

The diagnostic role of medical thoracoscopy in unexplained exudative pleural effusions: a single-center experience with 25 patients

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Резюме

Pleural effusion is an abnormal accumulation of fluid between the two pleurae. The approach to pleural effusions depends on the clinical picture and initial pleural fluid aspiration sample. Occasionally, pleural fluid analysis fails to establish a definitive diagnosis. **The aim** of the study to evaluate the value of medical thoracoscopy in cases of unexplained exudative pleural effusions. **Methods.** This cross-sectional study was conducted at the respiratory unit of Al Dowaly Private Hospital, Baghdad, Iraq, over a period of 9 months. Twenty-five patients with unexplained exudative pleural effusions, after non-diagnostic pleural fluid analysis, were included. Patients with hemodynamic instability, coagulopathy, serological or PCR evidence of current COVID-19 infection, or a previously established diagnosis of pleural effusion were excluded. **Results.** Medical thoracoscopy provided a definitive diagnosis in 19 out of 25 (76%) patients. Among these, malignancy was identified in 64% of cases, while tuberculosis accounted for the remaining diagnoses. **Conclusion.** Medical thoracoscopy is an important tool in diagnosis with high yield and minimal complications. It is recommended for patients with undiagnosed exudative pleural effusions following inconclusive initial work-up.

Key words: pleuroscopy, medical thoracoscopy, exudative, pleural effusion.

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Диагностическая роль торакоскопии при необъяснимом экссудативном плевральном выпоте: опыт одного центра с участием 25 пациентов

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Abstract

Плевральный выпот — это аномальное скопление жидкости между двумя плевральными оболочками. Подход к лечению плеврального выпота зависит от клинической картины и исходного образца аспирационной жидкости плевральной полости. Иногда анализ плевральной жидкости не позволяет установить окончательный диагноз. **Целью** исследования явилась оценка эффективности торакоскопии в случаях необъяснимого экссудативного плеврального выпота. **Материалы и методы.** Данное поперечное исследование проводилось в респираторном отделении частной больницы Аль-Довали (Багдад, Ирак) в течение 9 мес. В исследование были включены 25 пациентов, у которых был выявлен необъяснимый экссудативный плевральный выпот, при этом анализ плевральной жидкости оказался неинформативным. Из исследования были исключены пациенты, у которых наблюдались гемодинамическая нестабильность, коагулопатия, а также положительная реакция по результатам анализа крови или полимеразной цепной реакции на текущую инфекцию COVID-19 или ранее был установлен диагноз плевральный выпот. **Результаты.** По результатам торакоскопии окончательный диагноз установлен у 19 (76 %) из 25 пациентов. В 64 % случаев выявлены злокачественные новообразования, в остальных случаях — туберкулез. **Заключение.** Торакоскопия является важным высокоэффективным диагностическим инструментом с минимальными осложнениями. Торакоскопия рекомендуется пациентам с недиагностированным экссудативным плевральным выпотом и неубедительными результатами первоначального обследования.

Ключевые слова: плевроскопия, торакоскопия, экссудативный, плевральный выпот.

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Pleural effusion is defined as accumulation of fluid in the pleural space and usually indicates an underlying pathology. It usually result from imbalance of fluid formation and removal [1].

The diagnosis of the pleural effusion rests mainly on the likelihood of a particular disease the patient presented with. The four major causes of pleural effusions are congestive heart failure (CHF), malignancies, pneumonia, and pulmonary thromboembolism [2].

CHF and liver cirrhosis usually cause almost all transudative pleural effusions, whereas the other diseases are the three main causes of exudative pleural effusions. Viral infection and post coronary artery bypass surgery also causes exudative effusions [3].

Separation of exudate from transudate pleural effusion.

Thoracentesis (aspiration) is the first diagnostic step in patients presented with pleural effusion of sufficient amount (usually more than 1 cm in lateral decubitus chest radiography, sonography or computed tomography). Aspiration is not usually done in bilateral pleural effusions of likely exudative effusion such as HF, unless in the presence of atypical features or when the patient fails to respond to therapy [3]. Exudate and transudate differentiation is important before further tests. The pleural fluid analysis profile includes protein, glucose, Ph, lactate dehydrogenase (LDH), albumin, adenosine deaminase levels, cell counts, cytological examination and bacterial staining / cultures with tuberculosis screen [4 – 6].

Light's criteria [7] (Table 1) are the most sensitive for identifying exudates, with 98% sensitivity but have lower specificity (74%) [8, 9].

Available options when no diagnosis obtained after initial thoracentesis. The available options when the diagnosis is unclear following pleural aspirate are: CT angiography is considered first, to rule out pulmonary embolism, pulmonary infiltrate, pleural masses and mediastinal lymphadenopathy [10]. Next available options include either observation, needle biopsy, bronchoscopy, thoracoscopy or thoracotomy with open biopsy.

Medical thoracoscopy (Pleuroscopy). Medical thoracoscopy is a minimally invasive procedure used primarily for diagnostic purposes but also for some therapeutic applications with the pleural effusion is the leading indication for its use [11].

Medical thoracoscopy uses and advantages:

- Biopsy can be taken from the lung, pleura, diaphragm and mediastinum and the possibility to scan for TB and malignancy;
- Staging in pulmonary malignancy and mesothelioma;
- It is considered a gold standard for scientific studies;
- Pleural fluid drainage;
- Evaluation of the pulmonary re-expansion potential;
- Pleurodesis using materials such as talc.

The aim of the study to explore the value of medical thoracoscopy for diagnosis of unexplained exudative pleural effusions.

Methods

This cross-sectional study was performed in respiratory unit of Al-Dowaly private hospital between January and October 2021. Twenty-five patients were enrolled in the current study All patients underwent primary tests, including pleural fluid analysis for glucose, lactate dehydrogenase, protein, white blood cells and differential and cytological study all of which were negative for a specific diagnosis.

Exclusion criteria:

- Patients who underwent procedures for therapeutic purposes, those with previous histologically diagnosed exudative pleural effusion;
- Patients with Hemodynamically instability;
- Patients with thrombocytopenia (less than 75,000/micro/L) or coagulopathy.
- Laboratory/clinical evidence of acute/recent COVID 19 illness.

Basic patient information and detailed medical and surgical histories were recorded

The Medical thoracoscopy team comprised one consultant in interventional pulmonology, one interventional pulmonary Iraqi board fellow, Anesthesia specialist and one or two persons from nursing staff to assist during the procedure. The instrument used was Olympus LTF-160 (description provided see Tables 2, 3).

Lateral decubitus position was used for all patients and the effusion side is facing up.

Oxygen saturation and cardiac monitoring and were continuously observed during the procedure. Nasal cannula oxygen supply was given throughout the procedure.

The procedure was done under conscious sedation using intravenous propofol. Anesthesia locally was done using lidocaine 10%.

1-cm incision was made at the mid-axillary line between the fourth and seventh intercostal space, but when the imaging indicates a lower pleural sac abnormality, the thoracoscopy may be inserted through lower site incision.

After careful inspection of the pleural sac, biopsies were taken from suspicious areas and kept in formalin tube for histopathological diagnosis and in normal saline tube for mycobacterial diagnosis

After completing the above-mentioned steps, a chest tube was inserted in the place of the thoracoscope insertion site. The procedure took about 45 minutes on average.

After that, chest x ray was taken for all patients to exclude pneumothorax which sometime can happen after the procedure. All patients were observed for at least 24 hours.

Table 1
Light's criteria for exudative pleural effusion [7]

Таблица 1
Критерии Лайта для диагностики экссудативного плеврального выпота [7]

Criteria	Result
Pleural fluid protein/Serum protein	> 0.5
Pleural fluid LDH/Serum LDH	> 0.6
Pleural fluid LDH	> 2/3 of the upper normal limit for serum LDH

Note: LDH, lactate dehydrogenase; an effusion will be classified as exudative if one or more of the above criteria are met. If none are met, it is considered a transudate.

Примечание: выпот классифицируется как экссудативный, если соответствует одному или нескольким перечисленным критериям. Если ни один из критериев не выполняется, выпот считается трансудатом.

Table 2
Causes of pleural effusion

Таблица 2
Причины плеврального выпота

Transudative pleural effusions	Collagen vascular diseases
Congestive heart failure	Rheumatoid pleuritis
Cirrhosis	Systemic lupus erythematosus
Nephrotic syndrome	
Superior vena caval obstruction	<i>Drug induced lupus</i>
Urinothorax	Sjogren syndrome
Peritoneal dialysis	Familiar mediterranean fevers
Glomerulonephritis	Churg – Strauss syndrome
Myxedema	Wegner's granulomatosis
Cerebrospinal fluid leaks to pleura	<i>Drug induced pleural diseases</i>
Hypoalbuminemia	Nitrofurantoin
Sarcoidosis	Dantrolene
Exudative pleural effusions	Methylsergide
<i>Neoplastic diseases</i>	Ergot drugs
Metastatic disease	Dasatinib
Mesothelioma	Amiodarone
Body cavity lymphoma	Interlukin 2
Pyothorax associated lymphoma	Procarbazine
<i>Infectious diseases</i>	Methotrexate
Bacterial infections	Clozapine
Fungal infections	<i>Miscellaneous diseases and conditions</i>
Parasitic infections	Asbestos exposure
Viral infections	Post lung transplant
<i>Pulmonary embolization</i>	Post bone marrow transplant
<i>Gastrointestinal diseases</i>	Yellow nail syndrome
Pancreatic disease	Sarcoidosis
Sub phrenic abscess	Uremia
Intrahepatic abscess	Trapped lung
Intrasplenic abscess	Therapeutic radiation exposure
Esophageal perforation	Drowning
Post abdominal surgery	Amyloidosis
Diaphragmatic hernia	Milk of calcium pleural effusion
Endoscopic variceal sclerosis	Electrical burns
Post liver transplant	Extra medullary hematopoiesis
<i>Heart diseases</i>	Rupture of mediastinal cyst
Post coronary artery bypass graft surgery	Acute respiratory distress syndrome
Post cardiac injury	Whipple procedure
Pericardial disease	Iatrogenic pleural effusion
Post Fontan procedure	<i>Hemothorax</i>
Pulmonary venous stenosis post catheter ablation of atrial fibrillation	<i>Chylothorax</i>
<i>Obstetric and gynecologic syndrome</i>	
Ovarian hyper stimulation syndrome	
Fetal pleural effusion	
Post-partum pleural effusion	
Meigs syndrome	

Table 3
Profile of the Pleuroscope used

Таблица 3
Характеристика используемого плевроскопа

Specification	Value
Model	LTF-160
Distal End Outer Diameter	7.0 mm
Insertion Tube Outer Diameter	7.0 mm
Field of View	120 °
Depth of Field	3 – 100 mm
Angulation Range	UP 160 ° / DOWN 130 °
Working Length	270 mm
Total Length	520 mm
Channel Inner Diameter	2.8 mm
High Frequency Compatibility	YES
Laser Compatibility	YAG, 810 nm diode

Typical drainage period was 2 days depending on lung re-expansion, air leak, and fluid drainage amount. The drain is removed before discharge, unless there is a persistent air leak.

Discharged was done with advice to re-visit out patient's clinic in the coming weeks for further follow-up.

The study received ethical approval from the Iraqi Board for Medical Specializations. Patients were first interviewed after providing verbal consent, followed by their written informed consent regarding the intervention, relevant information, and participation in the study.

Statistical analysis. After data collection, data analysis was done using statistical package for social sciences (SPSS) version 24.

Counts and percentages were described for the qualitative data, means and standard deviations for the quantitative data.

Results

Demographics

In all the 25 studied patients, primary pleural fluid analysis was inconclusive. Medical thoracoscopy was performed for all those patients for diagnostic purposes.

The current study was carried out 25 patients, 13 (52%) patients were female and 12 (48%) patients were male.

The mean age was 59.6 years with range between (14 to 85) years with years and standard deviation 16.49. Age range is shown in Figure 1.

Pleural fluid profile

The minimum amount of aspired pleural effusion from all studied cases was 300 ml and maximum amount was 4 000 ml with median 1 500 ml and inter quantile.

As regards the affected site 12 (48%) patients had left sided effusions, 10 (40%) patients had right side effusion and 3 (12%) patients had bilateral pleural effusion.

Regarding the involved layer of pleura, the parietal layer was involved in 15 (60%) patients, the both layers were

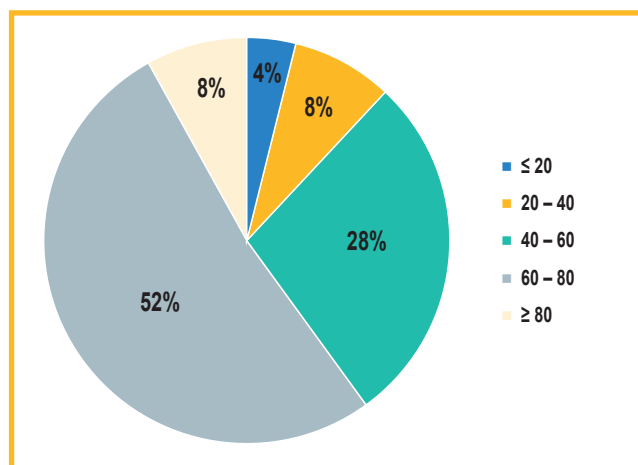


Figure 1. The distribution of the range of age of all studied cases
Рис. 1. Распределение обследованных пациентов по возрасту

involved in 9 (36%) patients and the visceral layer involved in 1 (4%) patient.

Finding of thoracoscopy are showing in Figure 2. The most common findings were random shape and size nodules in 11 (44%) patients.

Fluid character on aspiration is showing in Table 4. The most common color appearance is bloody 60%.

Table 4
Fluid character of all studied cases

Таблица 4
Характер плевральной жидкости у включенных в исследование пациентов

Pleural fluid color	Number	Percent, %
Bloody	15	60
Yellow	8	32
Dark yellow	2	8

The commonest final diagnosis of thoracoscopy was metastatic adenocarcinoma in 12 (48%) patients. Figure 3 shows the results.

The commonest minor complication was transient pleuritic type of chest pain (48%). Another reported complication is fever of short duration (32%). Less common complications were asymptomatic surgical emphysema (16%). No serious adverse events were recorded.

Discussion

Pleural effusions of exudative type like the malignant and tuberculous effusions, are usually associated with significant morbidity and mortality. Thoracoscopy, is also called pleuroscopy, remains the gold standard for providing diagnosis and treatment in such circumstances. We carried out this study to evaluate the diagnostic role of medical Thoracoscopy for the diagnosis of unknown source exudative pleural effusions.

In our study, the most common findings were random shape and size nodules in 11 (44%) patients, smooth pleura in 5 (20%) patients, hard and thick nodules in 5 (20%) patients, and small nodules in 3 (12%) patients. In a prospective study carried out by *K.A.Dar et al.* which included 125 patients, the common finding was multiple variable sizes nodules 53.6%, followed by sago grain infiltration in 15.2% [12]. In another study carried out by *L.Gong et al.*, the medical thoracoscopy showed that 66.7% of acute and chronic inflammation cases had pleural adhesions, nearly 70% of tuberculous pleuritis had severe pleural adhesions. Diffuse nodular changes found in all cases of malignant and tuberculous pleuritis and in 77.8% of acute and chronic inflammation cases [13].

Another study was carried by *K.M.Halima et al.* describe the diagnostic role of medical thoracoscopy in unexplained exudative pleural effusion of 6 years' experience at Al Hussein University Hospital in Egypt and 170 patients were en-

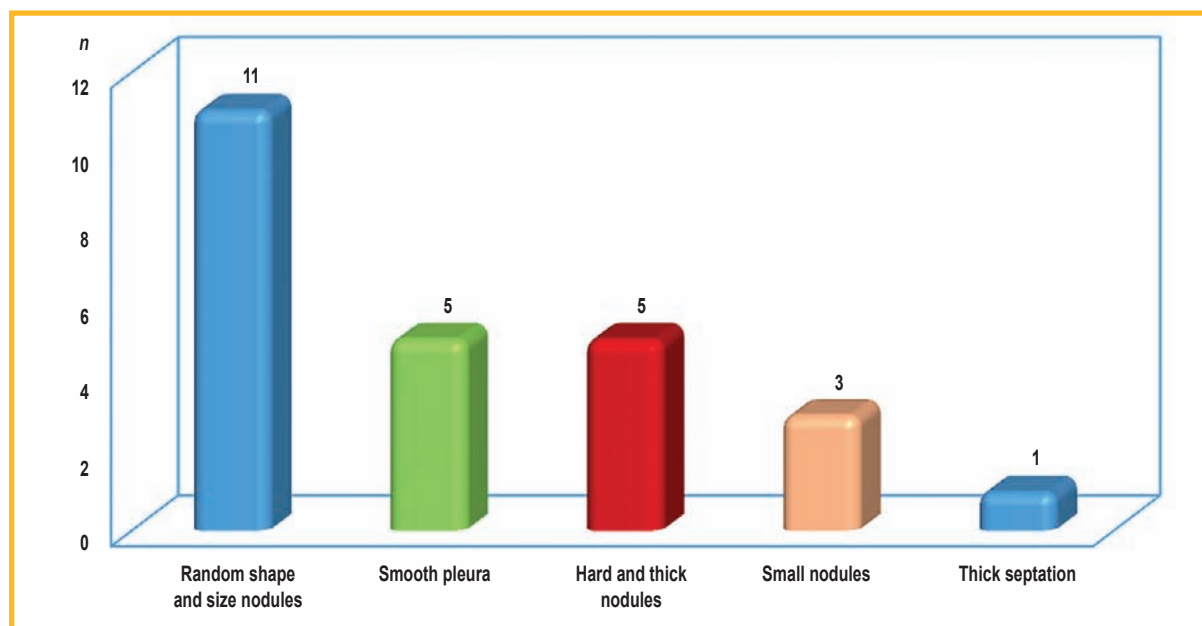


Figure 2. Distribution of findings of all studied cases

Рис. 2. Структура результатов обследования у включенных в исследование пациентов

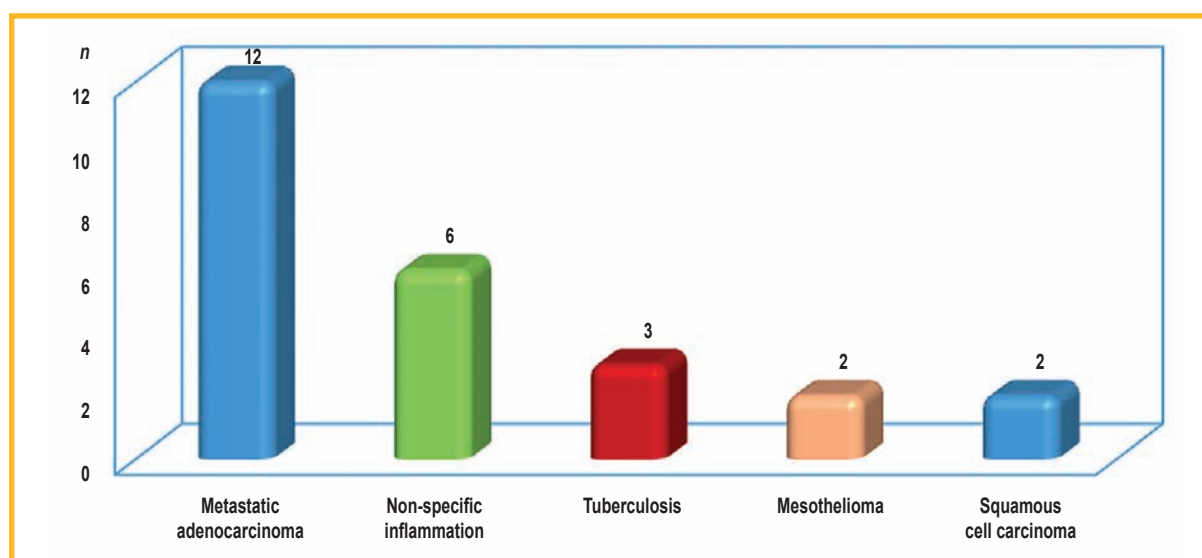


Figure 3. Distribution of diagnosis of all studied cases

Рис. 3. Структура диагнозов у включенных в исследование пациентов

rolled. Diffuse nodular changes were found in 109 (64.12%) patients [14].

In *B.A.Gao et al.* retrospective study of 215 patients; it was reported that pleuroscopic findings included pleural hyperemia, fibrinous adhesions and nodular bulges [15].

In our study, the most common aspirated pleural fluid was bloody tinged in appearance, followed by yellow and only 8% is dark yellow. In a study carried out by *V.Villena Garrido et al.* in Madrid, Spain, Serous and blood tinged were the most common presentations of pleural fluid at thoracentesis [16].

In our study, the final diagnosis of thoracoscopy was metastatic adenocarcinoma in 48% followed by non-specific inflammation (24%), tuberculosis (12%), mesothelioma (8%), and squamous cell carcinoma (8%).

In a study carried out by *V.K.Mootha et al.* in north India, medical thoracoscopy was diagnostic in 74.3%. Pleural malignancy was diagnosed in 48.6% of all patients. Nearly all cases of these malignant conditions were metastatic in origin [17].

Moreover, in *K.A.Dar et al.* study, Medical thoracoscopy was diagnostic in 90.4% of studied patients, pleural malignancy was the most common histopathological diagnosis (60.8%), of those; 50% were metastatic adenocarcinoma [12].

In a study carried out by *V.G.Prabhu and R.Narasimhan*, 68 patients went for thoracoscopy, malignancy was found in 24, TB in 16, nonspecific inflammation in 22 [18]. Empyema was found in 2 patients, 1 patient had sarcoidosis, 1 patient had normal pleura and it was non-diagnostic in 2 patients. The diagnostic yield of the thoracoscopy was 97% [18].

In a study carried out by *Y.B.Wu et al.* over 8 years (2005 – 2014), Medical thoracoscopy was done for 833 patients [19]. 342 patients had malignancy of which metastatic carcinoma and mesothelioma were the most common types. Immune histochemistry study showed that lung cancer was (85.2%), followed by breast cancer. In our study, we didn't order Immune histochemistry stain for the metastatic adenocarcinoma as the purpose of the study to

assess the diagnostic utility of medical thoracoscopy in differentiating the malignant from nonmalignant conditions among the unexplained exudative pleural effusion [19].

In another study carried out by *M.M.Ahmed et al.* in Egypt, which, fifty patients with unexplained pleural effusion were recruited [20]. Medical thoracoscopy yield a final diagnosis in 96%. Histopathologic biopsies shows that the most common diagnosis is malignancy (92%), followed by TB (2%), and nonspecific pleuritis (2%); no definitive diagnosis in 4%. Mesothelioma was found in (60%), while metastatic adenocarcinoma in (12%) [20].

Moreover, in a prospective study carried out by *C.B.Patil et al.* it was reported that the overall diagnostic yield of thoracoscopic pleural biopsy was (85.2%) in patients with unexplained exudative pleural effusion, and no diagnosis was made in (14.8%) of patient. Histopathological biopsy yielded malignancy in 66.4% patients, TB pleuritis in 28.2%, para-pneumonic effusion in 4 cases, followed by lupus pleuritis, multiple myeloma and pulmonary Langerhans histiocytosis one for each case [21].

R.Sodhi et al. describe their 2 years' experience of medical thoracoscopy. They found that pleural biopsy was diagnostic in 87.23%. Malignancy was diagnosed in 70.2% and tuberculosis in 10.6% [22].

Finally, the medical thoracoscopy is simple and relatively safe procedure. No serious adverse events were recorded among our studied cases and the most common minor complications were transient pleuritic pain (48%) followed by fever of short duration and asymptomatic surgical emphysema. In *Z.Wang et al.* study, their thoracoscopic procedure were carried out for tuberculous pleural effusion, the procedures were safe and no reported major adverse event apart from mild chest pain (43%) from the indwelling chest tube [23].

This study can be evaluated in light of its strengths and limitations. One strength of our study is that it's the second study in pulmonology subspecialty dealing with thoracoscopic pleural biopsy carried out by pulmonologist. A limitation of this study is the limitations of studied number of

patients, possibly due to low numbers of referred cases. Early referral of patients with unexplained pleural effusion to a pulmonologist to assess for need for thorascopic pleural biopsies is highly recommended. Early referral will make the procedure easy as the delay in doing thorascopic biopsies will make the procedure more difficult, possibly due to presence of adhesions, thickening or other complications of longstanding pleural effusion.

Conclusion

Medical thoracoscopy is considered a relatively safe procedure and has an excellent diagnostic yield in cases of undiagnosed exudative pleural effusions.

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Neama Abid Ali M. — supervision, methodology

Mazin Khazaal M. — statistical analysis, administration

Both authors made a significant contribution to the search and analysis for the article, read and approved the final version before publication, and are responsible for the integrity of all parts of the article.

Участие авторов

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Оба автора внесли существенный вклад в проведение поисково-аналитической работы при подготовке статьи, прочли и одобрили финальную версию до публикации, несут ответственность за целостность всех частей статьи.