Original Article

# Pleural biopsy: A superior procedure than pleural fluid cytology in diagnosing pleural malignancy

**Biswajit Biswas, Sudarshan Kumar Sharma[1], Rameshwar Singh Negi[2], Neelam Gupta[1], Virender Mohan Singh Jaswal[3], N. Niranjan[2], Balraj Singh[4]**

Department of Pathology, ESI-PGIMSR, Kolkata, West Bengal, Departments of [1]Pathology, [2]Pulmonary Medicine, [3]Biochemistry and [4]Community Medicine, IGMC, Shimla, Himachal Pradesh, India

## ABSTRACT

**Background:** The present study is designed to evaluate the role of pleural fluid cytology and pleural biopsy in diagnosing pleural diseases and to study the advantages and disadvantages of thoracocentasis and pleural biopsy. **Materials and Methods:** We prospectively included 66 consecutive indoor patients over a duration of 1-year. Pleural fluid was collected, cytological smears were made from the fluid. Plural biopsy was obtained in the same patient by Cope's needle. Adequate pleural biopsy tissue yielding specific diagnosis was obtained in 47 (71.2%) of cases. **Results:** Tuberculosis was the commonest nonneoplastic lesion followed by chronic nonspecific pleuritis comprising 60% and 33.3% of the nonneoplastic cases respectively and tuberculosis was predominantly diagnosed in younger age group. Majority (70.8%) of malignancy were in the age group of >50–70. Adenocarcinoma was found to be the commonest (66.7%) malignant neoplasm in the pleurae followed by small cell carcinoma (20.8%). **Conclusion:** Pleural biopsy is a useful and minimally invasive procedure. It is more sensitive and specific than pleural fluid smears.

**Key words:** Adenocarcinoma, pleural biopsy, pleural fluid, tuberculosis

## INTRODUCTION

The pleural space is a potential space between the visceral and parietal layers of the pleurae. The pleural space normally contains 0.1–0.2 ml/kg body weight of fluid.[1] Pleural effusion is an abnormal accumulation of fluid in the pleural cavity. Pleural effusion remains the most common manifestation of pleural pathology.[2] Although a variety of clinical conditions like heart failure, malignancy, pneumonia, tuberculosis may be the cause of a pleural effusion. The possibility of a malignant involvement of pleural cavity should always be considered in difficult to diagnose cases. Since percutaneous access of the pleural space is relatively simple, techniques like pleural biopsy and thoracoscopy have become very popular. However in a developing country like India, where such specialized facilities are available only in Advanced Pulmonary Medicine Centers, pleural fluid analysis and cytology remains the mainstay for diagnosing the various pulmonary diseases.[3]

Analysis of pleural fluid cytology has an important contribution for investigation of patients with pleural effusion.[4] Cytological examination not only helps for diagnosis of cancer but also for staging and prognosis of diseases.[5] Pleural biopsy is helpful to reach an etiological diagnosis of exudative pleural effusion, particularly when malignancy is suspected or when results of detailed pleural fluid study are inconclusive, especially in a set up where thoracoscope is not available.[2] Closed pleural biopsy provides the highest diagnostic yield in cases of pleural tuberculosis and malignancy, the two most important causes of exudative pleural effusion.[6]

The aim of this study is to obtain pleural fluid sample by thoracocentesis and to compare fluid cytology with

Access this article online

Quick Response Code:

Website: www.ccij-online.org

DOI: 10.4103/2278-0513.158457

**Address for correspondence:** Dr. Biswajit Biswas, 77/1 Masunda, K.G. Road, New Barrackpore, 24 Parganas North, Kolkata - 700 131, West Bengal, India. E-mail: drbiswajit2003@gmail.com

**Comparison of pleural fluid cytology and plural biopsy techniques in various neoplastic and non – neoplastic diseases by Epi Info and Open Epi software.**

**Sensitivity, specificity, positive predictive value, negative predictive value and likelihood ratios of positive and negative tests on pleural fluid cytology with histo-pathologically confirmed neoplastic and non – neoplastic diseases . (n=47)**

| Variable | Diagnostic Accuracy (%) | Sensitivity | | Specificity | | PPV[1] | | NPV[2] | | LHR[3] (Positive) | | LHR[4] (Negative) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | % | 95% CI[5] | % | 95% CI | % | 95% CI | % | 95% CI | Estimate | 95%CI | Estimate | 95%CI |
| Pleural Fluid cytology | 72.3 | 62.5 | 45.3-77.1 | 93.3 | 70.2-98.8 | 95.2 | 77.3-99.2 | 53.9 | 35.5-71.2 | 9.4 | 1.2-70.6 | 0.40 | 0.33-0.5 |
| | | | | | | | | | | | | | |

**Cohen's kappa (unweighted) = 0.47** (For pleural fluid cytology).

[1] PPV: Positive Predictive Value.
[2] NPV: Negative Predictive Value
[3] LHR (Positive): Likelihood ratio of a positive test.
[4] LHR (Negative): Likelihood ratio of a negative test.
[5] CI: Confidence Interval.

**Chart 1:** Comparison of pleural fluid cytology and plural biopsy techniques in various neoplastic and non – neoplastic diseases by Epi Info and open Epi software

a pleural biopsy to determine the etiology by various histopathological and cytological tests and to analyze the results.

## MATERIALS AND METHODS

We prospectively included 66 consecutive indoor patients over a duration of 1-year. Patients with transudative pleural effusion, pyothorax, chylothorax were excluded. Pleural fluid was collected by thoracocentesis under local anesthesia, cytological smears were made from the fluid. Plural biopsy was done in the same patient by Constantin Cope.[7] Adequate pleural biopsy tissue yielding specific diagnosis was obtained in 47 (71.2%) of cases [Table 1 and Chart 1]. The cytological smears were stained with Giemsa stain and Papanicolaou stain. Pleural biopsy was stained with Hematoxylin and Eosin staining.

## RESULTS

Age range of the patients were 18–84 years with a mean age of 51 years and 66.6% were males. The most common presenting symptom was shortness of breath (95.4%) followed by chest pain (89.4%) and productive cough (69.7%) and 48.5% patients had a history of smoking. Majority of the pleural fluid (69.7%) were hemorrhagic and rest (30.3%) were straw colored.

Tuberculosis was the most common nonneoplastic lesion followed by chronic nonspecific pleuritis comprising 60% and 33.3% of the nonneoplastic cases, respectively. Tuberculosis was the most common nonneoplastic disease in the younger age group (11–30 years) comprising 55.5% of all cases of tuberculosis.

Majority (70.8%) of malignancy were in the age group of >50–70. Adenocarcinoma [Figures 1a, b and 2a,b)] was found to be the commonest (66.7%) malignant neoplasm in the pleurae followed by small cell carcinoma [Figures 1c, d and 2d] (20.8%) and also these were more commonly encountered in male patients.

Only one patient (1.5%) suffered from pneumothorax after the pleural biopsy.

True positive – Positive in both biopsy and cytology.

True negative – Negative in both biopsy and cytology.

False positive – Negative in biopsy but positive in cytology.

False negative – Positive in biopsy but negative in cytology.

Sensitivity of pleural fluid cytology

$$= \frac{TP}{(TP + FN)} \times 100 = 62.5\%$$

Specificity of pleural fluid cytology

$$= \frac{TN}{(TN + FP)} \times 100 = 93.3\%$$

**Table 1: True positive, True negative, False positive and False negative Fluid Cytology**

| Sample | Test results | | | | Total |
|---|---|---|---|---|---|
| | TP | TN | FP | FN | |
| Fluid cytology | 20 | 14 | 1 | 12 | 47 |

TP: True positive, TN: True negative, FP: False positive, FN: False negative

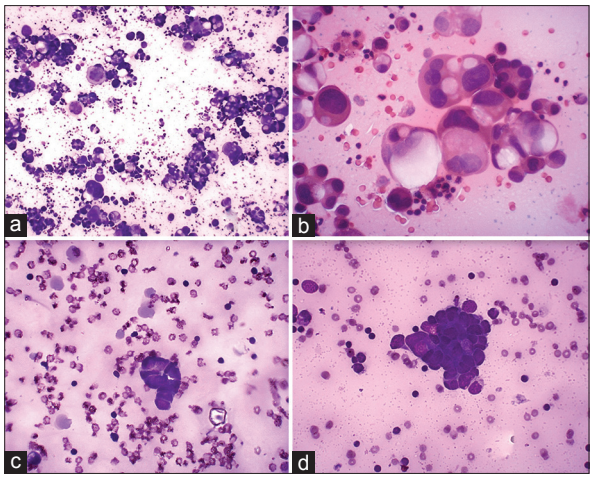


**Figure 1:** (a) Adenocarcinoma, pleural fluid (Giemsa, ×100). (b) Adenocarcinoma, pleural fluid (Pap, ×400). (c and d) Small cell carcinoma, pleural fluid (Giemsa, ×400)

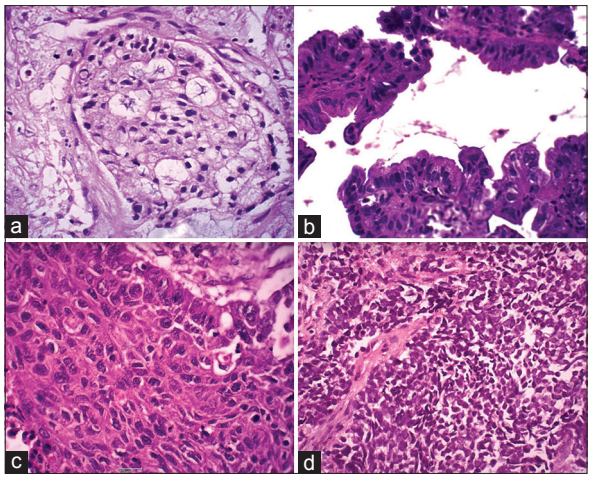


**Figure 2:** (a and b) Adenocarcinoma, pleural biopsy (H and E, ×400). (c) Squamous cell carcinoma, pleural biopsy (H and E, ×400). (d) Small cell carcinoma, pleural biopsy (H and E, ×400)

$$\text{Positive predictive value of pleural fluid cytology} = \frac{TP}{(TP + FP)} \times 100 = 95.2\%$$

$$\text{Negative predictive value of pleural fluid cytology} = \frac{TN}{(TN + FN)} \times 100 = 53.9\%$$

## DISCUSSION

Thoracocentesis has been a very popular diagnostic as well as therapeutic procedure for tapping pleural effusions and with very few procedural complications.[3] It is usually done through the 2nd intercostal spaces below the fluid level.[8] Medical thoracoscopy, by a pulmonologist is a safe and effective procedure for the diagnosis and therapy of various pleural diseases, but it is more invasive and expensive procedure, with a risk of complications like pneumothorax. Very few pulmonologist are trained in thoracoscopy and it is available only at selected centers, and furthermore its cost is very high for an economically average person, in a developing country like India.[3] A recent survey has also revealed that even in USA, only 6% of pulmonologists are currently trained in and perform a thoracoscopy.[9] Hence, thoracocentesis still remains a popular diagnostic procedure in cases of pleural effusion.

Gouda *et al*. compared the diagnostic sensitivity of both Cope's needle and Abrams LD and found it to be 85% for Cope needle and 57.5% for Abrams needle.[10] However, adequate pleural biopsy tissue yielding specific diagnosis was obtained in 47 (71.2%) of cases by Cope's needle in this study. Different complications have been noted in patients after pleural biopsy procedure, some of them being pain at the site of biopsy,[11,12] pneumothorax,[10-12] and hemothorax.

In their study, Bhattacharya *et al*. observed that cytological analysis of 3 consecutive samples of patients of pleural effusion increased the diagnosis rate of malignancy.[13] However in the present study, only one sample of the pleural fluid was obtained and compared with pleural biopsy.

In pleura, secondary tumors are more common than the primary tumors. The primary tumor may be pulmonary or extrapulmonary. The common pulmonary tumors infiltrating into the pleurae are squamous cell carcinoma, small cell carcinoma and adenocarcinomas and extrapulmonary neoplasms metastasizing into pleura are usually from breast, ovary, GIT, stomach, and pancreas.[14] Adenocarcinoma is the most common malignancy encountered in the pleural biopsy.[3,13,15] The second most common being small cell carcinoma.[3,13] However, Khan *et al*. (2011) in their study of 26 malignancies found mesothelioma as the second most common malignancy. In the present study also the most common malignancy metastasizing to pleura was adenocarcinoma [Figures 1a, b and 2a, b] (43.7%) followed by small cell carcinoma [Figures 1c, d and 2d] (15.6%) and squamous cell carcinoma [Figure 2c] (9.4%) which was quite similar to previous studies.[3,13]

Combining pleural fluid analysis with pleural needle biopsy can help in the diagnosis and morphological classification of the majority of malignant pleural lesions, leaving around 7–12% undiagnosed cases.[16] Thoracoscopy is the ideal procedure available to directly explore the pleural cavity and visualize the malignancies in early stages, which are confined up to visceral pleura of the lung. However, even after thoracoscopy, around 10% of effusions remain undiagnosed.[17,18]

## CONCLUSION

Pleural biopsy is a useful and minimally invasive procedure. It is more sensitive and specific than pleural fluid smears. In a country like India, where investigations and health facilities are inadequate and cost of treatment is often high, pleural fluid analysis, and cytology should continue to be the first line investigation in patients presenting with pleural effusion. It is not only cost effective but a reasonably safe procedure, which shows reasonably good sensitivity and specificity in diagnosing primary, as well as metastatic pleural malignancies.

## REFERENCES


1. Rahman NM, Chapman SJ, Davies RJ. Pleural effusion: A structured approach to care. Br Med Bull 2005;72:31-47.
2. Pandit S, Chaudhuri AD, Datta SB, Dey A, Bhanja P. Role of pleural biopsy in etiological diagnosis of pleural effusion. Lung India 2010;27:202-4.
3. Gaur DS, Chauhan N, Kusum A, Harsh M, Talekar M, Kishore S, *et al*. Pleural fluid analysis-Role in diagnosing pleural malignancy. J Cytol 2007;24:183-8.
4. Soe Z, Shwe WH, Moe S. A study on tuberculous pleural effusion. Int J Collab Res Intern Med Public Health 2010;2:32-48.
5. Maldhure BR, Bedarkar SP, Kulkarnl HR, Paplnwar SP. Pleural biopsy and adenosine deaminase in pleural fluid for the diagnosis of tubercular pleural effusion. Indian J Tuberc 1994;41:161-5.
6. Anwar R, Farooqi JI. Diagnostic yield of pleural biopsy in lymphocytic exudative pleural effusion. Rawal Med J 2004;29:61-4.
7. Cope C. New pleural biopsy needle; preliminary study. J Am Med Assoc 1958;167:1107-8.
8. Ihsanullah, Khan N, Jadoon H, Zaman M, Ahmed A. Yield of Abrams needle pleural biopsy in exudative pleural effusion. J Ayub Med Coll Abbottabad 2009;21:116-8.
9. Mathur PN, Loddenkemper R. Biopsy techniques in the diagnosis of pleural diseases. Eur Respir Monogr 2002;7:120-30.
10. Gouda AM, Dalati TA, Al-Shareef NS. A comparison between Cope and Abrams needle in the diagnosis of pleural effusion. Ann Thorac Med 2006;1:12-5.
11. Shah D, Amanullah, Shah N, Attaullah S, Haq A. Diagnostic yield of pleural biopsy in exudative pleural effusion. J Postgrad Med Inst 2007;21:278-82.
12. Khattak MI, Amin S, Shabbier G, Rehman S. Diagnostic value of pleural biopsy in exudative pleural effusion. Gomal J Med Sci 2011;9:156-8.
13. Bhattacharya S, Bairagya TD, Das A, Mandal A, Das SK. Closed pleural biopsy is still useful in the evaluation of malignant pleural effusion. J Lab Physicians 2012;4:35-8.
14. Husain AN. The lung. In: Kumar V, Abbas AK, Fausto N, Aster JC, editors. Robbins and Cotran Pathologic Basis of Disease. 8th ed. Philadelphia, PA: Saunders, Elsevier; 2012. p. 732.
15. Khan Y, Bilal, Zia S. Etiological spectrum of exudative pleural effusion in a tertiary care hospital based on closed pleural biopsy. Ann Pak Inst Med Sci 2011;7:133-6.
16. Prakash UB, Reiman HM. Comparison of needle biopsy with cytologic analysis for the evaluation of pleural effusion: Analysis of 414 cases. Mayo Clin Proc 1985;60:158-64.
17. Mårtensson G, Pettersson K, Thiringer G. Differentiation between malignant and non-malignant pleural effusion. Eur J Respir Dis 1985;67:326-34.
18. Cantó A, Blasco E, Casillas M, Zarza AG, Padilla J, Pastor J, *et al.* Thoracoscopy in the diagnosis of pleural effusion. Thorax 1977;32:550-4.


**Cite this article as:** Biswas B, Sharma SK, Negi RS, Gupta N, Jaswal VM, Niranjan N, *et al.* Pleural biopsy: A superior procedure than pleural fluid cytology in diagnosing pleural malignancy. Clin Cancer Investig J 2015;4:530-3.

**Source of Support:** Nil, **Conflict of Interest:** None declared.