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Original Article

Diagnostic Yield of Pleuroscopy in Undiagnosed Pleural Effusions

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ABSTRACT

Objective: To evaluate the diagnostic yield of pleuroscopy in undiagnosed pleural effusions.
Study Design: Cross-sectional study
Place and Duration of Study: Pulmonology Department of Pakistan Emirates Military Hospital (PEMH), Rawalpindi, Pakistan, from Mar to Aug 2023.
Methodology: This study selected ninety-eight patients having undiagnosed pleural effusions, aged 15-70 years. Both genders with symptoms of weight loss, fever, cough, and smoking were included through non-probability consecutive sampling. Informed consent was taken before enrolling patients, moderate sedation was given to the patients before the procedure. Complications were recorded.
Results: A total of 98 patients with mean age of 56.6±7.6 years, 24(24.49%) were female, and 74(75.51%) male patients were included. 64(64.3%) patients had malignancy, 22(22.5%) had benign pleural effusions and findings of 13(12.2%) had remained undiagnosed or inconclusive. The diagnostic yield after pleuroscopy was reported to be 87.7%. Post-Pleuroscopy complications comprised an overall rate of 9.2%, were identified.
Conclusion: The study demonstrates that Pleuroscopy offers a high diagnostic yield in evaluating undiagnosed pleural effusions, confirming its effectiveness and safety. The findings of the study confirm that Pleuroscopy should be considered a valuable tool in the diagnostic and therapeutic management of exudative pleural effusions. Its precision and patient satisfaction support its wider use in clinical practice.

Keywords: Diagnostic yield, Pleural Biopsy, Pleural Effusion, Pleuroscopy

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INTRODUCTION

Pleural effusion is a frequently encountered medical condition in the field of pulmonary and respiratory diseases.[1] The occurrence of undiagnosed pleural effusion is a common phenomenon; the precise identification of the cause of pleural effusion is a considerable challenge, given that a significant proportion, ranging from 25% to 40%, of cases remain unidentified.[2] Despite the utilization of diagnostic techniques such as cytological evaluation of specimens obtained by thoracentesis, the underlying cause of roughly 15% of pleural effusions remains unidentified.[3] Pakistan is endemic for tuberculosis (TB). Patients suspected of pleural TB but with inconclusive pleural fluid analysis were one of the concerns. Pleura is the site of metastasis for many tumours like adenocarcinoma, squamous cell carcinoma, epithelial neoplasm, etc.[2,4] According to recent studies, mesothelioma or asbestos-related effusions are common, effusions associated with entrapped lung, sometimes just viral pleurisy or autoimmune serositis like Familial Mediterranean, etc., all need definitive diagnosis. Pleural fluid analysis may remain inconclusive in many cases. Cytology can also be negative in malignant patients having chemotherapy/ radiotherapy can be due to the para-malignant effusions.[4,5]

Different techniques have been used for the diagnosis of unidentified pleural effusions, including video-assisted thoracoscopy surgery (VATS), Abraham's blind biopsy, etc. VATS had a higher diagnostic yield, but higher complications were determined by some studies, while Abraham's biopsy has an almost 70% yield.[6] It is recommended that patients presenting with pleural effusion undergo pleuroscopy as a means of establishing a definitive diagnosis. During the late 19th century, the medical practice of thoracoscopy was developed, which involved the exploration of the pleural cavity.[6]

Pleuroscopy, also known as medical thoracoscopy and this technique has emerged as a novel diagnostic approach for the examination of pleural disease, and it has gained widespread adoption as a diagnostic modality on a global scale due to beneficial visualization of pleura for diagnosing

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nodules, granulomas etc.[7] This technique differs from traditional procedures due to its minimally invasive nature, allowing it to be conducted with moderate sedation in the endoscopy suite, without the requirement of intubation or single-lung breathing. The procedure can be conducted in the OPD on the same day; no hospital admissions are required.[8] The diagnostic precision of this method is about 90-100%. The incidence of complications is relatively low, ranging from 2% to 5%, and these complications are generally of a minor nature, such as subcutaneous emphysema, haemorrhage, and infection. Furthermore, the fatality rate associated with these complications is less than 0.1%.[9] When performed by skilled professionals, pleuroscopy is a procedure that is safe and well-tolerated, exhibiting a high level of diagnostic accuracy and treatment effectiveness.[10]

This study aimed to assess the diagnostic yield of pleuroscopy, especially in undiagnosed pleural effusions, which can be performed by pulmonologists who are not surgeons within the endoscopic suite, utilizing local anesthesia and conscious sedation for patient comfort. The findings of the study will be beneficial for new doctors and trainees.

METHODOLOGY

The cross-sectional study was conducted at PEMH, Rawalpindi Pakistan, from March to August 2023. Ethical approval was granted before data collection from the institutional ethical review board (ERC EC/517/23). The sample size was calculated by considering 15% undiagnosed pleural effusions.[3] The sample size was calculated by an online open epi sample size calculator, and the calculated sample size was 100 patients with 7% margin of error. The data was collected through a non-probability consecutive sampling technique.

Inclusion Criteria: The study included individuals aged 15-70 years, of both genders, patients presented with symptoms of weight loss, fever, cough, smoking, and who had effusion that remained inconclusive despite fluid analysis or associated HRCT findings, Bronchial lavage, and sputum analysis. Patients had undiagnosed pleural effusions by thoracentesis, biochemical cultures, serologic examinations, and other diagnostic tests of the fluid were also included.

Exclusion Criteria: Patients with unstable hemodynamics, platelet counts under 75,000/microL, prothrombin times (PTs) greater than or equal to 10, and patients having comorbidities like chronic liver and kidney diseases were excluded. Patients with worst functional status, i.e., no benefit of diagnosis, and patients who received a therapeutic procedure and refused to participate in the study were also excluded.

All the patients who were voluntary, had undiagnosed exudative pleural effusion, required pleuroscopic examination, and met the inclusion criteria were selected. A written informed consent was taken before enrolling patients into the study. Patient's information, including demographics, clinical diagnosis, and other relevant information, was entered on a pre-designed proforma. The pleuroscopic procedure was performed by the skilled team. During the procedure, all patients were given local administration of 2% Lidocaine for anesthesia; anesthetic drugs used were Nalbuphine (Nelbin) 5mg, Midazolam (Dormicum) 5mg or Propofol 1ml. A 1.0 cm skin incision was made. Samples were taken in Formalin and Normal Saline. For histopathological analyses, all biopsy samples were transported in separate Formalin containers. Biopsy samples were processed according to the standard protocols. The patients received a follow-up chest X-ray radiograph after the procedure to ensure the observed complications.

Data was entered and analysed using Statistical Package for Social Sciences (SPSS) version 26.0. Descriptive and inferential statistics were applied. In descriptive statistics, mean (SD) and frequency (percentage) were calculated to determine the demographics, clinical findings, and diagnostic yield. Inferential statistics, including Pearson's chi-square test, Fisher's exact test, and independent sample t-test, were applied to assess the relationship between diagnostic variables. The p-value ≤ 0.05 was considered significant.

RESULTS

The study found that the diagnostic yield of pleuroscopy in individuals presenting with undiagnosed pleural effusion was 87.7%, with a complication rate of 9.2%. The study population did not report any major complications; a few minor complications, including hemoptysis (2%), bleeding (1%), hypoxia (2%), post-procedural fever (3%), and desaturation (1%), were reported. The findings of the current study revealed that 64% of patients had malignancy, 22.5% had benign pleural effusions, and 12.2% of patients' findings remained undiagnosed/ inconclusive. Additional distribution of the pleural effusion diagnosis showed that out of 64.3% (n=64) malignancies, 76.6% of patients had metastatic tumor,

11% had mesothelioma, 7.8% had lymphoma, and 4.7% had other types of malignancies. Adenocarcinoma, with a prevalence of 51%, was the most prevalent type of tumor in metastatic cancerous patients.

The study included 100 patients; two patients withdrew from the study, though 98 patients with a mean age of 56.64±7.56 years were recruited. Out of 98 patients, 24(24.5%) were female and 74(75.5%) male patients. 46(47.0%) patients were diabetic and 33(33.6%) were hypertensive. Patients were presented with sign and symptoms of cough 23(23.5%), shortness of breath 34(34.7%), smoking history 27(27.5%), fever 22(22.5%) and chest pain 18(18.4%). Demographics and clinical parameters of the study population are mentioned in Table-I.

Table-I: Demographics and Clinical Parameters of the Study Population (n=98)

Study Variables		n(%)
Age (years) Mean±SD		56.64±7.56
Gender	Male	74(75.5%)
	Female	24(24.5%)
Co-morbidities	Diabetics	46(47.0%)
	Hypertensive	33(33.7%)
	Smokers	27(27.5%)
Sign and Symptoms	Cough	23(23.5%)
	Shortness of breath	34(34.7%)
	Fever >38 oC	22(22.5%)
	Chest pain	18(18.4%)
Diagnostic Yield		87.7%)

Figure-1 shows that 64(64.3%) patients had malignancy, 22(22.5%) had benign pleural effusions, and findings of 12(12.2%) had remained undiagnosed/ inconclusive. Additional distribution of the pleural effusions is shown in Table-II, which shows types of malignancies and benign diseases. The diagnostic yield after pleuroscopy was reported to be 87.7%.

The results of Table-II showed that among malignant tumors, most (49; 76.6%) patients had metastatic tumors, while only 3(4.7%) had undetermined or other types of malignancies. The Metastatic tumor (49; 50%) was further categorized into Malignant Epithelial Neoplasm 7(14.2%), Lung Adenocarcinoma 12(24.5%), Adenocarcinoma 25(51%), Renal Cell Carcinoma 2(4.1%), Clear Cell Carcinoma 1(2%) and Small Cell Carcinoma 3(6.1%).

The reported complication rate of the study population was 9(9.2%). The study population showed no adverse event or major complication, few minor complications, including hemoptysis 2(2.0%), bleeding 1(1.0%), hypoxia 2(2.0%), post-procedural fever 3(3.0%), and desaturation 1(1.0%) were reported. Minor complications in post-pleuroscopy, with an overall complication rate of 9.2%, are depicted in Figure-2.

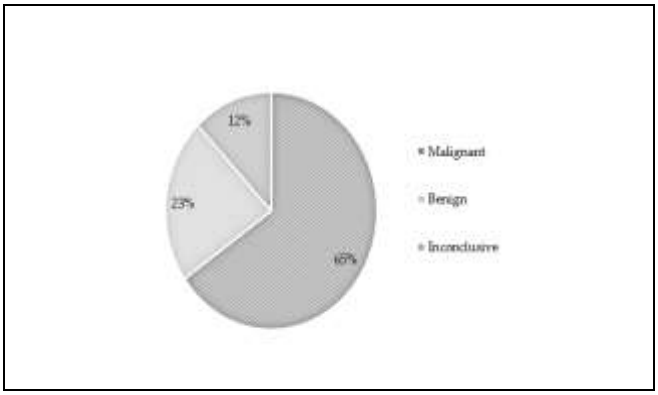

Figure-1: Diagnosis of Pleural Effusions (n=98)

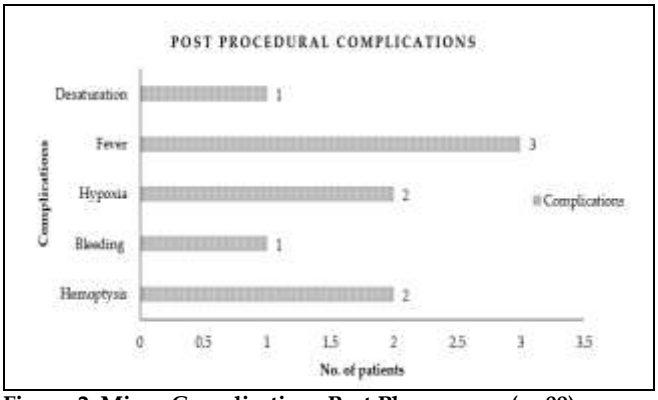

Figure-2: Minor Complications Post Pleuroscopy (n=09)

Comparison of patient's demographics and clinical characteristics showed that significant findings were observed with smoking (p=0.023), cough (p=0.009), shortness of breath (p<0.0001), fever (p=0.001) and chest pain (p=0.003), which can be considered as important indicators for diagnosing tumours (malignant and benign both mentioned in Table-III).

Table-II: Study Findings Predict Cause Distribution of Pleural Effusions (n=98)

Pleural Effusions		n (%)
Malignant (n=64)	Metastatic tumor	49(76.6%)
	Mesothelioma	7(11.0%)
	Lymphoma	5(7.8%)
	Undetermined/ Other	3(4.7%)
Benign (n=22)	Tuberculosis (TB)	15(68.2%)
	Chronic Pleuritis/ Non-specific inflammations	7(31.8%)
Inconclusive/ Undiagnosed		13(12.2%)

Table-III: Comparison of Demographics and Clinical Characteristics with Diagnosis (n=98)

Study Variables		Diagnosis of Pleural Effusion			*p*-value
		Malignant (n=64)	Benign (n=22)	Inconclusive (n=13)	
Gender	Male	49(76.6%)	16(72.7%)	9(75.0%)	0.936
	Female	15(23.4%)	6(27.3%)	3(25.0%)	
Diabetics		34(53.1%)	7(31.8%)	5(41.7%)	0.208
Hypertension		18(28.1%)	12(54.5%)	3(25.0%)	0.061
Smoking		13(20.3%)	7(31.8%)	7(58.3%)	0.023
Cough*	Yes	21(32.8%)	2(9.1%)	0	0.009
	No	43(67.2%)	20(90.9%)	12(100%)	
Shortness of breath (SOB)*	Yes	34(53.1%)	0	0	<0.0001
	No	30(46.9%)	22(100%)	12(100%)	
Fever*	Yes	22(34.4%)	0	0	0.001
	No	42(65.6%)	22(100%)	12(100%)	
Chest pain*	Yes	18(28.1%)	0	0	0.003
	No	46(71.9%)	22(100%)	12(100%)	
Type of complications*	Haemoptysis	2(3.1%)	0	0	0.083
	Bleeding	0	1(4.5%)	0	
	Hypoxia	1(1.6%)	0	1(8.3%)	
	Post-procedural Fever	1(1.6%)	1(4.5%)	1(8.3%)	
	Desaturation	0	0	1(8.3%)	
	None	60(93.8%)	20(90.9%)	9(75.0%)	

**Fisher exact test*

DISCUSSION

The results from the study inferred that Pleuroscopy is a safe and cost-effective treatment, which has been shown in almost all related clinical studies. In recent years, pulmonologists have commonly used pleuroscopy under local anaesthesia, which is less intrusive and has a diagnostic yield of 79–96%. Additionally, it has been suggested that pleuroscopy demonstrates superiority in terms of obtaining larger biopsy specimens and achieving a higher diagnostic yield, with an efficiency rate of 92.6%. The probability of complications is limited, as indicated by published data from China, ranging from 0.4% to 44.1%. The reported adverse effects encompass chest discomfort (24.9–44.1%), subcutaneous emphysema (8.0%), postoperative fever (5.3%), mild bleeding (4.6%), hypotension (0.5%), re-expansion pulmonary edema (0.5%), and empyema (0.4%).[11] It is worth noting that the majority of these complications are minor and do not result in an extended duration of hospitalisation.[12] A study by Beaudoin *et al.,* also observed a diagnosis yield of 100% in their study on pleuroscopy.[5] Patil *et al.,* evaluated a cohort of individuals with unexplained pleural effusion using thoracoscopy pleural biopsy. Their findings revealed a diagnostic yield of 85.2% for this diagnostic method.[14] Although the diagnosis yield reported by Hejazi *et al.,* was 66%.[15] By the findings of Ishii et al., the incidence of complications was reported to be 6.1%, with no instances of severe adverse events being documented.[13] The observed minor consequences encompassed slight pain in a single case and mild bleeding in another case, with a distribution of 54% malignant tumours and 46% benign disorders. The benign illnesses observed in the study were pyothorax (15.1%), nonspecific pleurisy (12.1%), and tuberculous pleurisy (9.1%).[13,17] Same findings were reported by our study, with the diagnostic yield of 87.7% and complication rate of 9.2%.

In a recent study conducted by Wang *et al.,* a comprehensive analysis was performed to evaluate the accuracy and outcome of pleuroscopy in diagnosing pleural effusion among a cohort of 833 patients.[16] The findings revealed that malignancies emerged as the predominant aetiology for misdiagnosed pleural effusions. It was shown that 41.1% of patients who had pleuroscopy were identified with Malignancies in Pleural Effusion (MPE). Lung cancer was identified as the primary aetiology in most cases of malignant pulmonary embolism, accounting for 67.8% of occurrences. Secondary carcinoma, mesothelioma, and lymphoma were also identified as contributing factors, representing 11.7%, 10.2%, and 2.9% of cases, respectively.

In a previous study by Helala *et al.,* similar diagnostic results for medical thoracoscopy were reported; they also demonstrated that 70% of their patients had malignant effusion.[18] Furthermore,

Mahmoodlou *et al.,* did a study in Iran with a sample size of just 31 participants. Despite the limited sample size, their findings match with the results of the current investigation, indicating that malignant diseases are the predominant underlying causes of undetected pleural effusion.[4] While the diagnostic approaches may not consistently yield relevant outcomes, favourable findings can help respirologists strategize their further investigations for comparable patients. The primary factors contributing to the prevalence of undetected pleural effusions are malignancies, pneumonia, TB, and pulmonary embolisms. Among these, malignancy was the most frequently observed finding in the patients' diagnostic evaluations, accounting for around 66.4% of reported cases.[2]

Tuberculous pleural effusion (TPE) is a prevalent aetiology of pleural effusion in regions with high endemicity, and individuals with compromised immune systems have an increased susceptibility to the development of tuberculous pleural effusion. The incidence of tuberculous pleural effusion as determined through medical thoracoscopy exhibits considerable variation among different countries, with rates ranging from over 80% in some regions to less than 2% in European countries and the United States. Research findings have demonstrated that medical thoracoscopy is a reliable and secure technique for managing cases of organised tuberculous pleural effusion. The results presented by the researchers revealed that an estimated 14% of patients exhibit tuberculous pleural effusion.[19]

The authors discussed the importance of conducting long-term follow-up for patients with "idiopathic pleuritis" due to the significant rate of changes in the definitive diagnosis, which occurred in up to 68% of these individuals throughout the course of the follow-up period.[19]

Future research should focus on investigating the optimal follow-up protocols for undetected pleural effusion, particularly regarding their length and the methods employed. This is particularly relevant in cases when medical thoracoscopy (MT) has already been performed. Additional prospective, randomized clinical trials are required to establish the diagnostic accuracy and safety of medical thoracoscopy (MT) in the context of pleural illnesses. In modern times, the utilisation of narrow band imaging (NBI) has been implemented in pleuroscopy to identify malignant lesions through the evaluation of pleural vascular patterns. This application has demonstrated its efficacy in detecting abnormal vascular patterns, which are indicative of malignant lesions, particularly in cases involving flat lesions. Additional research is required to ascertain the extent to which these emerging technologies, which enhance the visualisation of supplementary lesions during magnetic resonance imaging (MRI) guided thermal therapy (MT), contribute to clinical practice.[19] Meanwhile, it is noteworthy that pleuroscopy remained an invasive procedure requiring proper vigilant training and patient selection criteria. For instance, since significant pleural adhesion will result in non-existent pleural spaces, pleuroscopy should be considered for patients who do not have pleural adhesion. Before procedure, it is advised that a regular ultrasonography check be carried out to determine whether a pleural gap is present. The objective of this study is to determine the diagnostic yield of pleuroscopy in individuals presenting with undiagnosed pleural effusion in a Pakistani population.[20]

LIMITATION OF STUDY

The present study is subject to many limitations. Initially, it is noteworthy that the quantity of cases under examination is limited, hence necessitating an augmentation in the sample size. Furthermore, necessitating the conduct of a multicentre investigation on a larger sample size is required.

CONCLUSION

It is concluded that medical thoracoscopy exhibits a notable level of feasibility and accuracy when employed for the purpose of diagnosing exudative pleural effusion. Pleuroscopy is considered a safe, well-accepted procedure with adequate precision in the treatment of pleural effusions, with a diagnostic yield of 87.7%. The utilization of thoracoscopic intervention has demonstrated positive outcomes in the treatment of encapsulated pleural effusion. Consequently, it is advisable to consider recommending thoracoscopic procedures as part of the therapeutic management approach for exudative pleural effusion.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

IA & SAS: Conception, study design, drafting the manuscript, approval of the final version to be published.

MI & MH: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

KA & HR: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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