

## A study of Clinico-radiological and etiological profile of pleural effusion patients diagnosed at tertiary care hospital

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**Background:** Pleural effusion is an excess fluid that accumulates between two pleural layers. Pleural fluid analysis and cytology are the mainstays for diagnosing various pulmonary diseases. **Aim and objective:** To study the clinico-radiological and etiological profile of pleural effusion patients diagnosed at a tertiary care hospital. **Material and Method:** All the patients who are clinic radiologically suspected were broadly evaluated clinically by the presenting complaints, detailed history, general, followed by systemic examination, and routine investigations like a complete blood count (CBC), pleural fluid cytopathological, biochemical, microbiological, and CBNAAT (Cartridge-Based Nucleic Acid Amplification Test) examination were done. **Results:** The majority of patients were in the age group of 31–40 years (n = 25). 31.25% followed by 20-30 years (n = 17) 21.25%. The most common symptom was breathlessness (52.25%), followed by fever (45%), chest pain (35%), cough (31.25%), and weight loss (27.25%). 45 (52.25%) cases were of exudative effusion and 35 (43.75%) cases of transudative effusion. CCF (16/35) 45.71% is the commonest cause of transudative pleural effusion, followed by CKD (11/35) at 31.42% and cirrhosis (6/35) at 17.14%. Tuberculosis 40% was the common cause of exudative pleural effusion, followed by malignancy (28.89%), empyema (11.11%), and synpneumonic (8.88%). High levels of ADA (above 40) were seen in 55% (11/20). CBNAAT detected MTB in 13.75% cases among exudative effusion, while cytochemistry and pleural biopsy favor tuberculosis (13.75% and 1.25%, respectively) in exudative effusion. **Conclusion:** While evaluating a case of pleural effusion, a combined approach involving clinical evaluation, radiographic and sonographic evaluation, pleural fluid analysis, pleural fluid cytology, and in cases where possible thoracoscopic pleural biopsy, must be utilized for fruitful and accurate diagnosis. CBNAAT could also be a useful rapid diagnostic tool for suspected tuberculous pleural effusion/empyema.

**Keywords:** pleural effusion, Clinico-radiological, etiological profile

### Introduction

A pleural effusion, i.e., an excessive accumulation of fluid in the pleural space, indicates an imbalance between pleural fluid formation and removal. Accumulation of pleural fluid is not a specific disease but rather a reflection of underlying pathology. Pleural effusions accompany a wide variety of disorders of the lung, pleura, and systemic disorders. Therefore, a patient with pleural effusion may present not only to a pulmonologist but to a general internist, rheumatologist, gastroenterologist, nephrologist, or surgeon. To treat pleural effusion appropriately, it is important to determine its cause. With knowledge of the pleural fluid cytology, biochemistry, and clinical presentation, an etiological diagnosis can be established in approximately 75% of patients.[1] Pleural effusion is an indicator of a pathologic process that may be of primary pulmonary origin, of an origin related to another organ system, or occasionally the first evidence of some other systemic disease. It may occur in the setting of acute or chronic disease and is not a diagnosis in itself. The occurrence of

pleural effusion [PE] is a common finding, with a higher incidence of effusions secondary to non-infective pathology in the western studies and infective pathology in India [2]. India has the highest prevalence of tuberculosis in the world, with 2/3rd of all TB patients being in India [3]. Tuberculosis is the main cause of effusion in India as compared to the other countries where malignancy and parapneumonic effusions are more common. Pleural tuberculosis is second in frequency after TB lymphadenitis. Diagnosing the etiology of pleural effusions clinically with certainty is a challenging task for physicians.

Congestive heart failure is the biggest condition that produces transudative pleural effusion, followed by hepatic hydrothorax. Nephrotic syndrome and hypoproteinemia are some other common causes [4]. Common causes of exudative effusion include tuberculosis, parapneumonic effusion, viral infections, and malignancy [5]. Other causes include hypothyroidism, pulmonary embolism with infarction, connective tissue disorders, pancreatitis, esophageal rupture (Boerhaave's syndrome), collagen vascular disorders, chylothorax, and hemothorax. With various diagnostic aids like pleural fluid analysis, pleural fluid cytology, pleural biopsy, ultrasonography, bronchoscopy, and thoracoscopy, serological tests like ANA, ADA, rheumatoid factor, and CT thorax help the physician arrive at the diagnosis at an earlier course of the disease [6]. Determining the etiological and clinical profile of PE helps in the adoption of regionally optimized diagnosis and therapeutic approaches. Here we have made an attempt to arrive at the clinic-radiological and etiological diagnosis of pleural effusion by collecting relevant clinical as well as laboratory data using the recent modalities available in tertiary care hospitals.

## Material and Methods

This prospective study was conducted in the Department of General Medicine, Dr. KNS Memorial Institute of Medical Sciences, Gadia, Barabanki, UP, India. Institute Ethics Committee approval was obtained before starting the study. Informed and written consent was obtained from all the patients and/or attendants before enrollment in the study. Total 80 adult patients of both sexes were selected for the study.

All the patients who are clinic radiologically suspected were broadly evaluated clinically by the present complaints, detailed history, and general and systemic examination. Routine investigations like a complete blood count (CBC), pleural fluid cytopathological, biochemical, microbiological, and CBNAAT (Cartridge-Based Nucleic Acid Amplification Test) examination. Sputum examination was done for AFB staining by the Ziel Nelson technique in all cases, Gram staining, and culture & sensitivity in specific cases. Chest X-ray PA view was done in all cases, and chest sonography and CT chest were done if required. Other specific investigations, like pleural biopsy (by Abrahms needle) and fiberoptic bronchoscopy were done if required as per the nature of specific diseases.

## Inclusion criteria

All cases in which the patient or relative of the patient gives informed consent.

All cases of pleural effusion admitted in mgmc (age > 15 years) with clinically or radiologically documented pleural effusion were included in the present study.

### Exclusion criteria

- Patients who are moribund, not fit, refusal for consent
- Patients who have bleeding disorder.
- Patients with trauma chest will be excluded.

### Statistically analysis

The data was coded and entered into a Microsoft Excel spreadsheet. Analysis was done using SPSS version 23 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Descriptive statistics included the computation of percentages, means, and standard deviations. The data were checked for normality before statistical analysis using the Shapiro-Wilk test. The chi-square test and Fisher exact test were used for qualitative data whenever two or more than two groups were used to compare. The level of significance was set at  $P \leq 0.05$ . ROC curve was also.

### Obsevation and Result

**Table 1: Demographic details of the study subjects**

Age	N	%
20-30	17	21.25
31-40	25	31.25
41-50	15	18.75
51-60	13	16.25
≥60	10	12.5
Gender	Male	50
	Female	30
Residence	Rural	60
	Urban	20

**Table 2: Distribution of various symptoms in study subjects**

Symptoms	N	%
Breathlessness	41	52.25
Chest pain	28	35
Cough	25	31.25
Weight loss	22	27.5
Night sweats	15	18.75
Fever	36	45
Icterus	8	10

**Table 3: Etiologic spectrum of the study subjects**

Etiology		N	%
Transduative (N=35)	Cardiac causes-CCF	16	45.71
	CKD	11	31.42
	Cirrhosis	6	17.14
	Etiology unknown	2	5.71
	Tuberculosis	18	40
Exduative (N=45)	Malignancy	13	28.89
	Empyema (bacterial)	5	11.11
	Synpneumonic	4	8.88
	Pancreatitis	2	4.44
	Etiology unknown	3	6.67

**Table 4: Association of ADA levels with etiological spectrum**

<b>Etiology</b>	<b>&lt;40 IU</b>	<b>40-70IU</b>	<b>&gt;70 IU</b>	<b>Total</b>
<b>Tuberculosis</b>	8	9	2	19
<b>CCF</b>	9	6	2	17
<b>Malignancy</b>	8	4	2	14
<b>CKD</b>	5	2	1	8
<b>Cirrhosis</b>	4	2	1	7
<b>Empyema (Bacterial)</b>	0	3	2	5
<b>Synpneumonic</b>	1	1	1	3
<b>Pancreatitis</b>	2	0	0	2
<b>Etiology unknown</b>	3	1	1	5
<b>Total</b>		28	9	50
<b>P-value</b>				0.001

**Table 5: Radiological profile of the study subjects**

<b>Etiology</b>	<b>Mild</b>	<b>Moderate</b>	<b>Massive</b>	<b>Total</b>
<b>Tuberculosis</b>	6	12	2	20
<b>CCF</b>	6	9	2	17
<b>Malignancy</b>	7	5	1	13
<b>CKD</b>	3	5	0	8
<b>Empyema</b>	2	4	0	6
<b>Synpneumonic</b>	2	3	0	5
<b>Cirrhosis</b>		3	3	3
<b>Pancreatitis</b>	1	1	0	2

<b>Etiology</b>	1	2	3	6
<b>Total</b>	28	44	11	50

**Table 6: Diagnostic yield of various investigations**

<b>Microbiological method</b>	<b>N</b>	<b>%</b>
<b>CBNAAT detects MTB</b>	11	13.75
<b>Cytobiochemistry favors MTB.</b>	20	25
<b>Pleural biopsy in favor of MTB</b>	1	1.25
<b>AFB stain detects MTB.</b>	3	3.75

## Discussion

The present study was done on patients with pleural effusion reporting to a tertiary care teaching hospital. The total number of cases studied were 80 with male predominance, that is, 50 with a male-to-female ratio of 2:1. Most of the studies reported almost similar gender patterns with male predominate, and profiles of these are Pandit et al. (1.79:1) [7], Valdes L. [8] et al. (62.5% males and 37.5% females with a ratio of 1.6:1), while a little higher ratio of males was reported by Al Quorian et al. [9]. Of 201 cases, 145 were males (72%), and 56 were females (27.9%), with a ratio of 2.58:1. Though the general understanding is that the incidence of pleural effusion is equal between both sexes, unless there is a specific etiological profile, the ratio varies from study to study and probably depends on the nature of the selection of patients [10].

In our study, the patients are in the age groups between 15 and more than 61 years, with the mean age of the patients being 32 years. The similar mean age in cases of effusion was also reported as 34, 33, and 31 years by Valdes L et al., Sharma SK [11] et al., and Subhakar K [12] et al., respectively. In our study, near three-fourths (75%) of patients were from rural areas and near one-fourth (25%) from urban areas. This rural predominance could be due to our hospital catering to rural populations. The most common symptom in our study is breathlessness (52.25%), followed by fever (45%), chest pain (35%), cough (31.25%), and weight loss (27.25%). These similar findings are compatible with the studies done by Porcel and Vives (2003) [13]. Light RW and Ball WC [14] also observed 51% breathlessness in their study. Breathlessness is a predominant symptom that compels the patient to report a health facility. In our study, more than half of the cases (55%) were of moderate radiological grade, followed by near one-fourth mild (35%), and massive (13.75%), which was similar to Reddy L et al. [15].

In our study, a high level of ADA (above 20) was seen in 55% (11/20) of tuberculosis patients, and empyema was 100%. Pleural fluid ADA > 40 U/l was taken as a diagnostic cutoff for tuberculous effusion, and it yielded 97.1% sensitivity, 83.14% specificity, 82% positive predictive value, and 94.6% negative. Although a pleural fluid ADA 70 IU/L is diagnostic of tuberculosis. In another study by Bandrés Gimeno (1994) [16] et al., the cut-off value of ADA >23 U/L had sensitivity, specificity,

positive, and negative predictive values of 96%, 100%, 1.0%, and 0.94%, respectively, for differentiating tuberculous pleuritis or neoplasia with lymphocytic exudate. Sharma SK et al. also recorded a cutoff value of 35 IU/L with 83% sensitivity and 66% specificity in the Indian population. Gupta A et al. (2018) showed that about 70% had raised ADA levels, predominantly in exudative effusion (94%), and almost 99% of these patients had tuberculosis. It appears that pleural fluid ADA level above 70 U/L is highly suggestive of tuberculous pleuritis, whereas pleural fluid ADA level below 40 U/L virtually rules out the diagnosis of International Journal of Medical and Health Research tuberculosis [17]. This finding correlates well with our finding where 27 patients had an ADA level > 70 U/. The ADA value is a sensitive and specific test for the diagnosis of tuberculous pleurisy. Our study also supports that results of ADA levels should be interpreted in parallel with clinical findings and other pleural fluid parameters such as lymphocyte-to-polymorph ratio, glucose levels, and cytopathology to differentiate between tuberculous effusion and parapneumonic effusion. CBNAAT detected tuberculosis in 11 (31.42%) patients out of 35 patients with exudative pleural effusion. Out of 45 tubercular pleural effusions and 5 patients with empyema, CBNAAT detected MTB in 17 and 8 patients, respectively. Study by Gupta et al. showed 25% of total patients having exudative pleural effusion detected MTB by CBNAAT of pleural effusion, while study by Chakarborty A et al. [18] showed 32% (24/75) of cases of tubercular pleural effusion detected MTB by CBNAAT, out of which 2 were rifampicin resistant. In our study and other studies have shown CBNAAT has the potential to significantly authenticate tubercular etiology in pleural fluid specimens with rapid test results, and it has an added advantage to assess the rifampicin drug sensitivity.

There were about 56.25% cases of exudative effusion and 43.75% cases of transudative effusion in our study. A study done by Shashikant A and Gupta A (2017) [19] observed a similar pattern: 66% cases of exudative and 34% transudative. In our study, tuberculosis (18/45) 40% was the most common etiology of exudative pleural effusion. It was followed by malignancy (13/45) 28.89%, empyema (5/45) 11.11%, and synpneumonic (4/45) 8.88% in terms of etiology. Desai PP (1993) [20] et al. reported tubercular effusion comprises 22.4% and 64% were of malignancy. This study has a predominance of the elder age group, which may be the reason for malignancy out number tuberculosis. In our study, congestive cardiac failure (16/35) was the commonest etiology of transudative effusion, followed by CKD (31.42%) and cirrhosis (17.14%). In a study by Al Quarain [21] et al., the common etiology was tubercular (37%) followed by malignancy (18%), parapneumonic (14%), and congestive cardiac failure (14%); Valdes L et al. showed tubercular (25%), malignancy (22.9%), and transudative (17.9%) were the commonest causes of pleural effusion. Similar results were observed in a study done by Al Alusi FA (2003) et al. [22] in Iraq and by Afful B (1986) et al. [23], showing tuberculosis the leading cause of exudative pleural effusion and CCF among the commonest ethologies for transduative pleural effusion. Yam LT et al. [24] have shown that predominant lymphocytes in pleural fluid are suggestive of either tuberculosis or malignancy in the majority of cases. Pandit et al. reported that 75% and 41% of diagnosed tuberculosis and malignancy patients, respectively, had predominant lymphocytes in their pleural fluid.

In our study, pleural biopsy was needed in undiagnosed exudative pleural effusions of only 3 in number, out of which 1 was nonspecific inflammation followed by

tuberculosis 1 and malignant in 1 patient. A good number of studies are available in which they used pleural biopsy or medical thoracoscopy as a primary tool for the diagnosis of pleural effusion. A study by Hucker et al. [25] found 21 cases (20.6%), Hansen et al. [26] found 45 cases (31%), and Blanc et al. [27] observed 57 cases (38.2%) of chronic nonspecific inflammation. In a study by Patil C et al. [28], out of 18 cases, five patients the histopathology report had chronic inflammation, and in one patient it was normal pleura [29]. While we needed a biopsy only 7 out of 116 patients, we were able to make a diagnosis with simple biochemical, molecular, and cytopathological examination. Our study suggests that thoracoscopy/pleural biopsy is not required in all the cases of exudative pleural effusion; it should be limited to only undiagnosed pleural effusion.

The limitation of the study was that the number of patients is small and the duration is a shorter time period, which could limit the general applicability of our findings to the larger community setup and a possible selection bias, as patients with advanced malignancy may have been referred directly for palliative care without further investigations. In the present study, diagnosed cases of pleural effusion that might be on conservative management before enrollment were included. So, the effects of previous treatment, which may affect our diagnostic workup and differential diagnosis, were not taken into account.

## Conclusion

The present study concludes that despite the revised national tuberculosis control program in India, the tubercular effusions are still at large. The cause is usually the noncompliance with antitubercular therapy. The malignant pleural effusion cases are far less than tuberculosis, but their incidence is rising as compared to previous studies. While evaluating a case of pleural effusion, a combined approach involving clinical evaluation, radiographic and sonographic evaluation, pleural fluid analysis, pleural fluid cytology, and, in cases where possible, thoracoscopic pleural biopsy, must be utilized to produce a fruitful and accurate diagnosis. CBNAAT is also a useful rapid diagnostic tool for suspected tuberculous pleural effusion/empyema, considering the advantage of rapid test results and information about drug resistance patterns, especially in high-burden countries such as India.

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