

## Etiologies of Pleural Effusion in Assiut University Hospital: One Year Study

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### Abstract

**Background:** Etiological diagnosis of exudative pleural effusion is sometimes difficult despite cytological, biochemical and microbiological tests.

**Aim of Study:** Was to make an etiological diagnosis of exudative pleural effusion by pleural biopsy, thoracoscopy and PCR of pleural fluid.

**Patients and Methods:** This prospective study was performed from September 2015 to August 2016 in Chest Department, Assiut University Hospital A total of 50 patients with exudative pleural effusion in whom the diagnosis was uncertain after routine biochemical, cytological and microbiological evaluation of pleural fluid were included in the study. These patients underwent pleural biopsy by Abram's needle and histopathology was done to determine the etiology of pleural effusion. Also thoracoscopy was done to undiagnosed pleural effusion, and PCR of pleural effusion was done.

**Results:** Out of 50 patients, most (28,56%) were male. Majority was malignant pleural effusion (18,36%). Pleural fluid was straw color in 15 (100%) cases of tuberculous effusion and hemorrhagic in 11 (61.1%) cases of malignant effusion. Pleural biopsy diagnosed 14 (77.8%) cases of malignant effusion and 10 (66.7%) cases of tuberculous effusion, PCR of pleural fluid diagnosed 14 (93.3%) cases of tuberculous effusion.

**Conclusions:** Pleural biopsy was diagnostic in the patients with exudative pleural effusion. PCR of pleural fluid was diagnostic in Tuberculous effusion.

**Key Words:** Pleural biopsy– PCR Polymerase Chain Reaction.

### Introduction

THE pleural space is bordered by the parietal and visceral pleurae. The pleural space plays an important role in respiration by coupling the movement of the chest wall with that of the lungs in 2 ways. First, a relative vacuum in the space keeps the visceral and parietal pleurae in close proximity. Second, the small volume of pleural fluid, which

has been calculated at 0.13 mL/kg of body weight under normal circumstances, serves as a lubricant to facilitate movement of the pleural surfaces against each other in the course of respirations [1].

Although pleural effusion is a common disorder among patients presenting with respiratory symptoms, there is limited evidence on the accuracy and reliability of symptoms and signs for the diagnosis of pleural effusion [2].

The pleural effusion stands frequently in the faces of physicians as a diagnostic problem that has to be solved. Pleural effusion does not form a disease entity by itself, but is usually a presentation of many diseases. Pleural effusion is an important and common clinical finding. In some diseases, it represents the initial or the only symptom and its presence can alter the prognosis and the treatment of disease [3].

When pleural effusion is accompanied by obvious disease process in the lung or other organs, the etiology becomes readily apparent. However, the investigations and the traditional laboratory methods may sometimes fail to detect the underlying cause of effusion in good percent of cases. So bacteriological and cytological studies of pleural fluid combined with pleural needle biopsy are very important for etiological diagnosis [4].

In our study to clarify the etiology of pleural effusion by bacteriological and cytological examinations of pleural fluid as well as that pleural needle biopsy and PCR of pleural fluid. Thoracoscopy was performed in some cases not diagnosed by previous procedures.

**Aim of the study:**

Study of etiology of pleural effusion in Assiut University Hospital Chest Department in one year.

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## Patients and Methods

This study was designed as a case series study in a prospective manner. Patients with non-diagnosed exudative pleural effusion admitted to Chest Department, Assiut University Hospital during the period between September 2015 to August 2016.

The study design was approved by the Scientific Ethics Committee of Faculty of Medicine of Assiut University. After meeting inclusion criteria, informed consent is obtained from the patient.

All patients were subjected to the following:

- A Full history taken.
- Clinical examination was done show sign of pleural effusion: Dullness to percussion, decreased or absent tactile fremitus, decreased breath sounds, and no voice transmission.
- Plain Chest X-rays postero-anterior view and lateral view.
- Chest ultrasound confirming pleural effusion.
- Pleural fluid aspiration for biochemical, cytological and bacteriological examination.
- Blood sample to estimate serum albumin.
- Pleural biopsy.
- Thoracoscopy.
- Pleura fluid PCR.

## Results

50 patients with pleural effusion, malignant pleural effusion is most common cause about 18 patients (36%), then post-pneumoic effusion was second cause about 17 patients (34 %), then tuberculous pleural effusion was the third cause about 15 patients (30%) as show in Table (1).

Table (1): Different diagnosis of pleural effusion.

Diagnosis	No. (n=50)	%
Malignant effusion	18	36.0
Post pneumonic effusion	17	34.0
Tuberculous effusion	15	30.0

In post pneumonic effusion 7 cases (41.2%) age between 40-60 years with mean age  $\pm$  SD was  $50 \pm 15.85$  ( $p$ -value 0.175), in malignant pleural effusion 9 cases (50 %) age above 60 years with mean age  $\pm$  SD was  $58.61 \pm 13.91$  ( $p$ -value 0.036),

and Tuberculous effusion 9 cases (60%) age below 40 years ( $p$ -value 0.003) and mean age  $\pm$  SD was  $37.13 \pm 17.35$  ( $p$ -value 0.001).

In post pneumonic effusion male about 15 cases (88.2%), in malignant pleural effusion male about 10 cases (55.6%) but in tuberculous effusion were female 12 cases (80%) as demonstrated in Table (2).

The clinical features of different etiology of pleural effusion. In caes of malignant pleural effusion dyspnea is common presenting symptom about 16 (88.9%) cases then dull aching chest pain 13 (72.2%) cases, in tuberculous pleural effusion, post pneumonic effusion pleuritic chest pain about 15 (100%), 17 (100%) respectively, then dry cough 13 (86.6%) in tuberculous pleural effusion as in Table (3).

Malignant effusion presented by massive effusion in chest X-ray 16 cases (88.9%), while Tuberculous effusion presented by moderate effusion in chest X-ray in 9 cases (60%),  $p$ -value (0.003) as in Table (4).

Chest ultra-sound in malignant effusion showed homogenous effusion in 10 cases (55.6%) and pleural nodules 11 cases (61.1%) but in tuberculous effusion chest ultra-sound show complex separted 10 cases (66.7%) and consolidation in 12 cases (70%) in post pneumonic effusion as show in Table (5).

Colour of pleural effusion in tuberculous effusion straw in 15 cases (100%), purulent 12 cases (70%) in post pneumonic effusion and haemorrhagic in 11cases (61.1%) of malignant effusion as show in Table (6).

In Tuberculous effusion lymphocytes was common in 14 cases (93.3%) but in Malignant effusion lymphocytes present in 6 cases (33.3%) as in Table (7).

Sensitivity of closed pleural biopsy in diagnosis of tuberculous effusion 66.7%, specificity 100%. Moreover positive predictive value and negative predictive value was 100% and 87.5% respectively, but sensitivity of PCR in diagnosis of tuberculous effusion 93.3% and specificity 100%. Moreover positive predictive value and negative predictive value was 100% and 97.2% respectively as seen in Table (8).

Sensitivity of pleural fuild cytology in diagnosis of malignant effusion was 44.4% and specificity

about 100%, Moreover positive predictive value and negative predictive value was 100% and 76.1% respectively.

Sensitivity of closed needle pleural biopsy in diagnosis of malignant effusion was 77.8% and specificity about 100%, Moreover positive predic-

tive value and negative predictive value was 100% and 88.9% respectively as in Table (9).

Closed needle pleural biopsy diagnosed 14 of 18 cases malignant effusion (77.8%) While, there was four cases (22.2%) diagnosed by pleural thoracoscopy (Table 10).

Table (2): Age and sex distribution in relation to etiology of pleural effusion.

	Post-pneumonic effusion		Malignant effusion		Tuberculous effusion		<i>p</i> -value <sup>1</sup>	<i>p</i> -value <sup>2</sup>	<i>p</i> -value <sup>3</sup>
	No.	%	No.	%	No.	%			
<i>Age: (years)</i>									
<40	4	23.5	2	11.1	9	60.0	0.402	0.036*	0.003*
40-60	7	41.2	7	38.9	4	26.7	0.890	0.388	0.458
>60	6	35.3	9	50.0	2	13.3	0.380	0.229	0.026*
Mean age ± SD	50±15.85		58.61±13.91		37.13±17.35		0.175	0.036*	0.001*
<i>Sex:</i>									
Male	15	88.2	10	55.6	3	20.0	0.060	0.000*	0.037*
Female	2	11.8	8	44.4	12	80.0			

Table (3): Clinical features among 50 patients of pleural effusion.

	Post-pneumonic effusion		Malignant effusion		Tuberculous effusion		<i>p</i> -value <sup>1</sup>	<i>p</i> -value <sup>2</sup>	<i>p</i> -value <sup>3</sup>
	No.	%	No.	%	No.	%			
<i>Cough:</i>									
No cough	0	0.0	9	50.0	0	0.0	0.001*		0.001*
Dry	5	29.4	9	50.0	13	86.7	0.214	0.001*	0.026*
Productive	12	70.6	0	0.0	2	13.3	0.000*	0.001*	0.199
<i>Dyspnea:</i>									
Yes	7	41.2	16	88.9	6	40.0	0.003*	0.946	0.003*
No	10	58.8	2	11.1	9	60.0			
<i>Chest pain:</i>									
No	0	0.0	2	11.1	0	0.0	0.486	—	0.489
Pleuritic	17	100.0	3	16.7	15	100.0	0.000*	—	0.000*
Dullaching	0	0.0	13	72.2	0	0.0	0.000*	—	0.000*

Table (4): Comparison between Malignant and Tuberculous pleural effusion as regard chest X-ray findings.

	Malignant pleural effusion		Tuberculous pleural effusion		<i>p</i> -value <sup>1</sup>	<i>p</i> -value <sup>2</sup>
	No.	%	No.	%		
<i>Opacity:</i>						
All hemothorax	16	88.9	3	20.0	0.691	0.000*
Mid & lower	2	11.1	9	60.0	0.162	0.003*
Lower	0	0.0	3	20.0	0.691	0.083

Table (5): Chest ultra-sound findings of different diagnosis of pleural effusion.

	Post-pneumonic effusion		Malignant effusion		Tuberculous effusion		<i>p</i> -value <sup>1</sup>	<i>p</i> -value <sup>2</sup>	<i>p</i> -value <sup>3</sup>
	No.	%	No.	%	No.	%			
<i>Chest ultrasonography:</i>									
Anechoic	4	23.5	4	22.2	1	6.7	0.927	0.338	0.346
Homogeneous echogenic	11	64.7	10	55.6	1	6.7	0.581	0.001*	0.000*
Complex non-sepated	2	11.8	3	16.7	3	20.0	0.679	0.645	0.805
Complex sepated	0	0.0	1	5.6	10	66.7	0.324	0.000*	0.000*
<i>Others:</i>									
Consolidation	12	70.6	0	0.0	0	0.0	0.000*	0.000*	0.000*
Pleural nodules	0	0.0	11	61.1	0	0.0	0.000*		0.000*
Pleural thickening	0	0.0	4	22.2	0	0.0	0.104		0.108
No	5	29.4	3	16.7	15	100.0	0.443	0.000*	0.000*

Table (6): Colour of pleural fluid among 50 patients.

	Post-pneumonic effusion		Malignant pleural effusion		Tuberculous pleural effusion		P-value <sup>1</sup>	P-value <sup>2</sup>	P-value <sup>3</sup>
	No.	%	No.	%	No.	%			
<i>Pleural fluid color:</i>									
Straw	2	11.8	6	33.3	15	100.0	0.228	0.000*	0.000*
Purulent	12	70.6	0	0.0	0	0.0	0.000*		
Serosanguinous	3	17.6	1	5.6	0	0.0	0.338	0.000*	0.354
Hemorrhagic	0	0.0	11	61.1	0	0.0	0.000*	0.229	0.000*

Table (7): Pleural fluid cytology according different etiology of pleural effusion.

	Malignant effusion		Tuberculous effusion		Post-pneumonic effusion	
	No.	%	No.	%	No.	%
Lymphocyte	6	33.3	14	93.3	0.0	0.0
Polymorphs	0	0.0	0	0.0	13	76.5
Pus	0	0.0	0	0.0	15	88.2
Reactive mesothelial cell	4	22.2	1	6.7	0	0.0
Atypical mesothelial cell	4	22.2	0	0.0	0	0.0
Metastatic adenocarcinoma	8	44.4	0	0.0	0	0.0

Table (8): Comparison between Closed needle pleural biopsy and PCR of pleural fluid in diagnosis of tuberculous pleural effusion.

	Closed needle pleural biops	PCR of pleural fluid
Sensitivity	66.7%	93.3%
Specificity	100%	100%
PPV	100%	100%
NPV	87.5%	97.2%

Table (9): Comparison between pleural fluid cytology and closed needle pleural biopsy in diagnosis of malignant pleural effusion.

	Pleural fluid cytology	Closed needle pleural biopsy
Sensitivity	44.4%	77.8%
Specificity	100%	100%
PPV	100%	100%
NPV	76.1%	88.9%

Table (10): Sensitivity, Specificity of closed needle pleural biopsy in diagnosis of malignant pleural effusion.

No.	Disease present				Disease absent				PPV	NPV
	True positive (Sensitivity)		False negative		False positive		Trueneegative (Specificity)			
	No.	%	No.	%	No.	%	No.	%		
50	14	77.8	4	22.2	-	-	32	100.0	100.0	88.9

**Discussion**

This study included 50 patients with pleural effusion, malignant pleural effusion is most common cause about 18 patients (36%), then post-pneumonic effusion was second cause about 17 patients (34%), then tuberculous pleural effusion was the third cause about 15 patients (30%).

In this study, malignant pleural effusion was diagnosed in 18 patients, the age and sex distribution among those patients show that malignant pleural effusion was frequent in males 10 (55.6%) than female 8 (44.4%). The mean age of malignant group was 58.61 ± 13.91. These result of age and

sex distribution were in agreement those obtained by Khald et al., [5].

Tuberculous pleural effusion was diagnosed in 15 patients (30%) in this study. Female were 12 (80%) and males were 3 (20%) disagreed with Porcel [6] as tuberculous pleural predominates in men, with an overall male-to-female ratio of 2:1. As regard, the mean age of tuberculous group was 37.13 ± 17.35. This was agreed with Porcel [6] as tuberculous pleural affects mainly younger adults (mean age=34 years). The difference in the age between the malignant and tuberculous pleural effusion was highly significant.

Das [7], the mean and median age of malignant (54 years) higher than that of tuberculous/granulomatous lesion patients (34 and 33 years, respectively). So tuberculous effusion was mostly a disease of those aged <40 years, malignant effusion was a commonly found in the  $\geq 50$  years age group.

Liam et al., [8]. Observed that the median age of patients with malignant effusions (68.5 years) was significantly higher than that of patients with tuberculous effusions (34.5 years,  $p < 0.001$ ), and a higher percentage of patients with malignant pleural effusion (44%) presented with large effusions than patients with tuberculous effusion (12%,  $p = 0.001$ ).

Antonangelo et al., [9]. Observed a significant difference in the age between tuberculosis ( $38.7 \pm 13.6$ ) and cancer ( $58.5 \pm 14.5$ ) in pleural effusion ( $p < 0.001$ ), and sex distribution between tuberculosis (Male: Female=132: 50) versus cancer (Male: Female=49: 95) was also significant ( $p < 0.001$ ).

Malignant pleural effusion the most common presenting symptom is dyspnea in 16 case (88.9%), dull aching chest pain in 13 case (72%) and dry cough in 9 cases (50%). This agreed with Antony et al., 2001 as dyspnea is most common presenting symptom due to massive pleural effusion but not only cause of dyspnea, it also due to several factors may be involved, including a decrease in the compliance of the chest wall, contralateral shifting of the mediastinum, a decrease in the ipsilateral lung volume, and reflex stimulation from the lungs and chest wall, Antony et al., [10].

Tuberculous pleural effusion the most presenting symptom was chest pain (pleuritic in nature) in 15 (100%), then dry cough in 13 (86.7%) cases, and fever in 15 (100%) cases. That result agreed with Gopi et al., [11], as the most common presenting symptoms are pleuritic chest pain (75%) and non productive cough (70%). And agreed with Porcel [6], as Tuberculous pleural effusion most commonly manifests as an acute or subacute illness causing fever, cough, and pleuritic chest pain in more than 70% of patients.

Chest X-ray in cases of malignant pleural effusion is massive in 16 cases (88.9%) that is agreed with Porcel and Light [12] but in case of tuberculous pleural effusion is moderate 9 (60%) of cases that agreed with Gopi et al., [11], TB pleural effusions, typically unilateral and small to moderate in size, usually occupy less than two thirds of a hemithorax.

As regard chest ultrasound of pleural effusion, tuberculous pleural effusion was showed complex

separated in 10 cases (66.7%), complex non separated 3 cases (20%) disagreed with Chen et al., [13] as tuberculous pleural effusion 41% was complex non separated, a complex septated pattern in 47% but malignant pleural effusion was showed homogenous pleural effusion 10 cases (55.6%) disagreed with Chen et al., [13] as a complex non septated pattern in 85%, an anechoic pattern in 11%, and a complex septated pattern in 4%, homogenous echogenic in 11 cases (64.7%) of post-pneumonic effusion. Also noted in chest ultrasound, pleural nodules is present in 11 cases (61.1%) patients with malignant pleural effusion, and pleural thickening about 4 patients (22.2%). Disagreed with Qureshi et al., [14], The presence of nodular pleural thickening was observed in (42%) with malignant effusions, Parietal pleural thickening was detected in 21 patients, measuring >1cm in (42%) patients with a malignant effusion.

Inspection of the the pleural fluid showed that the colour of the pleural fluid in patients with tuberculous pleural effusion was predominantly straw coloured 15 (100%), that result were agreed Gopi et al., [11]. A tuberculous pleural effusion is typically clear and straw colored; however, it can be turbid or serosanguinous but is virtually never grossly bloody.

In patients proved to be malignant pleural effusion, the fluid was haemorrhagic in 11 cases (61.1%), that agreed with Porcel and Light [12] and straw colour in 6 cases (33.3%) and serosanguinous in 1 cases (5.6%). Although blood tinged fluid itself has no diagnostic importance, haemorrhagic fluid with RBC's count of more than 100,000/mm<sup>3</sup> are highly suggestive of malignancy, infarction or trauma.

In our study, among 15 patients with tuberculous pleural effusion, pleural needle biopsy achieve diagnosis of tuberculous pleurisy (tuberculous granuloma) in 66.7%. This result agreed with Gopi et al., [11] as pleural biopsy reveals granulomas in 50 to 97% of patients. Disagreed with Porcel [6] as Closed pleural biopsy performed by experienced physicians demonstrates granulomas, with or without caseous necrosis, in approximately 80% of the cases. However, its diagnostic yield rises to 90% if the pleural tissue is sent for culture.

The closed pleural needle biopsy sensitivity and specificity in diagnosis of tuberculous pleural effusion was 66.7% and 100% respectively. Moreover, the positive predictive value and negative predictive value was 100% and 87.5% respectively.

As regard PCR of pleural effusion in diagnosis of tuberculous pleural effusion. Sensitivity and specificity about 93.3% and 100% respectively, the positive predictive value and negative predictive value was 100% and 97.2% respectively in our study. that result agreed with Gopi et al., [11], as the efficacy of PCR for diagnosis of pleural tuberculosis, a sensitivity ranging from 20 to 90% and specificity from 78 to 100%.

As regard, Pleural fluid cytology, Lymphocytes was common in tuberculous effusion in 14 cases (93.3%) and malignant effusion 6 cases (33.3%), similar findings have been reported by Spieler [15] and Esmat et al., [16]. The predominance of lymphocyte in tuberculous and malignant effusion probably reflects the role of T. Lymphocytes in cellular immune reaction against mycobacterium tuberculous and neoplasia [17].

Pleural fluid for cytology was proved malignant pleural effusion in 8 (44.4%) patients, so sensitivity and specificity of pleural fluid cytology about 44.4% and 100% respectively, positive predictive value and negative predictive value was 100% and 76.1% respectively. That result agreed Johnson, [18] as pleural cytology 33% for diagnosis of malignancy, Bueno et al., [4]. Ong et al., [19] concluded that examination of pleural fluid for malignant cells may leads to the diagnosis in 40% to 90% of malignant effusion.

And Villena, et al., [20] Pleural fluid cytology is among the tools offering the highest yield for diagnosing malignancy. The sensitivity of this test ranges from 40% to 87% depending mainly on the cytologist's training, the extent of pleural involvement, and tumor type (yield is higher in adenocarcinoma).

That disagreed with Porcel [6] and Hooper et al., 2010, as Cytology is positive in approximately 60 percent of malignant pleural effusions.

The closed pleural needle biopsy proved malignant pleural effusion 14 patients of 18 (77.8%), this result agreed with Antony et al., [10], as pleural biopsy a diagnostic in 45-75% for malignant pleural effusion. But disagreed with Hooper et al., [21] as pleural biopsy is diagnostic in 57% for malignancy. So sensitivity and specificity of pleural needle biopsy was 77.8% and 100% respectively and positive predictive value and negative predictive value was 100% and 88.9% respectively.

Thoracoscopy was used in diagnosed 4 cases (22.2.%) of malignant pleural effusion when those

cases was negative with the pleural needle biopsy and malignancy was suspected. But thoracoscopy not routinely used in all cases of pleural effusion as it invasive technique.

#### Conclusion:

- 1- Common etiology of pleural effusion was malignancy in Assuit University, Chest Department.
- 2- Pleural needle biopsy has diagnostic information for different etiology of pleural effusion.
- 3- PCR has diagnostic role of tuberculous pleural effusion.

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## أسباب الأنسكاب البللوري في مستشفى أسيوط الجامعي خلال سنة

المقدمة: الأنسكاب البللوري يعد أحد المشاكل الطبية التي تمثل تحدياً صعباً في الوصول إلى تشخيص صحيح للمرض المسبب للأنسكاب البللوري، وفي ظل وجود كثيراً من الأمراض المسببة للأنسكاب البللوري حيث يوجد العديد من الوسائل التي تساعد على المرض المسبب له، لذلك جاء هدف الرسالة معرفة الأسباب المختلفة للأنسكاب البللوري وذلك في دراسة عملية بداخل أروقة مستشفى جامعة أسيوط قسم أمراض الصدر خلال الفترة من سبتمبر ٢٠١٥ حتى أغسطس ٢٠١٦.

المرضى والطرق: تم فحص ٥٠ مريض مصاب بالأنسكاب البللوري، وقد تم أخذ التاريخ المرضي وإجراء الفحص الطبي الكامل لهؤلاء المرضى مع عمل الفحوصات الطبية المناسبة مثل استخدام الأشعة السينية وأشعة الموجات فوق الصوتية على الصدر.

وقد تم أخذ عينة من السائل البللوري وتحليلها من الناحية السيتوباثولوجية من كل المرضى الذين أشتملت عليهم الدراسة وأخذ عينة من الغشاء البللوري باستخدام إبرة كوب من بعض المرضى.

وفي بعض الحالات التي لم تتمكن من الوصول إلى التشخيص على الرغم من استخدام كل لفحوصات السابقة تم اللجوء إلى منظار بللوري.

الأستنتاجات: خلال هذه الدراسة مان عدد المصابين بالأنسكاب البللوري السرطاني ١٨ حالة وكذلك عدد المصابين بالأنسكاب البللوري الناتج عن ألتهابات رئوية عدد ١٧ حالة، بالإضافة إلى عدد المصابين بالأنسكاب البللوري الناتج عن ألتهاب الدرن بالبللورا عدد ١٥ حالة، لذلك كان الأنسكاب البللوري السرطاني من أهم الأسباب المسببة للأنسكاب البللوري في قسم أمراض الصدر في جامعة أسيوط خلال عام.

وكذلك أخذ عينة من الغشاء البللوري يساعد في تشخيص الأسباب المسببة للأنسكاب البللوري.

وكذلك فحص السائل البللوري بـ PCR يساعد في الأنسكاب البللوري الناتج عن الألتهاب الدرني بالغشاء البللوري بالرئة.