Pleural Effusion: Characterization With contrast CT Appearance and CT Attenuation Values

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Summary:

Background: A number of different types of fluid may accumulate in the pleural space, the most common being transudate, exudate (thin or thick), blood and chyle. All types of pleural effusion are radio graphically identical, though historical, clinical and other radiological features may help limit the diagnostic possibilities. Sometimes, also CT and MRI can help to specify the diagnosis.

Objective: To determine the accuracy of computed tomography (CT) in enabling differentiation of pleural exudates from transudates.

Patients and methods: forty three consecutive patients (43 effusions) underwent contrast-enhanced CT. Thoracocentesis was performed to measure pleural and serum total protein values. Effusions were classified as exudates with accepted criteria. CT scans were evaluated for the presence and appearance of: parietal pleural thickening**,** visceral pleural, thickening, extra pleural fat thickening**,** measurement of CT attenuation values for each of the pleural fluids.

Results: 34 effusions were exudates and 9 were transudates. Twenty of the 34 exudates (59%) were associated with parietal pleural thickening. 67% of empyema and 86% of the parapneumonic exudative effusions had pleural thickening. The specificity of this finding in diagnosing the presence of an exudate is 88%. The mean value in Hounsfield units of an effusion was determined using a region of interest on the three slices with the greatest quantity of fluid.

Conclusion: Ultrasound is done to detect pleural effusion ,which sometimes cannot be detected by conventional radiography , but characterization of the pleural fluid cannot be done by ultrasound because CT attenuation with additional pleural CT appearance features such as fluid loculation, pleural thickness, and pleural nodules are helpful in differentiating exudates from transudates, because we found that their prevalence is higher among exudative effusions .so ultrasound is done to detect the effusion ,but its characterization is done by CT.

Keywords: pleural exudate, pleural transudate, CT attenuation value.

Introduction:

Pleural effusion is a common clinical finding with many causes (1).The first step in the evaluation of a pleural effusion is to determine whether the pleural fluid is a transudate or an exudate. The formation of a transudate usually results from increased capillary hydrostatic pressure or from decreased colloid osmotic pressure. The main cause of transudates is usually congestive heart failure (CHF). The formation of an exudate usually results from an increased permeability of the pleural capillaries, generally due to inflammatory or neoplastic processes (2). Thoracocentesis is routinely used as the first step in the characterization of a pleural effusion as transudate or exudate. Biochemical, cytologic, and microbiological analysis of the effusion can lead to determination of the cause in most cases(1). Diagnostic thoracocentesis carries small but significant risks.The most common complication is pneumothorax, occurring in around 12% of the procedures with 5% of patients requiring chest tube insertion (3). Minor complications include pain, shortness of breath, cough, and hematoma. Relative contraindications for thoracocentesis include a bleeding diathesis, systemic anticoagulation, a small volume of pleural fluid, mechanical ventilation, inability of the patient to cooperate, and cutaneous disease such as herpes zoster or other infection at the needle insertion site(4).

A noninvasive method to characterize pleural fluid would be valuable for avoiding the potential risks associated with thoracocentesis and may help to guide therapy. CT is frequently used to assess patients with pleural abnormalities associated with neoplasm, pneumonia, and empyema.Exudates usually contain high levels of protein, lactate dehydrogenase (LDH), bilirubin, and cholesterol(1) , thus potentially they may show greater attenuation values on CT.Parietal pleural thickening at contrast-enhanced CT usually indicates the presence of a pleural exudates . A pleural exudate in the absence of pleural thickening occurs most frequently in patients with malignancy or parapneumonic effusion. It

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has been recently reported that the finding of parietal pleural thickening at contrast-enhanced CT can help distinguish pleural effusions representing exudates or empyema from those representing transudates (1). Transudative pleural effusions and a large percentage of malignant exudates do not show parietal pleural thickening or enhancement. Also, several studies have described extra pleural fat thickening and edema in association with pleural thickening or effusion; we reviewed the appearance of the pleura on contrast-enhanced CT scans obtained in 43 consecutive patients with pleural effusions to determine the accuracy of CT in enabling differentiation of pleural exudates from transudates on the basis of parietal pleural thickening. The appearance of extrapleural fat was also assessed.

Patients and methods:

Data were collected at Baghdad teaching hospital from June 2010 to May 2011. Forty three patients with pleural effusions were evaluated with contrast-enhanced CT and diagnostic thoracocentesis. Patients were selected for the study if they met the following criteria: (a): presence of a pleural effusion at contrast-enhanced CT (b): pleural total protein values obtained at thoracocentesis and (c): CT attenuation values. There were 11female patients and 32 male patients aged 15-70 years (mean: 43 years). Thoracocentesis was performed an average of 3-4 days before or after the CT examination. For the purposes of this study, a pleural effusion was classified as an exudate or a transudate in accordance with definitions proposed by Light (2). Modifications of Light's criteria have been shown to increase the specificity in detecting exudates (3); however, we chose to adhere to the original criteria, which are followed at our hospital laboratory.

To be classified as an exudate, an effusion should met the following criteria: A pleural fluid total protein/serum total protein ratio of more than 0.5. Effusions were classified as transudates if they did not meet the above criteria. Patients were excluded from the study if there were insufficient laboratory data with which to evaluate the nature of the effusion.

Pleural effusions were also analyzed for the presence of infectious organisms by means of staining (including gram, fungal, and mycobacterial stains), culture (aerobic, anaerobic, fungal, and mycobacteial), and cytologic examination. Parapneumonic effusions are usually defined as those associated with pneumonia, lung abscess, or bronchiectasis, and an empyema is considered to be a complicated parapneumonic effusion in which pus is present and the culture is positive (2,3).In our study, effusions were considered to be empyemas only if culture results were positive. Otherwise, all effusions associated with pulmonary infections were classified as Para pneumonic effusions. Malignant effusions were defined by the presence of positive cytologic results. Effusions with negative cytologic results were classified as effusions "associated with malignancy," in distinction to the truly malignant effusions.

Scanning parameters: Contrast-enhanced CT was performed and 5-8 mm-thick sections were obtained with the Toshiba 4 slices and Philips multidector CT, All patients received 60-120 ml of iohexol (Omnipaque 300 at a rate of. 3 ml/sec).

Data acquisition: CT scans were reviewed blindly by two observers who reached a consensus. Studies were evaluated for the CT attenuation values and the presence of parietal and visceral pleural thickening. Parietal pleural thickening was diagnosed only if a pleural line was visible internal to the ribs in areas in which pleural effusion was also seen (4). When visible, the thickness of parietal pleura was measured and its extent and appearance classified as focal or diffuse and irregular or smooth. Pleural thickening was considered diffuse if it was visible in all locations in which fluid was visible. The presence of visceral pleural enhancement and thickening adjacent to fluid collections was also assessed. The extrapleural fat adjacent to the ribs was evaluated for visibility, thickness, asymmetry, and attenuation. Extrapleural fat was arbitrarily considered normal if it was less than 2 mm thick. The attenuation of the extrapleural fat was estimated to be the same as that of the chest wall fat, the same as that of the musculature of the chest wall, or intermediate, between that of fat and musculature.

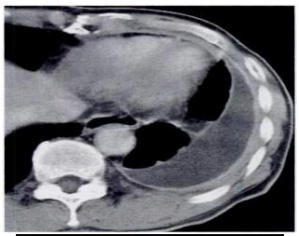

Fig (1): contrast enhanced CT of thorax of a 70 years old man with lung metastasis ,there is parietal pleural thickening

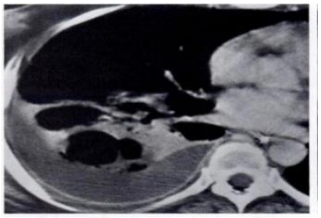

Figure (2) Contrast-enhanced CT scan of the thorax of showing visceral pleural thickening and extra pleural fat thickening

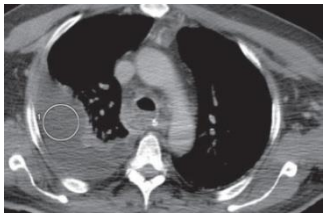

Fig. 3—Contrastenhanced CT scan of chest at level of aortic arch in 73-year-old mm with right-sided empyema shows loculated pleural effusion (circle) on right

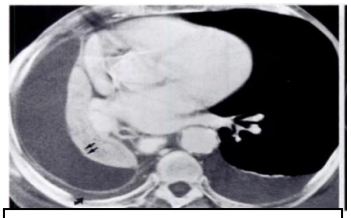

Figure (4) Contrast-enhanced CT scan of a chest with congestive heart failure .the right lung is collapsed, and the parietal and visceral (straight arrows) pleura are diffusely thickened. The sub pleural fat (curved arrow) is thicker than that in the left side.

Results:

Parietal pleural thickening Thirty four exudates were evaluated with CT .Twenty showed focal or diffuse parietal pleural thickening thus, the sensitivity of parietal pleural thickening as seen at CT in the detection of the presence of a pleural exudate was 58% (confidence interval, 40%-73%) (Table 1).

Table (1) summary of CT finding in 34 exudates and 9 transudate

Group	Parietalpleural thickening	Extrapleuralfat thickening	Visceralpleural thickening
Exudates	33	21	13
Transudate	1	1	1

Pleural thickness measured 2-4 mm is seen in 15 of the 34 cases with thickening, and the thickness of the pleura did not appear to correlate with the diagnosis. Of the 20 effusions associated with parietal pleural thickening, 12 showed diffuse, smooth, parietal pleural thickening in association with the pleural effusion (Fig 1) and three had diffuse, irregular thickening (Table 4). The remaining 14 effusions were associated with irregular or smooth focal pleural thickening. All effusions were crescentic and unilocular. Focal, irregular thickening was seen in the presence of malignancy; however, only two effusions were associated with this finding. Focal, irregular, pleural thickening was seen with malignancy. Fourteen pleural exudates did not show parietal pleural thickening (Table 1). These included 5 effusions associated with malignancies, one parapneumonic effusions, two of unknown cause, and one occurring after chest trauma. Parietal pleural thickening was visible in 5 of 7 empyemas (Fig 3) but was present in only 6 (86%) of 7 parapneumonic exudates. Neither the characteristics of the pleural thickening nor the thickness of the parietal pleura were helpful for distinguishing empyema from an uninfected parapneumonic exudate (Tables 4). However, none of the transudative parapneumonic effusions were associated with pleural thickening.

Of the 9 transudates, only one showed parietal pleural thickening. Thus, the specificity of this finding in diagnosing the presence of an exudate is 88% (confidence interval, 50%-99%; positive predictive value, 97%; negative predictive value, 54%) (Table1). Of the remaining 9 transudative effusions, 8 were crescentric and unilocular. One transudative effusion caused by congestive heart failure showed unilateral loculation of fluid in the fissures without pleural thickening. Of the 9 transudates, most occurred in patient with history of malignancy but were associated with benign pleural fluid at cytologic examination of were parapneumonic effusion in the abscense of empyema. Of the 33 exudates associated with parietal pleural thickening 21 showed extrapleural fat thickening; therefore, the sensitivity was 95% (confidence interval, 75% ^ 99%) (Table 1). 6 of these exudates were empyemas and 5 were parapneumonic effusions (Table 5). The extra pleural fat was 2-4 mm thick in 6 cases and at least 4 mm thick in 4 cases (Table 5); five additional cases had an extrapleural fat layer that was less than 2 mm thick, which was considered normal Only one of the 14 exudates without parietal pleural thickening was interpreted as showing extrapleural fat thickening; this occurred in a patient with a parapneumonic effusion. Fat thickening was associated with a transudate only in the patient with parietal pleural thickening. The specificity of this finding was 80 % (confidence interval, 65% - 90%).

Visceral pleural thickening was visible in 13 patients with exudates (five with pneumonia, five with empyema, and three with malignancy) (Fig 4) and in the patient with a transudative effusion and pleural thickening (Fig4). Thickened visceral pleura measured less than 2 mm in all patients. The sensitivity of this finding was 22% and the specificity 96%. Of the 24 effusions in patients with malignancies, 17 were exudates (Table3). Ten showed parietal pleural thickening. Nine of the 10 had negative findings at cytologic examination, and six had positive findings (Fig 2). There was no difference in the degree or appearance of pleural thickening between those patients with positive and negative cytologic findings. (Tables 1, 2). Of the 7 exudates associated with malignancy that did not show parietal pleural thickening, 5 had positive cytologic findings Of the effusions associated with lung cancer, none of those associated with pleural thickening had positive cytologic findings; two of three effusions associated with lymphoma, breast cancer, or other tumors had pleural thickening and positive cytologic results.. Extrapleural fat thickening was visible in three of the 23 exudative effusions.

According to Light's criteria, 34 of the 43 pleural effusions were exsudates and 9 were transudates. Table (2) summarizes the different causes of pleural effusions and their respective mean attenuation in Hounsfield units. The mean attenuation of exudates (7.2 HU; [SD] 9.4 HU) was not significantly lower than that of transudates (10.1 HU; 6.9 HU), ($p = 0.24$). The attenuation of exudates ranged from -21 to 28 HU and the attenuation of transudates ranged from 0.3 to 32 HU. All 13 negative attenuation values were found in exudates .Eight of these patients were found to have acute pneumonia, three had chronic effusion due to malignant disease, and two had pleural effusion of unknown cause. There was a mild but significant positive relationship between mean Hounsfield units and pleural total protein The overall accuracy for identifying exudates was low, ($A z = 0.582$; 95% CI, 0.479-0.680), resulting primarily from the overlap in scores between 0 and 13 HU, which constituted 64% of effusions. The optimal threshold value for exudates was determined to be £ 8.5, which showed a sensitivity of 55.1% and specificity of 68.2%.

Table (2): summary of causes and attenuation value for pleural effusion

Characterstic	All effusions	Transudate	CHF	Others	Exudates	Malignancy	Pneumonic effusion	Pulmonary embolism	Others	unknown
No. of lesions	43	9	1	8	34	24	5	1	1	3
Mean /SD(HU)	7.9/9.0	10.1/6.9	11.1/6.4	0.3/0	7.2/9.4	7.2/8.5	5.8/9.9	5.0/5.5	10.8/8.0	-3.3/12.4

Table (3): characteristic of 24 pleural effusions associated with malignancy

Diagnosis	No. of exudates	No. of transudates	No.with thickened parietal pleura	No.with no thickening parietal pleura
Lymphoma				
Positive cytologic findings	3	0	2	1
Negative cytologic findings	2	3	2	3
Breast cancer				
Positive cytologic findings	3	0	1	2
Negative cytologic findings	1	2	1	2
Lung cancer				
Positive cytologic findings	3	0	0	3
Negative cytologic findings	2	0	2	0
Others				
Positive cytologic findings	2	0	1	1
Negative cytologic findings	1	2	1	2
Total	17	7	10	14

Table (4): characteristic of parietal pleural thickening in 43 exudate

		Focal Thickening		Diffuse Thickening	
Diagnosis	Normal	Smooth	Irregular	Smooth	Irregular
Malignancy					
Positive cytologic finding	5	1	3	1	1
Negative cytologic finding	2	3	4	2	0
Pneumonia	1	1	0	5	0
Empyema	2	1	0	4	0
Pulmonary embolus	1	0	0	0	1
Trauma	1	0	0	0	0
Undiagnosed	2	0	1	0	1
Total	14	6	8	12	3

Table (5) thickness of extrapleural fat in34 exudate

Diagnosis	Normal	2mm	2-4 mm	>4mm
Malignancy				
Positive cytology	9	0	0	1
negative cytology	4	3	2	1
Pneumonia	2	1	0	1
Empyema	1	0	4	1
Pulmonary embolism	1	0	0	0
Trauma	1	0	0	0
Unknown	1	1	0	0
Total	19	5	6	4

Discussion:

Exudative effusions can have a variety of causes. They often reflect the presence of pleural inflammation, infection, or neoplasm, and in such cases are thought to be due to an increased permeability of abnormal pleural capillaries and the release of high-protein fluid into the pleural space (2,3). Transudative effusions are not associated with pleural disease and are considered to be the result of systemic abnormalities that cause an imbalance in the hydrostatic and osmotic forces leading to the formation of pleural fluid. This results in an outpouing of low-protein fluid from the pleural capillaries and, occasionally, the parenchymal interstitium into the pleural space. Common causes of a transudative effusion include congestive heart failure, cirrhosis,and nephrotic syndrome

.Differentiating an exudate from a transudate can be important in clinical management, particularly in patients with infection and malignancy. Exudates and transudates differ in many ways, but according to generally accepted criteria proposed by Light (2), exudative effusions are considered to be those with a pleural fluid total protein/serum total protein ratio of more than 0.5. A pleural fluid-specific gravity exceeding 1.016 or a pleural fluid protein exceeding 3 g/dL are other citeia used to diagnose exudate, but these have a somewhat lower specificity (4). Sonography can be useful for detecting pleural fluid characteistics compatible with an exudative effusion. Burgher Lw (4) found that all effusions with septation, complex non septation, or homogeneous echogenicity at sonography were exudative. Anechoic effusions, however, could be either transudative or exudative. The sensitivity of sonography in their study was 66%, with a specificity of study was 66%, with a specificity of 100% and a positive predictive value of 100%

Ultrasound allows the detection of small amounts of pleural locular fluid, with positive identification of amounts as small as 3 to 5 ml, that cannot be identified by x-rays, which is only capable of detecting volumes above 50 ml of liquid. Contrary to the radiological method, ultrasound allows an easy differentiation of pleural locular liquid and thickened pleura. And it`s efficient in pinpointing thoracocentesis, even in small fluid collections.

The ultrasound image of pleural effusion is characterized by an echo-free space between the visceral and parietal pleura. Ultrasound can also be used to enable percutaneous diagnostic or therapeutic drainage (thoracocentesis).

CT scanning is excellent for detecting small amounts of fluid and is also often able to identify the underlying intrathroacic causes (e.g malignant pleural deposits or primary lung neoplasm) or as well as subdiaphragmatic diseases (e.g.subdiaphragmatic abscess) In addition CT can also help to distinguish between a pleural effusion and pleural empyema. In our study, parietal pleural thickening was shown at contrast-enhanced CT in 59% of exudates, and this finding had a specificity of 88% and a positive predictive value of 97%. Bartter T (1) have reported that CT shows pleural thickening and enhancement in almost all patients with empyema or parapneumonic effusion.In their study, 24 of 25 empyemas demonstrated pleural thickening and enhancement at CT; however, some patients underwent thoracostomy tube insertion before undergoing CT.

In our study, CT was sensitive in detecting pleural thickening in empyema; 4 of 6 empyemas showed pleural thickening. Conversely, pleural thickening was seen in 56% of the uninfected exudative (culture-negative) parapneumonic effusions. Included in this group with pleural thickening, however, are all of the complicated parapneumonic effusions (n = 5), which were treated with chest-tube drainage. 20% percent of parapneumonic effusions were transudates and did not show pleural thickening. Pleural thickening was less frequent when associated with malignancy, and if these cases are excluded, the sensitivity of parietal pleural thickening in diagnosing an exudate increases to 69%. Of 24 effusions in patients with neoplasm, 4 (16%) were transudates and were not associated with pleural thickening; none of these were malignant effusions.

Thickening and increased attenuation of extrapleural fat is another finding that is suggestive of pleural inflammation or infection and has been reported in patients with empyema, malignancy, and asbestos expo sure (1,4). A pior study (4) has demonstrated increased attenuation of extrapleural fat in a larger percentage of empyemas than was seen in our study. Bartter T (1) found an increase in attenuation of Extrapleural fat thickening was also common in those patients with pleural thickening associated with parapneumonic effusions. Increased attenuation of extrapleural fat, presumably representing edema or inflammation, was present in 10 patients with fat thickening; eight had empyema or parapneumonic effusion. This finding may indicate inflammation in the absence of thickening or could reflect a volume-averaging phenomenon. CT can play an important role in the diagnosis of exudative and transudative effusions. Pleural thickening associated with a pleural effusion in a patient with pneumonia indicates the presence of an exudate, and thoracocentesis is warranted. In patients with malignancy, the presence of pleural thickening indicates the presence of an exudate; the absence of parietal pleural thickening does not exclude the presence of an exudate or malignant effusion, and thoracentesis should be performed for diagnosis. The degree of pleural thickening is not helpful for predicting the diagnosis, although the presence of extrapleural fat thickening is suggesive of an empyema or a parapneumonic effusion. Irregular pleural thickening is suggestive of a neoplasm. The mean CT attenuation values in our study were almost identical for both types of effusion. We found a considerable overlap in values with the majority of effusions in the 0-13 HU range (64%). Before this study, we expected to see increased attenuation in exudates because exudative fluid usually contains high levels of protein, LDH, and bilirubin, which all potentially can show increased attenuation on a CT scan. Only one clinical study has been published on the characterization of pleural effusions using CT attenuation. Burgher Lw. (4) Examined 145 patients and found that the mean attenuation of exudates was 17.1 HU compared with a mean attenuation of 12.5 HU for transudates. The authors concluded that the overall accuracy of CT attenuation was moderate, with an optimal threshold value of 13.4 HU that showed a specificity of 71% and sensitivity of 83% for differentiating transudates from exudates. In our study, mean attenuation of exudates was 7.2 HU compared with 10.1 HU for transudates, and the overall accuracy for identifying exudates was

low (A z = 0.582). Thus, CT attenuation value was found to be a poor indicator for characterizing an effusion. Grogan DR. (3) found that the elevated pleural cholesterol in exudates is the result of the underlying disease (e.g., malignancy, pneumonia, or tuberculosis) rather than a reflection of the serum cholesterol level. A possible explanation for the elevated pleural cholesterol may be greater cellular degeneration or in- creased pleural permeability in exudates compared with transudates (3). Elevated cholesterol levels can also result from chylothorax, mainly due to trauma or lymphoma, and from pseudochylothorax, mainly due to tuberculosis, rheumatoid arthritis, or empyema (4). Waite et al. (5) found pleural thickening in 27 of 65 patients with exudates and none among 20 patients with transudates (42% sensitivity, 100% specificity). Our study, on the other hand, found pleural thickening in 1 of the 9 transudates (11%) compared with 20 of 34 exudates (59%). Loculation of the effusion was found in 24 of 211 patients in the study of Burgher Lw (4), all of them in patients with exudates. Our study, on the other hand, found loculated pleural effusion in 3 of the 9transudates (33%) compared with 19 of 34 exudates (56%). Both pleural thickening and loculation were found in more than one third of the patients with transudates in our study. This clearly contradicts the finding of the four relatively large studies mentioned (3,4). A possible explanation for this difference may be that all four studies were performed 10 years ago or more. The quality and resolution of the CT images in our study were probably higher than those of the previous studies, thus elevating the sensitivity of these finding but decreasing their specificity in the present study. Our study has several limitations. First, it is a retrospective study, and the thoracocentesis and CT were not performed at the same time in most of our patients. As mentioned, diuresis can alter pleural biochemistries (1, 2).Thus, some pleural fluids of patients with heart failure might have been misclassified as exudates. Moreover, treatment success or failure in patients with pneumonia might also influence biochemistries of pleural fluid or CT appearance. To minimize the effect of this limitation on our results, we limited the time interval between thoracocentesis and CT to 72 hours.All of the previous clinical series mentioned had a maximal interval between CT and thoracocentesis of from 7 to 20 day (1,2). Another limitation is that chest CT in our study was performed using two different scanning parameters and two different scanners. In addition, some patients received IV contrast material and others did not. Nevertheless, there were no noticeable differences in measurements by the two radiologists, and the analysis presented in the results suggested that IV contrast material did not affect the attenuation values. It should be emphasized that CT is more sensitive than both conventional chest radiography and sonography for differentiating pleural fluid from pleural thickening, assessing fluid loculation, identifying focal masses, and assessing lung infiltrates (4,6).

Conclusion:

Ultrasound is done to detect pleural effusion ,which sometimes cannot be detected by conventional radiography , but characterization of the pleural fluid cannot be done by ultrasound because CT attenuation with additional pleural CT appearance features such as fluid loculation, pleural thickness, and pleural nodules are helpful in differentiating exudates from transudates, because we found their prevalence is higher among exudative effusions .so ultrasound done to detect the effusion ,but characterization is by CT.

References:

*1. **Bartter T, Santarelli R, Akers SM, Pratter MR**. The evaluation of pleural effusion. Chest 2004; 106:1209-1214.*

*2. **Broaddus VC, Light RW.** What is the origin of pleural transudates and exudates? (editorial) Chest 1992; 102:658-659.*

*3. **Grogan DR, Irwin RS, Channick R, et al**. Complications associated with thoracocentesis: a prospective, randomized study comparing three different methods. Arch Intern Med 1990; 150:873-877.*

*4. **Sokolowski JW, Burgher LW, Jones FL, Patterson JR, Selecky PA**. Guidelines for thoracocentesis and needle biopsy of the pleura. Am Rev Respir Dis 2000; 140:257-258.*

*5. **Leung , A.N.,Muller,R.R** CTin differential diagnosis of diffuse pleural disease. American Journal of Roentgenology, (2011) .154 487 – 492 .*

*6. **Henschke , C.T.. Davis ,S.D., Romano .p.M, Yankctvit / D .F** the pathogenesis .radiological evatuation and therapy of pleural effusions . Radiologie Clinics of north Anne riea , (2011), 27, 241 – 1255.*