ISSN 2515-8260 Volume 10, Issue 1, 2023

ETIOLOGICAL, CLINICO-RADIOLOGICAL AND MICROBIOLOGICAL PROFILE OF EXUDATIVE PLEURAL EFFUSION

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ABSTRACT:

BACKGROUND: There are various causes of exudative Pleural effusion, rather than assumption of a diagnosis by clinical suspicion, proper diagnosis is needed in guiding specific targeted treatment. Exudative pleural effusions necessitate thorough investigation and specialized diagnostic methods. The main objective of this study is to determine the aetiologies of exudative pleural effusion, and to assess clinical profile along with radiological and microbiological profiling in current scenario in Western Maharashtra.

MATERIALS AND METHODS: A prospective, observational and cross-sectional study was done on 114 patients of exudative pleural effusion in a tertiary care centre. Patients above 10 years of age with biochemical evidence of exudative effusion were only included in the study. Biochemical, cytological and microbiological tests were done on their pleural fluid and their clinical profile was noted. In selected cases, Patients underwent pleural biopsy, Video Bronchoscopy and Image guided Lung Biopsy.

RESULTS: In young population, females were more affected (57%) whereas in middle age and in elderly population, males were more affected. Dyspnoea was the most common symptom. Radiological profiling showed majority had moderate effusion and preferably right sided effusion and >50% effusion were loculated. 70.2 % were of tubercular aetiology, 14 % were of malignant effusion, 10.5 % were of Para pneumonic effusion and 5.3 % were effusion secondary to pancreatitis. Estimation of pleural fluid adenosine deaminase plays an important role in the diagnosis of tubercular effusion. Fluid cytology and closed pleural biopsy helped in diagnosis of malignant effusion.

CONCLUSION: Tuberculosis is still the commonest causes of exudative effusions in western Maharashtra after which there is Para pneumonic effusions and malignant effusion. All patients should undergo ultrasonography of thorax to see for loculated pleural effusion. Though Pleural fluid ADA levels are highly sensitive with specificity for the diagnosis, along with that Pleural biopsy, Pleural fluid cytology and Image guided lung biopsy are necessary in indicated cases to correlate with the diagnosis. In case of workup of undiagnosed exudative effusion, Bronchoscopy and CT Pulmonary Angiogram (CTPA) proved to be an important investigation in arriving to a conclusion.

INTRODUCTION:

Pleural effusion is caused by either an excess of pleural fluid getting collected in the pleural space or a failure in pleural lymphatic absorption [1]. Normally, the pleural space contains 0.13 mL/kg body weight of pleural fluid. During respiration, the parietal and visceral pleura slide along smoothly due to the minimal amount of fluid that serves as a lubricant. The equilibrium between intrapleural pressure and hydrostatic, oncotic pressure of pleural capillaries ensures that the normal amount of fluid is maintained.[2, 3]

Excessive fluid will accumulate in the pleural area as a result of any imbalance in the aforementioned mechanism. The clinician faces a hurdle when trying to ascertain the cause of the pleural effusion once it has been identified.[4] Transudative pleural effusions are quite simple to diagnose because the underlying reasons are apparent from the history, physical examination, and a few routine laboratory tests.[5,6]

Contrarily, the majority of exudative pleural effusions are challenging to diagnose and necessitate initial thoracentesis, a series of biochemical, cytological, and microbiological investigations and specialized diagnostic

methods like computed tomography (CT) scan of thorax, pleural biopsy, bronchoscopy, and thoracoscopy. The location, patient and age, and advancements in diagnostic techniques for underlying causes each play a role in the aetiology distribution of pleural effusions in different series.[7, 8]

There is still a gap in our understanding of the etiological diagnosis and clinical profile of pleural effusion due to the small number of studies conducted in various regions. This study is done to determine the etiological diagnosis of pleural effusion; we also wanted to assess the effectiveness and complications of various diagnostic tests. This is because knowledge of the aetiology of pleural effusion requires to be augmented in selecting the most appropriate diagnostic tool in an actual scenario.

MATERIAL AND METHODS:

A prospective, observational and cross-sectional study was done on 114 patients of exudative pleural effusion in a tertiary care centre in western Maharashtra in the Department of Respiratory Medicine, for 2 years between October 2020 and October 2022. Detailed History, Physical examination, correlation of radiological, Biochemical and cytological investigation were done. Patients of both gender of more than 10 years of age with clinical, radiological and biochemical evidence of Pleural effusion which is exudative in nature were included in the study. Written and informed consent were taken. Patient with transudative Pleural effusion, hemothorax, non-tappable pleural effusion (after image-guided) were not included in the study. Hemodynamically unstable patients and patients unwilling to give valid consent are excluded from the study.

The subjects for the study were selected from the IPD and OPD of Department of Respiratory medicine after fulfilling the inclusion and exclusion criteria and after obtaining informed written consent. Pre-treatment assessments were performed which included detailed history with chief complaints, history of presenting illness and co-morbidity history and physical examination.

Renal function test, Serum Proteins, Serum LDH, Thyroid Function test, Random Blood Sugars wherever indicated in suspected cases.

Radiological tests included CXR films Postero-anterior view, USG Thorax and Abdomen-pelvis, and CT chest if done for certain patients. Chest X-ray was done to establish the diagnosis of Pleural effusion. Ultrasound Thorax was done to quantify fluid, and for marking for Diagnostic/Therapeutic Thoracocentesis. Diagnostic thoracocentesis was done on all subjects with tappable Pleural effusion and the Pleural fluid was sent for the following tests: Pleural Fluid for Total and differential Leucocyte count, Glucose, Proteins, and LDH. Light's criteria 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.

Patients with Exudative pleural effusion were chosen for our study and pleural fluid samples are sent for ADA, Culture and sensitivity, AFB Culture, CBNAAT for M.TB, Staining techniques (Gram stain/ZN stain/Fungal stain) and malignant cytology. Pleural biopsy, FNAC and Fibre-optic bronchoscopy with bronchoalveolar lavage was done in certain cases. In certain indicated cases, Image guided lung biopsy, CTPA were also done.

RESULTS:

A total of 114 consecutive cases of pleural effusion had been included in this study.

CLINICAL PROFILE:

Peak age of incidence was 20-30 years & 40-50 years with 24% of cases each. . Overall males 59% and females were 40 %. In young population, females were more affected (around 57%) than males (40%) whereas in middle age and in elderly population, males were more affected compared to females as shown in table 1.

Table 2 shows different etiology of pleural effusion. Out of 114 patients 70.2 % were of tubercular aetiology, 14 % were of malignant effusion, 10.5 % were of Para pneumonic effusion and 5.3 % were effusion secondary to pancreatitis.

On assessing symptoms of patient having pleural effusion as shown in Table 3,it reveals around 73% patients had non-productive cough and 15% had productive cough in which half of the patients had acute cough <3 weeks and rest patients had sub-acute and chronic cough. Only 4 % of subjects had haemoptysis. Coming to breathlessness, 90.5 % (n=103) of the overall subjects, in which 26.2% (n=27) had symptoms of dyspnoea <1 week, 15.5% (n=16) had 1-2 weeks duration, 27.2 % (n=28) had 2-4 weeks duration and 31.1 % (n=32) had >28

days duration of dyspnea. With grading, 14.6% (n=15) had grade 1 dyspnea, whereas 45.6% (n=47) had grade 2, 32% (n=33) had grade 3 and 7.8% (n=8) had grade 4 dyspnea. Overall, 31.1% (n=32) had >28 days of dyspnea and 45.6% (n=47) had grade 2 dyspnea. A total of 69.3% patients had fever in which 46.5% had low grade fever and 22.8% had high grade fever.

Figure 3 shows on comparing comorbidities with etiology, in patients with tubercular effusion, around 18% had Diabetes mellitus and 17.5 % had Hypertension, whereas in Para pneumonic effusion, around 50% of the patients had either Diabetes or hypertension or both. In malignant effusion patients, 37.5% patients had hypertension and 18% had diabetes.

RADIOLOGICAL PROFILE:

Figure 4 shows type of effusion, in which more than half of the patients (52.6%, n=60) had loculated effusion whereas 47.4% (n=54) had non loculated effusion. Figure 2 shows on comparing the grading of effusion with etiology, Majority of tubercular effusion and Para pneumonic effusion patients had moderate effusion, whereas majority of malignant effusion patients and effusion sec. to pancreatitis were gross effusion.

MICROBIOLOGICAL PROFILE:

Table 4 shows Microbiological Profile of patients were analysed using various samples of sputum, bronchoalveolar lavage, and pleural fluid analysis. Microbiological evidence in pleural fluid – Out of 12 Para pneumonic effusion cases, in only 5 cases there were growth in pleural fluid culture in which 2 were streptococcus, 2 were MRSA (Methicillin-resistant Staphylococcus aureus) and 1 was acinetobacter. In case of CBNAAT, only 11 cases were CBNAAT positive for M.tb. Among 15 patients who underwent bronchoscopy with bronchoalveolar lavage, 5 patients were BAL CBNAAT positive for mycobacterium tuberculosis, for 6 patients, BAL and TBLB yielded the diagnosis of malignancy and 4 patients had evidence of bacterial growth on BAL fluid (1 MRSA, 2 Klebsiella and 1 streptococcus). Patients underwent closed pleural biopsy with Abram's needle and samples were sent for histopathological examination, in which 13 had findings suggestive of tubercular pleuritis, and 9 had findings suspicious of malignancy among which few gave definite diagnosis of malignancy.

Out of 15 malignant effusion cases, 10 cases had malignant cells in their pleural fluid. USG Guided lung biopsy was done in 2 cases, CT Guided lung biopsy in one case. 3 cases had Mtb detected by CBNAAT in sputum sample and one patient had MRSA isolated in sputum

FLUID CHARACTERISTICS:

Table 5 shows Differential counts in pleural fluid – More than 77.2% patients (n=88) had lymphocytic predominance whereas only 22.8% (n= 26) had neutrophil predominance. On comparing differential counts with etiology, most of the tubercular patients (82.5%, n=66) had lymphocytic predominance, in rest of the 17.5% patients (neutrophil predominance) few cases were tubercular empyema. In case of malignant effusion patients, all (100%) were lymphocytic predominant. In case of Para pneumonic effusion, all (100%) were neutrophil predominant. 52.6 % (n=60) patients had right sided effusion whereas 47.4% (n=54) had left sided effusion.

Pleural fluid ADA (Table 6) Around 36.8 % patients had ADA in the range of 40- 70, whereas 25.4% patients had ADA less than 30 and 23.7% patients had ADA in the range of 70-100, 8.8% patients had 30-40 and 5.3% patients had >100. On comparing the ADA with different etiologies, All Malignant effusion cases had ADA <30, 48.8% of tubercular effusion patients had ADA 40-70 and 33.8 % tubercular patients had ADA 70-100 and around 80% Para pneumonic effusion patients had ADA <40. ADA was sensitive in diagnosing tubercular effusion and in malignant effusion.

DISCUSSION:

The main purpose of this study is to determine the prevalence and the etiologies of exudative effusions among patients hospitalized for pleural effusion, and to correlate pleural effusion with some potential risk factors.

In our study females were more commonly affected in young population whereas males in elderly population. Dyspnoea were the most common symptom. Radiological profiling showed majority had moderate effusion and preferably right sided effusion and >50% effusion were loculated. 70.2 % were of tubercular aetiology, 14 % were of malignant effusion, 10.5 % were of Para pneumonic effusion and 5.3 % were effusion secondary to pancreatitis. Malignant effusion had .pleural fluid ADA level 30IU/L.48.8% tubercular effusion had pleural fluid level about 70-100IU/Differential count of pleural fluid showed predominance of lymphocytes.

Dhital et al 2009[9] in his study he aimed to assess most common cause of unilateral and bilateral pleural effusion. Among 100 patients that the most common cause of unilateral pleural effusion is tuberculosis followed by Para pneumonic effusion and many cases of those belong to younger age group (21-30 yrs) and most common cause of bilateral pleural effusion is congestive cardiac failure. The mean age of the patient was 44.89 ± 21.59 and must patients with pleural effusion belong to age group 21- 30. Most common cause of pleural effusion was found to be tubercular effusion followed by Para pneumonic effusion. Right sided effusion was seen in most cases of tubercular Para pneumonic and malignant effusion whereas bilateral effusion was seen in 87.5% of the patient (7 out of 8) having congestive heart failure and all cases of renal disease (4 out of 4). Shortness of breath (83%), cough (67%) and fever (66%) are the most common mode of clinical presentation.

Maikap et al 2015[10] The most common cause pleural effusion in this study was tuberculosis (68.8%),followed by malignancy (14%), empyema (6%), and transudative effusion (2.8%). Pleural effusion was commonly seen in male (66%). Even after thorough investigations with the help of closed pleural biopsy, fibre optic bronchoscopy, CT scan and CT guided fine needle aspiration cytology and others, 5.2% of cases could not be diagnosed. He concluded that thoracoscopic pleural biopsy will narrow down the gap in diagnosing such cases.

Desai et al 2018 [11] he studied the exudative pleural effusion profile among Bhuj people. He found that the majority were tubercular in origin (67%),13%,8%,3%and 6% were malignant effusions, Synpneumonic effusion, pancreatic effusions and empyema respectively. In his study he could not Diagnose 3% of effusions. Massive effusions were seen in 53.8% of malignant effusions and 33.3% of empyema. Lymphocyte predominant effusions were seen in 84.6% and 89.6% of malignant and tubercular effusions. Positive cytology was seen in 61.5% of malignant effusions Tubercular effusion had a pleural fluid ADA more than 40 IU/L. and 92.3% of malignant effusion had pleural fluid ADA less than 30IU. Pleural effusion is a commonly encountered in medical practice and in our country, the commonest cause is tuberculosis.

Reddy et al 2019 [12] he conducted a study, 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. Majority of the study population (63.4%) were between 20 and 60 years of age. 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 Para pneumonic effusion (28.5%) and malignant pleural effusion (22.2%).

Ibrahim et al 2021 [13]conducted a retrospective cross sectional study in beirut which showed that 78% of patients had exudative pleural effusion, while the rest 22% had transudative effusion. Cardiovascular diseases were the most common etiology of transudative effusion (76.6%) and infectious Para pneumonic effusions were the most common causes of exudates (48.8%).

CONCLUSION:

Tuberculosis is still the commonest causes of exudative effusions in western Maharashtra after which there is Para pneumonic effusions and malignant effusion. All patients should undergo ultrasonography of thorax to see for loculated pleural effusion. Though Pleural fluid ADA levels are highly sensitive with specificity for the diagnosis, along with that Pleural biopsy, Pleural fluid cytology and Image guided lung biopsy are necessary in indicated cases to correlate with the diagnosis. In case of workup of undiagnosed exudative effusion, Bronchoscopy and CT Pulmonary Angiogram (CTPA) proved to be an important investigation in arriving to a conclusion.

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Table 1: Age and Gender

Age group (years)	Female		Male	
	n	%	n	%
<20	4	57.1	3	42.9
20-30	16	59.3	11	40.7
30-40	6	35.3	11	64.7
40-50	12	42.9	16	57.
50-60	5	27.8	13	72.2
>60	3	17.6	14	82.4
Total	46	40.4	68	59.6
Chi square p value=0.11 (Not significant)				

Fig 1: Gender

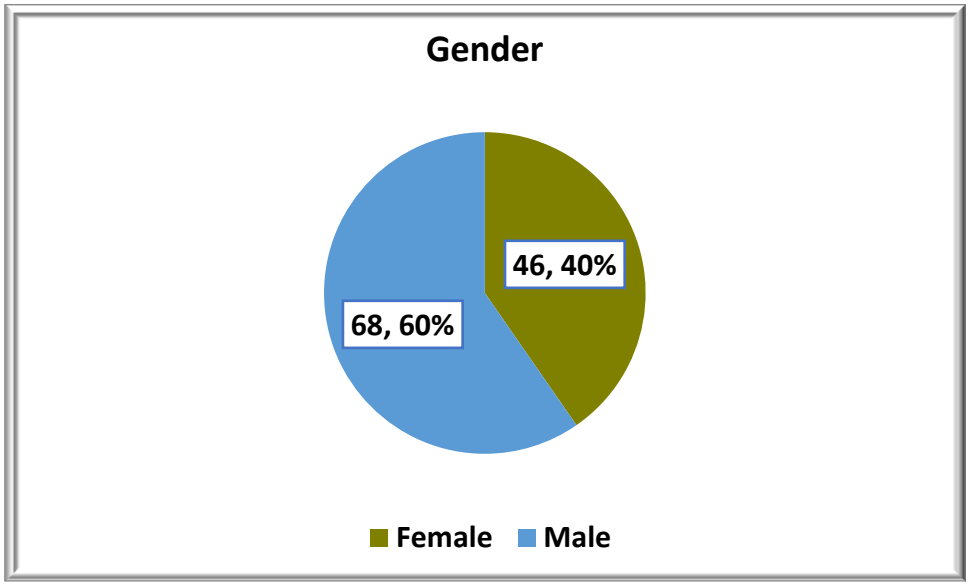

Table 2: Etiology

Etiology	Number	Percentage
Tuberculosis	80	70.2

ISSN 2515-8260 Volume 10, Issue 1, 2023

Malignant effusion	16	14.0
Parapneumonic effusion	12	10.5
Effusion secondary to pancreatitis	6	5.3
Total	114	100.0

Table: 3 Symptoms

Symptoms	**Number**	**Percentage**
cough		
No cough	13	11.4
Dry cough	84	73.7
productive	17	14.9
Duration of cough		
<3 weeks	51	50.5
3-8 weeks	29	28.7
>8 weeks	21	20.8
Sputum	17	26.3
Haemoptysis	4	3.5
Fever		
No	35	30.7
Low grade	53	46.5
High grade	26	22.8
Chest pain	84	73.7
Breathlessness	103	90.5
Duration of breathlessness		
<1 week	27	26.2
1-2 weeks	16	15.5
2-4 weeks	28	27.2
>4 weeks	32	31.1
Grading of dysponea		
Grade I	15	14.6
Grade II	47	45.6
Grade III	33	32.0
Grade IV	8	7.8

ISSN 2515-8260 Volume 10, Issue 1, 2023

Figure 2: Grading effusion in different etiology

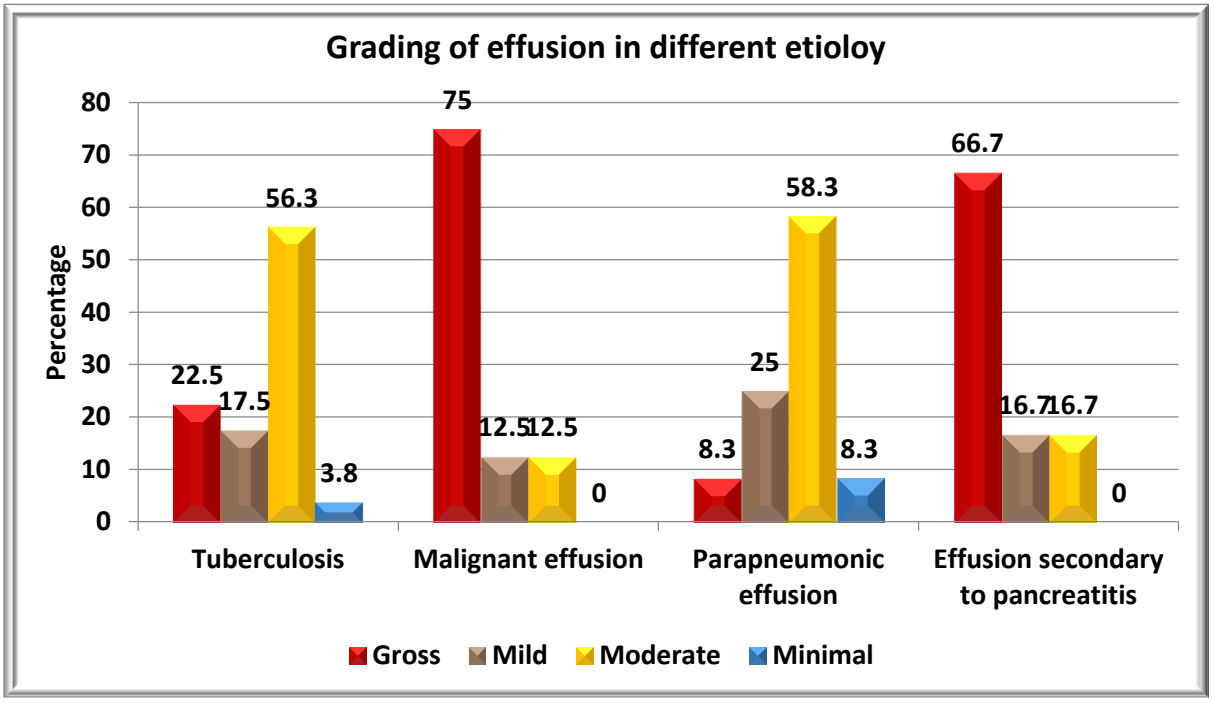

Figure 3: Comorbidities with etiology

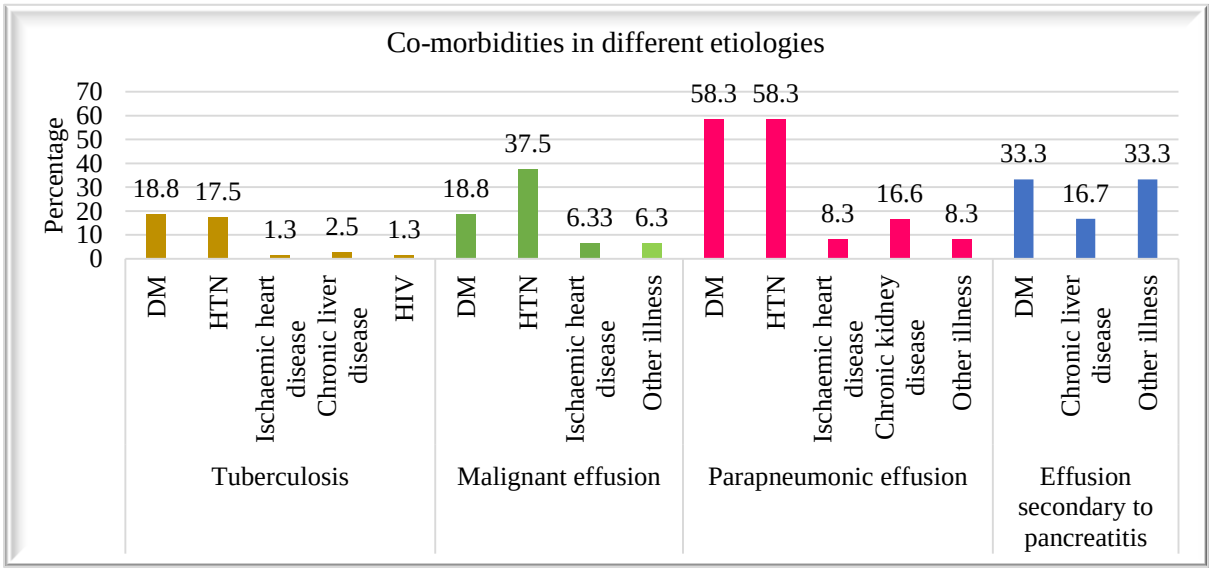

Figure 4: Type of effusion

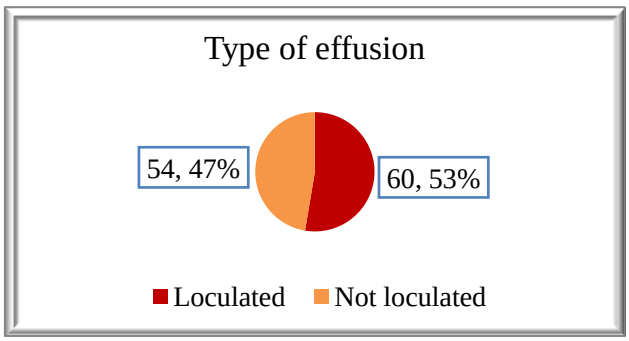

Table 4: Microbiological profile

Parameter	Number	Percentage
Cobweb		
Present	51	44.7
Absent	63	55.3
Growth in Pleural fluid C/S		
Absent	111	97.4
Present	3	2.6
Acinetobacter	1	-
Streptococcus	2	-
Pleural fluid CBNAAT		
Detected	11	9.7
Not Detected	103	90.3
Relevant FNAC/Other findings		
USG guided lung biopsy	2	
CT guided lung biopsy	1	
Sputum CBNAAT-MTB detected	3	
Sputum C/S-MRSA	1	

Table 5: Differential count analysis with etiology

Differential count	Etiology								Total	P-value
	Tuberculosis		Malignant effusion		Parapneumonic effusion		Effusion secondary to pancreatitis			
	n	%	n	%	n	%	n	%		
Lymphocyte predominant	66	82.5	16	100.0	0	0	6	100	88	**<0.001**
Neutrophil predominant	14	17.5	0	-	12	100	0	0	26	
Total	**80**	**100**	**16**	**100**	**12**	**100**	**6**	**100**	**114**	

Table 6: Association of ADA categories with etiology

ADA ctegories	Etiology								Total	P-value
	Tuberculosis		Malignant effusion		Parapneumonic effusion		Effusion secondary to pancreatitis			
	n	%	n	%	n	%	n	%		
<30	4	5.0	16	100	7	58.3	2	33.3	29	**<0.001**
30-40	4	5.0	0	-	4	33.3	2	33.3	10	
40-70	39	48.8	0	-	1	8.3	2	33.3	42	
>70	27	33.8	0	-	0	-	0	-	27	
>100	6	7.5	0	-	0	-	0	-	6	
Total	**80**	**100**	**16**	**100**	**12**	**100**	**6**	**100**	**114**	