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Diagnostic yield and etiological spectrum of medical thoracoscopy-guided pleural biopsy in various exudative pleural effusions: experience from a rural tertiary center in north India

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Abstract

Exudative pleural effusions still today remain a frequent diagnostic challenge. Approximately 20-40% of cases remain undiagnosed after a pleural fluid study and closed pleural biopsy. Medical thoracoscopy (MT), a new tool, enables direct visualization and targeted pleural biopsy, substantially improving diagnostic accuracy. The objective of this study was to determine the diagnostic yield, etiological profile, and procedure-related complications of MT-guided pleural biopsy in various groups of moderate to massive exudative effusions from a rural tertiary center in north India. In secondary objectives, we also analyzed the same in undiagnosed, hemorrhagic, and pyothorax patients as our experience with MT. This cross-sectional study was conducted and collected data over the years (2015-2024). A total of 103 patients (67 males, 36 females; mean age 47.2±17.4 years) with exudative pleural effusion (per Light's criteria) and met inclusion exclusion criteria underwent semi-rigid MT under conscious sedation. Undiagnosed effusion was defined as exudative effusion with negative microbiological (cartridge-based nucleic acid amplification test, Gram stain culture, tuberculosis (TB) culture) and malignant cytological investigations, and pleural fluid ADA <70 U/L was considered. Histopathological findings were analyzed to determine diagnostic yield, etiological distribution, and complications. The overall diagnostic yield was 95.1% (98/103). Malignancy accounted for 37 (35.9%), TB for 29 (28.2%), and inflammatory lesions for 31 (30.1%); 1 case (0.97%) was sarcoidosis, and 5 (4.9%) were non-diagnostic. In the undiagnosed group (n=67), diagnostic yield was 94.0%, with malignancy [37 (55.2%)] as the leading cause, followed by TB [16 (23.88%)] and inflammatory lesions [9 (13.43%)]. Metastatic adenocarcinoma was the most common malignant subtype (35.1%). Among hemorrhagic effusions (n=30), 70% were malignant. Among 37 cases of pyothorax, it was detected that, based on histopathology, 9 patients (24%) had tuberculous pyothorax and one malignant case. Complications occurred in an overall 10.7% of patients, predominantly minor and safe. Mean chest tube duration was 2.8 days for TB, 5.8 days for inflammatory, and 6.7 days for malignant effusions. Overall, MT-guided pleural biopsy is a safe, minimally invasive, and high-yield diagnostic tool for exudative pleural effusions. It should be prioritized for undiagnosed pyothorax and hemorrhagic effusions to ensure definitive etiological diagnosis and evidence-based personalized management to avoid empirical use of antitubercular therapy.

Key words: medical thoracoscopy, pleuroscopy, exudative pleural effusion, undiagnosed pleural effusion, pleural biopsy, CBNAAT, tuberculosis.

Introduction

Pleural effusion presents as one of the common day to day clinical problems encountered by a Pulmonologist, with an estimation of around 1.5 million cases annually in US alone [1]. Worldwide epidemiology varies widely, but Tuberculosis and Malignancy remain predominant in this part of the world or more to say developing countries [2]. The diagnostic approach in Pleural fluid analysis for etiology starts with thoracocentesis for pleural fluid sample to laboratory based biochemical, cytological and microbiological examinations [3]. Light's criteria, established in 1972, remains the gold standard for differentiating transudates from exudates, requiring at least one of the following: pleural fluid protein to serum protein ratio >0.5, pleural fluid lactate dehydrogenase (LDH) to serum LDH ratio >0.6, or pleural fluid LDH >2/3rd upper normal limit of serum LDH as per British Thoracic Society Guidelines 2010 [4].

Even after comprehensive initial evaluation by pleural fluid analysis and closed pleural biopsy, around 20-40% of exudative pleural effusions remain Undiagnosed [5-8]. This diagnostic gap leads to the need of more invasive procedures to obtain larger pleural tissue samples under direct visualization to confirm etiology. In real world Medical thoracoscopy (MT), a technique pioneered by Hans-Christian Jacobaeus in 1910 was used for the treatment of Tuberculous pneumothorax [9]. Since then, MT has evolved as an essential diagnostic and therapeutic instrument in modern Respiratory medicine [10]. Unlike VATS (Video Assisted Thoracoscopic Surgery) that needs general anaesthesia with single-lung ventilation, Medical thoracoscopy (MT) is less invasive. Being performed in spontaneously breathing patients under conscious sedation, MT has become more accessible to modern day Pulmonologists as a suitable daycare procedure [11].

Extensive International literature has now established the superior diagnostic yield of MT compared to blind closed pleural biopsy with reported sensitivities exceeding 95% for Malignancy and 99% for Tuberculosis [12]. That’s being significantly higher for MT than 44% and 51% respectively for closed pleural biopsy [12-15]. The major advantage of MT being easy access for Pulmonologists to get a direct visualization of visceral pleura, parietal pleura and recesses to locate the target abnormal lesions. This enables us to acquire larger tissue biopsy specimens needed for histopathological examinations and immunohistochemistry [16]. Adequate tissue samples become particularly invaluable in cases of malignant mesothelioma and metastatic pleural disease, where architectural patterns and immunohistochemical studies play a distinctive role in differentiation [17].

While Medical thoracoscopy (MT) has become standard practice in many tertiary centres worldwide, data documentation from Rural tertiary care centres in India, where the high disease burden, resource constraints and delayed referrals differ significantly from urban settings, remains limited. The etiological spectrum of pleural effusions in rural settings may vary due to Tuberculosis or malignancy prevalence, occupational exposures, smoking patterns, and access to early diagnostic facilities. Furthermore, the safety and feasibility of performing MT in resource limited settings with appropriate training but potentially limited back up surgical support requires documentation to encourage future works [18,19].

The MT-Pleura Study was therefore designed to evaluate the diagnostic yield and etiological spectrum of Medical thoracoscopy-guided pleural biopsy in patients with various types of exudative pleural effusions at a Rural tertiary care centre in North India. Working in a Rural setting often patient referrals are delayed and lost to follow up occurs. We also particularly emphasized on Undiagnosed, Pyothorax and Haemorrhagic effusions and the changing epidemiological patterns of pleural diseases in these settings.

Objectives

Primary objectives

To determine the diagnostic yield and etiological spectrum of Medical thoracoscopy-guided pleural biopsy among patients with various exudative moderate to massive pleural effusions.

Secondary objectives

1. To determine the diagnostic yield and etiological distribution specifically in Undiagnosed pleural effusions (67 cases).
2. To determine the etiological distribution specifically in Haemorrhagic pleural effusions (30 cases) and Pyothorax (37 cases)
3. To document and analyze complications encountered during and after the Medical thoracoscopy procedure.

Materials and Methods

Study design and settings

This was a hospital based cross-sectional Observational study (**The MT-Pleura Study**) conducted in the Department of Respiratory Medicine, U.P University of Medical sciences (UPUMS), Saifai, UP - a Rural based tertiary care centre with outpatient and inpatient

departments. Data was collected over the years (January 2015 - December 2024), however COVID 19 disrupted the study and was restarted later with no change in study protocol of recruitment. Around 156 patients were screened and evaluated out of which 103 patients were enrolled for the study based on consent and inclusion-exclusion criterias over the years. Written informed consent was obtained from all participants after detailed explanation of the study protocol in their native language and after the Institutional ethical clearances (53 R/RIMS&R/2014-15).

Study population - The MT-Pleura Study

Inclusion criteria

1. Diagnosed exudative moderate to massive pleural effusion cases as per Light's criteria: (a) Ratio of pleural fluid protein to serum protein >0.5, OR (b) Ratio of pleural fluid LDH to serum LDH >0.6, OR (c) Level of pleural fluid LDH >2/3rd upper normal limit of serum LDH (any one or more criterion positive; transudate excluded by all three criteria negative) as per British Thoracic Society Guidelines 2010 [4]
2. Male or female patients 18 to 70 yrs of age attending the inpatient or outpatient - Department of Respiratory Medicine with exudative pleural effusion.
3. Moderate to massive pleural effusion confirmed on chest radiography and ultrasonography, suitable for intercostal drain insertion and Medical Thoracoscopy.

Exclusion criteria

1. Patients with transudative pleural effusion as per Light's criteria.
2. Clinically and medically unfit for interventional procedures including hemodynamic instability, coagulation defects (altered bleeding time, clotting time, prolonged prothrombin time by >4 seconds, INR >1.5, platelet count <50,000/mm^3), severe hypoxemia, or intractable cough.
3. Patients aged below 18 years or above 70 years.
4. Extensive pleural adhesions with narrow intercostal spaces precluding safe thoracoscopy access.
5. Moderate to massive effusion with positive CBNAAT/TB culture or malignant cytology in diagnostic pleural fluid study.

Definitions

Undiagnosed Pleural effusion: defined as failure to achieve a diagnosis by initial pleural fluid analysis including pleural fluid adenosine deaminase (ADA) levels <70 U/L and negative CBNAAT/Bactec culture/TB culture and malignant cytology [19]. Because the study was conducted in a high tuberculosis-burden setting where empirical antitubercular therapy is frequently initiated on intermediate ADA values, a conservative ADA threshold of 70 U/L was pre-specified rather than the conventional rule-in cutoff of 40 U/L, so that patients in the intermediate 40–70 U/L band underwent histopathological confirmation rather than empirical treatment.

Pyothorax - Empyema thoracis: frank pus in pleural cavity. Pyothorax, the diagnosis is established by any one of [4,19]:

1. Frank pus on pleural aspiration (grossly purulent fluid), OR
2. Positive pleural fluid Gram stain, OR
3. Positive pleural fluid culture.

Haemorrhagic pleural effusion was defined by grossly blood-stained pleural fluid on aspiration (macroscopic appearance), in the absence of criteria for haemothorax (pleural fluid haematocrit <50% of peripheral blood) [19].

Diagnostic yield

Proportion of patients in whom a definitive histopathological diagnosis was established through medical thoracoscopy-guided pleural biopsy, calculated as (number of patients with conclusive diagnosis / total number of patients who underwent thoracoscopy) × 100.

Study procedure

Pre-procedure evaluation

All patients enrolled in the study underwent clinical evaluation which included detailed history and physical examination. Baseline investigations included - complete blood count, renal function test, liver function test, coagulation profile, INR & platelet count, and routine serology tests. Chest radiography (posteroanterior view) and Ultrasonography of thorax for localization, quantification and entry site marking. Effusion volume was estimated sonographically using the Balik formula (V = 20 × maximum interpleural distance in mm) in the supine position; effusions estimated at 500–1500 mL was classified moderate and >1500 mL massive [20]. Contrast enhanced computed tomography (CECT) were performed as needed to assess the

feasibility of thoracoscopy and evaluate parenchymal lesions. Electrocardiography and echocardiography were performed to assess cardiovascular fitness.

Pleural fluid analysis included cell count and differential, biochemical analysis (protein, glucose, LDH), Adenosine deaminase (ADA) estimation, Gram stain and culture sensitivity, acid fast bacilli (AFB) smear, CBNAAT for TB, TB culture, fungal KOH stain and culture (if needed) and Malignant cytology (2 samples) examinations were done routinely. Serum LDH was measured simultaneously for Light's criteria calculations. Those with CBNAAT/TB culture or malignant cytology positive in pleural fluid were not subjected to MT.

Medical thoracoscopy procedure

MT was performed under conscious sedation as a single port procedure using a semi-rigid video Thoracoscope (Olympus CV190 EVIS EXERA III 190 series, Japan). Patients were kept fasting for 6 hours prior to the procedure. Patients were positioned in lateral decubitus with the diseased side up and the ipsilateral arm positioned above the head to widen intercostal spaces and improve access.

The procedure was performed under the conscious sedation using midazolam (0.05 mg/kg body weight) and intravenous tramadol (100 mg) for analgesia. Supplemental doses were administered as needed during the procedure. In case of inadequate analgesia with tramadol, intravenous pethidine (25 mg) was administered as rescue analgesia in selective cases. Continuous monitoring of vital signs, oxygen saturation and level of consciousness was performed throughout the procedure.

After sterile dressing & draping preparation, local anaesthesia was achieved by infiltrating the skin, subcutaneous tissue, intercostal muscles, and parietal pleura with 10-20 mL of 2% lignocaine at the 5th or 6th intercostal space in the mid-axillary line. A 1.5-2 cm skin incision was made along the line of the intercostal space, followed by blunt dissection of subcutaneous tissue and intercostal muscles using curved artery forceps. A 10 mm diameter cannula with blunt trocar was inserted into the pleural cavity, and the trocar was replaced with the semi-rigid video thoracoscope.

Pleural fluid was suctioned through catheter to enable clear visualization of the entire pleural surface. Systemic examination of the visceral pleura, parietal pleura, diaphragmatic pleura and costophrenic recess was performed. Adhesions were gently lysed using the thoracoscope or biopsy forceps when necessary to allow complete visualization. Multiple pleural biopsies (typically 4-6 samples) were taken from the suspicious areas on the parietal pleura using the

"peeling of pleura" technique - grasping the parietal pleura with biopsy forceps introduced through the working channel and performing a shearing movement.

Following completion of biopsy, the thoracoscope and cannula were removed and a 28-32 French intercostal chest tube was inserted through the same port and secured with sutures. The chest drain was connected to an underwater seal drainage system. Post-procedure chest radiography was performed after 12 hours to assess lung expansion and rule out complications.

Post-procedure care and drain removal

The intercostal chest drain (ICD) was removed when lung expansion was complete and drain output decreased to less than 100 mL per 24 hours for three consecutive days (BTS 2010 drain removal by 12-72 hrs) [4] or earlier. Biopsy specimens were immediately placed in 10% formalin for histopathology and immunohistochemistry while NS samples for CBNAAT/TB culture and BACTEC culture for examination at the Department of Pathology, UPUMS, Saifai.

Data collection and statistical analysis

Demographic data (Age, sex), clinical presentation, radiological findings, pleural fluid analysis parameters, thoracoscopic findings, histopathological diagnosis, complications and duration of chest tube drainage were systematically recorded in structured proforma. Data was entered into Microsoft Excel and analyzed using SPSS software for Windows version 26 (IBM Corp., Armonk, NY, USA). Diagnostic yield was calculated as proportion of patients with conclusive histopathological diagnosis.

Results

Baseline characteristics

A total of 103 patients with exudative pleural effusions underwent medical thoracoscopy during the study period. The mean age of the patients was 47.2 ± 17.4 years (range 18-70 yrs). The study population comprised 67 males (65%) and 36 female (35%) with male to female ratio 1.86:1. Age distribution analysis revealed that Tuberculosis was more prevalent in the younger age group (18-30 years, 48.3%), while Malignancy showed increasing incidence with age, 61-70 years age group (45.9%). Inflammatory lesions were predominantly seen in younger patients (18-30 years, 32.2%).

Based on radiological evidence, pleural effusions were right sided in 60 patients (58.3%), left sided in 41 patients (39.8%) and bilateral effusion in 2 patients (1.9%). The distribution of

cases included 53 pleural effusions (51.45%), 19 pyopneumothorax (18.44%), 18 pyothorax (17.47%), and 13 hydropneumothorax (12.6%). Among the total cohort, 67 patients (65.04%) had Undiagnosed pleural effusions with ADA <70 U/L. Pleural fluid analysis of 103 patients based on ADA levels had: median 41.0 U/L (IQR 21.9–116.4; mean 74.4 ± 77.2; range 2.7–392.3). Tubercular effusions were predominantly lymphocytic and Pyothorax had neutrophil predominance and exudative as per Light's criteria.

Overall diagnostic yield and etiological spectrum (n=103)

Medical thoracoscopy-guided pleural biopsy achieved an overall diagnostic yield of 95.14% (98/103 patients). The etiological distribution in the entire cohort was as follows - Malignancy 37 cases (35.9%), Inflammatory lesions 31 cases (30.1%) - comprising acute inflammation 3 cases, acute-on-chronic 12 cases, and chronic inflammation 16 cases, Tuberculosis 29 cases (28.2%), Sarcoidosis 1 case (0.97%) and Non-conclusive 5 cases (4.85%) (Figure 1). Nondiagnostic cases were on the base of Pathology reporting of Nonspecific inflammation (3 cases) and Nonconclusive (2 cases) and repeat biopsy request for sample inadequacy and loss of tissue in processing.

Among the 37 malignancy cases, the histopathological subtypes included: Poorly differentiated carcinoma (8 cases, 21.6%), Adenocarcinoma (13 cases, 35.1%), Squamous cell carcinoma (5 cases, 13.5%), non-small cell lung cancer requiring further immunohistochemistry (3 cases, 8.1%), Small cell/round cell carcinoma (3 cases, 8.1%), Mesothelioma (2 cases, 5.4%), Lymphoma (2 cases, 5.4%), and AdenoSquamous carcinoma (1 case, 2.7%). The predominance of metastatic pleural disease (35/37 cases) over primary pleural mesothelioma (2/37 cases) was notable (Table 1). Etiology by ADA band (full cohort, n=103, MT-histopathology reference standard): ADA range of 40-70 U/L becomes very difficult to determine the etiology even in endemic country like India without biopsy evidence. Malignancy was found in 30 and 7 cases with ADA <40 U/L and 40-70 U/L. Tuberculosis was found in 10 and 6 cases with ADA <40 U/L and 40-70 U/L respectively (Table 2).

Among the 29 cases of tuberculosis diagnosed by histopathology showing caseating granuloma in all the cases, CBNAAT and TB culture was positive in 9 (31%) and 5 (17%) cases respectively from the biopsy samples only seen on follow up.

Diagnostic yield in undiagnosed pleural effusions (n=67)

Among 67 patients of Undiagnosed pleural effusion (65.04%), medical thoracoscopy achieved a diagnostic yield of 94.03% (63/67 patients). The etiological distribution in this subgroup demonstrated a markedly different pattern compared to the overall cohort: Malignancy 37 cases (55.2%) - representing the predominant diagnosis, Tuberculosis 16 cases (23.88%), Inflammatory lesions 9 cases (13.43%), Sarcoidosis 1 case (1.49%), and non-conclusive 4 cases (5.97%) (Figure 2).

Hemorrhagic pleural effusions (n=30)

In our study Haemorrhagic pleural effusions were identified in 30 patients in total (29.13%). This type of effusion may have malignant or benign etiologies. Among these, Medical thoracoscopy achieved a diagnostic yield of 96.66% (29 out of 30 patients). The etiological distribution was: Malignancy 21 cases (70%) [Adenocarcinoma 5 cases (23.8%), Squamous cell carcinoma 4 cases (19.04%), Poorly differentiated carcinoma 5 cases (23.81%), Small cell/round cell carcinoma 2 cases (9.53%), Non-small cell lung cancer 2 cases (9.53%), Mesothelioma 2 cases (9.53%), Lymphoma 1 case (4.76%)], Tuberculosis 5 cases (16.7%), Chronic inflammation 2 cases (6.7%), Sarcoidosis 1 case (3.33%), and Non-conclusive 1 case (3.33%). The predominance of Malignancy (70%) as the cause of haemorrhagic effusions aligns with established clinical understanding.

Pyothorax cases (n=37)

In our study among 37 patients out of total 103 patients presented with Pyothorax (35.9%) with diagnostic yield 97.3%. Histopathological examination after MT revealed: Tuberculosis in 9 patients (24%), acute inflammation in 3 patients (8%), acute-on-chronic inflammation in 12 patients (32.4%), chronic inflammation in 11 patients (30%), Malignancy (AdenoSquamous carcinoma) in 1 patient (3%), and non-conclusive in 1 patient (3%). The finding of Malignancy in a patient presenting with pyothorax highlights the importance of histopathological examination even in apparently Infectious presentations, probably a Secondary infection of a malignant effusion. Repeat pleural fluid culture and biopsy culture was positive for Streptococcus species and was treated with antibiotics as per sensitivity.

Complications

MT related complications occurred in 11 patients (10.68%) out of 103 procedures. The spectrum of complications included: Bleeding 4 cases (3.9%) – all four patients had borderline coagulation parameters (Normal range being - bleeding time 5-7 min, clotting time 2-5 min, aPTT 50-75 sec, prothrombin time 10-13 sec). Local bleeding was managed conservatively with local pressure application and intravenous tranexamic acid in one case. Surgical emphysema 2 cases (1.94%) - both resolved spontaneously within 7 days without intervention. Poor wound healing 2 cases (1.94%) - both patients had Diabetes mellitus and healing improved with glycemic control and regular wound dressing; pleurocutaneous fistula 1 case (0.97%) - self-limiting, resolved spontaneously. Death occurred in 1 case (0.9%) - occurred 24-72 hours post-procedure in patients with severe disseminated malignancy (Lymphoma with massive effusion and embolism). The patient was hemodynamically stable immediately post-procedure for 48hrs, suggesting that the death was attributable to underlying disease severity rather than the procedure-related complication.

Duration of chest tube drainage

Post MT intercostal chest tube drainage, mean duration varied according to the underlying etiology: Tuberculosis 2.8 days (range 2-7 days), Inflammatory lesions 5.8 days (range 3-14 days), Metastatic pleural effusions 6.7 days (range 4-21 days), and Malignant mesothelioma 6.9 days (range 5-27 days). The longer drainage duration of drainage in Malignant effusions reflects the tendency for persistent fluid accumulation and entrapped lung in these cases. Chest-tube drainage duration was compared across the three principal etiological groups using the Kruskal-Wallis test. All pairwise comparisons were significant (TB vs inflammatory and TB vs malignancy, both $p<0.001$; inflammatory vs malignancy, $p=0.042$).

Discussion

Our study (The MT-Pleura Study) from a Rural tertiary care centre in North India demonstrates that MT guided pleural biopsy has high overall diagnostic yield 95.14% even in various exudative pleural effusions. In-particular high diagnostic yield per se was observed in - Undiagnosed effusion (94.03%), Haemorrhagic effusion (96.6%), Pyothorax (97.3%). We demonstrated that Malignancy is emerging as the predominant etiology (55.2%) surpassing Tuberculosis (23.8%). Literature reviews evidently show that these findings are consistent with the established International literature reporting diagnostic yields of 90-95% for Medical

thoracoscopy [21-23] substantially higher than the 44-51% yield of closed pleural biopsy [12-15].

Diagnostic yield: comparison with existing literature

Our overall diagnostic yield (DY) of 95.14% aligns closely with multiple published studies like Loddenkemper and Boutin [24] who reported DY exceeding 90% in their European experiences. In Denmark Hansen et al [18] reported DY of 90.4% in 146 patients undergoing MT. Similarly, earlier Indian studies like Mootha et al [25] from North India reported 94.3%, Agarwal et al [26] and Haridas et al [27] documented sensitivity of 93% and superiority of MT over closed pleural biopsy. Hence our approach to MT as an early intervention in Undiagnosed effusions (65.04% of our cohort), Haemorrhagic effusions and Pyothorax may be considered for etiology guided personalized management in exudative pleural effusions perse.

Etiological spectrum: rising burden of pleural malignancy

Most distinctive finding of our study is the predominance of pleural Malignancy (55.2%) over Tuberculosis (23.88%) in Undiagnosed pleural effusions. It probably signals toward a gradual paradigm shift from historic pattern in India, where Tuberculosis traditionally accounted for the majority of exudative effusions [28]. Our findings do echo with the other latest studies from India: Mootha et al [25] reported 45.7% malignancy versus 22.9% tuberculosis in undiagnosed effusions from a North Indian tertiary centre. This changing epidemiological pattern may reflect due to multiple factors including improvement in TB control programs, increasing lung cancer incidences in India associated with tobacco smoking and indoor air pollution, increasing age and early access to better diagnostic facilities even in rural resource limited settings. Moreover, Western studies likewise do report even a higher proportion of malignancy. Hucker et al [29] found 59% malignancy, Hansen et al [18] reported 62%, and Kendall et al [30] found no cases of Tuberculosis in their UK cohort.

However, the persistence of Tuberculosis in Undiagnosed (23.88%), Haemorrhagic effusion (16.7%) and Pyothorax (24%) in our study underscores the burden of TB in India. Rather it highlights the need of MT to uncover the etiological possibilities of Tuberculosis even in pleural effusions with low ADA (<70 mg/dl) level.

Malignancy subtypes and clinical implications

Among the 37 malignant cases, Metastatic disease 35 cases (94.6%) predominated over the primary pleural Mesothelioma 2 cases (5.4%). This distribution is in align with the global pattern where metastatic pleural malignancy accounts for 95% of malignant pleural effusions (MPE) [31,32]. In our study there is predominance of metastatic Adenocarcinoma (35.1%) and Poorly differentiated carcinoma (21.6%) reflecting the most common histological spectrum of lung cancer, in line with the literature of malignant pleural effusions [33,34]

Safety profile and complications

The overall complication rate of 10.68% in our study is within the acceptable range but higher than some published series reporting 3-5% complications [18,28,34]. The difference was probably due to inclusion of sicker patients with advanced malignancy, performance of the procedure in a resource-limited setting, and transparent reporting of all adverse events. Our bleeding rate (3.9%) falls within the reported range of 0.3-0.4% to 5% [18,25,35]. Importantly, all 4 bleeding cases occurred in patients with borderline coagulation parameters (INR 1.5-1.6 and platelet count 50,000 to 80,000/ml), suggesting the need for more stringent cut-offs in patient selection.

From our study, Surgical emphysema (1.94%) and Pleurocutaneous fistula (0.97%) were well-recognized minor complications. Literature reported incidence of subcutaneous emphysema ranges from 0.6% to 4.9% [18,35] and our rate falls well within this range. Noteworthy, the one death (0.9%) that occurred 24-72 hours post-procedure in patients with advanced malignancy. While temporally associated with the procedure, the severe underlying disease and hemodynamic stability immediately post-procedure suggest disease progression rather than procedure-related complications as the primary cause. No cases of empyema (reported rate 0.5-2.7% [18,35]) major air leak, or tumour seeding were observed in our study.

Clinical implications and practice recommendations

The high diagnostic yield demonstrated in this study supports the early incorporation of medical thoracoscopy in the diagnostic algorithm for exudative pleural effusions, particularly in undiagnosed, haemorrhagic and pyothorax subgroups after initial pleural fluid analysis. Clinical suspicion of Malignancy based on age, gender, smoking history, massive effusions, recurrent haemorrhagic effusions where malignancy is the leading differential diagnosis, MT based biopsy with diagnostic confirmation is needed [36-39]. The procedure can be safely

performed by trained Pulmonologists in Rural tertiary centres with appropriate patient selection, equipment, and backup support. It is wise that MT training programs may emphasize more on patient selection criteria, meticulous technique, complication recognition with management, and adequate tissue samples acquisition for comprehensive histopathological and molecular analysis.

Strengths and limitations

Strengths - This study (**The MT-Pleura Study**) provided valuable data and insight from a Rural tertiary care centre about the etiological possibilities and the need of Medical thoracoscopy as a newer modality in the field of Interventional Pulmonology for treatment and personalized management of exudative pleural effusions.

Limitations - The study was a single centre experience, and future multicenter study needs to be planned for representation of general population. Rural setting also leads to delayed patient referrals and loss to follow up leads to further delayed diagnosis. More access to extended immunohistochemistry panels will facilitate further subtyping of Poorly differentiated malignancy cases.

Conclusions

Medical thoracoscopy-guided pleural biopsy is a safe, minimally invasive diagnostic procedure that achieves high diagnostic yield (95.14%) in patients with exudative pleural effusions. However, in the challenging subsets MT also maintains the high diagnostic yield per se - Undiagnosed effusion (94.03%), Haemorrhagic effusion (96.6%), Pyothorax (97.3%) with Malignancy emerging as the predominant etiology (55.2%) followed by Tuberculosis (23.8%). Careful patient selection and apt full management of complications hold the key. Moreover, early definitive diagnostic approach through Medical thoracoscopy can pave a way towards personalized evidence-based treatment approach for pleural effusions.

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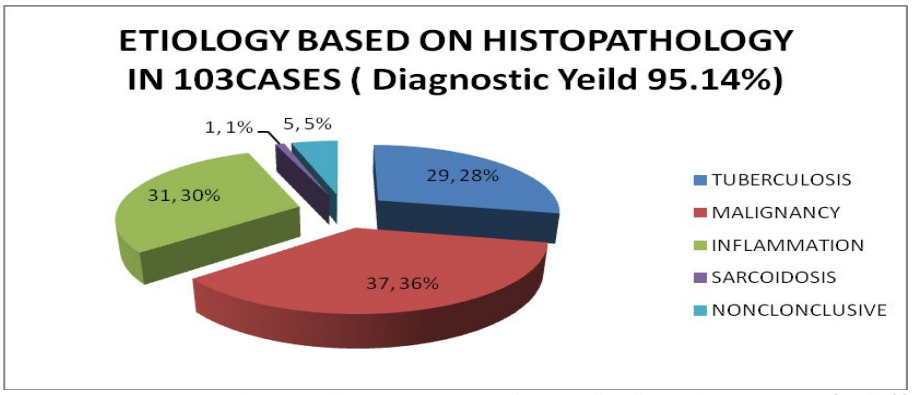

Figure 1. Pie chart showing etiological distribution of different diagnosis based on histopathology done after pleural biopsy in 103 exudative effusions.

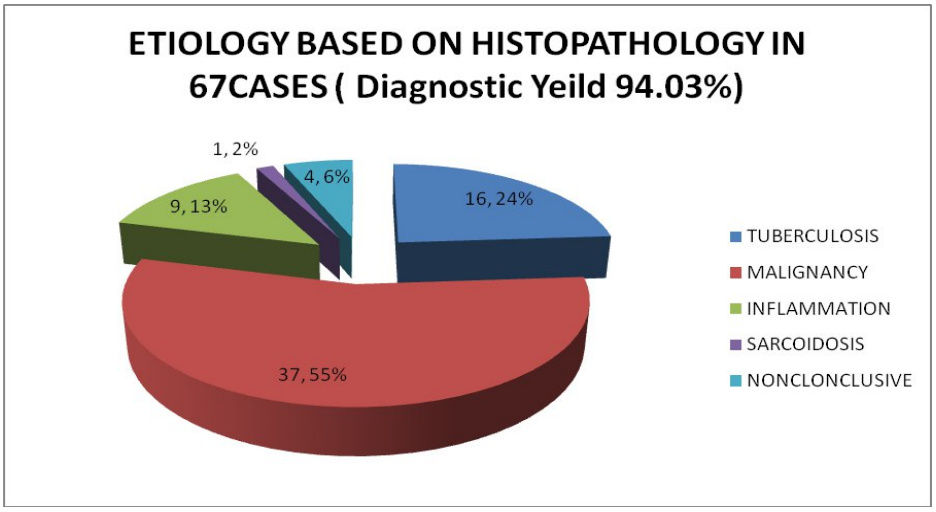

Figure 2. Pie chart showing etiological distribution of different diagnosis based on histopathology done after pleural biopsy in undiagnosed effusions 67 (65.04%).

Table 1. Distribution of pleural malignancy subtypes

TYPES OF MALIGNANCY	**n (%)**	
Adenocarcinoma	13 (35.1)	
Squamous Cell Ca	5 (13.5)	
Poorly differentiated Ca	8 (21.6)	
Small Cell/Round Cell Ca	3 (8.1)	
Nsclc Ca	3 (8.1)	
Lymphoma	2 (5.4)	
Mesothelioma	2 (5.4)	
Adenosquamous Cell Ca	1 (2.7)	
Total	**37 (35.9)**	

Table 2. Etiological distribution by pleural fluid ADA band (n=103)

ADA band	**n**	**Malignancy**	**Tuberculosis**	**Inflammatory**	**Sarcoidosis**	**Non-conclusive**
<40	51	30 (58.8%)	10 (19.6%)	7 (13.7%)	1 (2.0%)	3 (5.9%)
40–70	16	7 (43.8%)	6 (37.5%)	2 (12.5%)	0	1 (6.2%)
>70	36	0 (0%)	13 (36.1%)	22 (61.1%)	0	1 (2.8%)
Total	**103**	**37**	**29**	**31**	**1**	**5**

ADA, adenosine deaminase (U/L). Row percentages are of the band total (n). Diagnosis assigned by medical thoracoscopy–guided pleural biopsy histopathology. Undiagnosed cohort corresponds to ADA <70 U/L (bands 1–2 combined, n=67).