest radiograph, thoracic ultrasonography (USG), computed tomography (CT) and magnetic resonance imaging of the thorax, amongst others. Pleural fluid (Pf) analysis included biochemical, cytopathological analysis, nucleic acid amplification test (NAAT), bacterial culture and histopathology.

Diagnostic criteria for each clinical diagnosis were as follows. Pleural effusion was categorised as exudative applying either of the two definitions.[2,3] As per Light's criteria,[2] if one or more of the following criteria were present, the pleural effusion was classified as exudative: (i) The ratio of pleural fluid protein-to-serum protein is >0.5; (ii) the ratio of pleural fluid lactate dehydrogenase (LDH)-to-serum LDH is >0.6 and (iii) the pleural fluid LDH level is greater than two-thirds of the upper limit of normal for serum LDH.[2] As per another definition,[3] pleural effusion was classified as exudate if one or more of the following criteria were present: (i) pleural fluid protein >2.9 g/dL; (ii) pleural fluid cholesterol >45 mg/dL; and (iii) Pf LDH >0.45 times upper limit of normal serum LDH.[3] Pleural effusion was classified as transudative if none of the above-mentioned criteria were present.

Based on the chest X-ray, the pleural effusion was graded as mild, moderate and massive: (i) only costophrenic angles are blunted (mild); (ii) blunting of costophrenic angle and positive meniscus sign seen and fluid level below second intercostal space (moderate); and (iii) blunting of costophrenic angles, when fluid level is above the second intercostal space, complete opacification of hemithorax and mediastinal shift (massive).[4]

Patients were diagnosed with confirmed tuberculosis (TB) pleural effusion if one of the following criteria was met: (i) acid-fast bacilli (AFB) smear-positive when pleural fluid was used as the source specimen, and the *Mycobacterium tuberculosis* bacterium was grown in culture or was detected by cartridge-based NAAT (CBNAAT); (ii) in the absence of granulomatous lung disease for other reasons, a pleural biopsy revealed a granulomatous lesion with or without caseous necrosis and (iii) sputum mycobacterial culture was positive for *M. tuberculosis* and the pleural effusion improved with anti-TB treatment (ATT).[5] Probable TB pleural effusion is defined as lymphocyte-predominant exudates with adenosine deaminase (ADA) >40 IU/L in pleural fluid in the absence of evidence of malignancy and improves after ATT.[5]

Para-pneumonic effusion was diagnosed as **(**i) typical para-pneumonic pleural effusion if pleural fluid glucose was more than 40 mg/dL, pH >7.2, and LDH <3 × upper limit normal for serum, Gram's stain and culture being negative; (ii) borderline complicated pleural effusion if pleural fluid pH was between 7.0 and 7.20 or LDH was elevated more than 3 times upper limit normal and glucose more than 40 mg/dL, Gram's stain and culture negative and (ii) simple complicated pleural effusion if pleural fluid pH was <7.0 or glucose <40 mg/dL or Gram's stain or culture positive (excluding skin contaminants), but there are no loculation and no frank pus. The pleural effusion was categorised as complicated pleural effusion if pleural fluid pH was <7.0 and/or glucose was <40 mg/dL or Gram's stain or culture were positive and the pleural effusion was multiloculated. Simple empyema was diagnosed if frank pus was present, but it was free flowing. In complex empyema, frank pus was present along with multiloculation.[6]

Malignant effusions were also divided into confirmed and probable categories as per standardised criteria.[7]

A diagnosis of definitive TB empyema was defined as the presence of frank pus on pleural aspiration with Pf smear and/or culture being positive for AFB and/or *M. tuberculosis* on two or more occasions.[8] Probable TB empyema was defined as empyema in patients who had radiological evidence of active pulmonary TB on CT scan (nodular consolidation in apical segments/tree-in-bud appearance/mediastinal lymphadenopathy with central necrosis) or concomitant-positive sputum smears for AFB. Tuberculin skin test (TST) was considered positive as per standard case definition.[9]

The outcome studied was variables such as diagnosis at the time of discharge/discharge on request/death/discharge against medical advise (DAMA), length of stay in hospital, clinical/laboratory/treatment profile of admitted patients, details of preadmission workup and treatment outside and surgical intervention (s); if any and follow-up post-discharge at months: 2, 4 and 6; wherever feasible.

Statistical analysis

Data were described in terms of range, mean ± standard deviation (SD), frequencies as appropriate. All statistical calculations were done using IBM Statistical Package for the Social Sciences (SPSS) for Windows, version 21 (IBM Corp., Armonk, N.Y., USA).

RESULTS

Over a period of 1 year (January 2019 to December 2019), 116 patients aged ≥18 years were admitted with unilateral pleural effusion. Their mean age was 51.5 ± 17.2 years; there were 81 (69.8%) males. Majority of the patients (n = 46, 39.6%) were in the age group of 41-60 years. Most of them were from urban area (59.5%).

The average duration of symptoms before admission was 21 days. The most common symptoms observed in this study were shortness of breath (56%), followed by fever (53.4%), cough (52.5%) and chest pain (35.3%) (Table 1). Fever was continuous in 15 (13%) patients and intermittent in 47 (41%) patients. It was associated with chills and rigors in 49 (42%) patients. Shortness of breath was Grade 3 (Modified Medical Research Council grading) in 36 patients (31%).

Right-sided (n = 25, 21.6%) pleuritic chest pain was more common than left sided (n = 16, 13.7%). Character of chest pain was sharp in most of the patients (n = 41, 35.3%).

Table 1: Presenting complaints

Presenting complaints	No. (%)
Fever	62 (53.4)
Continuous	15 (12.9)
Constitutional symptoms	
Intermittent	47 (40.5)
Chills and rigors	49 (42.2)
Anorexia	40 (34.5)
Evening rise	23 (19.8)
Weight loss	22 (19.0)
Night sweats	13 (11.2)
Fatigability	6 (5.2)
Respiratory symptoms (MMRC Grade)	
Shortness of breath	65 (56.0)
1	51 (44.0)
2	15 (12.9)
3	36 (31.0)
4	14 (12.1)
Cough	61 (52.6)
Chest pain	41 (35.3)
Site	
Left	16 (13.8)
Right	25 (21.6)
Character	
Sharp	41 (35.3)
Onset	
Insidious	33 (28.4)
Sudden	5 (4.3)
Course	
Progressive	35 (30.2)
Severity	
Mild	13 (11.2)
Moderate	20 (17.2)
Severe	1 (0.9)
Increase with inspiration and cough and decrease with expiration	39 (33.6)
Haemoptysis	2 (1.7)
Others	
Pain abdomen	16 (13.8)
Vomiting	12 (10.3)
Nausea	5 (4.3)
Abdominal distension	4 (3.4)
Altered sensorium	4 (3.4)
Jaundice	3 (2.6)
Burning micturition	3 (2.6)
Palpitations	2 (1.7)
Constipation	2 (1.7)
Lower back ache	2 (1.7)
Loose stools	1 (0.9)
Increased frequency of micturition	1 (0.9)
Decreased urine output	1 (0.9)
Headache	1 (0.9)
Seizures	1 (0.9)
Quadriparesis	1 (0.9)
Hemiparesis	1 (0.9)

MMRC=Modified Medical Research Council

There were 36 patients (31%) with a history of diabetes mellitus (DM), 34 (29.3%) patients with hypertension, 25 (21.6%) patients with coronary artery disease (CAD), 19 patients (16.4%) with a history of TB, 18 (15.5%) patients with chronic kidney disease (CKD), 12 (10.2%) patients with diagnosed malignancy, 11 (9.5%) patients with hypothyroidism, 8 (6.9%) patients with chronic liver

disease (CLD), 8 (6.9%) patients with chronic obstructive pulmonary disease (COPD), 4 (3.4%) patients with old cerebrovascular accident, 3 (2.6%) patients with bronchial asthma, 2 (1.7%) patients with *cor-pulmonale* and 1 (0.9%) patient each with interstitial lung disease, seizure disorder, people living with HIV, inflammatory bowel disease and valvular heart disease (Table 2).

Table 2: Comorbid conditions

Comorbidities	No. (%)
DM	36 (31.0)
HTN	34 (29.3)
CAD	25 (21.6)
TB	19 (16.4
Pulmonary TB	15 (12.9)
Abdominal TB	2 (1.7)
Disseminated TB	1 (0.9)
Other	1 (0.9)
CKD	18 (15.5)
Malignancy	12 (10.3)
Hypothyroidism	11 (9.5)
CLD	8 (6.9)
COPD	8 (6.9)
CVA	4 (3.4)
BA	3 (2.6)
Cor pulmonale	2 (1.7)
ILD	1 (0.9)
OSA	1 (0.9)
Valvular heart disease	1 (0.9)
Coeliac disease	1 (0.9)
Seizure disorder	1 (0.9)
PLHIV	1 (0.9)
IBD	1 (0.9)

PLHIV=People living with human immunodeficiency virus; IBD=Inflammatory bowel disease; BA=Bronchial asthma; OSA=Obstructive sleep apnoea; ILD=Interstitial lung disease; COPD=Chronic obstructive pulmonary disease; CVA=Cerebrovascular accident; CAD=Coronary artery disease; CLD=Chronic liver disease; DM=Diabetes mellitus; HTN=Hypertension; CKD=Chronic kidney disease; TB=Tuberculosis

Amongst the 19 patients (16.4%) with a history of TB, 15 patients (12.9%) had pulmonary TB, 2 patients (12.9%) had abdominal TB, 1 patient (0.9%) had disseminated TB and 1 patient (0.9%) had skeletal TB in the past.

On general physical examination, sensorium was normal in 109 (93.9%) patients. Seven patients were found to be drowsy because of hepatic encephalopathy (n = 4; 3.4%), uraemic encephalopathy (n = 2; 1.7%) and brain metastasis (n = 1; 0.9%). Pallor (n = 72, 62.10%), pitting oedema (n = 24, 20.7%) and lymphadenopathy (n = 7, 5.1%) were the most common physical signs. Out of 7 patients with lymphadenopathy, 4 had cervical, 2 had axillary and 1 had supraclavicular lymphadenopathy.

Chest radiograph showed right-sided pleural effusion in 67 (57.8%) patients and left sided in 49 (42.2%) patients. It was observed that there were a greater number of patients with mild pleural effusion (n = 64, 55.2%; this include 20 patients with secondary pleural effusion) as compared to moderate (n = 42, 36.2%) and severe (n = 10, 8.6%). Other chest radiograph findings were consolidation (n = 21, 18.1%) and cavitatory changes (n = 4, 3.4%).

Ultrasonography of the chest was done in 52 patients (44.8%). Unilateral pleural effusion was seen in all of 52 (44.8%), septations were present in 14 (12.1%), consolidation in 5 (4.3%) and pleural thickening in 1 patient.

Diagnostic aspiration was done in all cases (n = 116, 100%). Gross appearance of pleural fluid sample was straw coluored in 53 patients (45.7%), haemorrhagic in 24 patients (20.7%), clear in 20 patients (17.2%), turbid yellow in 12 patients (10.3%) and 7 patients (6%) had pus. There was no chylous pleural effusion observed in the present study (Table 3).

Table 3: Gross appearance of pleural fluid

Gross appearance	No. (%)
Straw coloured	53 (45.7)
Haemorrhagic	24 (20.7)
Clear	20 (17.2)
Turbid, yellow	12 (10.3)
Pus	7 (6.0)
Total	116 (100.0)

Of all admitted patients (n = 116), 99 (85.3%) patients had exudative and 17 (12.1%) patients had transudative (14.7%) nature of pleural effusion. Amongst the 99 patients with exudative pleural effusion, 53 (45.7%) patients had TB pleural effusion, 15 (12.9%) patients had para-pneumonic pleural effusion, 12 (10.3%) patients had malignancy, 7 (6.1%) patients had empyema, 4 (3.4%) patients had pleural effusion secondary to acute pancreatitis, 3 (2.6%) patients had haemothorax, 1 (0.9%) patient had pleural effusion reactionary to abdominal surgery and 4 (3.4%) patients had unknown cause.

There were 13 patients who were confirmed cases and 40 patients who were probable case of TB pleural effusion. Amongst the 15 patients with para-pneumonic effusion, four had typical para-pneumonic effusion, four had simple complicated para-pneumonic effusion and seven had complex complicated pleural effusion. Out of seven patients with empyema, only one patient had TB empyema and the rest were bacterial. Out of 12 patients with malignant pleural effusion, 12 were confirmed and 3 were probable case of malignant pleural effusion. Among 6 patients with empyema, two were simple and four were complex empyema.

Amongst 17 patients with transudative and pseudo-exudative pleural effusion, 5 (4.3%) patients had heart failure (HF) with reduced ejection fraction (HFrEF) along with CKD, 2 (1.7%) patients had anaemia and hypoproteinaemia, 2 (1.7%) patients had CKD, 1 (0.9%) patient had CLD, 1 (0.9%) patient had hypothyroidism, 1 (0.9%) patient had HFrEF, 1 (0.9%) had HF with normal ejection fraction (HFnEF), 1 (0.9%) patient had *cor pulmonale*, 1 (0.9%) patient had HFrEF along with acute kidney injury (AKI) and hypoproteinaemia and 2 (1.7%) patients had unknown cause.

Amongst the patients with TB pleural effusion, pleural effusion analysis showed exudative nature in all (n = 53) the patients. Lymphocyte predominance was seen in 52 (98.1% in this subgroup) patients. ADA was more than 40 IU/dL in all 53 patients. Pleural effusion CBNAAT was positive in 9 patients (16.9% in this subgroup) and line probe assay (LPA) was positive in two patients (3.7% in this subgroup). Sputum smear AFB was positive in three patients (5.6%) and sputum CBNAAT was positive in two patients (3.7% in this subgroup). Other supportive evidence found was positive TST in 15 patients (28.3% in this subgroup), and the history of TB was present in 13 patients. Twelve patients (22.6% in this subgroup) had radiological suspicion of TB.

In patients with malignant pleural effusion, carcinoma of lung (n = 3, 2.6%), carcinoma of breast (n = 3, 2.6%), renal cell carcinoma (n = 2, 1.7%), carcinoma of ovary (n = 1, 0.9%), carcinoma of pancreas (n = 1, 0.9%), carcinoma of gall bladder (n = 1, 0.9%) and unknown primary (n = 1, 0.9%) were the aetiology of pleural effusion. Out of 12 patients with malignant pleural effusion, 9 were confirmed cases and 3 were probable cases. Amongst confirmed malignant pleural effusion, one was histopathologically proven, seven were cytologically proven and four were radiologically proven. Malignant cell from Pf sample was positive in seven patients which constitutes 58.3% of malignant pleural effusion cases.

Forty eight (90.6%) of straw-coloured pleural effusion sample had TB aetiology. All the malignant pleural effusion had haemorrhagic pleural effusion sample. Pleural effusion protein-to-serum protein ratio is maximum in case of TB pleural effusion followed by para-pneumonic effusion and malignancy.

Pleural effusion ADA was tested in 113 (97.4%) patients. Mean ± SD of pleural fluid ADA values in TB, para-pneumonic and malignant pleural effusion was 140.9 ± 84.7 IU/L, 94.7 ± 118.5 IU/L and 37.6 ± 79.5 IU/L, respectively. Out of 113 patients (97.4%) whose Pf ADA was done, ADA >40 IU/L was present most commonly in TB pleural effusion (n = 52, 44.8%) followed by empyema (n = 4, 3.4%), para-pneumonic (n = 8, 6.9%), malignant pleural effusion (n = 3, 2.6%), unknown (n = 1, 0.9%) and HFrEF and CKD (n = 1, 0.9%). It was observed that, out of 53 patients with TB pleural effusion, 52 patients had ADA >40 IU/L.

Mean pleural fluid glucose value was 109.9 mg/dL. Minimum observed value for pleural fluid glucose was seen in empyema and para-pneumonic effusion. Pleural fluid glucose level <40 mg/dL was evident in 14 patients (12.1%), amongst whom 8 patients (6.9%) had para-pneumonic effusion, 5 patients (4.3%) had empyema and 1 patient (0.9%) had TB empyema.

Amongst all aetiologies, para-pneumonic effusion had the highest LDH value. Higher value of LDH specifically Pf LDH-to-serum LDH ratio of more than 2 was seen in patients with TB pleural effusion (n = 27, 23.3%), para-pneumonic effusion (n = 13, 11.2%), malignant pleural effusion (n = 9, 7.7%) and empyema (n = 7, 6.0%). All seven patients with empyema had Pf LDH ratio more than 2. Pf pH analysis was done in 106 patients. Maximum number of the patients (n = 65, 61%) had pH between 7.2 and 7.4. pH <7 was seen in 10 patients, 4 (3.4%) were empyema and 6 (5.2%) were para-pneumonic effusion.

Pf analysis showed lymphocyte predominance in 90 patients (77.6%), whereas neutrophil predominance in 26 patients (22.4%). Lymphocyte predominance was seen in TB pleural effusion (n = 52, 98.1% in this subgroup), malignant pleural effusion (n = 12, 100% in this subgroup), HFrEF and CKD (n = 5, 100% in this subgroup), pancreatic (n = 4, 100% in this subgroup) and other transudative causes. It was observed that neutrophil predominance was seen in patients with para-pneumonic effusion (n = 14, 93.3% in this subgroup), empyema (n = 5, 100% in this subgroup) and haemothorax (n = 3, 100% in this subgroup).

Pf lymphocyte-to-neutrophil (L/N) ratio of >0.75 increases the specificity for diagnosing TB pleural effusion. TB pleural effusion (n = 52; 98% in this subgroup), malignant pleural effusion (n = 12; 100% in this subgroup), pancreatic pleural effusion (n = 4; 100% in this subgroup), pleural effusion reactionary to abdominal surgery (n = 1; 100% in this subgroup) and unknown cause (n = 2; 50%

in this subgroup) had Pf L/N ratio of >0.75 in this study. Sensitivity and specificity of Pf L/N ratio of >0.75 to diagnose TB pleural effusion were 56.52% and 95.83%, respectively.

In the present study, TB, para-pneumonic and malignant pleural effusion had mean ADA value of 140.9 ± 84.7 IU/L, 94.7 ± 118.5 IU/L and 37.6 ± 79.5 IU/L, respectively. TB pleural effusion (98.1%) had ADA value >40 IU/L ($P = 0.001$), whereas most malignant pleural effusion (75%) had ADA value <40 IU/L ($P = 0.01$). There were 58 patients who had both ADA >40 and L/N ratio >0.75. It includes 52 patients (89.6% in this subgroup) with TB pleural effusion, 3 patients (5.2% in this subgroup) with malignant pleural effusion, 1 patient (1.7% in this subgroup) with bacterial empyema, 1 patient (1.7% in this subgroup) with TB empyema and 1 patient with HFrEF and CKD (1.7% in this subgroup). When ADA and L/N ratio were analysed simultaneously, it was found that 98% ($n = 52$) of patients with ADA >40 and L/N ratio >0.75 had TB aetiology. The sensitivity and the specificity increase up to 89.7% and 98.3%, respectively (Table 4).

Table 4: Sensitivity and Specificity of pleural fluid L/N ratio >0.75 and ADA>40 to diagnose TB pleural effusion

L/N ratio >0.75 and ADA>40	%	95% CI
Sensitivity	89.7	78.8-96.1
Specificity	98.3	90.8-100.0
Positive predictive value	50.00	40.6-59.4
Negative predictive value	98.1	88.2-99.7
Accuracy	90.5	81.7-95.3

L/N ratio=Lymphocyte-to-neutrophil ratio; ADA=Adenosine deaminase; CI=Confidence intervals; TB=Tuberculosis

Mean Pf total leucocyte count (TLC) was 2015.6 ± 3088.2 cells/mm^3. Mean TLC of TB pleural effusion was 2399.3 ± 3381.4 cells/mm^3. Mean TLC of para-pneumonic effusion was 2516.7 ± 4571.6 cells/mm^3 and that of empyema was 3435.5 ± 4489.4 cells/mm^3. Mean TLC count of malignant pleural effusion was 1487.5 ± 1587.8 cells/mm^3. It was observed that two patients (1.7%) had Pf TLC more than 10,000 amongst which one patient (0.9%) had empyema and one patient (0.9%) had para-pneumonic effusion.

Pf culture revealed growth of organism in 13 cases out of 17 cases of complicated para-pneumonic effusion and empyema cases. Pf routine aerobic and anaerobic culture was done in all the patients. *Staphylococcus aureus* was the most commonly ($n = 4$, 3.4%) isolated organism from Pf. Out of these four patients, 2 had methicillin-resistant *S. aureus* (MRSA). Other organisms isolated were *Burkholderia* spp. ($n = 1$, 0.9%), *Pseudomonas* spp. ($n = 1$, 0.9%), *Klebsiella* spp. ($n = 1$, 0.9%), *Sphingomonas* spp. ($n = 1$, 0.9%) and vancomycin-resistant *Enterococcus* ($n = 1$, 0.9%) and *Candida* ($n = 1$, 0.9%). There was a growth of contaminant such as *Staphylococcus epidermidis* and *Staphylococcus hemolyticus* in three patients (2.6%).

Pf CBNAAT was performed in 112 patients (96.6%), out of which 8.0% ($n = 9/112$) were positive and 91.9% ($n = 103/112$) were negative. Pf LPA was performed in seven patients (6.0%) amongst which two were positive. Malignant cell from Pf sample was positive in seven patients which constitutes 58.3% of malignant pleural effusion cases.

The haematological and biochemical profile of all the patients was observed at the time of admission and discharge. In the current study, anaemia (haemoglobin [Hb] <12 g/dL) and severe anaemia (Hb <8 g/dL) were seen in 74 (63.8%) and 11 (9.5%) patients, respectively. Leucopenia (TLC <4000/mm^3) was not seen in any patient, whereas leucocytosis (TLC >12000/mm^3) was seen in 38 (32.8%) patients. Thrombocytopenia (platelet count below 150,000/mm^3) was seen in 13 (11.2%) patients.

Biochemical profile including renal function tests and liver function tests were studied to assess organ dysfunction. A total bilirubin ≥1.5 mg/dL and serum glutamic-oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) ≥50 IU/L were considered for assessing hepatic dysfunction. Hyperbilirubinaemia with a total bilirubin ≥1.5 mg/dL was seen in 11 (9.5%) patients and transaminitis, i.e., SGOT and SGPT ≥50 IU/L were seen in 23 (19.8%) and 21 (18.1%) patients, respectively. Forty-five (38.8%) patients having raised ALP >125 IU and 81 (69.8%) patients with serum albumin <3.5 g/dL were also considered to be having hepatic dysfunction Twenty-three (19.8%) patients with serum creatinine ≥1.5 mg/dL had renal dysfunction. Electrolyte disturbances, i.e., hyponatraemia (sodium <135 mM) and hypernatraemia (sodium >145 mM) were seen in 42 (36.2%) and 6 (5.2%) patients, respectively. Hypokalaemia (potassium <3.5 mM) and hyperkalaemia (potassium >5.0 mM) were seen in 14 (12.1%) and 17 (14.7%) patients, respectively.

Sputum analysis culture and sensitivity revealed growth in nine cases which showed *Pseudomonas* spp. in 5 patients (4.3%), *Klebsiella* spp. in 2 patients (1.7%),

Klebsiella spp. as well as fungal growth in 1 patient (0.9%), 1 patient (0.9%) had both *Klebsiella* spp. and *Acinetobacter* spp. growth and 1 patient (0.9%) had *Acinetobacter* spp. along with *Escherichia coli* and fungal growth. Sputum CBNAAT was positive in two patients only

Chest radiograph showed right-sided pleural effusion in 67 (57.8%) patients and left sided in 49 (42.2%) patients. It was observed that TB pleural effusion ($n = 33$, 63.3% in this subgroup), malignant pleural effusion ($n = 7$%, 58.3% in this subgroup), para-pneumonic effusion ($n = 10$, 66.6% in this subgroup), empyema ($n = 4$, 66.6% in this subgroup), haemothorax ($n = 2$, 66.6% in this subgroup) and effusion secondary to surgery ($n = 1$, 100% in this subgroup) was more common on the right side. Pancreatic effusion is more common on the left side. All the four patients with pancreatic effusion had left-sided effusion. Out of 64 patients with mild pleural effusion, 29 were TB in aetiology, whereas out of 10 patients with massive pleural effusion, 5 were malignant (Table 5).

Table 5: Distribution of subjects according to grade of pleural effusion and aetiology*

Aetiology	Grade of pleural effusion			*P-value*
	Mild	Moderate	Severe	
TB	29 (55)	22 (42)	2 (4)	
Para-pneumonic	10 (67)	5 (33)	0	
Malignant	3 (25)	4 (33)	5 (42)	
Others	22 (61)	11 (31)	3 (8)	
Total	64 (55)	42 (36)	10 (9)	
				0.002

*Data are presented as No. (%)
TB=Tuberculosis

Abdominal USG was done in 17 patients (14.7%). Free fluid in the abdomen was seen in 11 patients (9.5%), renal parenchymal change in 10 patients (8.6%), hepatomegaly in 9 patients (7.8%), splenomegaly in 7 patients (6.0%) and liver echotexture changes in 4 patients (3.4%). CT chest was done in 77 patients (66.4%). Mediastinal LAP was observed in 12 patients (10.3%), consolidation in 12 patients (10.3%), cavitatory lesion in 7 (6.0%) patients (single cavity in 4 patients and multiple in 3 patients), nodular shadow in 6 (5.2%) patients, bronchiectasis and/or fibrosis in 5 (4.3%) patients, lung mass in 3 (2.6%) patients, pleural thickening in 3 (2.6%) patients, ground-glass opacification (GGO) in 3 (2.6%) patients, miliary mottling in 2 (1.7%) patients and pulmonary thromboembolism in 1 (0.9%) patient. Probable aetiology based on CT chest was TB in 17 (14.7%) patients, malignant in 7 (6.0%) patients and non-TB pathology in 23 (19.8%) patients. Echocardiography was done in 43 (36.2%) patients and 8 (7.8%) patients had HFrEF, whereas one patient had HFnEF.

Medical management of patients with unilateral pleural effusion includes 55 (47.4%) patients with ATT, 35 (30.2%) patients were given intravenous (IV) antibiotic, 14 (12.1%) patients with supportive treatment, 12 (10.3%) patients with decongestive therapy, 6 (5.2%) patients with antifungal and 4 (3.4%) patients with chemotherapy.

Therapeutic aspiration was done in 26 cases (22.4%). These patients had moderate-to-severe respiratory distress. These patients include 10 (8.6%) with malignant pleural effusion, 9 (7.7%) with TB pleural effusion, 2 (1.7%) with effusion of unknown aetiology, 1 (0.9%) with HFrEF and CKD, 1 (0.9%) with CKD, 1 (0.9%) with HFrEF, 1 (0.9%) with cor pulmonale and 1 (0.9%) with CLD.

Intercostal drainage tube insertion was done in forty patients (34.9%). Among these 40 patients, 11 (9.5%) had TB pleural effusion, 11 (9.5%) had para-pneumonic effusion, 6 (5.2%) had malignant pleural effusion, 6 (5.2%) had empyema, 3 (2.6%) had haemothorax, 1 (0.9%) had TB empyema and 2 (1.7%) were of unknown aetiology. In the present study, streptokinase was inserted in 14 (12.1%) patients in view of incompletely drained Pf. It includes three patients with empyema (50% in this subgroup), 7 patients with para-pneumonic effusion (46.6% in this subgroup) and 4 patients with TB pleural effusion (7.5% in this subgroup). Video-assisted thoracoscopic surgery and broncho-pleural fistula closure and decortication were done in one (0.9%) patient in the current study.

The mean age of the patients with TB pleural effusion was 47.9 years and that of malignant and para-pneumonic pleural effusion was 52.7 years and 56.6 years, respectively. Hence, patients with TB aetiology of pleural effusion were comparatively younger as compared to patients with malignant and para-pneumonic pleural effusion.

Out of the 116 admitted patients, 98 (84.5%) patients were discharged, 18 (15.5%) patients went DAMA and no mortality was observed during the course of hospitalisation. Of 18 patients who went DAMA, 14 had exudative and 4 had transudative nature of pleural effusion. Amongst the exudative group, 5 (4.3%) were para-pneumonic, 3 (2.6%) were TB, 3 (2.6%) were malignant, 2 (1.7%) were unknown aetiology and 1 (0.9%) was empyema. Amongst transudative group, 1 (0.9%) patient had CKD in, 1 (0.9%) patient had HFrEF along with AKI and hypoproteinaemia, and 1 (0.9%) patient had anaemia and hypoproteinaemia and 1 (0.9%) patient had unknown aetiology (Table 6).

Table 6: Distribution of patients according to aetiology of pleural effusion and outcome

Aetiology	DAMA	Discharge	Total
Exudative			
TB	3	50	53
Para-pneumonic	5	10	15
Malignant	3	9	12
Empyema	1	5	6
Pancreatic	0	4	4
Unknown - exudative	2	2	4
Haemothorax	0	3	3
Reactionary to abdominal surgery	0	1	1
TB empyema	0	1	1
Transudative			
HFrEF and CKD	0	5	5
CKD	1	1	2
Unknown - transudative	1	1	2
Anaemia and hypoproteinaemia	1	1	2
HFnEF	0	1	1
HFrEF	0	1	1
Cor pulmonale	0	1	1
CLD	0	1	1
Hypothyroidism	0	1	1
HFrEF, AKI and hypoproteinaemia	1	0	1
Total	18	98	116

DAMA=Discharge against medical advice; TB=Tuberculosis; HFrEF=Heart failure with reduced ejection fraction; HFnEF=Heart failure with normal ejection fraction; CKD=Chronic kidney disease; CLD=Chronic liver disease; AKI=Acute kidney injury

On the other hand, on those who were discharged, the most common aetiology was TB (n = 50, 43.1%), followed by parapneumonic (n = 15, 12.9%), malignant (n = 9, 7.6%), empyema (n = 5, 4.3%), HFrEF and CKD (n = 5, 4.3%), pancreatic (n = 4, 3.4%), haemothorax (n = 3,2.6%), unknown (n = 2, 1.7%), reactionary to abdominal surgery (n = 1, 0.9%), TB empyema (n = 1, 0.9%), CKD (n = 1, 0.9%), anaemia and hypoproteinemia (n = 1, 0.9%), HFnEF (n = 1, 0.9%), HFrEF (n = 1, 0.9%), hypothyroidism (n = 1, 0.9%), CLD (n = 1, 0.9%), cor pulmonale (n = 1, 0.9%) and unknown transudative (n = 1, 0.9%).

The average duration of stay in hospital was 11.3 days. The average duration of stay in ward was 8.6 days and in intensive care unit (ICU) was 2.7 days. 15 (12.9%) patients required ICU care during their course of hospitalisation. Aetiology of pleural effusion among patients requiring ICU care was TB pleural effusion (n = 8, 8.9%), para-pneumonic (n = 2, 1.7%), malignant (n = 1, 0.9%), pancreatitis (n = 1, 0.9%), haemothorax (n = 1, 0.9%), HFrEF with AKI and hypoproteinaemia (n = 1, 0.9%) and cor pulmonale (n = 1, 0.9%).

Out of 116 patients, 113 patients were available for follow-up at 2 months, 109 patients at 4 months and 93 patients at 6 months. In patients (n = 113) who followed up at 2 months, 71 (62.8%) showed improvement in constitutional symptoms. In 109 patients who followed up at 4 months, 90 (82.5%) showed improvement at 4 months. At 6 months, 93 patients were followed up, out of which 77 (85.5%) patients showed improvement in constitutional symptoms. The most common cause of mortality was malignancy followed by para-pneumonic effusion and empyema (Table 7).

Fifty-one patients with TB pleural effusion were followed up at 2 and 4 months and 43 patients were followed at 6 months and it was found that 68.6% (n = 35/51), 92.2% (n = 47/51) and 97.6% (n = 41/42) showed improvement, respectively. Two (3.8% in this subgroup) patients showed ATT-induced hepatitis. Eight (15.1% in this subgroup) patients were readmitted with fever which on evaluation was found to be because of empyema (n = 4, 7.5% in this subgroup), pneumonia (n = 2, 3.7% in this subgroup), Pott's spine (n = 1, 1.9% in this subgroup) and urinary tract infection (n = 1, 1.9% in this subgroup). Two (3.8% in this subgroup) patients required repeat therapeutic tap. One patient (1.9% in this subgroup) developed hydropneumothorax. Two patients (3.7% in this subgroup) stopped ATT on follow-up. One patient (1.9% in this subgroup) was later diagnosed with carcinoma lung.

Amongst 12 cases of malignant pleural effusion, 5 patients died at 2 months of follow-up and all these patients had non-pulmonary malignancy. Four patients died at 4-month follow-up and all of them also had non-pulmonary malignancy. One patient each had undergone decortication, pleurodesis, chest tube insertion in view of hydropneumothorax and therapeutic tap on follow-up.

Out of 20 patients with para-pneumonic effusion and empyema followed at 2 months, 50% (n = 10/20) showed improvement. 100% (n = 15/15) showed improvement at 4 months of follow-up and 100% (n = 11/11) showed improvement at 6 months of follow-up.

DISCUSSION

The male-to-female ratio was 2.3:1. In a previous study done from South India, 68% of patients were males, and 32% of patients were females which were in concordance with results in the present study.[10] Similarly, in another study by Parikh *et al*. from Western India, 68% of patients

Table 7: Distribution of subjects according to follow-up

Aetiology	No.	2 months F/U Constitutional features				4 months F/U Constitutional features				6 months F/U Constitutional features			
		Improved	Not improved	Loss to F/U	died	Improved	Not improved	Loss to F/U	Died	Improved	Not improved	Loss to F/U	Died
Exudative													
TB	53	35	16	2	0	47	3	2	1	41	1	10	1
Malignant	12	0	7	0	5	1	2	0	9	0	2	1	9
Typical para-pneumonic	4	1	3	0	0	3	0	1	0	2	0	2	0
Simple complicated para-pneumonic	4	3	0	0	1	3	0	0	1	3	0	0	1
Complex complicated para-pneumonic	7	4	1	1	1	4	0	2	1	3	0	3	1
Empyema	6	2	4	0	0	5	0	1	0	3	0	3	0
Unknown	4	2	2	0	0	3	1	0	0	2	0	2	0
Pancreatic	4	3	1	0	0	4	0	0	0	4	0	0	0
Haemothorax	3	3	0	0	0	3	0	0	0	3	0	0	0
Reactionary	1	1	0	0	0	1	0	0	0	1	0	0	0
TB empyema	1	1	0	0	0	1	0	0	0	1	0	0	0
Transudative													
HFrEF and CKD	5	5	0	0	0	5	0	0	0	5	0	0	0
CKD	2	1	1	0	0	1	1	0	0	1	0	0	1
Anaemia	2	2	0	0	0	2	0	0	0	1	0	1	0
HFnEF	1	1	0	0	0	1	0	0	0	1	0	0	0
HFrEF and CKD	1	1	0	0	0	1	0	0	0	1	0	0	0
Cor pulmonale	1	1	0	0	0	1	0	0	0	1	0	0	0
CLD	1	1	0	0	0	1	0	0	0	1	0	0	0
Hypothyroidism	1	1	0	0	0	1	0	0	0	1	0	0	0
HFrEF and AKI	1	1	0	0	0	0	0	1	0	0	0	1	0
Unknown	2	2	0	0	0	2	0	0	0	2	0	0	0
Total	116	71	35	3	7	90	7	7	12	77	3	23	13

F/U=Follow-up; No.=Number of patients; HFrEF=Heart failure with reduced ejection fraction; HFnEF=Heart failure with normal ejection fraction; CKD=Chronic kidney disease; CLD=Chronic liver disease; AKI=Acute kidney injury; TB=Tuberculosis

were males, and the male-to-female ratio was found to be 2.2.[11] Similar observations were noted in other studies from other regions of the world.[12,13] The age of the patients ranged between 18 and 90 years, with a mean age of 51.5 ± 17.2 years in the present study. Maximum patients (63.8%) were in the age group of 20–60 years. In a study from Hyderabad, the mean age of the study population was 48.8 years, with most common age group being 20–60 years of age.[14] Another study from Qatar[15] showed that mean age group of study population was 47.4 ± 18.2 years. In a study[16] from Kerala, majority of the patients were in the age group of 30–60 years with a mean age of 46.5 years. A possible explanation for the greater percentage of middle age and older patients in the current study may be the varied aetiology of unilateral pleural effusion in these subgroups as compared to younger population group requiring admission and evaluation.

The average duration of clinical symptoms was 21 days in the present study with a range of 1–180 days before requiring admission to our centre. Loss of appetite, loss of weight and fatigability were the chronic symptoms. Similar results were found in a study from Telangana in India, where majority of the study population had 3–4-week duration of symptoms before reporting for admission.[14] A similar study from Ethiopia[17] showed that the mean duration of the symptoms was 66 days before hospital visit with a range of 3–365 days which was high when compared to the current study. This may be due to better availability of healthcare facilities in India compared to Ethiopia.[17]

The most common presenting symptoms in the present study was shortness of breath (n = 65, 56%), fever (n = 62, 53.4%), cough (n = 61, 52.5%), chest pain (n = 41, 35.3%), anorexia (n = 40, 34.5%), weight loss (n = 22,18.9%), pain abdomen (n = 16, 13.7%), night sweats (n = 13, 11.2%), vomiting (n = 12, 10.3%) and fatigability (n = 6, 5.1%). In a study[14] from Telangana, the most common presenting symptom was dyspnoea (84%), followed by cough (80%), fever (65%), chest pain (43%) and loss of weight and loss of appetite (27%). Another study form Kerala,[16] showed that the most common presenting symptoms were dyspnoea (77%), pleuritic chest pain (66%), cough (45%), weight loss (42%) and fever (40%). Similar results were also seen in another study[18] from Nepal, which found that

shortness of breath (83%), cough (67%) and fever (66%) were the most common mode of clinical presentation in patients with pleural effusion.

In the current study, 36 patients (31%) had a history of DM, 34 (29.3%) patients had hypertension (HTN), 25 (21.6%) patients had CAD, 19 patients (16.4%) had a history of TB, 18 (15.5%) patients had CKD, 12 (10.2%) patients with malignancy, 11 (9.5%) patients had hypothyroidism, 8 (6.9%) patients had CLD and 8 (6.9%) patients had COPD. In a study[19] from Central Indian state of Madhya Pradesh, a history of TB was present in 36.4% of cases, followed by DM in 27.6% and CLD and CAD in 13.6%.

Pallor (n = 72, 62.10%), pitting oedema (n = 24, 20.7%) and LAP (n = 7, 5.1%) were the most common physical signs. Out of seven, four patients had cervical LAP, two had axillary LAP and one had supraclavicular LAP. Similar results were seen in a study[19] from Central India, which showed that 50% of patients had pallor, 23% had oedema and 14% had icterus. It was observed that reduced respiratory movements, decreased tactile vocal fremitus, diminished breath sound and stony dull note on percussion on the affected side were the most common findings present on chest examination. Similar findings were observed in another study[20] from West Bengal in Eastern India.

Diagnostic aspiration of Pf was done in all the patients. It was observed that most of the Pf s (n = 53, 45.7%) were straw coloured. Pf was haemorrhagic, clear, yellow and turbid and pus coloured in 20.7% (n = 24), 17.2% (n = 20), 10.3% (n = 12) and 6.0% (n = 7) of patients, respectively. Most of straw-coloured (n = 48/53, 90.57%) Pf was found to be TB, whereas the most of haemorrhagic Pf (n = 12/24; 50%) was found to be malignant. In a study[10] from Karnataka in South India, TB effusion was predominantly straw coloured, whereas malignant effusion was haemorrhagic. Another study[16] showed that 49 out of 54 TB effusions were grossly straw coloured in appearance and 12 out of 14 malignant effusions were haemorrhagic.

The first algorithmic step in the diagnosis of pleural effusion is to differentiate between transudative and exudative effusion. In clinical practice, this is conventionally done using Light's criteria. 99 patients (85.3%) had exudative and 17 patients (14.6%) had transudative effusion in the current study. Similar results were seen in a study[21] from the United Kingdom, which showed that 101 patients (80%) had exudative and 19 (15%) had transudative pleural effusion. Another study from Bristol in the United Kingdom showed that, out of 921 patients with unilateral pleural effusion in their study, 803 patients (87%) had exudative and 118 patients (13%) had transudative nature of pleural effusion.[22] A possible explanation for exudative pleural effusions being predominantly right-sided could be as follows. Transudative pleural effusions occur due to systemic cause, wherein Pf accumulates because of an imbalance between the hydrostatic and oncotic pressures. In contrast, an exudative pleural effusion occurs when the local factors influencing the accumulation of Pf are altered, resulting in exudative pleural effusion being more frequently unilateral.

The aetiology of exudative pleural effusion was TB in 53 (45.7%) patients, para-pneumonic in 15 (12.9%) patients, malignant in 12 (10.3%) patients, empyema in 7 (6.1%) patients, pancreatic in 4 (3.4%) patients, haemothorax in 3 (2.6%) patients and effusion reactionary to abdominal surgery in 1 (0.9%) patient. Aetiology was unknown in 4 (3.4%) patients. In our country, TB pleural effusion was the most common cause probably due to the higher prevalence of TB in India due to resource-limited settings. In a study from Telangana, the most frequent cause of pleural effusion was TB in 38% of patients, followed by para-pneumonic effusion (28.5%) and malignant pleural effusion (22.2%).[14] Another study[23] from Nigeria in Africa observed that the most common aetiology was TB (42.2%), followed by para-pneumonic effusion (14.07%) and malignancy (12.08%).[23] A study[23] from Qatar in Western Asia showed that the most common cause of pleural effusion was TB, para-pneumonic effusion, malignant effusion and cardiac failure in 32.5%, 19%, 15.5% and 13% of patients, respectively.[15] Similarly, a study[18] from Nepal found that the most common cause of pleural effusion was TB (32%), para-pneumonic (30%) and malignancy (18%).

A study[24] in Tamil Nadu concluded that TB was the leading cause of pleural effusion accounting for 46% of cases followed by para-pneumonic effusion (24%) and malignancy (14%). Similar results were seen in studies conducted in resource-limited countries like Iraq, Ghana and Pakistan.[25-27] The occurrence of para-pneumonic effusion as observed in the present study from India was higher as compared to resource-rich–developed countries as shown in a study[28] conducted in Lithuania in Europe. This study[28] showed that malignant pleural effusion was seen in 16.5% of patients, whereas para-pneumonic aetiology was found only in 13% of patients.

In the present study, among 15 patients with para-pneumonic effusion, 4 patients had uncomplicated and 11 had complicated para-pneumonic effusion. Empyema was present

in 8 patients, among which only 1 was TB and rest were bacterial empyema. A study[29] from Spain observed 34.7% were uncomplicated para-pneumonic effusion, 37.1 were complicated pleural effusion and 28.2% were empyema.[30] In a study from Western India, it was observed that 48% of patients had uncomplicated para-pneumonic effusion, 42% had complicated para-pneumonic effusion and 10% had empyema. The present study conducted in a resource-limited setting in India had a greater number of patients with complicated para-pneumonic effusion and empyema. This is primarily due to a higher number of patients with complicated effusion getting referred and admitted to DMCH, Ludhiana, as it is a tertiary care hospital with a patient referral from the North Indian region of Punjab, Himachal Pradesh, Haryana as well as Jammu and Kashmir.

Amongst transudative pleural effusion, HF was an important cause (n = 8, 6.9%) in this study. Out of 8 patients with HF, 7 were HFrEF and 1 had HFnEF. Five patients out of 8 had accompanying CKD. In a study[31] from West Bengal in Eastern India, HF (2%) was the most common cause amongst transudative group; whereas TB (68.8%) was the most common cause in exudative group. In a study[18] from neighbouring country of Nepal, amongst transudative pleural effusion, HF was the most common cause (8%).

It was observed in the present study that most of the effusions showed lymphocyte predominance (n = 90; 76.7%) on cytological analysis of Pf. Aetiology of pleural effusion amongst the lymphocyte-predominant subset of Pf was TB in 52 (44.8%) patients, malignant in 12 (10.3%) patients and HFrEF and CKD in 5 of patients. Amongst the neutrophil-predominant subset of Pf, the most common cause was found to be para-pneumonic effusion in 14 (11.2%) patients and empyema in 5 patients. A study[32] from West Bengal concluded that predominantly lymphocytes are commonly found in TB pleural effusion and predominantly neutrophils are commonly found in para-pneumonic effusion and empyema, which is concordant with results of the current study. Similar results were found in a study[25] from a resource-limited country like Iraq in Western Asia, which concluded that, in both TB and malignant effusions, the cellular content of the fluid was predominantly lymphocytic.

On biochemical analysis of Pf, it was observed that two patients had Pf of 0 mg/dL, out of which one patient had complicated para-pneumonic effusion and the other patient had empyema. Mean Pf glucose value was minimum for empyema (mean 37.5 ± 54.4 mg/dL) and para-pneumonic effusion (mean 67.40 ± 74.24 mg/dL). More than 3 g/dL of mean Pf protein was seen in TB pleural effusion (4.98 ± 1.21 g/dL), para-pneumonic effusion (mean 4.25 ± 0.96 g/dL) and malignant pleural effusion (mean 4.02 ± 0.89 g/dL). The observations in the current study were similar to observations reported in studies from Telangana[14] in Southern India and Nepal.[18]

Higher Pf LDH (Pf -to-serum LDH ratio more than 2) was seen in patients with empyema (7/7), para-pneumonic (13/15), malignancy (9/12) and TB pleural effusion (27/53; 51% in this subgroup). Pf LDH was low in effusion due to HF and CKD. Similar results were seen in the study[18] from Nepal, which concluded that raised level of LDH was seen in inflammatory conditions such as TB and para-pneumonic effusion and low in other conditions such as congestive HF and liver disease.

In the present study, TB, para-pneumonic and malignant pleural effusion had mean ADA value of 140.9 ± 84.7 IU/L, 94.7 ± 118.5 IU/L and 37.6 ± 79.5 IU/L, respectively. TB pleural effusion (98.1%) had ADA value >40 IU/L (P = 0.001), whereas most of malignant pleural effusion (75%) had ADA value <40 IU/L (P = 0.01). A meta-analysis from Japan observed that there was a statistically significant difference according to the levels of Pf ADA between TB pleural effusion and malignant pleural effusion group and confirmed that ADA is a very useful parameter for the differentiate TB and malignant pleural effusion.[33] Another study[16] from Kerala in Southern India also observed that all cases of TB effusion had Pf ADA >40 IU/L and most of the malignant effusions had ADA level of <30 IU/L.

The cut-off value of >40 IU/L of ADA had a sensitivity of 75.4%, specificity of 97.7%, PPV of 98.1% and NPV of 71.7% for diagnosing TB pleural effusion. A study[19] from Madhya Pradesh in Central India concluded that if ADA >70 IU/L was taken as cut-off, it was exclusively seen in case of TB pleural effusion with an accuracy of 99%, sensitivity of 100% and specificity of 98.6%. Another study[14] from Telangana in South India showed that >30 IU/L of ADA cut-off value had 92% sensitivity, 100% specificity, 1.00 PPV and 0.85 NPV for diagnosis of TB pleural effusion.

Two main diseases other than TB pleural effusion that is associated with a high Pf ADA are empyema and rheumatoid pleural effusion, but the latter two diseases do not have Pf lymphocytosis. Pf L/N ratio of >0.75 increases the specificity for diagnosing TB pleural effusion.[34] In the present study, TB pleural effusion (n = 52) had Pf L/N ratio of >0.75. The sensitivity and specificity of Pf L/N

ratio of >0.75 to diagnose TB pleural effusion were 56.52% and 95.83%, respectively. When ADA and L/N ratio were analysed simultaneously, it was found that 98% (n = 52) of patients with ADA >40 and L/N ratio >0.75 had TB aetiology. The sensitivity and the specificity increase to 89.7% and 98.3%, respectively. Hence, along with ADA, clinical evaluation, L/N ratio and glucose levels are necessary to separate these entities.[34]

TST was positive only in 28.3% of patients (n = 15/53) of TB effusion. In a study[10] from Southern India, TST was negative in the majority of diagnosed cases of TB pleural effusion, which is concordant with the present study. However, another study[16] from Southern India found that TST was positive in 61.10% of patients with TB effusion, which was contrary to the findings of the present study. As TST was not conducted in 42.3% (n = 49) patients in the present study, it would be difficult to use positive TST as a comparison variable with other studies.

Pf CBNAAT was performed in 112 patients, out of which 9 were positive and 103 were negative. It was seen that the sensitivity of CBNAAT in TB pleural effusion in the present study was 16.67%. Similar results were seen in a study[35] from Karnataka in Southern India with a sensitivity of CBNAAT in TB pleural effusion between 22.7% and 51.4%. A study[36] concluded that sensitivity and specificity of CBNAAT were 4.76% and 87.5%, respectively, for TB pleural effusion. The low sensitivity of CBNAAT in the diagnosis of TB pleural effusion is attributed to paucibacillary nature of TB pleural effusion.

In this study, 7/53 patients had a history of TB. In a similar study[11] done in Gujarat in Western India, amongst 62 patients of TB effusion, 4 patients (6.5%) had a history of TB. Carcinoma of lung and carcinoma of breast (n = 3 each) were the most common primary responsible for malignant pleural effusion in the present study. Other primary with malignant pleural effusion in the present study included renal cell carcinoma (n = 2), carcinoma ovary, carcinoma of head of pancreas, carcinoma of gallbladder and carcinoma of unknown primary (n = 1 each). 1 out of 3 patients with carcinoma of lung had adenocarcinoma variant on histopathology. In a study[30] from Spain in Europe, lung (37%) and breast (36%) carcinoma were the most common tumours presenting with malignant pleural effusion. Their study also concluded that cytology had an accuracy of 51% to diagnose malignant pleural effusion. Another study[37] from Spain found that the most frequent locations of the primary tumour among the neoplastic effusion group were lung (32.6%), breast (11.5%) and lymphoma (10.8%).

Malignant cell Pf cytology was positive in 7/12 patients with malignant pleural effusion in the present study. A study from Mayo Clinic found that malignancy as the cause was established by cytology in 57% of the patients only, which is consistent with the present study.[38] In a study from Iraq in Western Asia, malignant cells were positive in 15 of the 25 patients of malignant effusion.[25]

Pf cultures revealed growth of organisms in 10/22 of patients with para-pneumonic effusion and empyema. The most common organism isolated from Pf culture was *S. aureus* (n = 4; 2 of these were MRSA). In a study[29] from Eastern India, MRSA (4%), *Pseudomonas* spp.(4%), *Acinetobacter* spp.(2%), *E. coli* (2%) and *Peptostreptococcus* spp.(2%) were isolated from Pf culture. In a study[13] from France in Europe, bacterial culture results were positive in 39% of patients, which was similar to the microbiological yield in the present study. In another study[30] from Spain, only 30% of cultures yielded positive results in infectious pleural effusion. The microbiological yield in the present study was also less as compared to a similar microbiological study[39] from the Eastern United States. The low yield of Pf and sputum culture positivity in the present study could be attributed to prior antibiotic use before getting admitted to the hospital. Unfortunately, empirical use of antimicrobial therapy without evidence-based documentation of bacterial infection is very common in resource-limited countries.

Patients with TB pleural effusion were comparatively younger as compared to patients with malignant and para-pneumonic pleural effusion. The mean age of patients with TB, malignant and para-pneumonic pleural effusion was 47.9 years, 52.7 years and 56.6 years, respectively. A study[11] from Western India observed that TB pleural effusion was more common in young patients; whereas malignant pleural effusion was more common in older age patients, which was concordant with the present study.

It was observed that right-sided pleural effusion (57.8%) was more common as compared to left-sided pleural effusion (42.2%). Most of the unilateral pleural effusions (n = 64, 55.2%; including 20 with secondary pleural effusions) were found to be mild both clinically and radiologically. In a study[16] from Kerala in Southern India, 66% of patients had right-sided effusion and 52% of patients had mild pleural effusion. In the present study, TB and malignant pleural effusion were found to be more common on the right side. A study[32] in West Bengal showed that both TB and malignant pleural effusion cases were more commonly observed on the right side.

Other studies from different regions in the world have also concluded that unilateral pleural effusion was most common on the right side.[18,24] The possible explanation is right lung is larger and has more pleural surface area; hence more surface area for the secretion of Pf. Moreover, anatomically, major openings such as vena caval hiatus as well as minor venous openings are more numerous in the right hemidiaphragm than on the left side.

Loculated pleural effusion was present in 19 (16.4%) patients in the present study. In a study[17] from Ethiopia, loculated effusion was found in 2.7% of patients only. It can be postulated that more number of patients with complicated para-pneumonic effusion and empyema were observed due to better access to advanced imaging techniques in India as compared to Ethiopia in Africa.

Haematocrit level was determined for all patients, and 74 patients (63.8%) had anaemia. Similar results were seen in the study[17] from Ethiopia with anaemia in 64 (66%) patients. The reason might be the similar prevalence of malnutrition in the in the two geographically different resource-limited settings.

Out of the 116 patients, 98 (84.5%) patients were discharged and 18 (15.5%) went DAMA. There was no mortality. The mean length of stay in hospital was 11.3 days. In the present study, 2 (3.9%) patients showed anti-tuberculosis treatment (ATT) induced hepatotoxicity. Eight (15.6%) patients were readmitted with fever which on evaluation was found to be because of empyema ($n = 4$), pneumonia ($n = 2$), Pott's spine and urinary tract infection 1 patient each. 2 (1.7%) patients required repeat therapeutic tap. One patient had developed hydropneumothorax. Two patients showed improvement in spite of stopping ATT on follow up. One patient was later diagnosed with carcinoma lung.

Malignant pleural effusion (n=12) had high mortality. At 2 months follow-up, 5 patients had died; by 4 months, 9/12 patients had died. A study[40] from a resource-rich setting like the United States also showed that the median survival of a patient with malignant pleural effusion was 4 months. Another study[41] from Europe concluded that patients with malignant pleural effusion had median survival ranging from 3 to 12 months, and mostly, the management remained palliative.

Two of the 21 patients with para-pneumonic effusion and empyema had died. Complicated para-pneumonic effusion and empyema had a higher mortality rate as compared to uncomplicated para-pneumonic effusion. A study[29] from the United States also observed that mortality is highest amongst complicated para-pneumonic effusion and empyema.

The limitation of the current study is that it is a single-centre study with study duration of 1 year; hence, this may limit the general applicability to a larger pool of patients admitted to different hospitals in a vast country like India with varied socio-economic differences.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Sahn SA, Heffner JE. Pleural fluid analysis. In: Light RW, Lee YC, editors. Textbook of Pleural Diseases. 2nd ed. London: Arnold Press; 2008. p. 209e26.
2. Light RW. Pleural effusions. Med Clin North Am 2011;95:1055-70.
3. Heffner JE. Non-malignant pleural effusion. In: Grippi MA, Elias JA, Fishman JA, Kotloff RM, Pack AI, Senior RM, editors. Fisherman's Pulmonary Diseases and Disorders. 5th ed. New York: Mc Graw Hill Education; 2015. p. 1164-75.
4. Balachandran G. Pleural effusion – A pictorial essay. Radiol Forum 2016;6:121-27.
5. Zhao T, Chen B, Xu Y, Qu Y. Clinical and pathological differences between polymorphonuclear-rich and lymphocyte-rich tuberculous pleural effusion. Ann Thorac Med 2020;15:76-83.
6. Light RW, Girard WM, Jenkinson SG, George RB. Parapneumonic effusions. Am J Med 1980;69:507-12.
7. Blakiston M, Chiu W, Wong C, Morpeth S, Taylor S. Diagnostic performance of pleural fluid adenosine deaminase for tuberculous pleural effusion in a low-incidence setting. J Clin Microbiol 2018;56:e00258-18.
8. Malhotra P, Aggarwal AN, Agarwal R, Ray P, Gupta D, Jindal SK. Clinical characteristics and outcomes of empyema thoracis in 117 patients: A comparative analysis of tuberculous vs. non-tuberculous aetiologies. Respir Med 2007;101:423-30.
9. De Lima Corvino DF, Shrestha S, Kosmin AR. Tuberculosis Screening. In: Stat Pearls. Treasure Island (FL): Stat Pearls Publishing; 2020.
10. Mohan MK, Ravindran C. Aetiology and clinical profile of pleural effusion in a teaching hospital of south India: A descriptive study. Pulmon 2012;14:89-96.
11. Parikh P, Odhwani J, Ganagajalia C. Study of 100 cases of pleural effusion with reference to diagnostic approach. Int J Adv Med 2016;3:328-31.
12. Maldhure BR, Bedukar SP, Kulkarni HP, Papinwar SP. Pleural biopsy and adenosine deaminase in pleural fluid for the diagnosis of tuberculous pleural effusion. Indian J Tuberc 1994;41:161-5.
13. Hirsch A, Ruffie P, Nebut M, Bignon J, Chrétien J. Pleural effusion: Laboratory tests in 300 cases. Thorax 1979;34:106-12.
14. Reddy RS, Varaprasad K, Narahari NK, Bhaskar K, Varma GR, Paramjyothi GK. Clinical and etiological profile of an exudative pleural effusion in a tertiary care center. Indian J Respir Care 2019;8:22-6.
15. Khan FY, Alsamawi M, Yasin M, Ibrahim AS, Hamza M, Lingawi M, *et al*. Aetiology of pleural effusion among adults in the state of Qatar: A 1 year hospital-based study. East Mediterr Health J 2011;17:611-8.
16. Raghavan S, Jayachandran R, Mosses S. Clinical and etiological profile of patients with pleural effusion in a tertiary care centre. JMSCR

2017;5:553-8.
17. Desalew M, Amanuel A, Addis A, Zewdu H, Jemal A. Pleural effusion: Presentation causes and treatment outcome in a resource limited area, Ethiopia. Health 2012;4:15-9.
18. Dhital KR, Acharya R, Bhandari R, Kharel P, Giri KP, Tamrakar R. Clinical profile of patients with pleural effusion admitted to KMCTH. Kathmandu Univ Med J (KUMJ) 2009;7:438-44.
19. Shashikant A, Archana G. A study on clinicoetiological profile of patients with pleural effusion. IOSR-JDMS 2017;16:23-7.
20. Hasan M, Islam MR, Matin A, Khan R, Rahman M, Islam MR, *et al*. Clinical Profile of children with pleural effusion admitted in a tertiary care hospital of Bangladesh. JMSCR 2012;4:7-9.
21. Hooper C, Lee YC, Maskell N; BTS Pleural Guideline Group. Investigation of a unilateral pleural effusion in adults: British thoracic society pleural disease guideline 2010. Thorax 2010;65 Suppl 2:i4-17.
22. Arnold DT, De Fonseka D, Perry S, Morley A, Harvey JE, Medford A, *et al*. Investigating unilateral pleural effusions: The role of cytology. Eur Respir J 2018;52:1801254.
23. Godwin CM, Benneth CA, Eugenia OO, Emmanuel NA. Pleural effusion: Aetiology, clinical presentation and mortality outcome in a tertiary health institution in eastern Nigeria – A five-year retrospective study. J AIDS Clin Res 2015;6:2.
24. Selvamani G, Manimaran A, Karthick G, Vanithamani P, Venkatesan R. Aetiology underlying pleural effusion in Thanjavur Medical College and Hospital: A descriptive study. Int J Sci Study 2019;6:171-3.
25. Al-Alusi F. Pleural effusion in Iraq: A prospective study of 100 cases. Thorax 1986;41:492-3.
26. Afful B, Murphy S, Antunes G, Dudzevicius V. The characteristics and causes of pleural effusions in Kumasi Ghana – A prospective study. Trop Doct 2008;38:219-20.
27. Khan Y, Zia SB. Etiological spectrum of exudative pleural effusion in a tertiary care hospital based on closed pleural biopsy. Ann Pak Inst Med Sci 2011;7:133-6.
28. Zablockis R, Nargela R. Diagnostic value of pleural fluid cytologic examination. Medicina (Kaunas) 2002;38:1171-8.
29. Singh S, Bargaje MD, Deoskar RB, Anokar AT. Clinical profile of parapneumonic effusion and empyema at a tertiary center in western India -changing behavior of microorganisms in superbug era. SM J Pulm Med 2017;3:1028.
30. Porcel JM, Esquerda A, Vives M, Bielsa S. Etiology of pleural effusions: Analysis of more than 3,000 consecutive thoracenteses. Arch Bronconeumol 2014;50:161-5.
31. Maikap MK, Dhua A, Maitra MK. Aetiology and clinical profile of pleural effusion. Int J Med Sci Public Health 2018;7:316-21.
32. Bar PK, Mandal S, Banik T, Barman R, Mandal A. A clinicopathological study of pleural effusion with special reference to malignant aetiology in a tertiary care hospital in West Bengal. Int J Med Res Rev 2019;7:266-72.
33. Goto M, Noguchi Y, Koyama H, Hira K, Shimbo T, Fukui T. Diagnostic value of adenosine deaminase in tuberculous pleural effusion: A metaanalysis. Ann Clin Biochem 2003;40:374-81.
34. Burgess LJ, Maritz FJ, Le Roux I, Taljaard JJ. Combined use of pleural adenosine deaminase with lymphocyte/neutrophil ratio. Increased specificity for the diagnosis of tuberculous pleuritis. Chest 1996;109:414-9.
35. Chakraborty A, Ramaswamy S, Shivananjiah AJ, Puttaswamy RB, Chikkavenkatappa N. The role of genexpert in the diagnosis of tubercular pleural effusion in India. Adv Respir Med 2019;87:276-80.
36. Biswas D, Mukherjee S, Begum S, Paul A, Ghosh P, Sarkar S. Role of cartridge-based nucleic acid amplification test in diagnosis of tuberculous pleural effusion compared to tuberculous empyema in HIV seronegative patients. Int J Sci Stud 2017;5:125-9.
37. Valdés L, Alvarez D, Valle JM, Pose A, San José E. The etiology of pleural effusions in an area with high incidence of tuberculosis. Chest 1996;109:158-62.
38. Prakash UB, Reiman HM. Comparison of needle biopsy with cytologic analysis for the evaluation of pleural effusion: Analysis of 414 cases. Mayo Clin Proc 1985;60:158-64.
39. Brook I, Frazier EH. Aerobic and anaerobic microbiology of empyema. A retrospective review in two military hospitals. Chest 1993;103:1502-7.
40. Heffner JE, Nietert PJ, Barbieri C. Pleural fluid pH as a predictor of survival for patients with malignant pleural effusions. Chest 2000;117:79-86.
41. Psallidas I, Kalomenidis I, Porcel JM, Robinson BW, Stathopoulos GT. Malignant pleural effusion: From bench to bedside. Eur Respir Rev 2016;25:189-98.