e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(1); 1120-1130

Original Research Article

Role of Pleural Biopsy in Exudative Pleural Effusions

M Sandhya Swaroopa[1], VS Rajesh Khanna[2]

[1]Assistant Professor, Department of Pulmonary Medicine, Dr Patnam Mahender Reddy Medical College, Chevella dist Ranga Reddy

[2]Assistant Professor, Department of Anaesthesia and Critical Care, Maheswara Medical College, Isnapur, Patancheruvu

Received: 25-10-2023 / Revised: 23-11-2023 / Accepted: 18-12-2023

Corresponding Author: Dr. M Sandhya Swaroopa

Conflict of interest: Nil

Abstract:

Pleural effusion is the commonest clinical expression of pleural disease. Once light's criteria differentiate the transudate from exudate, the latter poses a clinical challenge in making an etiological diagnosis, we conducted the study with an aim of finding the role of pleural biopsy in exudative pleural effusion it was a Prospective observational study Seventy consecutive patients of exudative pleural effusions were selected from the outpatient and inpatient department of our medical college hospital setting at district headquarters.

Conclusions and Summary: We recommend closed pleural biopsy should still be the initial step in the diagnostic algorithm for undiagnosed exudative pleural effusions especially in a high tb-burdened and resource limited country like India and other Asiatic countries. CPB is safe and should be a routine complimentary diagnostic procedure in patients with exudative pleural effusions, in view of its negligible morbidity and mortality.

Introduction

Pleural diseases affect over a million individuals annually, and physicians in most subspecialities encounter pleural effusions [1], which always would pose a diagnostic dilemma. Thus, pleural disease affects approximately 300 subjects per 100,000 population per year world over. [2] The first endoscopic inspection of the pleura was performed as early as in 1866; Needle biopsy of the parietal pleura was introduced by Defrancis in 1955, an important advancement in the diagnostic evaluation of pleural effusions. [3] In this context the pleural biopsy (and thoracoscopy) can virtually diagnose two main disorders, viz., malignancy and tuberculosis of the pleura, where cytological, biochemical and microbiological analysis of pleural fluid did not yield any diagnostic clues.

Cope and Abram's needles began the era of closed pleural biopsy technique, providing a safe, bed side procedure in the evaluation of an undiagnosed exudative pleural effusion. Closed pleural biopsy provides the highest diagnostic yield in pleural tuberculosis, especially in high tuberculosis prevalent country like India. The yield for pleural tuberculosis from combined pleural fluid and closed pleural biopsy does not differ from that obtained by thoracoscopy [4]. Hence, in the case of tuberculous pleuritic, the option of CPB might be even stronger because of the high diagnostic sensitivity, which in some studies approximates that of thoracoscopy [5]. Similarly, CPB can be easily performed with minimal complications in malignant pleural effusions; about 7-12% of patients with these effusions can be diagnosed by CPB when cytology is negative [6]

In this regard, the alternative of CPB can be offered to the patients if further work up is considered in the treatment. In these individual cases, a diagnostic sensitivity of 45% for CPB, although low compared to 95% for thoracoscopy, might still be a reasonable option [7]. However, even in suspected tuberculosis, in case of a nondiagnostic CPB, especially reporting as "nonspecific pleuritis", best option remains thoracoscopy, especially if the subject is an elderly person. Whatever the pros and cons of CPB vis a vis thoracoscopy, the local skill and expertise and the availability of trained man power, the general condition of the patient to withstand the procedure and the financial constraints on the part of the patient may ultimately decide the choice of the procedure in the diagnostic work up of exudative pleural effusions.

Subjects and Methodology

I) Design of the Study: Prospective observational study

II) Setting: Seventy consecutive patients of exudative pleural effusions were selected from the outpatient and inpatient department of our medical college hospital setting at district headquarters.

III) Period of study: July 2013 to September 2014

IV) Inclusion Criteria:

1. Age above 14 years
2. Exudative effusions meeting at least one of the following criteria:

a) Pleural fluid protein to serum protein ratio greater than 0.5

b) Pleural fluid LDH to serum LDH ratio greater than 0.6

c) Pleural fluid LDH greater than two thirds of the upper limit of normal for the serum LDHs

3. Mild, Moderate (25-75% of hemithorax) and Massive (>75% of the hemithorax) Pleural effusions had been taken into study by clinical and radiological examination.

V) Exclusion Criteria:

1. Pyothorax.
2. Pleural effusions secondary to well documented chronic history of heart failure nephrotic syndrome, liver cirrhosis probably transudative effusion.
3. pyoderma, herpes zoster, bleeding diathesis, respiratory failure, patients on oral anticoagulants.
4. Inability of the patient to cooperate.
5. Refusal for consent

All patients subjected to detailed clinical history and physical examination and useful investigations were done to confirm the effusion. Routine investigations like

CBP, ESR, Blood Sugar, Blood Urea, Serum Creatinine, Bleeding Time, Clotting Time, APTT, HIV HBSAG, Sputum for AFB staining, Sputum for bacterial culture and sensitivity, Mantoux test, ECG, Chest x-ray PA view, Ultrasound abdomen and chest done in all cases and CT Chest done wherever necessary.

Diagnostic thoracocentesis was done and pleural fluid was sent for pleural fluid analysis for:

1. cell count
2. Biochemical analysis for protein, sugar, ADA
3. AFB staining and culture
4. Cytology for malignant cells
5. About 50ml of pleural fluid is sent for cytology

Pleural tissue taken by the COPE's biopsy needle sent for:

1. Histopathology
2. Smear for AFB
3. Pleural biopsy for AFB culture

Needle Biopsy of the Pleura: In this study needle biopsy of the pleura was done with Cope's pleural Biopsy needle.

Observations and Results

A total of 70 subjects were taken into our study who had an exudative pleural effusion and out of which 48(68.5%) were males and 22 were females (31.5%). Among them 30(42.85%) subjects were from the urban background and 40 (57.15%) patients were from rural background. There were 28 illiterates (40%) overall with 17(24.14%) of males and 11(15.62%) were females. Illiterates were more among rural background of about 55% compared to 20% from Urbanites. About 17(24.2%) completed primary school, urban vs rural being 16.6% and 30% respectively. 2.5% of rural patients and 13.3% of urbanites completed secondary education. About 13.3%of urban patients completed intermediate education compared to 7.5% of rural patients. There were 16.6% undergraduates from urban and 25% from rural background. Number of postgraduates were more in urban (20% vs 2.5%). The number of patients with higher education was more in urban population(n=15,30%) which is 21.4% overall compared to 12.5% of rural population in our study which was only 7.14% overall. Similarly, males completed higher education at a level of 33.3% compared to 18.18% of females.

Thirty out of 70 studied population (42.8%) were smokers all of them being males. High percentage of smokers was found in our study which was 62.5% among males. Eight out of 30 urban males (26.6%) were smokers compared to 22out of 40 rural patients (55%). The mean S.I among illiterates was 440 compared to 313 among primary completers and 50 patients with graduation. The S.I was also higher among rural population (395 Vs 183) and among lower income group (392 Vs 231). So, in our study not only literacy rate was low in rural population but also majority of them were smokers.

One patient with small cell carcinoma had a very high smoking Index of 1200.Adenocarcinoma is the most likely malignancy with a high S.I(mean S.I 820) whereas mean S.I of 202 was noted among squamous cell carcinoma. In patients with tuberculosis and non-specific diagnosis the mean value of S.I was 125 to 200 except in one patient with tuberculosis who had a S.I of 600. In patients with CT chest mass, pleural biopsy report showed most of the times adenocarcinoma (n=8) which was 80% compared to one who had small cell carcinoma1 (10%) and one who had squamous cell carcinoma 1(10%).

Twenty one out of 48 males are alcoholics (43.75%) compared to only 2 out of 22 females (9%). Alcoholics were more in rural population (n=23, 57.5%) compared to 23.3% of urban population. Sixty out of 70 subjects complained of cough (85.7%). Among them 43 males and 17 females complained of cough and predominantly patients had dry cough 71.4%. 17% of patients with cough complained of expectoration. chronic cough was seen in 30 patients (50%). Breathlessness of grade 2 or more was complained by 29 patients which had equal preponderance in

males (41.6%) and females (40.9%). Twenty out of 21 males with dyspnea had grade of 2 and 3 and 8 out of 10 females had grade 2 and 3 dyspn A total of 26 subjects complained of chest pain (37.1%), majority having Peripheral pleuritic chest pain. 57.14% patients complained of of fever. About 30 out of 48 males (62.5%) and 10 out of 22 females (45.5%) complained of fever. Majority of subjects had less than 1 month fever (37 out of 40) and fever of two to three months was complained by 3 patients (7.5%).

Acute fever (less than 1 week) was seen in only one subject, subacute (1 week to 4 weeks) was seen in 36 subjects (i.e 90% with fever). About 16 subjects complained of hemoptysis (22.8%)and nearly 90% of them had mild hemoptysis. No patient had massive or life-threatening hemoptysis. Among subjects with sputum patient production nine had increased mucoid production in mild quantities. Only one subject had moderate quantity of muco purulent sputum.

Loss of appetite was seen in 20(28.6%) of cases. Among them 80% were males and 20% where females History of weight loss was seen in 34.3%of (n=24) subjects and among them 71% were males and 29% were females and out of them 50%had significant weight loss. 32 patients (45.6%) had past medical illness. Among them majority had diabetes 17(24.3%) and hypertension in 6(8.6%) patients. Both the diseases had been in 9 (12.9%) patients.

Diabetes was under control in all the patients. Patients with diabetes had moderate or massive effusion (80.76% Vs 19%) compared to mild effusions. Past respiratory illness was seen in 19 diabetics (15.7%). Among them COPD was seen in 8(11.4%) overall and pulmonary tuberculosis treatment history in 4.3%(n=3).

No significant past respiratory illness was seen in 72.9%(n=51). Among the rest pulmonary tuberculosis was seen in four subjects (15.78%), COPD in 8(42.10%). Smoking Index was found to be higher among COPD patients (525.0) compared to past tuberculosis patients(150.0).

Past history of tuberculosis treatment was seen in 4 patients (5.7%) and all of them completed treatment. Sputum for Ziehl Nelson staining was positive in 2 (2.9%) subjects (1 male and 2 females). These patients had tuberculous pleural effusion with parenchymal lesions. Sputum did not show any bacterial or fungal growth among all patients.

Tuberculin skin test (TST) was evaluated in 59(84.3%) subjects. Among them 19 (32.20%) had positive reaction of more than 10mm.1-5mm was seen in 23 subjects (39%) and 6-10mm was seen in 17 (28.8%).

Equal number of males and females (n=8) had parenchymal lesion on a digital chest X ray PA view.

All the patients showed pleural effusion on chest X ray. Free pleural effusion was noted in 59 out of 70 patients (84.2%) and 15.7% of patients (n=11) had loculated pleural effusion. Among patients with free pleural effusion 40 (67.79%) were males and 19 (32.20%) were females.

There were 8 males and 3 female patients with loculated pleural effusion. Loculated effusion was more in males (16.6%) compared to females (13.6%). All the loculated effusions were confirmed with ultrasound chest.

On chest X ray among 10 (14.3%) cases with mild pleural effusion 9 are males Among moderate pleural effusions of 38(54.28%), 26 are males (68.4%) and 12 females12 (31.5%). Among massive pleural effusions of 22(31.4%), 13(59.09%) are males and 9 (40.91%) females. So, most of the females had moderate and massive effusion, ultrasound scan of chest showed similar results.

Among males 9(18.75%) had mild effusions, 26(54.16%) had moderate effusions and 13(27%) had massive effusions. Similarly, in females1(4.54%) had mild effusions and 12(54.54%) had moderate effusions and 9(40.9%) had massive effusions.

Eight (11.36%) of males had associated parenchymal disease and8(11.36%) of females had associated parenchymal disease. Associated parenchymal disease was noted more in massive pleural effusions of 54.54% compared to 10.5% in moderate and none in mild effusions.

Based on CT chest there were 12 cases of mediastinal involvement (17.14%), massive effusions were associated with 45% moderate effusions 5.2%and none in mild effusions. Among 5 out of 22 massive effusions on chest x-ray and 10 out of 22 with CT chest had mediastinal lesions (22.7%) and (45%) compared to none with moderate effusions on chest x ray and 5.2% with CT chest.

So, parenchymal disease and mediastinal disease was seen more frequently with massive pleural effusions. Out of 5 cases, adenocarcinoma was noted in 4 cases (80%) after closed pleural biopsy and only one case of tuberculosis had mediastinal lesion; among adenocarcinoma diagnosed by pleural biopsy right sided adenocarcinoma had more preponderance for a mediastinal spread based on chest X ray. TST was done in 59 subjects (84.3%). Among them 23(33%) had 1-5 mm induration, 17(24.3%) had 6-10mm induration and 19(27.1%) had > 10mm induration. Among diabetics >10mm induration was observed in 4 cases (out of 26).

In mild pleural effusion, the fluid aspirated was between 300ml to 500ml, in moderate effusion among 500 to 1000ml was aspirated and more than 1000ml was aspirated in all the cases of massive effusions.

Straw colored fluid was noted in 42.9% (n=30), dark yellow colored fluid in 26(37.1%) of cases and 14(20%) of patients had hemorrhagic effusion. Hemorrhagic effusion was more common in females than in males (31.8% Vs 14.5%). There were no major complications after pleural fluid aspiration in our study.

All the patients had exudative pleural effusion based on LIGHT's criteria. Pleural fluid protein was between 3 to 5 gms/dl in 68.1%(n=43) and >5 gms/dl in 38.6% (n=27). Males had higher pleural fluid protein content in our study (41.6% Vs 31.8%). Pleural fluid sugar content of < 50mg/dl was found in 3(4.3%), 50 to 80mg/dl in 43(61.4%) and > 80mg/dl in 24(34.3%) of cases.

Pleural fluid ADA levels<20 units/ L in 15(21.4%), 20-40 units/L in 20(28.5%) and 40- 60 units /L in 35(50%) cases. In tuberculous effusions ADA is >40units/L in 31(77.5%) out of 40 cases. Pleural fluid cell count was between 50- 500 cells/ mm3 in 19(27.1%), 500-1000 in 27(38.6%), 1000-1500 cells in 17(24.3%) and >1500 cells in7(10%) cases.

Pleural fluid cytology revealed malignant cells 14.3%(n=10), out of 20% overall who were confirmed as malignancy. Therefore, the yield of pleural fluid cytology in malignant effusion for diagnosing malignancy in 71.4% in our study. One case of squamous cell carcinoma was positive on pleural fluid cytology, one case of small cell carcinoma was also positive on pleural fluid cytology, whereas 8 out of 12 adenocarcinoma (66%) showed adenocarcinoma in pleural fluid cytology examination.

Pleural fluid staining with ZN staining yielded positive in cases in our study (2.9%) overall and 2(5%) in tuberculous effusion). Pleural fluid AFB culture was initially positive in 4 (5.7%) patients, 2 each in males and females.

Tuberculosis was diagnosed in 40 cases of pleural effusions with pleural biopsy in our Study (57%). Among them mild effusions were seen in 6(15%), moderate effusions were seen in 26(65%) and massive effusions in 8(20%) of cases. Pleural biopsy for AFB smear was positive in 11(21.15%) cases out of 52 cases of tuberculosis.

Among 70 cases in our study 10 (14.2%) were diagnosed as malignancy on pleural biopsy; among them all (n=10) had massive pleural effusions. Among non-specific pleuritic (n=20) (initial diagnosis prior to thoracoscopy) 4 had mild effusions.12 had moderate effusions and 4 had massive pleural effusions (20% Vs 60% Vs 20% respectively).

Four patients who underwent thoracoscopy were histopathologically diagnosed as adenocarcinoma and incidentally all of these patients had moderate pleural effusions. So, among patients with moderate pleural effusions where pleural biopsy was done 68.42% had tuberculosis, 10.5% had malignancy and 21.05% had non specific diagnosis.

All the malignant effusions were massive effusions. 9 out of 10 malignant effusions had mediastinal involvement. 1 case of adenocarcinoma did not have mediastinal involvement. So, a massive effusion with mediastinal involvement mustprobably turned out as malignancy with pleural biopsy in our study. All the malignant cases diagnosed prior to pleural biopsy also had a parenchymal mass on CT scan of the chest. Chest X ray was less sensitive in detecting mediastinal or parenchymal lesions in malignant effusion in our study. Pleural biopsy which revealed malignancy in 10 cases, 8(40%) were adenocarcinoma, 5(25%) in males and 3(15%) in females, small cell carcinoma in 1 (5%) male patient and 1squamous cell carcinoma in 1(5%) female patient.

Among mild effusions 60% (6 out of 10) had tuberculosis and remaining 4 patients were diagnosed as nonspecific with pleural biopsy. Among massive effusions 8 patients (36.3%) were diagnosed as tuberculosis 10(45.5%) patients had malignancy and 4 (18%) had nonspecific diagnosis in pleural biopsy. The yield of current study where a specific diagnosis could be confirmed on pleural biopsy was 71.4% (50 out of 70) and nonspecific diagnosis was seen in 20 cases (28.5%).

Out of 20 nonspecific pleuritic cases,15(75%) were males and 5(25%) were females. 9 (45%) cases were of >55 years age group, 4 patients (20%) less than 30years and 7 (35%) patients are between 30 to 55 years. Out of them 7(35%) cases were smokers. Among them 4(20%) were of mild effusion,12(60%) was of moderate effusion and 4(20%) were of massive effusion. Among the nonspecific cases 7(35%) were diabetic. None of them were hypertensives.

Out of 20 nonspecific pleuritic cases, chest X rays of two patients showed parenchymal changes. ESR was normal in 13(65%) patients, and it was about 30-50mm/1hr in 7(35%) of the cases. Montoux test showed 1-5mm, 5-10mm, >10mm in 13(65%), 6(30%),1(5%) patients respectively.

Four pleural biopsy bits were sent in 7(35%) cases. Four patients who underwent thoracoscopy were his to pathologically diagnosed as adenocarcinoma, incidentally all of these patients had moderate pleural effusions with an age group of more than 55 years. Depending on clinical and radiological background 12(60%) patients of nonspecific pleuritis were suspected to be of tuberculous effusion and were started on anti-tuberculosis drugs and where the patients showed response to the treatment and clinically improved. 4(20%) cases of nonspecific pleuritic left untreated were followed for 12months and they did not show any clinical deteoriation.

Right sided tuberculosis was seen in 22 cases and left side in 18 cases. Adenocarcinoma was more

common on right side (7 out of 8 cases). Tuberculosis was also found to be more common on right side. The number of pleural biopsy bits sent were 3 bits in 37 patients (52.58%) and 4 bits were sent in 33 patients (47.1%).

Two patients (2.9%) developed a small pneumothorax, which subsided on conservative management One patient (1.42%) developed same side surgical emphysema which subsided over three days with oxygen therapy and 1(2.9%) patient developed vasovagal attack.

Table 1: Demography

		Number of Cases	Percent
Sex	Males	48	68.6
	Females	22	31.4
Age	Mean Age	49.30	
	Range	60	
Residency	Urban	30	42.9
	Rural	40	57.1
Socio Economic Status	Lower	38	54.3
	Lower Middle	22	31.4
	Upper Middle	10	14.3
	Upper	0	0
Smoking	Yes	30	42.9
	No	40	57.1
Alcohol	Yes	23	32.9
	No	47	67.1

Table 2: Symptoms

Symptoms	No of Cases	Percent
Cough	60	85.7%
Fever	40	57.1%
Dyspnea	29	41.4%
Chest Pain	26	37.1%
Weight Loss	24	34.3%
Loss of Appetite	20	28.6%

Table 3: Pleural effusion in chest xray

		Gender		Total	
		Male	Female		percentage
Pleural Effusion in Chest Xray	Mild	9	1	10	14.3
	Moderate	26	12	38	54.3
	Massive	13	9	22	31.4
	Total	48	22	70	100

Table 4: Diagnosis of pleural biopsy

Diagnosis Of Pleural Biopsy	No Of Cases	Percentage (%)
RT side kochs plueritis	22/70	31.4%
LT side kochs plueritis	18/70	25.7%
LT side adenocarcinoma	1/70	1.4%
RT side adenocarcinoma	7/70	10%
RT side squamous cell carcinoma	1/70	1.4%
LT side small cell carcinoma	1/70	1.4%
RT side non specific pleuritis	10/70	14.2%
LT side non specific pleuritis	10/70	14.2%

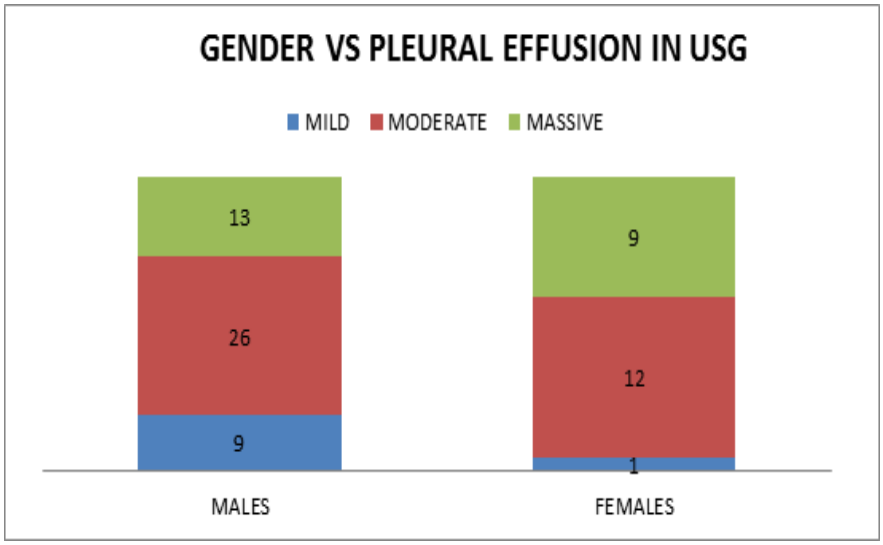

Chart 1: Gender Vs Pleural Effusion in USG

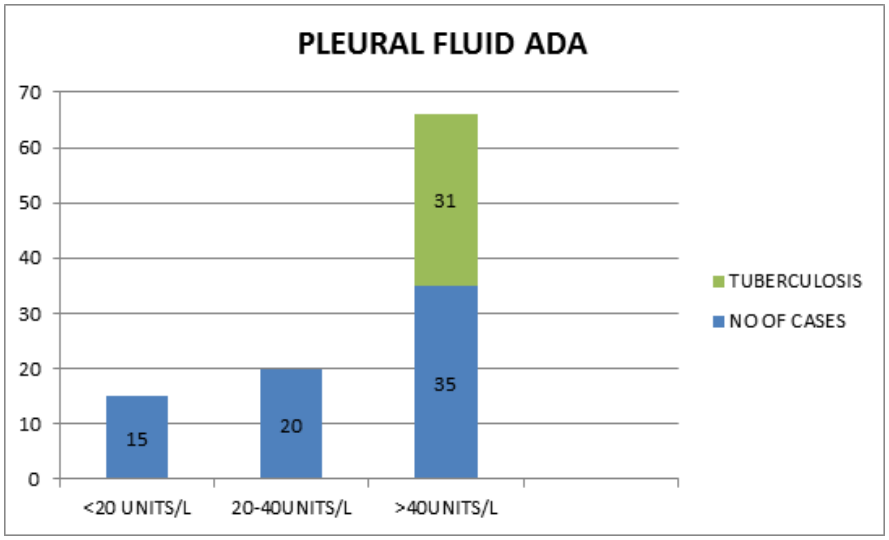

Chart 2: This chart showing pleural fluid ADA levels where >40 units/L were seen in 35 cases out of which 31 were tuberculous effusions

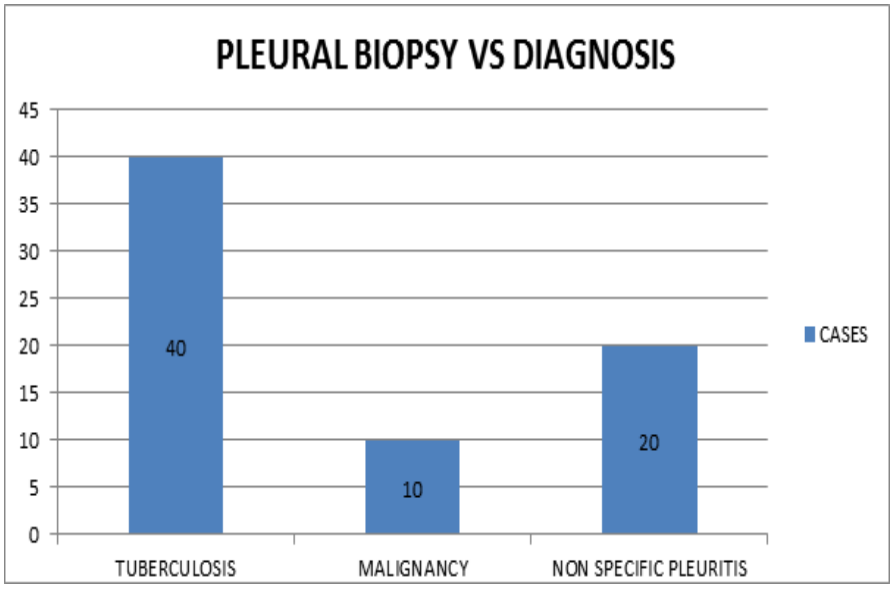

Chart 3: Out of 70 cases 40 were diagnosed as tuberculosis ,10 cases were malignancy and 20 cases were diagnosed as nonspecific pleuritis with closed pleural biopsy

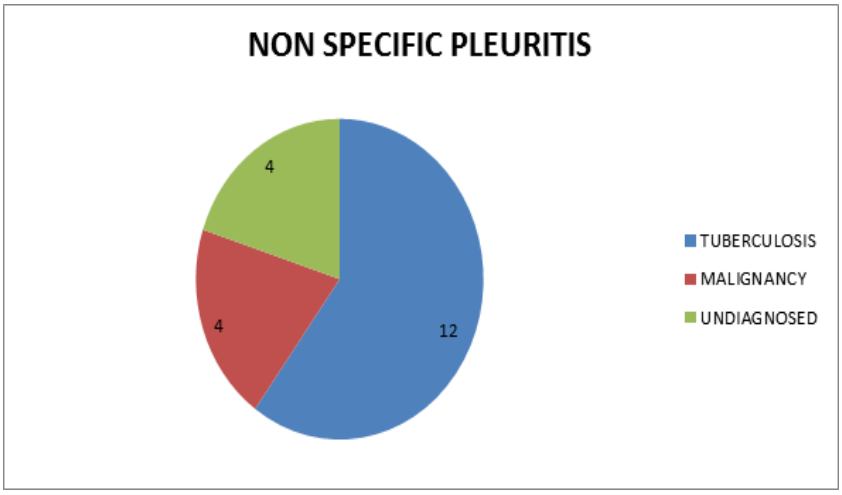

Chart 4: Out of 10 nonspecific pleuritis 4 cases were diagnosed as malignancy,12 cases showed response with att drugs and remaining 2 cases were undiagnosed

Discussion

Etiological diagnosis of exudative pleural effusion is elusive inspite of the technological advances in the field of modern medicine. It poses a stiff clinical challenge.[8]

In this prospective study we attempted to approach this problem with the clinical profile of the patients and blind biopsy technique with cope biopsy needle. [9]

Age: The present study includes 70 subjects, with the mean age of 49.30 years. The patients with tuberculosis were younger than the patients with malignancy. In the current study most of the subjects were (43.47%) between 40-to-70-year age range, comparable with the other studies. [10]

Sex: There were more number of male patients in our study; 48 (68.6%) of the 70 subjects were males and 22 (31.4%%) were females earlier studies reported similar male preponderance [11,12]

Manju R et al reported 60% males and 40% females in their study of 30 subjects submitted to cope needle biopsy [13]

Smoking: In our current sudy there were more smokers among illiterate and rural population. Themean S.I among illiterates was 440 compared to 313 among primary completers and 50 patients with graduation. The S.I was also higher among rural population (395 Vs 183) and among lower income group (392 Vs 231). One patient with small cellcarcinoma had a very high S.I of 1200. Adenocarcinoma is the most likely malignancy with a high S.I(mean S.I 820) whereas mean S.I of 202 was noted among squamous cell carcinoma. In patients with tuberculosis and non-specific diagnosis the mean value of S.I was 125 to 200 except in one patient with tuberculosis who had a S.I of 600. In patients with CT chest mass, pleural biopsy report showed most of the times adenocarcinoma (n=8) which was 80% compared to one who had small cell carcinoma 1(10%) and one who had squamous cell carcinoma 1(10%).

Symptoms: In the present study Fever and cough were the commonest symptoms 60(57.1%) and 40(85.7%) respectively, followed by breathlessness and chest pain 29(41.4%), 26(37.1%) respectively, comparable with the study of Mohammad ish aq khattak et al in which non-productive cough was mostly found in 43 (86%) patients, chest pain in 33 patients (66%), with 18 patients (36%) presented with breathlessness whereas 22 patients (44%) had fever[15], sudipta pandit et al study reported fever and cough as the commonest symptoms (69.2%).

Tuberculin Skin Test: In our study tuberculin skin test (tst) was evaluated in 59(84.3%) subjects. Among them 19 patients (32.20%) had positive reaction of more than 10mm. 1-5mm was seen in 23 patients (39%) and 6-10mm was seen in 17 patients (28.8%) in tuberculous pleural effusion TST yielded positive reaction of more than 10mm in 18(45%) of the 40 patients.

In a study conducted by goud et al [25] 49 patients (92%) had ppd positive (<10 mm) and only 4 of 53 patients had tst negative (1-5 mm) in another study conducted by h.s hira et al TST was positive in 25% and negative tst was seen in 30% patients.

Pleural Effusion on Chest X Ray: In our prospective study among 70 cases on chest x- ray mild pleural effusion was noted in10(14.3%), Moderate pleural effusion was noted in 38 (54.3%) patients and massive effusions in 22(31.4 5%) comparable with a study conducted by Alaa M. Gouda, where most of the cases were found to have moderate to massive pleural Effusions [25].

Dr Balchand Motiani et al performed a study in which he found mild pleural effusion in 30 (38%) patients, moderate pleural effusion in 38 (48%)

patients, and large pleural effusion in 11 (14%) patients [17].

In our study most of the effusions were present on right side in 40(57.14%) cases and 30(42.85%) were on left side, similar to Yaseen khan at el study where right sided pleural effusion was found in 55% cases, left sided in 40% cases and 5% were having both sided pleural effusion[14]. Similar results of Right-side dominance of pleural effusion is also found in other studies by Mousa E. Khadadah et al[19] and WK kalaajieh[32].

In the current study all cases diagnosed as malignancy by pleural biopsy were of massive effusions (n=10,71.42%), Similar to results found in a study by Somnath Bhattacharya et al[10] and WK kalaajieh.

Based on CT chest there were 12 cases of mediastinal involvement (17.14%), mass lesions in 11(15.7%) cases in which massive effusions were most commonly associated (45%). Parenchymal disease and mediastinal disease was seen more frequently with massive pleural effusions. Out of 5 cases, adenocarcinoma was noted in 4 cases (80%) and only one case of tuberculosis had mediastinal lesion.

Somnath Bhattacharya et al showed similar results on CT scan of thorax which revealed mass lesion in 26 cases (39%), collapse in 13 cases (20%), and mediastinal lymphadenopathy in 19 (29%) case of which 14(21%) were massive effusions[10].

Pleural Fluid Ada: In our present study Pleural fluid ADA levels of <20 units/ L were seen in 15(21.4%), 20-40 units/L in 20(28.57%) and 40- 60 units /L in 35(50%) cases; ADA levels of >40units/L were mostly seen seen in tuberculous effusions in 31(77.5%) of our patients.

In a study conducted by Danielle M. Lima et al the mean value of ADA activity levels in all 45 patients was 43.6 U/L. Among the patients with the diagnosis of tuberculosis, the mean ADA activity level was 53 U/L, while in the group of patients where the diagnosis of tuberculosis was ruled out, it was 37 U/L. Considering 40 U/L as a cutoff value, the test result was considered positive in 11 patients with tuberculosis; however, in the samples in which the tuberculosis diagnosis was ruled out, 8 patients presented activity levels >40 U/L, which lowers the sensitivity (68.8%) and specificity (72.4%) of the test.

Pleural Fluid for Z-N Staining: In our study Pleural fluid with ZN staining yielded positive results in 2 cases (2.9%) overall and 2(5%) in diagnosed patients of tuberculous effusion, this is comparable with a study done by Prince James et al [12] where Pleural fluid smear positive for AFB was seen in 1 of (4.8%) 48 cases.

Pleural Fluid for Culture Afb: In our current study pleural fluid culture was positive for AFB in 4 patients (5.7%) overall and 4(10%) in tuberculous effusion comparable with a study conducted by Alaa m. gouda et al [25] where mycobacterium tuberculosis grew from pleural fluid culture, only in 4/53 patients.

In another study done by prince james et al. [12] pleural fluid mycobacterial culture is found positive in up to 30% cases of tubercular pleural effusion.

Arun gopi et al. [5] in his study concluded that culture requires a minimum of 10 to 100 viable bacilli and, therefore, is more sensitive with a yield ranging from 12 to 70%.

Pleural Tissue for Afb Smear: In the present study pleural biopsy tissue for AFB smear was positive in 11(27.5%) of 40 patients of tuberculous pleural effusions.

In a study conducted by sudipta pandit et al showed pleural tissue for acid fast stain was positive in 16 cases (22%)[8].

similarly in a study conducted by h.s.hira et al pleural tissue was submitted for ziehl-nelsen (zn) stain for presence of mycobacterium tuberculosis. it was positive in 2 (10.5) of 19 patients [9].

Pleural Fluid Cytology for Malignant Cells: In our study Pleural fluid cytology revealed malignant cells in 14.3%(n=10) out of 70 cases overall. Therefore, the yield of pleural fluid cytology in malignant effusion for diagnosing malignancy is 71.4% in our study. One case of squamous cell carcinoma was positive on pleural fluid cytology, one case of small cell carcinoma was also positive on pleural fluid cytology, whereas 8 out of 12 adenocarcinoma (66%) showed adenocarcinoma in pleural fluid cytology examination.

In a study conducted by sudipta pandit et al showed pleural fluid cytology for malignant cells were positive in 14 out of 72(19.4%) cases[8]. Similarly in another study conducted by wk kalaajeih et al. pleural fluid cytology for malignant cells were positive in 70% comparable with our present study.

In another study done by Prince James et al Pleural fluid cytology alone was diagnostic of malignancy in only two (14.3%) cases out of 28 cases.

Similarly in another study conducted by Ihsanullah et al pleural fluid cytology for malignant cells were positive in 5 cases out of 24 cases.[20]

Somnath Bhattacharya et al performed a similar study where pleural fluid cytology for malignant cells was positive in 46(69%).

Tuberculosis: In our study Tuberculosis was diagnosed in 40 cases of pleural effusions with pleural biopsy in (57.14%). Among them mild effusions

were seen in 6(15%), moderate effusions were seen in 26(65%) and massive effusions in 8(20%) of cases.

In a study conducted by Alaa M. Gouda the overall diagnostic sensitivity in pleural effusions with Cope's pleural biopsy was 82%, compared to 54% for Abram's needle [25]. The diagnostic sensitivity in TB pleurisy for Cope pleural biopsy was 85% (17/20), compared to 57.5 (19/33%) for Abrams needle (P = 0.08). In a study conducted by Prince James et al closed pleural biopsy yielded the diagnosis in 76.2% cases of tubercular pleural effusion [12], and in 66.7% cases, pleural biopsy was the only diagnostic test. This 76.2% yield was with single pleural biopsy, in an Indian study on role of serial pleural biopsies in the diagnosis of pleural effusion [12]. Mousa E. Khadadah et al performed a similar study in assessing the diagnostic yield of percutaneous pleural biopsy, approximately 74 (52%) patients had a definitive diagnosis, of whom 66 (46%) showed definitive granulomas (caseating or non-caseating)in their samples.[19]

Malignancy: In the current study among 70 cases, 10 (14.2%) were diagnosed as malignancy on pleural biopsy; among them all (n=10) had massive pleural effusions. Mungal et al performed similar study on 55 cases of which malignancy was proved histopathologically in 47.3% cases Similar study was done by Sudipta Pandit et al where pleural biopsy showed malignancy in (33.4%) cases [8]. Somnath Bhattacharya performed a similar study where pleural biopsy showed positive for malignancy in (48%) [10]. In a study done by Biswajit Chakrabarti pleural biopsy showed positive for malignancy in 27% [21] In an Indian study, Christopher et al [11] reported that the diagnostic yield of pleural biopsy was 71% for pleural malignancy.

Type of Malignancy: In our current study pleural biopsy revealed malignancy in 10 cases, 8(40%) were adenocarcinoma, 5(25%) in males and 3(15%) in females, small cell carcinoma in one (5%) male patient and one squamous cell carcinoma in 1(5%) female patient.

In a study done by Biswajit Chakrabarti pleural biopsy showed positive for malignancy of which 9(69%) were adenocarcinoma, 2(15.5%) were diagnosed as mesothelioma and 2(15.5%) were diagnosed as non-small cell carcinoma on histopathological examination [21]. Prince James et al performed a similar study where pleural biopsy showed bronchogenic carcinoma in 4(28.6%), Mesothelioma in 2 (14.3%), Papillary carcinoma in one (7.1%) Malignant effusion with unknown primary in 5 (35.7%) and Lymphoma in two (14.3%) cases [12].

Relationship between Number of Biopsy Specimens and Diagnosis of Malignancy: In our study 4 pleural biopsy specimens (biopsy bits) were sent in 5 cases of malignancy out of which three were diagnosed as adenocarcinoma, one squamous cell carcinoma and one small cell carcinoma. In another 5 cases of malignancy 3 biopsy specimens were sent out of which all the 5 were diagnosed as adenocarcinoma. However, this difference in diagnostic yield did not reach statistical significance.

In a study done by Biswajit Chakrabarti et al 25 blind biopsy procedures were done in which up to three specimens were sent; malignancy was diagnosed in four patients 1 NSCLC (16%) and mesothelioma in 1 case, while in the 40 procedures in which 4 to 6 samples were obtained, 13 samples (32.5%) were diagnostic of malignancy of which (adenocarcinoma were 7; mesothelioma were 3; NSCLC, were 1; others in 2 cases respectively)[21]. However, this difference in diagnostic yield did not reach statistical significance similar to that of our study.

Non-Specific Pleuritis: In the current study among 70 cases, 20 (28.57%) were diagnosed as non-specific pleuritis on pleural biopsy, (diagnosis prior to thoracoscopy) of which 4 had mild effusions,12 had moderate effusions and 4 had massive pleural effusions (20%, 60%, 20% respectively). Four patients who underwent thoracoscopy were histopathologically diagnosed as adenocarcinoma, incidentally all of these patients had moderate pleural effusions with an age group of more than 55 years. Depending on clinical and radiological background 12(60%) patients of non- specific pleuritis were suspected to be of tuberculous etiology and were started on antituberculosis drugs and the patients showed response to the treatment and they clinically and radiologically improved. 4(20%) cases of nonspecific pleuritis were left untreated and were followed for 12months and they did not show any clinical deteoriation.

In a study by Biswajit Chakrabarti et al [21] pleural biopsy showed nonspecific pleuritis in 22 patients (29%) after no recurrence of the effusion or the subsequent development of neoplasia was identified on regular clinical follow up for a minimum of 12 months following initial blind pleural biopsy (range of follow-up, 12 to 48 months).

In a study by et al one hundred and twenty-two pleural biopsies were performed in 116 patients using cope needle in 39, Abram's needle in 83 cases. A non- specific diagnosis was obtained in 56 (50.9%) cases [22].

Final Diagnosis and Yield of Pleural Biopsy: The yield of our study where a specific diagnosis could be confirmed on pleural biopsy was 71.4% (50 out of 70) of which tuberculosis is seen in (57.14%), malignancy 10(14.2%) and nonspecific pleuritic 20(28.57%) respectively.

Another study done by Frank et al showed the diagnostic yield of pleural biopsy in 40–70% cases in both tuberculous and malignant pleural effusion. In a study performed by R. manju et al diagnostic yield of pleural biopsy was 55.6%. Arnab Maji et al conducted a similar study of which pleural biopsy showed a diagnostic yield of 45.34% which is consistent with that of 43% to 57% reported in other studies.

Somnath Bhattacharya et al performed a similar study where pleural biopsy showed diagnostic yield of 48% in malignant effusions[10]. Yaseen Khan et al conducted a similar study in which pleural biopsy showed tuberculosis, malignancy and non-specific inflammation in 53%, 28% and 19% cases respectively with a diagnostic yield of 81% [14]

Relationship between Number of Biopsy Specimens and Diagnosis: In our study the number of pleural biopsy bits sent were 3 bits in 37 patients (52.58%) and 4 bits were sent in 33 patients (47.1%). The difference in pleural yield between the group in which three samples were obtained and those in which four samples were obtained did not reach statistical significance(p=0.57). Furthermore, when examining all biopsy proven cases of TB pleuritis, the proportion of those with 4 samples and more (≥4), and those with size of 3 mm and above (≥3 mm) increases significantly to 78.8% and 93.9%, among TB pleurisy patients [19].

Complications: In our study 2 patients developed complications such as pneumothorax and required intercostal tube drainage. One patient developed same side surgical emphysema which subsided over three days with conservative management and 1 patient developed vasovagal attack.

Yaseen Khan et al conducted a similar study in which he concluded that eight patients out of 100 developed subcutaneous emphysema at biopsy site which resolved in next few days. Most were having mild pain at biopsy site which resolved with NSAIDs. There were no major complications in his study, illustrating the safety of the procedure.

Conclusions and Summary

We recommend closed pleural biopsy should still be the initial step in the diagnostic algorithm for undiagnosed exudative pleural effusions especially in a high tb-burdened and resource limited country like India and other Asiatic countries.

CPB is safe and should be a routine complimentary diagnostic procedure in patients with exudative pleural effusions, in view of its negligible morbidity and mortality.

It needs minimal manpower support and hospitalization. this recommendation for closed pleural biopsy is all the more justified in a resource poor country like India where the facilities and expertise for imaging-guided pleural biopsies and thoracoscopy are not available. Medical thoracoscopy needs initial training competence of at least 20 supervised procedures and substantially greater capital equipment costs and larger procedure support team.

Though tuberculous pleurisy is noted in the older individuals, moderate to massive pleural effusions reported as ‘nospecific pleuritis’ on CPB should be aggressively evaluated or reffered for thoracoscopic evaluation to exclude or confirm a malignant pleural effusion.

Usually obtaining three or four biopsy samples by blind biopsy technique would suffice for diagnostic evaluation of tb pleuritis and malignant pleural effusions in combination with peural fluid analysis and cytology. it has been stated that at least three specimens would be sufficient for a diagnostic yield of tb pleuritis and fourth specimen would give higher yield for suspected malignancy.

Unlike for medical thoracoscopy , the competency in cpb requires knowledge of thoracentesis with an initial five procedures under supervision ; in the present study which is carried by first year trainee postgraduate in pulmonology the cpb yield was more than 70%.[26]

There is no difference over the priority of pleural biopsy needles (abrams verses cope) since various studies did not note any superiority over the other regarding diagnostic yield.

Hence, sensitivity alone might not be the only criterion for a physician to opt a diagnostic test. it should be more prudent to chose the most feasible option for a given patient on a case by case basis and the available facilities and manpower.[27]

References

1. Puchalski J et al. Pleural diseases preface. Clin Chest Med. 2013; 34(12).
2. Koegelenberg CF, Diacon AH Pleural controversy: close needle pleural biopsy or thoracoscopy-which first? Respirology. 2011; 16(5): 738-46.
3. Defrancis N, Klosk E, Albano E . Needle biopsy of the parital pleura. N Engl J Med. 1955;252: 948-949.
4. Michael H Baumann. Closed pleural biopsy not dead yet. Chest. 2006;129(6):1398-1400.
5. Gopi A, Madhavan SM, Sharma SK, Sahn SA. Diagnosis and treatment of tuberculous pleural effusion in 2006. Chest. 2007; 131:880-889.
6. Loddenkemper R, Grosser H, Gabler A, Mai J, Preussler H, Brandt HJ et al. Prospective evaluation of biopsy methods in the diagnosis of malignant pleural effusion: Intrapatient comparison between pleural fluid cytology, blind needle biopsy and thoracoscopy. Am Rev Respir Dis. 1983; 127(4): 114.

7. Psathakis K and Skouras V. Blind needle biopsy of pleura: Why not? Eur Resp Rev. 20(120):120-122.
8. Pandit S, Chaudhuri AD, Datta SB, Dey A, Bhanja P. Role of pleural biopsy in etiological diagnosis of pleural effusion. Lung India. 2010; 27(4):202-4.
9. H. S. Hira and Rajiv Ranjan Role of percutaneous closed needle pleural biopsy among patients of undiagnosed exudative pleural effusion Lung India. 2011; 28(2): 101–104.
10. Somnath Bhattacharya, Tapan D Bairagya, and Sibes K Das Closed Pleural Biopsy is Still Useful in the Evaluation of Malignant Pleural Effusion J Lab Physicians. 2012 J; 4(1): 35–38.
11. Christopher DJ, Peter JV, Cherian AM. Blind pleural biopsy using a Tru-cut needle in moderate to large pleural effusion--an experience. Singapore Med J. 1998 ;39(5):196-9.
12. Prince James, Richa Gupta, D. J. Christopher and T. Balamugesh. Evaluation of the diagnostic yield and safety of closed pleural biopsy in the diagnosis of pleural effusion. Indian J Tuberc. 2010; 57:19-24.
13. R Manju, R Venkateswara Babu, S Vinod Kumar, Bhawana Ashok Bade. Pleural Biopsy in Exudative Effusions - A Comparative Study Using Abram's and Cope Needles World journal of medical sciences. 2012;7(3):151-154.
14. Yaseen Khan, Bilal, Sumera Zia Etiological spectrum of exudative pleural effusion in a tertiary care hospital based on closed pleural biopsy Y Ann. Pak. Inst. Med. Sci. 2011; 7(3):133-136.
15. Mohammad ishaq khattak, Said amin, Ghulam shabbier, Sadiq ur rehman Diagnostic value of pleural biopsy in exudative pleural effusion Gomal Journal of Medical Sciences. 2011; 9(2):156-158.
16. Khan.H U, Rahman-ud-din, Mahsud I U, Khattak A M, Ihsan Waheed, S. Humayun shah Aetiology of exudative pleural effusion in district D. J. khan biomedica 2007; 23 (14):57-59
17. Dr Balchand Motiani, Nadeem Rizvi, Fakhir Raza Haidri Diagnostic role of pleural biopsy in exudative pleural effusion. PJCM 2008; 14(1):4-13.
18. Hoda M. Bahr, Mohamed H. El-Shafey, Mohamed S. Hantera, Gehan H. Abo-El magd Ahmed H. El-Batsh Ultrasound guided needle pleural biopsy in patients with undiagnosed pleural effusion Egyptian Journal of Chest Diseases and Tuberculosis. 2014; 63:113–118.
19. Mousa E. Khadadah et al, Closed percutaneous pleural biopsy A lost art in the new era. Saudi Med J 2009; 30(6): 793-797.
20. Ihsanullah, Nisar Khan, Huma Jadoon, Munawar Zaman, Ashfaq Ahmed Yield of Abrams needle pleural biopsy in exudative pleural effusion J Ayub Med Coll Abbottabad. 2009;21(1):116-118.
21. Biswajit Chakrabarti, MBBS, FRCP; Ida Ryland, MSc;John Sheard, MD, FRCPath; Christopher J. Warburton, MD, FRCP; and John E. Earis, MD, FRCP The role of abrams percutaneous pleural biopsy in the investigation of exudative pleural effusions. Chest. 2006; 129(6):1549–1555.
22. Al-Shimemeri AA, Al-Ghadeer HM, Giridhar HR Diagnostic yield of closed pleural biopsy in exudative pleural effusion. Saudi Med J. 2003; 24(3):282-6.
23. Jiménez D, Pérez-Rodriguez E, Diaz G, Fogue L, Light RW. Determining the optimal number of specimens to obtain with needle biopsy of the pleura. Respir Med. 2002 ;96(1):14-7.
24. Nusair S, Breuer R, Amir G, Berkman N Closed pleural needle biopsy: predicting diagnostic yield by examining pleural fluid parameters. Respir Med. 2002 ;96(11):890-4.
25. Alaa M. Gouda, Tarek A. Dalati, Nasser S. Al-Shareef A comparison between Cope and Abrams needle in the diagnosis of pleural effusion Annals of Thoracic Medicine - 2006;1(1):12-15.
26. Carl M. Kirsch, D. Mark Kroe, Raymond L. Azzi, William A. Jensen, Frank T Kagawa, MD, John H Wehner, The Optimal Number of Pleural Biopsy Specimens for a Diagnosis of Tuberculous Pleurisy CHEST. 1997; 112:702-06.
27. Ashutosh Sachdeva, MBBSa, Ray Wesley Shepherd, MDb, Hans J. Lee, MDb, Thoracentesis and Thoracic Ultrasound: State of the Art in 2013. Clin Chest Med. 2013;34: 1–9.