Research article

Medical thoracoscopy – Diagnostics of pleural effusion with indefinite etiology

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ABSTRACT

Introduction: Pleural effusion occurs when extra fluid accumulates in the pleural space of the body. Pleural effusion is a symptom of underlying pathology caused by lung, pleural, and systemic diseases. In approximately 75% of patients, cytobiochemical and microbiological investigation of pleural fluid can provide an etiological diagnosis. Despite thoracentesis diagnostics and its concerned workup, the root cause remains unidentified. Despite primary tests, medical thorocoscopy plays an important role in undiagnosed pleural effusion. This study is planned in order to appraise as to what would be the diagnostic yield on implementing medical thoracoscopy in a tertiary care centre where patients were being treated for pleural effusion of unknown etiology.

Methodology: From June 2021 to June 2022, Saveetha Medical College and Hospital in Thandalam, Kanchipuram, initiated a prospective, interventional, and non-randomised study. Our institution conducted a study on pleural effusion cases that were not diagnosed following the initial biochemical and cytological analysis of their respective pleural fluids.

Results: This study included 53 patients with pleural effusion. 42 patients(79.25%) had definitive diagnosis and 11 patients(20.75%) had inconclusive histopathological report. It was noted that 30 (56.6%) patients with definitive diagnosis had cancer, 10 (18.9%) had tuberculosis, and 2 (3.8%) had empyema. In our investigation, the diagnostic yield on implementing medical thoracoscopy was 79.25%. The overall sensitivity in our study was 89.36%, with specificity at 100%, positive predictive assessment at 100%, and negative predictive assessment at 54.5%.

Conclusion: Medical thoracoscopy is a minimally invasive, well-tolerated, and safe process that aids in the accurate identification of pleural effusion of unknown etiology. It also allows for the provision of therapeutic approaches such as pleurodesis and adhesiolysis. As a consequence, patients having pleural effusion in which the etiology is not known should opt for medical thoracoscopy.

Keywords: Medical thoracoscopy; Pleuroscopy; Unknown pleural effusion.

INTRODUCTION

Semi-rigid pleuroscope (Olympus Corporation, Tokyo, Japan) and flexible bronchoscope have been reported to be similar in handling and design; therefore, the former is now common in usage. Trocars, thoracoscopes/pleuroscopes, biopsy forceps, light sources, video systems, aspiration systems, chest tubes, and drainage systems are all required. The semi-rigid pleuroscope's standard diameter is 7 mm. Semi-rigid pleuroscopes and flexible optic bronchoscopes have the same 'look and feel' and so the former is easily used for medical thoracoscopy by respiratory physicians. It also aids in maintaining a flawless optical field; this is done by implementing suctioning techniques similar to those applied for flexible bronchoscopy, thereby allowing the physician to move its flexible tip to view the pleural space in altered ways and from one place to another in the location of adhesions. The flexible tip also makes it easier to insufflate talc (via a catheter) into not just the parietal pleura but into the visceral pleura as well; this is done via the working channel. Patients tolerate medical thoracoscopy/pleuroscopy well when executed under the influence of local anaesthesia and IV conscious sedation(1).

MATERIALS AND METHODS

In our study, patients having exudative pleural effusion in which its etiology was not known were admitted to the Department of Respiratory Medicine at Saveetha Medical College and Hospital in Thandalam, Kanchipuram. The study time frame started in June 2021 and continued till June 2022.

Inclusion criteria

All in-patients with unknown etiology having exudative pleural effusions were included in the study.

Exclusion criteria

Patients with transudative effusion, exudative effusion with ADA >40 U/L, children under the age of 18, patients suffering from blood coagulation disorder, patients refusing to consent to medical thoracoscopy were excluded.

Methodology

This is a prospective, interventional, non-randomised study being carried out at Saveetha Medical College and Hospital in Thandalam, Kanchipuram, to establish what could be the diagnostic yield on implementing procedures like medical thoracoscopy for patients being treated for exudative pleural effusion of unknown etiology. At our institution, all patients who continued to have pleural effusion that endured being undiagnosed even after preliminary screening of the pleural fluid with biochemical and cytological investigation were signed up for this study. Pleural effusion in which etiology is when any microbiological or biochemical analysis of the initial pleural fluid fails to provide an etiologic diagnosis; the analyses usually include tests for protein, sugar, and lactate dehydrogenase, as well as Gram staining, acid fast bacilli (AFB) smearing, GeneXpert and bacterial culture, pleural fluid adenosine deaminase (ADA) levels <40, and pleural fluid cytology being negative for malignant cells. We took a detailed history of each patient, including smoking practises and noteworthy previous medical history such as diabetes mellitus, systemic hypertension, malignancy, and so on. Thereafter, medical procedure thoracoscopy was implemented on all appropriate patients after anaesthetist clearance. All the patients gave informed consent and the process was videotaped.

All patients, 6 hours preceding the process, were given instruction to withhold food and fluids. Patients were then positioned in lateral decubitus, having the side that was affected faceup. Throughout the procedure, the anaesthetist continuously monitored all vital factors of the patient; these were monitored with electrocardiogram readings, blood pressure readings, and oxygenation levels. Thoracoscopy was performed under conscious sedation with intercostal nerve block at the preferred incision spot. In some cases, the process was achieved under general anaesthesia. The entry port was determined based on ultrasound screening, and it was usually the 5^{th} or 6^{th} intercostal space in the midaxillary line. Thereafter, a 2-cm incision along with blunt dissection of the subcutaneous tissue and muscles was done to extend up to the pleura. At that point, using a corkscrew motion, a trocar having a cannula was introduced through the chest wall; thereafter, any pleural fluid present was aspirated, with both the pleura and pleural cavity being explored using a semi-rigid thoracoscope.

Statistical analysis

For all measurements, a statistical software package (SPSS) was used. Mean and standard deviations were used to express descriptive data. The statistically significant p value was noted to be lesser than 0.05.

RESULTS

In this study, 53 patients who were reported to have pleural effusion were involved. The patients mean age was 54.98 years ± 13.30 (range 18-80 years; Fig. 1). There were 30 men (56.6%) and 23 women (43.4%). Eight of them (15.1%) were smokers and 45 patients (84.9%) never smoked. Shortness of breath followed by cough is the most common presenting symptoms, 84.9% patients had shortness of breath and 77.4% had cough. Mean duration of symptoms was 30.21 days to 28.75 days. 54.7% of patients had symptoms for less than 2 weeks before presenting to the hospital.

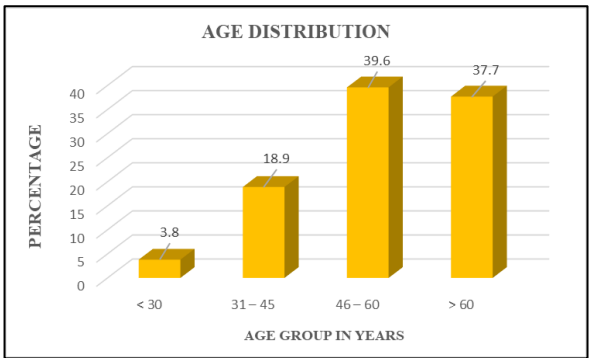

Fig.1: Age-wise distribution
The mean age group in the study is 54.98 years ± 13.30.

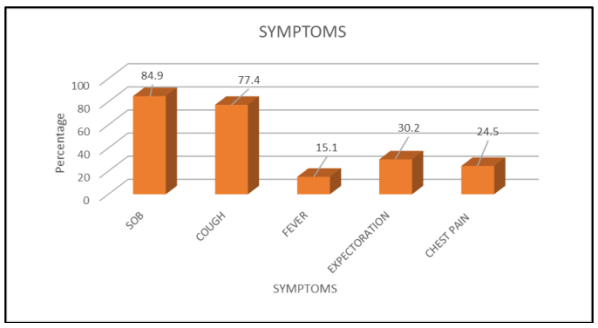

Fig. 2: Symptoms of patients

Fig. 2 shows symptoms of patients. Shortness of breath(84.9%) followed by cough (77.4%) were the predominant symptoms in our study population

Systemic hypertension (32.1%) and diabetes mellitus (28.3%) were the most common comorbid condition. Chest X-ray in postero-anterior view revealed 45% had right sided, 39.6% had left sided and 15.1% had bilateral pleural effusion. Mild, moderate, and massive effusion were detected in 21%, 45% and 25% respectively. Four patients had loculated effusion and one patient had hydropneumothorax.

Table 1: Description of pleural fluid parameters(n=53)

Parameters	**Mean**± SD
ADA (U/L)	31.44±14.646
LDH (U/L)	633.26±103.37
Sugar (mg/dl)	106.30±55.007
Protein (g/dl)	4.68±0.850

Most of the patients (49.1%) had ADA between 31-40 U/L in our study group. Pleural fluid was lymphocytic

predominant in 60.4% patients and polymorph predominant in 39.6%. Mean value of pleural fluid ADA was 31.44 ± 14.646, LDH 633.26 ± 103.37, Sugar 106.3± 55.007, Protein 4.68 ± 0.850 (Table 1). Forty-five patients (84.9%) underwent thoracoscopy under conscious sedation and 8 patients (15.1%) underwent the procedure under general anesthesia.

Table 2: Cross tab with diagnosis and pleural fluid ADA

Observed frequency				
Diagnosis/ ADA	**>20**	**21-30**	**31-40**	**Total**
Inconclusive	2	6	3	11
Metastatic Deposits	4	4	4	12
Primary Lung CA/ Pleural CA	1	8	9	18
Empyema/TB	0	2	10	12
Total	7	20	26	53
Expected frequency				
0.038130479	>20	21-30	31-40	
Inconclusive	1.45283019	4.1509434	5.39622642	
Metastatic Deposits	1.58490566	4.52830189	5.88679245	
Primary Lung Ca/ Pleural Ca	2.37735849	6.79245283	8.83018868	
Empyema/Tb	1.58490566	4.52830189	5.88679245	

Table 3: Cross tab with diagnosis and LDH

Observed frequency				
Diagnosis/ LDH	**<300**	**301-1000**	**>1001**	**Total**
Inconclusive	3	5	3	11
Metastatic deposits	8	3	1	12
Primary lung CA/ pleural CA	6	11	1	18
Empyema/TB	5	4	3	12
Total	22	23	8	53
Expected frequency				
Diagnosis/ LDH	**<300**	**301-1000**	**>1001**	
Inconclusive	4.56603774	4.77358491	1.66037736	
Metastatic deposits	4.98113208	5.20754717	1.81132075	
Primary lung CA/ pleural CA	7.47169811	7.81132075	2.71698113	
Empyema/TB	4.98113208	5.20754717	1.81132075	

There was a significant correlation between diagnosis and pleural fluid ADA (Chi-square value =0.038130479, p<0.05) (Table 2) indicating the diagnosis to have an effect on the pleural fluid ADA. However, it was also seen that the diagnosis had no effect on the pleural fluid LDH (Chi-square value =0.204082333, p>0.05) (Table 3). Similarly, no significant correlation between diagnosis and differential count predominance was observed (Chi-square value =0.113908528, p>0.05) (Table 4).

Table 4: Cross tab with diagnosis and differential cell count predominance

Observed frequency			
Diagnosis/polymorph/lymphocyte predominance	**Polymorph predominant**	**Lymphocyte predominant**	**Total**
Not achieved	5	6	11
Metastatic deposits	3	9	12
Primary lung CA/ Pleural CA	5	13	18
Empyema/TB	8	4	12
Total	21	32	53
Expected frequency			
Diagnosis/polymorph/lymphocyte predominance	**Polymorph predominant**	**Lymphocyte predominant**	
Inconclusive	4.358490566	6.641509434	
Metastatic deposits	4.754716981	7.245283019	
Primary lung CA/ pleural CA	7.132075472	10.86792453	
Empyema/TB	4.754716981	7.245283019	

Fig. 3 shows pleural fluid was lymphocytic predominant in 60.4% patients. Fig. 4 shows 45.3% patients had right sided effusion, 39.6% had left sided effusion and 15.1% had bilateral effusion.

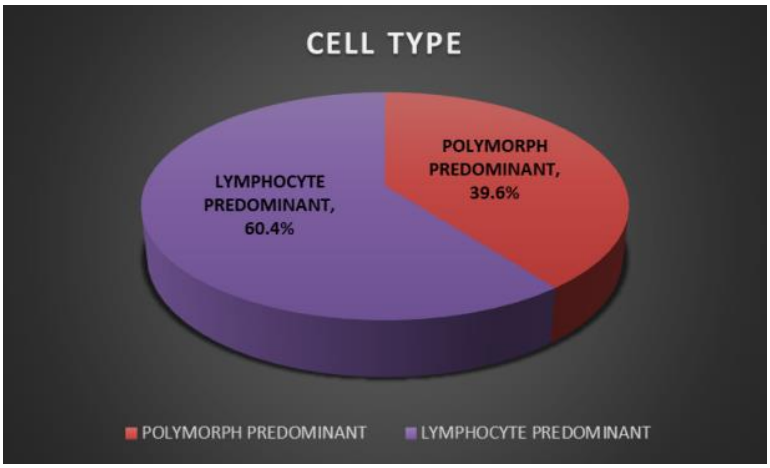

Fig. 3: Differential cell count

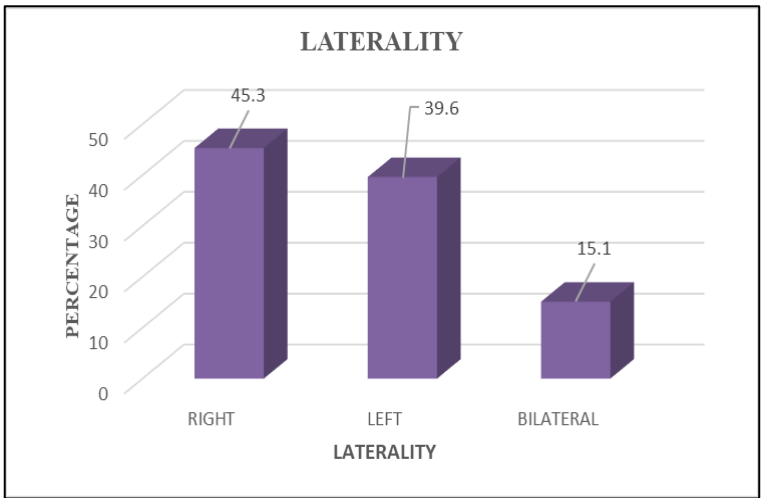

Fig. 4: Laterality of pleural effusion

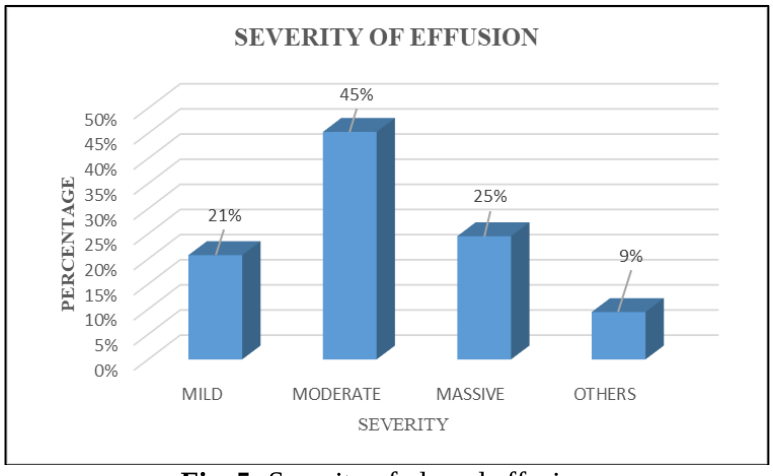

Fig. 5: Severity of pleural effusion

Fig. 5 indicates 45% patients had moderate pleural effusion while 25% had massive effusion, 21% had mild pleural effusion.

In this study**,** 45.3% patients had right-sided effusion, 39.6% had left-sided effusion and 15.1% having bilateral effusion.45% patients had moderate pleural effusion**,** 25% had massive effusion, 21% had mild pleural effusion. 4 patients had loculated pleural effusion and 1 patient had hydropneumothorax.

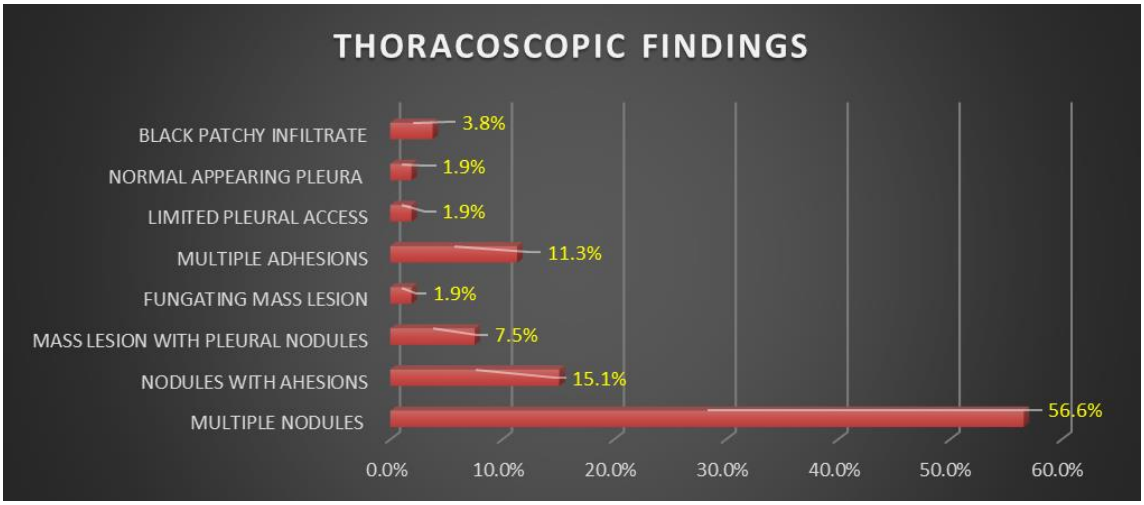

Fig. 6: Thoracoscopic morphological distribution

Fig. 6 indicates multiple nodules were the predominant thoracoscopic finding followed by nodules along with adhesions. Fig. 7 shows that primary lung malignancy is the most common histopathological diagnosis. Fig. 8 indicates 79.25% patients who underwent thoracoscopy achieved diagnosis.

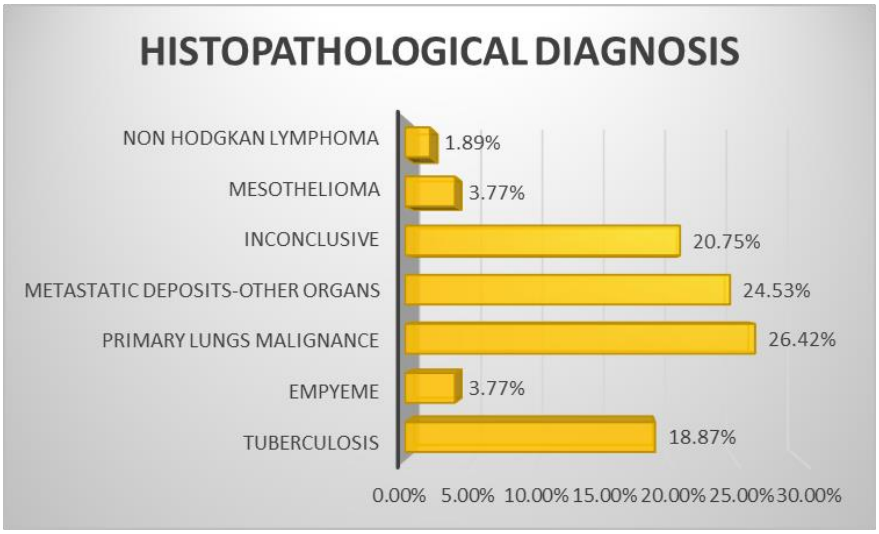

Fig. 7: Histopathological diagnosis

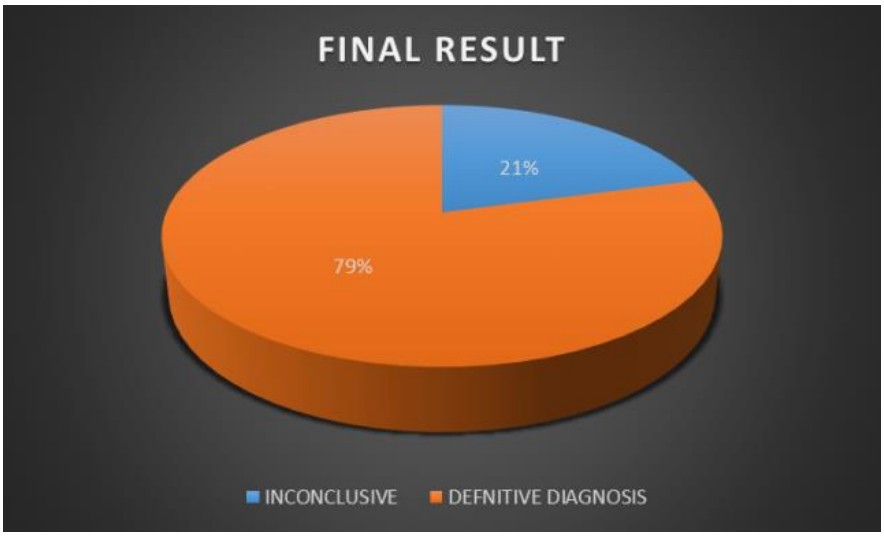

Fig. 8: Distribution of inconclusive report

Nodule, adhesions, and mass were the abnormal thoracoscopic outcomes noted in our study. Moreover, it was noted that multiple nodules over parietal, diaphragmatic and visceral pleura (56.6%) were the other most common thoracoscopic outcomes. 24F ICD and 28F ICD were inserted post procedure in 45 and 7

patients respectively. ICD was not inserted in 1 patient since the patient underwent the procedure under general anesthesia by actively collapsing the lung through bronchial blocker.

Forty-two patients (79.25%) had definitive diagnosis and 11 patients (20.75%) had inconclusive histopathological reports. In patients with definitive diagnosis, 30(56.6%) had malignancy, 10(18.9%) had tuberculosis and 2(3.8%) had empyema. Out of 30 malignancies, 2 were malignant mesothelioma, one was non-Hodgkin lymphoma, 14 were metastasis from lung, 6 were metastasis from breast, 6 were metastasis from other organs, one was metastasis from unknown primary. Among malignant histopathological diagnosis, adenocarcinoma lung (36.66%) was the most prevalent followed by metastasis from carcinoma breast (20%) and squamous cell lung carcinoma (6.67%).

Of those 11 patients with inconclusive thoracoscopic histopathological report, 3 underwent CT guided biopsy which resulted in diagnosis of adenocarcinoma lung, lymphoma, and tuberculosis respectively. Two patients underwent Bronchoscopy and TBNA which resulted in diagnosis of lymphangitis carcinomatosis among one patient and other patients had inconclusive reports. One patient underwent ultrasound-guided omental biopsy which showed serous cell adenocarcinoma. One patient was lost to follow up. Remaining 4 patients were followed up and medically managed. There were no obvious symptoms or deaths associated with the procedure. The general sensitivity, specificity, positive predictive assessment, and negative predictive assessment of thoracoscopic pleural biopsy were 89.3%, 100%, 100%, and 54.5% in our study, respectively.

DISCUSSION

Sensitivity and specificity were comparable to other studies such as Nattusamy *et al.*, (3) and Mohamed *et al.* (4) as shown in table 5. In one research (5), 86 semi-rigid thoracoscopy were performed on patients who were reported to have pleural effusion for which its etiology was not known; the diagnostic yield was at 95%. Moreover, it was noted that malignancy was a repeated diagnosis and so was determined as the most common, accounting for 45% of all cases. Malignancy was the cause of 56.6% of our cases. In research conducted in Hong Kong (6), diagnostic yield was 70% in 20 patients who were reported to have exudative pleural effusion, thereafter undergoing subsequent medical thoracoscopy (14 patients). Some minor complications were also noted in 20% of the patients; these included self-limited fever, limited emphysema, and transitory air leak; however, there were no deaths in the study. Moreover, our study noted no other complications such as limited emphysema or air leak.

In Indian research findings (7-10), the diagnostic yield on implementing procedures like medical thoracoscopy was noted at 67%. When the sample size included 21, 45, 25, and 68 patients, the outcomes were 73%, 80%, and 97%, respectively. The most common etiology was malignancy, with adenocarcinoma being the most common malignancy; tuberculosis was the second most common etiological finding. Our research yielded similar results. Two other studies (7, 9) found no significant complications like the one found in our study.

A study conducted in Egypt on 40 patients who were having exudative pleural effusions noted that 95% of all processes had definitive diagnosis in the case of undiagnosed pleural effusions, whereas 79.25% were conclusive in our study; pleural nodule was found in 28 patients, and 10 of these 28 patients were diagnosed with mesothelioma. In comparison to other studies, this study had a higher prevalence (11). As in previous studies, two of our 53 patients had malignant mesothelioma.

Loddenkemper (12) demonstrated that the diagnostic yield of pleural effusion analysis for malignancy and tuberculosis was 62% and 28%, respectively, while the yield of closed pleural biopsy was 44% and 51%, respectively. The combined results of the two mentioned tests were 74% and 61%, respectively. Medical thoracoscopy yielded 95% and 99% for malignancy and tuberculosis, respectively.

Table 5: Comparison of sensitivity and specificity of MT with other studies

Parameters	**Our study**	**Mohamed *et al.*,**	**Nattusamy *et al.*,**
Sensitivity	**89.36%**	95.80%	96.77%
Specificity	**100%**	100%	100%
Positive predictive value	**100%**	100%	100%
Negative predictive value	**54.50%**	50%	66.67%

Medical thoracoscopy had a sensitivity (true positive rate) of 89.36%. All other studies, including ours, had 100% specificity and positive predictive values. The ability of medical thoracoscopy, on the other hand, to truly identify those who do not have the disease, *i.e.*, negative predictive value, was 54.5%.

CONCLUSION

In our research, the diagnostic yield on implementing medical thoracoscopy was at 79.25%.

The overall sensitivity in our study was 89.36%, with specificity at 100%, positive predictive assessment at 100%, and negative predictive assessment at 54.5%. The main advantage of medical thoracoscopy is the ability to perform biopsy under direct vision on any pleural lesion or nodule located on the exterior of the lung for which the physician is suspicious that it could be other outcomes. In our setting, medical thoracoscopy is a minimally invasive, well-tolerated, and safe process that aids in the accurate identification of pleural effusion for which its etiology is not known. It also allows for the provision of therapeutic approaches such as pleurodesis and adhesiolysis. As a result, in patients having exudative pleural effusion for which its etiology is not known, medical thoracoscopy has a more promising outcome and so should be considered.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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