SJIF Impact Factor: 5.464

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 5.
Issue: 5.
Page N. 53-58
Year: 2021

Original Article www.wjahr.com

DIAGNOSTIC YIELD OF CYTOLOGY AND ABRAMS CLOSED PLEURAL BIOPSY IN LYMPHOCYTIC EXUDATE PLEURAL EFFUSIONS

***[1]Ahmed Alhusein, [2]Malek Hejazie and [3]Zuheir Alshehabi**

[1]Department of Pulmonary Medicine, Tishreen University Hospital Lattakia, Syria. Cancer Research Center, Tishreen University.
[2]Department of Pulmonary Medicine, Tishreen University Hospital and Al sham private university Lattakia, Syria.
[3]Department of Pathology at Tishreen University Hospital, Lattakia, Syria / Cancer Research Center at Tishreen University.

Received date: 14 July 2021 **Revised date:** 04 August 2021 **Accepted date:** 24 August 2021

***Corresponding Author: Ahmed Alhusein**

Department of Pulmonary Medicine, Tishreen University Hospital Lattakia, Syria. Cancer Research Center, Tishreen University.

ABSTRACT

Objective: to evaluate the diagnostic yield and safety of Cytology and closed pleural biopsy in Lymphocytic exudate pleural effusions. **Methods:** This prospective cohort study was carried out in pulmonary and pathology departments at Tishreen university hospital, Lattakia, Syria between March 2020 and March 2021.The number of patients involved in this study is 49. Cytology is considered diagnostic when malignant cells are detected in the specimen of 50 ml Aspirate. Tuberculosis is diagnosed by the detecting caseating granulomas in tissue specimens obtained by closed pleural biopsy. Malignancy will be detected by observing malignant cells in pleural fluid or tissue samples obtained by closed pleural biopsy. **Results:** Cytology detected malignancy in 6 cases, and the other 43 cases were classified as negative. The overall diagnostic yield of cytology is very low (12.9%). Cytology sensitivity in malignancies is about 21.4%. Over all diagnostic yield of CPB were 68.75% CPB sensitivity in malignancies is 71.4 % with 100 % specificity. In tuberculosis, the sensitivity were up to 93.3%. **Conclusion:** Cytology and closed pleural biopsy are good choices to diagnose pleural effusions. Cytology has low yield in malignancy whereas CPB is very effective in Tuberculosis pleural effusions and can be the first choice. We recommend CPB in malignant pleural effusions when the patient had chronic diseases that may prevent general anesthesiaand when Pleuroscoby is not available as in low economic countries.

KEYWORDS: Abrams, Closed Pleural Biopsy, Cytology, Pleural Effusion.

INTRODUCTION

Pleural effusions are very common in clinical practice, It affects about 3000 per million of population a year.[2] Most common causes of pleural effusions are : Malignancy, Tuberculosis, Pneumonia, Congestive Heart Failure, Renal Failure, connective Tissue Disease and Pulmonary Embolism.[1,2] The initial symptom of the effusion is related to the main etiology, as well as, many patient do not have symptoms at all.[3] Most popular symptoms are pleuritic chest pain, dyspnea, dry cough and impaired sleep quality.[3-6]

The first diagnostic procedure to define the underlying etiology is initial thoracentesis and can be used for therapeutic purposes.[7,8] Thoracentesis can classify the effusions to two different types according to the amount of protein and lactate dehydrogenases(LDH) in the fluid, transudate (low protein and LDH) and exudate (high protein or LDH levels). Light's criteria are the most common criteria used in clinical practice in the world since light created them in 1972.[9,10] Congestive Heart Failure, Renal Failure, Liver Cirrhosis and Hypoalbumenia are the most common causes in transudate effusions.[10] Otherwise, malignancies, tuberculosis, Para-pneumonic effusions and empyema are the mainstay etiologies in exudate effusions.[10]

Complete white blood cells count and differential is very important diagnostic test in exudate effusions and can diminish the diagnostic possibilities.When the fluid is full of neutrophils that lead us to Para-pneumonic effusions and empyema. Lymphocytic pleural effusions (> 50%), are caused by malignant neoplasms or tuberculosis in most cases.[11-15]

Cytology is very good choice when malignant pleural effusion is suspected.[16] Its diagnostic value is widely different (sensitivity is between 40-87%), due to a lot of factors like pathologist experience, lake of typical cells,amount of fluid received, type of neoplasm.[16] Cytology can make definitive diagnoses of malignant neoplasms.Cytology fails to diagnose tuberculosis and most cases of malignancies.[16]

When cytology fails, our options are closed pleural biopsy(CPB) and medical Thoracoscoby.[17]

Closed pleural biopsy(CPB) was first described by *DE Francis et a*. in 1955, and he used *Vim-Silverman* needle.[1] Indications of CPB included all undiagnosed pleural effusions since American Thoracic Society (ATS) shortened them to only exudate effusions with high suspicious of tuberculosis.[18,19] Diagnostic sensitivity is (40-87%) depends on the country, center and the expert of pulmonogist and pathologists.[18,19] The most popular needles are Cope and Abrams. Abrams are used in many centers in the world including our center. Topical anesthesia are used. Abrams needle has three parts are External trocar, Inner cannula and Stylet.[20,21]

In malignancies, the lesions invades the pleura in patchy distribution and that will diminish the sensitivity and the diagnosis opportunities with CPB alone. Tuberculosis lesions spreads in all over the pleural surface and that makes the diagnostic sensitivity of CPB in TB up to 90% in some studies.[22]

Some studies suggest that we can increase the diagnostic yield of CPB, by having more than two tissue pieces with the needle.[19] In one study, the sensitivity of CPB is 89% in Tuberculosis when 4 biopsies taken, and 54% when only one biopsy obtained.[23]

Pneumothorax is the most serious complication (3-15 %), and its incidence is very low with expert hands. Most cases don't need surgical interventions and resolved spontaneously. Other complications are pain, bradycardia, Hemothorax,spleen or liver damage, and spot infection.[1]

Medical Thoracoscoby is the *gold standard* with sensitivity up to 100% in some studies. But it is has important disadvantages includes: unavailable in most centers, needs experiment which is not often exist, very expensive and needs general anesthesia.[24-26]

We need to reevaluate the diagnostic yield of cytology and closed pleural biopsy with Abrams needle to redefine the indications, complications and the need to refer the patient to Pleuroscoby.

METHODS

This prospective cohort study was carried out in pulmonary and pathology departments at Tishreen university hospital, Lattakia, Syria between March 2020 and March 2021. The initial study included 129 patient with pleural effusion, but Only 49 patients meeting including criteria were selected and included in the study. The study has got the approval from scientific research congress at university presidency *(registration number: 1364/25-2-2020*), on behalf of the ministry of higher education and scientific research.

All patients with suspected pleural effusion has gone through routine investigations, history, clinical examination,chest x ray, initial primary thoracentesis, laboratory tests (Protein, LDH, Glucose, Cholesterol, PH if necessary,AFB smear and Culture and Sensitivity in certain patients).All data was recorded.

All effusions assessed by lights criteria to distinguish transudate from exudate ones.lights criteria are : (1.fluid protein/serum protein > 0.5, 2.fluid LDH / serum LDH > 0.6, 3.fluid LDH is more than 2/3 upper LDH normal limits).

Transudate and exudate with neutrophil predominance effusions were excluded. Patients with lymphocytic exudate pleural effusion were included in the study.

written consent was obtained from all patients before starting further investigations.

Pleural fluid cytology and closed pleural biopsy have been done to all patients.

Cytology is considered diagnostic when malignant cells are detected in the specimen of 50 ml of fluid. Tuberculosis is diagnosed by the detecting caseating granulomas in tissue specimens obtained by CPB. Malignancy will be detected by observing malignant cells in pleural fluid or tissue samples obtained by CPB.CPB will be considered diagnostic when tuberculosis or malignancy is detected. When Cytology and CPB did not help, further investigations has been conducted to get the definite diagnosis such as, TB NAAT,Tumor markers, bronchoscopy, Pleuroscoby..etc. Sensitivity, specificity and both negative and positive predictive values were calculated for cytology and CPB by using a decision matrix.

RESULTS

The initial study included 129 patient with pleural effusion. Only 49 patients meeting including criteria were selected and included in the study, *Figure 1*.The mean age was 55 years old (between 18- 80 years old).Closed Pleural biopsy(CPB) and Cytology were done to all patients (100 %), and CPB repeated only 3 times with no additional diagnostic benefit. Patients' demographic characteristics are listed below, *Table 1*.

The final diagnosis was obtained in 48 of 49 patient. Closed pleural biopsy diagnosed 32 (65.3%), cytology diagnosed 6(12.24%).CPB were diagnostic in all positive cytology samples. Patients that did not have final

diagnoses by Cytology and CPB went to other procedures like bronchoscopy, Adenosine De Aminase, biopsy from other organs to find malignant cells and computed tomography pulmonary angiogram (Pulmonary Embolism protocol).

The final diagnosis included neoplasms 28(57.1%), tuberculosis 15(30.6%) and other less common diseases listed in *Table 2*. Neoplasms were the most common cause of pleural effusions 28(57.1%) in our study as we mentioned earlier. Secondary malignancies are much more common (93.9% of all cases) than primary which confirmed in only 3 cases (3.6 %).The most common malignancy was Lung cancer (50%), and breast cancer (14.3 %). Lung adenocarcinoma made 50 % of lung cancer cases. The distribution of malignancies in this study comes in, *Table 3*.

Cytology detected malignancy in 6 cases, and the other 43 cases were classified as negative. The overall diagnostic yield of cytology is very low (12.9%). The most important thing is to calculate the sensitivity in malignant pleural effusions, because cytology cannot be diagnostic in tuberculosis and other pleural effusions deferential diagnosis. Cytology sensitivity in malignancies is about 21.4% (6/28).

Closed pleural biopsy results were classified into five categories: malignancy, tuberculosis, muscle cells, non-specific inflammation and inconclusive. only malignancy and tuberculosis were considered diagnostic, other undiagnosed patients went through other procedures. Malignancy detected in 20(40.8%), tuberculosis 15(30.6%), inconclusive 3(6.1%), non-specific inflammation 9(18.4%) and muscle cells 2(4.1%).

Over all diagnostic yield of CPB were 68.75%.CPB sensitivity in malignancies is 71.4 % with 100 % specificity. In tuberculosis, the sensitivity were up to 93.3%.Many studies suggested that the diagnostic yield of CPB is related to the number of passes of Abrams needle which give the pathologist bigger sample and give us better results. So we divided the patients to two separated groups: less than 2 passes and more than 2.We studied the relationship between the number of passes and the ability to get definite diagnosis using fisher exact equation and statistical relationship was proven (P value =0.04). All cases of tuberculosis needed more than 2 passes to be proven, as well as, most cases of malignancy. forty cases did not suffer any complication (81.63%).Complications happened in only 18.36%.The most common complication was Hypotension and bradycardia due to vasovagal stimulation 5 (10.2% together).All complications were tolerated with no deaths or invasive procedure needed(no cases of pneumothorax).

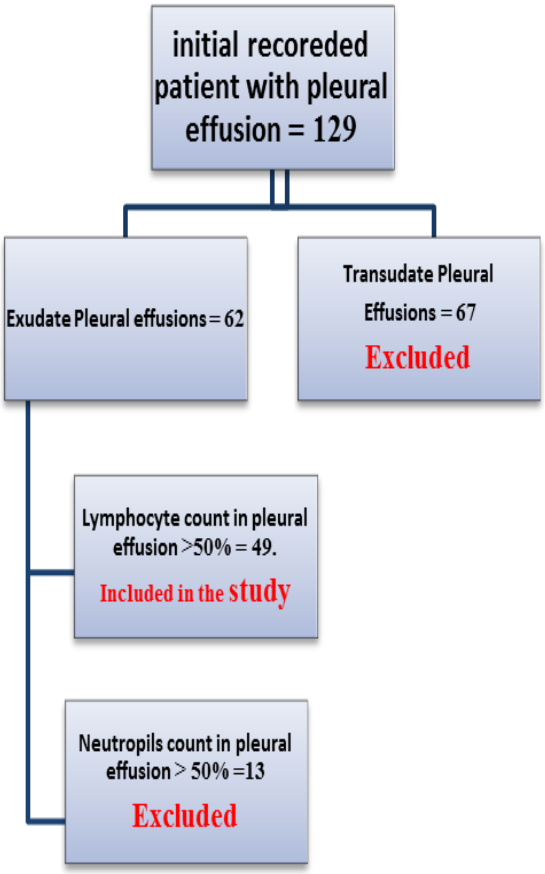

Figure (1): Included and excluded patients of the study.

Table (1): Patients' demographic characteristics.

Patients and characteristics	N(%)
Number	49
Mean age	55
Gender Male Female	 23(46.9%) 26(53.1%)
Smoking Yes No	 31(63.3%) 18(36.7%)
Side of the effusion Unilateral Bilateral	 24(49) 25(51)
Color of the effusion Hemorrhagic others	 29(59.2) 20(40.8)
Extent of the effusion Mild to moderate Massive	 19(38.8) 30(61.2)
SD(standard deviation)	

Table (2): The final diagnosis of 49 patients included in the study.

Final Diagnosis	N(%)
Neoplasms	28(57.1)
Tuberculosis	15(30.6)
Pulmonary Embolism	2(4.1)
Para pneumonic Effusion	1(2)
Post cardiac injury syndrome	1(2)
Rheumatoid Arthritis	1(2)
Idiopathic	1(2)

Table (3): The distribution of 28 patient with malignant pleural effusion.

Tumor	N (%)
Primary Mesothelioma Secondary	 3(10.7)
Lung Adenocarcinoma Squamous Cell Carcinoma Small Cell Carcinoma Large Cell Carcinoma	14(50) 7(25) 4(14.3) 2(7.1) 1(3.6)
Breast	4(14.3)
Ovarian	2(7.1)
Hodgkin Lymphoma	2(7.1)
Thyroid	1(3.6)
Prostate	1(3.6)
Kidney	1(3.6)

DISCUSSION

Undiagnosed pleural effusions are a matter of challenge in medicine. Cytology and CPB are very common ways to have a proper diagnosis. We noticed that cytology sensitivity is very low in our study when compared to other studies.Cytology diagnostic yield ranged between 44-69.2 % in some studies. *Porcel et al*,[27] (Spain 2016), studied cytology in 414 patient and cytology yield was about 44%.As well as, *Arnold et al*.[28] study in England(2018) with similar sensitivity (46.4%).We are sure that the small number of patients, using only smear cell technology are the reason of low sensitivity.

Our results are so close to worldwide studies when talking about CPB. Many studies concluded that CPB diagnostic yield in malignancy ranged between 51.5-82.4 %. The sensitivity in malignancies is 71.4% in our study which makes CPB an important procedure in malignant pleural effusion. The sensitivity is 58.9%, 59.2%, 60%, 63.1%, 77% in these studies respectively: *Solooki et al.*,

Pereyra et al., Poe et al., Jakubec et al., and Saldana et al.[29-33]

Complications are more common in our study (18.36%), but all complications were under control. No deaths or pneumothorax happened which is the most important complication. *Saha et al.*[23] study says that complications counts about 10.98 %, with 3,66% cases of pneumothorax. Thirty patients had pneumothorax in *Saldana et al.*[29] study.

Subcutaneous Atropine might be a good choice to prevent Hypotension and bradycardia during CPB, but to have a final recommendations we need more investigations and larger studies.

CONCLUSION

Cytology and CPB are good choices to diagnose pleural effusions.

Cytology detected malignancy in 6 cases, and the other 43 cases were classified as negative. The overall diagnostic yield of cytology is very low (12.9%). Cytology sensitivity in malignancies is about 21.4%.

Over all diagnostic yield of CPB were 68.75%.CPB sensitivity in malignancies is 71.4 % with 100 % specificity. In tuberculosis, the sensitivity were up to 93.3%

CPB is very effective in Tuberculosis pleural effusions and can be the first choice. We recommend CPB in malignant pleural effusions when the patient had chronic diseases that may prevent general anesthesia and when Pleuroscoby is not available as in low economic countries like Syria.

ACKNOWLEDGMENT

To all workers, nurses, and Technicins in pulmonary and pathology departments.

Consent

Writte informed consents were obtained from all patients before starting further investigations

Financial support and sponsorship

No financial support or sponsorship received.

Conflicts of interest

No Conflicts of interest declared.

REFERENCES

1. C. F. N. Koegelenberg and A. H. Diacon, “Pleural controversy: Close needle pleural biopsy or thoracoscopy - Which first?,” *Respirology*, 2011; 16(5): 738–746. doi: 10.1111/j.1440-1843.2011.01973.
2. N. Haridas, K. P. Suraj, T. P. Rajagopal, P. T. James, and R. Chetambath, “Medical thoracoscopy vs closed pleural biopsy in pleural effusions: A randomized controlled study,” *J. Clin. Diagnostic Res.*, 2014; 8(5): 14–17. doi: 10.7860/JCDR /2014/7476.4310.
3. B. Jany and T. Welte, “Pleural effusion in adults - Etiology, diagnosis, and treatment,” *Dtsch. Arztebl. Int.*, 2019; 116(21): 377–386. doi: 10.3238 /arztebl.2019.0377.
4. T. W. Shields, C. Reed, J. LoCicero III, and R. Feins, “General Thoracic surgery 7th edition,” *Philadelphia, LWW*, 2009.
5. R. Thomas, S. Jenkins, P. R. Eastwood, Y. C. Gary Lee, and B. Singh, “Physiology of breathlessness associated with pleural effusions,” *Curr. Opin. Pulm. Med.*, 2015; 21(4): 338–345. doi: 10.1097/MCP.0000000000000174.
6. B. F. Marcondes *et al.*, “Sleep in patients with large pleural effusion: Impact of thoracentesis,” *Sleep Breath.*, 2012; 16(2): 483–489. doi: 10.1007/s11325-011-0529-6.
7. A. H. Bartal, Y. Gazitt, G. Zidan, B. Vermeulen, and E. Robinson, 2: 0601–3140.
8. C. D. Chen, M. Y. Wu, H. F. Chen, S. U. Chen, H. N. Ho, and Y. S. Yang, “Prognostic importance of serial cytokine changes in ascites and pleural effusion in women with severe ovarian hyperstimulation syndrome.,” *Fertil. Steril.*, 1999; 72(2): 286–292, Aug, doi: 10.1016/s0015-0282(99)00206-x.
9. R. W. Light, M. I. Macgregor, P. C. Luchsinger, and W. C. Ball, “Pleural effusions: the diagnostic separation of transudates and exudates.,” *Ann. Intern. Med.*, 1972; 77(4): 507–513. doi: 10.7326/0003-4819-77-4-507.
10. N. A. Maskell and R. J. A. Butland, “BTS guidelines for the investigation of a unilateral pleural effusion in adults,” *Thorax*, vol. 58, no. SUPPL, 2003; 2: 8–17 doi: 10.1136/thx.58.suppl_2.ii8.
11. M. NOPPEN *et al.*, “Volume and cellular content of normal pleural fluid in humans examined by pleural lavage,” *Am. J. Respir. Crit. Care Med.*, 2000; 162(3): 1023–1026.
12. “Mesothelial cells: their structure, function and role in serosal repair,” *Respirology*, 2002; 7(3): 171–191.
13. V. Villena, A. López-Encuentra, R. García-Luján, J. Echave-Sustaeta, and C. J. A. Martínez, “Clinical implications of appearance of pleural fluid at thoracentesis.,” *Chest*, 2004; 125(1): 156–159. Jan. doi: 10.1378/chest.125.1.156.
14. N. A. Maskell, S. Batt, E. L. Hedley, C. W. H. Davies, S. H. Gillespie, and R. J. O. Davies, “The bacteriology of pleural infection by genetic and standard methods and its mortality significance,” *Am. J. Respir. Crit. Care Med.*, 2006; 174(7): 817–823. doi: 10.1164/rccm.200601-074OC.
15. A. Ferrer *et al.*, “Prospective clinical and microbiological study of pleural effusions.,” *Eur. J. Clin. Microbiol. Infect. Dis. Off. Publ. Eur. Soc. Clin. Microbiol.*, 1999; 18(4): 237–241, doi: 10.1007/s100960050270.

16. H. B. Grosu, F. Kazzaz, E. Vakil, S. Molina, and D. Ost, "Sensitivity of Initial Thoracentesis for Malignant Pleural Effusion Stratified by Tumor Type in Patients with Strong Evidence of Metastatic Disease," *Respiration*, 2018; 96(4): 363–369. doi: 10.1159/000490732.
17. B. CHOMET, P. HELLER, and W. F. KELLOW, "Needle biopsy of the parietal pleura.," *N. Engl. J. Med.*, 1956; 255(15): 684–690. doi: 10.1056/NEJM 195610112551502.
18. K. C. Devkota, R. Chokhani, and S. Gautam, "Diagnostic yield of pleural biopsy in exudative pleural effusion," *Nepal Med. Coll. J.*, 2014; 16(1): 13–16.
19. C. M. Kirsch, D. M. Kroe, R. L. Azzi, W. A. Jensen, F. T. Kagawa, and J. H. Wehner, "The optimal number of pleural biopsy specimens for a diagnosis of tuberculous pleurisy.," *Chest*, 1997; 112(3): 702–706. doi: 10.1378/chest.112.3.702.
20. Title or year in M. L. Search by author, "Image-guided pleural biopsies: indications, technique, and results in 10 patients.," *Radiology*, 1988; 169(1): 1–4. doi: 10.1148/radiology.169.1.3047781.
21. N. Morrone, E. Algranti, and E. Barreto, "Pleural biopsy with Cope and Abrams needles.," *Chest*, 1987; 92(6): 1050–1052. doi: 10.1378/chest.92.6.1050.
22. L. J. Walsh, J. T. Macfarlane, A. R. Manhire, M. Sheppard, and J. S. Jones, "Audit of pleural biopsies: an argument for a pleural biopsy service.," *Respir. Med.*, 1994; 88(7): 503–505. doi: 10.1016/s0954-6111(05)80331-2.
23. K. Saha, A. Maji, A. Bandyopadhyay, and D. Jash, "Diagnostic Yield of Closed Pleural Biopsy in Undiagnosed Exudative Pleural Effusions.," *Maedica*, 2021; 16(1): 34–40. doi: 10.26574/maedica. 2020.16.1.34.
24. R. Loddenkemper, P. Mathur, M. Noppen, and P. Lee, *Medical thoracoscopy/pleuroscopy: manual and atlas+ dvd*, 2011.
25. V. B. Antony, R. Loddenkemper, P. Astoul, C. BOUTIN, and P. GOLDSTRAW, "Management of malignant pleural effusions," *Am. J. Respir. Crit. Care Med.*, 2000; 162(5): 1987–2001.
26. C. Boutin, P. Astoul, F. Rey, and P. N. Mathur, "Thoracoscopy in the diagnosis and treatment of spontaneous pneumothorax.," *Clin. Chest Med.*, 1995; 16(3): 497–503.
27. J. M. Porcel, M. Quirós, S. Gatius, and S. Bielsa, "Examination of cytological smears and cell blocks of pleural fluid: Complementary diagnostic value for malignant effusions," *Rev. Clínica Española (English Ed.*, 2017; 217(3): 144–148. doi: https://doi.org/10.1016/j.rceng.2016.11.002.
28. D. T. Arnold *et al.*, "Investigating unilateral pleural effusions: The role of cytology," *Eur. Respir. J.*, 2018; 52(5): 1–9. doi: 10.1183/13993003.01254-2018.
29. R. Báez-Saldaña *et al.*, "Accuracy of closed pleural biopsy in the diagnosis of malignant pleural effusion," *J. Bras. Pneumol.*, 2017; 43(6): 424–430. doi: 10.1590/s1806-37562016000000323.
30. P. Jakubec *et al.*, "[Closed pleural biopsy in the diagnostics of malignant pleural involvement].," *Vnitr. Lek.*, 2014; 60(5–6): 423–430.
31. S. A. Emamian, M. Kaasbøl, J. F. Olsen, and J. F. Pedersen, "Original article Accuracy of the diagnosis of pleural effusion on supine chest X-ray,", 1997; 13: 57–60.
32. R. H. Poe, R. H. Israel, M. J. Utell, W. J. Hall, D. W. Greenblatt, and M. C. Kallay, "Sensitivity, Specificity, and Predictive Values of Closed Pleural Biopsy," *Arch. Intern. Med.*, 1984; 144(2): 325–328. doi: 10.1001/archinte.1984.00350140139020.
33. M. F. Pereyra *et al.*, "Role of blind closed pleural biopsy in the management of pleural exudates, 2013; 13(3): 011–367.