Pak. J. Chest Med. 2023;29(04)

Original Article

journal homepage: https:/www.pjcm.net/

Pakistan Journal of Chest Medicine

Official journal of Pakistan Chest Society

Diagnosis and Etiologies of Unilateral Pleural Effusion in a District General Hospital in the United Kingdom

Uzma Basit[1], Syed Ali Abbas[2], Ayesha Akhtar[2]✉, Fatima Zaina[2], Gohar Fatima[3]

[1]Department of Chest Diseases, Withybush General Hospital, Fishguard Rd, Haverfordwest, United Kingdom [2]Department of Respiratory Medicine, Dr Ziauddin University Hospital, Karachi – Pakistan [3]Liaquat National Hospital, Karachi - Pakistan

Corresponding Author:
Ayesha Akhtar
Department of Respiratory Medicine, Dr Ziauddin University Hospital, Karachi - Pakistan
Email: aysh92@live.com

Article History:

Received:	Aug 15, 2023
Revised:	Oct 28, 2023
Accepted:	Nov 27, 2023
Available Online:	Dec 02, 2023

Author Contributions:
AA conceived idea, SAA FZ UB drafted the study, UB collected data, UB AA GF did statistical analysis and interpretation of data, UB SAA FZ critical reviewed manuscript. All approved final version to be published.

Declaration of conflicting interests:
The authors declare that there is no conflict of interest.

How to cite this article:
Basit U, Abbas SA, Akhtar A, Zaina F, Fatima G. Diagnosis and Etiologies of Unilateral Pleural Effusion in a District General Hospital in the United Kingdom. Pak J Chest Med. 2023;29(04):462-469.

A B S T R A C T

Background: The lungs are enveloped by a serous membrane called visceral pleura, while the chest wall and pericardium are covered by parietal pleura. Lung hila connect these layers, and a small amount of fluid in the pleural space lubricates movement. Pleural effusion, excess fluid in the pleural cavity, indicates underlying pulmonary, pleural, or extra-pulmonary diseases.

Objective: To study the various causes of unilateral pleural effusion in patients presenting to a District General Hospital in the United Kingdom.

Methodology: This was a prospective study conducted at Worsecter Royal Infirmary, UK, during July 2021 to June 2022. All (58) adult patients (age above 18 years) admitted to chest ward from various sources with unilateral pleural effusion were included. Case notes were reviewed and data collected. Diagnostic pleural tap was performed in every case and aspirate was sent for biochemical, microbiological and cytological analysis. Pleural biopsies were taken where diagnosis could not be established with the help of other investigations.

Results: Among 58 patients with unilateral pleural effusion (34 men, 24 women), most were aged 50-89 (mean age 69). Among study cases, 16% were referred for surgery (VATS or thoracotomies), with an average 11-day waiting period. Effusions were transudate (15) or exudate (43), and malignancy was confirmed in 31 cases. Complications included intercostal drain dislodgement (19%) and subcutaneous emphysema (12%). Malignancy was the most common cause of unilateral pleural effusion, followed by parapneumonic effusion, left ventricular failure, TB, and asbestos-related benign effusion.

Conclusion: In conclusion, this study highlights malignancy as the primary cause of unilateral pleural effusion, confirmed through cytology and biopsies. Managing these patients is complex, involving prolonged hospitalization, multiple thoracocentesis attempts, and often prompt surgical intervention. Imaging, especially contrast CT chest, is crucial for lesion identification. Complications like drain dislodgement and subcutaneous emphysema underscore the challenges in pleural effusion management.

Keywords: Unilateral Pleural Effusion; Malignancy; Parapneumonic Effusion; Tuberculosis

Introduction

Pleural effusion is the abnormal accumulation of fluid in the pleural cavity, resulting from an imbalance between fluid formation and absorption. It can be caused by various pulmonary or extrapulmonary factors. Pleural effusions are broadly classified into transudative and exudative types based on their protein content. Transudative effusions, with pleural protein less than 29g/L, commonly occur in conditions like congestive heart failure, cirrhosis, and hypo-proteinemic states. Exudative effusions, with pleural protein exceeding 30g/L, are often associated with more serious conditions such as tuberculosis, malignancies, or autoimmune diseases. An alternative classification method involves Light's criteria, which considers pleural fluid and serum LDH and protein ratios. This approach aids in distinguishing between transudative and exudative effusions, enhancing diagnostic accuracy. Pleural effusions can have diverse etiologies, including those with different biochemical compositions like blood, pus, and chyle. Recognizing these distinctions is crucial for understanding the underlying diseases leading to effusion, such as pulmonary embolism, systemic lupus erythematosus, and rheumatoid arthritis. Symptoms of pleural effusion, such as cough, breathlessness, and pleuritic chest pain, typically arise once a significant fluid volume accumulates. The severity and nature of symptoms correlate with the effusion's volume, rate of accumulation, and the underlying pathology.

Unilateral pleural effusion is a common presentation encountered by clinicians in district general hospitals, necessitating a systematic and thorough approach to diagnosis. The condition often manifests with symptoms such as dyspnea, cough, and chest pain, prompting the need for timely and accurate identification of its root cause. The diverse range of potential etiologies underscores the complexity of this clinical scenario, making it essential to explore the specific challenges faced by healthcare professionals in the United Kingdom.

District general hospitals play a crucial role in the healthcare infrastructure of the United Kingdom, serving as primary points of care for a wide spectrum of medical conditions. Understanding the nuances of diagnosing and managing unilateral pleural effusion in this setting is vital for providing optimal patient care. Limited resources, diverse patient demographics, and the need for efficient and cost-effective diagnostic strategies contribute to the distinctive challenges faced by healthcare professionals in district general hospitals when confronted with unilateral pleural effusion cases.

Diagnosing the cause of unilateral pleural effusion is a multifaceted process, often requiring a combination of clinical evaluation, imaging studies, and invasive procedures. In district general hospitals, where access to specialized resources may be constrained, healthcare providers must navigate this complexity judiciously. The role of diagnostic modalities such as chest X-rays, ultrasound, computed tomography (CT) scans, and pleural fluid analysis becomes pivotal in establishing an accurate diagnosis. Challenges in interpretation and the need for timely interventions underscore the significance of exploring the diagnostic landscape specific to district general hospitals.

Unilateral pleural effusion can arise from a myriad of conditions, including infectious, neoplastic, inflammatory, and cardiac etiologies. The unique demographic and environmental factors in the United Kingdom contribute to a distinct spectrum of potential causes, necessitating an in-depth exploration of the prevalence and diagnostic considerations for each. Tuberculosis, malignancies, pneumonia, and heart failure are among the common contributors to unilateral pleural effusion, each requiring a tailored diagnostic and therapeutic approach.

A meticulous diagnostic approach is essential, involving a detailed history, clinical examination, and early diagnostic pleural tap. Analyzing pleural fluid through biochemical assays, including protein content and Light's criteria, helps narrow down differentials. Imaging modalities, such as chest X-rays, ultrasound, and CT scans of the thorax and abdomen, further enhance diagnostic precision.

In challenging cases, pleural biopsies contribute to diagnostic yield, aiding in the identification of malignancies or inflammatory conditions. Integrating these findings with clinical data provides a comprehensive understanding, enabling targeted therapeutic strategies.

Objective

To study the various causes of unilateral pleural effusion in patients presenting to a District General Hospital in the United Kingdom.

Methodology

This prospective study was conducted at the Chest Unit at Worcester Royal Infirmary, UK. All adult patients admitted with newly diagnosed unilateral pleural effusion between July 2021 and June 2022 were included. Those with known pleural effusion or bilateral pleural effusions were excluded. Based on their clinical presentation 58 patients suspected to have unilateral pleural effusion were enrolled in the study. This diagnosis was subsequently confirmed either with plain chest radiograph or ultrasound thorax. A detailed record of patients' history and clinical examinations were made. Routine blood tests were sent. All patients underwent diagnostic pleural tap and pleural fluid was sent for biochemical analysis, cytology and routine microbiology. Simultaneous, blood and pleural fluid for total protein, albumin and lactate

dehydrogenase (LDH) level were also checked. Pleural fluid was also sent for AFB smear and culture. Pleural fluids were not sent for Gene Xpert. In cases where pleural biopsies were taken, samples were sent for histopathology. Additional investigations included bronchoscopy, ultrasound abdomen, ECG (Electrocardiogram), transthoracic echocardiogram and CT scan chest, abdomen and pelvis. Patients' journey throughout the hospital stay was reviewed. A detailed record of intercostal drain insertion including number of thoracocentesis attempts, site of drain insertion, daily output, drain related complications and its outcome was recorded. Seldinger technique was used to insert Thal-Quick chest drain tubes under ultrasound guidance where pleural cavity drainage was deemed necessary.

Results

During the study period, 58 patients were found eligible for enrollment, 34 (59%) were men. Majority 46 (79%) were in the age range between 50-89 years with mean age of 69 years. Nearly half of the admitted patient 28 (48%) were referred by their general practitioners via Medical Admission Unit. Only 14 (24%) were admitted acutely via Emergency Department. Once admitted for evaluation of unilateral pleural effusion, the average length of stay was more than seven days for majority of patients 38 (65%), (range 7 to more than 21 days). All patients underwent thoracocentesis and 21 (36%) needed this procedure more than once either to obtain more sample or for the removal of large amount of effusion (therapeutic tap to relieve symptoms). Contrast enhanced CT scan was performed in 42 (72%) cases which resulted in identification of pulmonary lesions in 11 (26%) and pleural lesions 7 (17%) cases. 9 patients were referred to thoracic surgeons, 6 underwent VATS and 3 thoracotomy. Biopsies obtained during surgery helped in establishing diagnosis in 7 cases and the remaining 2 remained inconclusive and needed further investigation. Average delay between referral and to surgeons and procedure/ biopsies was 12 days.

Pleural effusion was exudative in 43 (74%) cases. CT guide pleural biopsies were taken in 4 (6%) cases only. 9 (15%) of patients who underwent surgery also had pleural biopsies. Malignancy was the most common cause of unilateral effusion found in 31 (54%) cases. Other causes included parapneumonic effusion 8 (14%), congestive cardiac failure in 6 (10%), pleural tuberculosis 5 (8%), benign asbestos related effusion 3 (5%), Chronic liver disease 3 (5%) and others 5 (8%). No definitive diagnosis could be established in 2 (3%) cases (Table 5). Only 19 (61%) of the 31 cases showed malignant cells on pleural fluid cytology, 20 were treated with pleurodesis using talc slurry which was unsuccessful in 5 (25%) cases requiring either further pleurodesis or other options. Among the 42 intercostal drains that were placed, 8 (19%) either fell out or dislodged. 5 (12%) developed drain related subcutaneous/ surgical emphysema. Leaking from the drain site, small iatrogenic pneumothorax, drain blockage requiring regular flushing and minor hematoma were seen in 8 (19%) cases (Table 2).

Discussion

Pleural effusion has a wide differential diagnosis. Evaluation of the patient with pleural effusion is challenging because the differential diagnosis is broad and includes both benign and life-threatening conditions and also the cause may be local or systemic. Moreover, the invasive and noninvasive tests required to make an etiological diagnosis may not be readily available in a primary care setting, and patients may need referral to a hospital equipped with skills of managing pleural diseases. Despite the challenges inherent to different settings, an organized approach to diagnosis and treatment is necessary. Based on their actual etiology, the treatment differs, often requiring drainage of the fluid with the help of intercostal tube. Insertion of chest drain may be associated with certain complications.

This study included male predominance a finding consistent with available literature. In a study performed in Nigeria on patients in pleural effusions male to female ratio was found to be 1.3:1 in march-April 2017.[6] Mean age group of our study was 69 years with 46 patients (79%) falling in ages between 50-89 years supporting that the incidence of pleural effusion is higher in older age in our population. This finding contradicts the finding by Oliver j. Bintcliffe et-al in a study of 130 patients at a pleural tertiary centre found slightly higher mean age of 75 years.[7] In contrast a study from Nigeria reported that the median age of the cases with pleural effusion was 38 years.[12] and this figure was similar to 37.8 years which was reported for other parts of Nigeria,[8] but these finding were less than what was reported from another part of the world.[9-10] Mean age of 48 years was found in a similar study from Pakistan.[25]

In our study, thirty-nine patients needed hospitalization for 1 week for diagnosis, management and needing intervention (thoracocentesis, VATS, pleural biopsy). In one the studies done on factors influencing length of hospital stay in patients with bacterial pleural effusion, they concluded that the patients with parapneumonic effusions and empyema who required longer hospitalization were those with purulent fluid, underlying disease, surgical drainage and/or decortication, with unfavorable radiological outcome and higher pleural fluid levels of lactate dehydrogenase and polymorphonuclear elastase.[11] Median duration of the hospital stay in that study was 17 days; much higher than reported in our study. Similar findings of prolonged hospital stay have

Table 1. Baseline characteristics of study cases

Characteristics	Frequency	Percentage
Gender		
Male	34	59.0
Female	24	41.0
Age Groups (Years)		
<30	3	5.1
30 – 39	3	5.1
40 – 49	6	10.2
50 – 59	12	20.6
60 – 69	10	17.2
70 – 79	11	18.9
80 – 89	13	22.4
Sources		
GP via MAU	28	48.2
GP via OPA	14	24.1
A & E	9	15.5
Other Specialties	7	12.0
Number of Thoracentesis		
1	36	62.0
2	18	31.0
3	3	5.1
4	1	1.7
CT Chest Done		
Yes	42	72
No	16	28
Pulmonary Lesion on CT (n=42)		
Yes	11	26
No	31	74
Pleural Lesion on CT (n=42)		
Yes	7	17
No	35	83

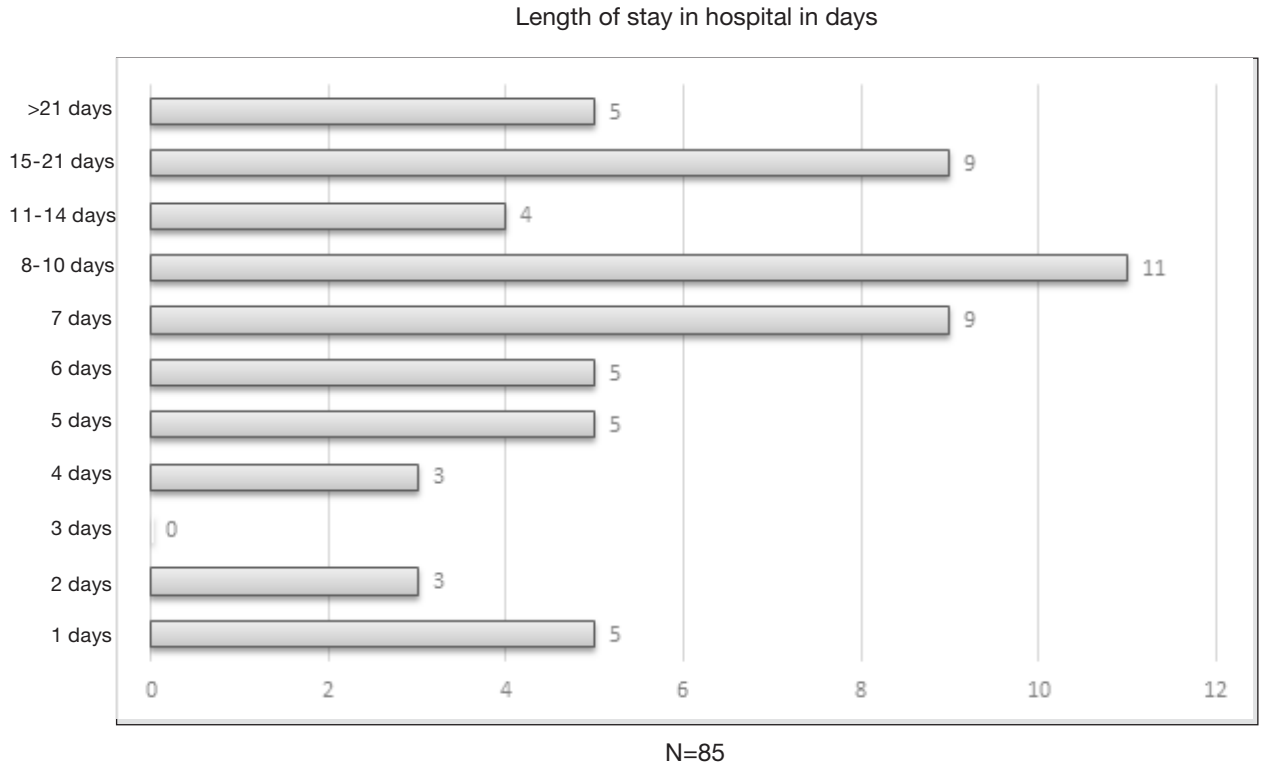

Figure 1. Distribution of study cases on the basis of stay in hospital

been reported in other studies.[12-13] In a similar study from Pakistan 64% of the study population needed to stay in hospital for more than seven days if they got admitted for assessment of their pleural effusions.[25] In a study conducted by Ferguson et al, [12] a total of 119 patients with purulent fluid were analysed. The findings revealed that the median duration for discharge was 21 days in cases when tube drainage or aspiration was effective, but it was 26 days when the treatment was deemed failed. In their study, Lindstrom and Kolbe.[13] examined a cohort of 46 individuals diagnosed with empyema, which was characterised by the presence of purulent fluid, non-purulent fluid with positive culture and biochemical data. The researchers found that the average duration of hospitalisation for these patients was 22 days. Furthermore, they observed that the length of hospital stay was significantly longer in cases where pleural sepsis did not involve Streptococcus milleri, individuals had debilitating illnesses, and frank pus was present. In a study conducted by Alfageme et al,[14] a total of 82 patients with either purulent fluid or non-purulent fluid with positive culture were examined. The average duration of hospitalisation was found to be 37 days. Notably, patients who had nosocomial infections or bronchopleural fistula experienced significantly longer periods of hospitalization. In a study conducted by Davies et al,[15] a cohort of 85 patients with effusions who underwent drainage tube insertion and intrapleural fibrinolytic therapy were examined. The researchers observed a median duration of hospitalization of 15 days.[15]

Thoracentesis is indicated for the symptomatic treatment of large pleural effusions or for treatment of empyema. It is also indicated for pleural effusions of any size that require diagnostic analysis.[16] Thoracentesis and pleural biopsy should always be performed under image guidance to improve its diagnostic sensitivity and prevent complications. Nucleic acid amplification tests, pleural tissue cultures, and collection of pleural fluid in blood culture bottles improve the diagnostic yield of pleural fluid cultures.[17] Different diagnostic modalities are used for evaluation of pleural effusion. CT thorax with contrast is used to assess effusions of mild quantity and effusions that are not evident on chest X-ray.

This research reported that 7 had primary pleural lesion and 11 had pulmonary lesion associated with pleural effusion. A CT examination demonstrating definite malignant features had a 44.6% sensitivity and 100% specificity for the identification of patients with pleural malignancy. A CT study demonstrating probable or definite malignant features had a sensitivity of 64.6% and specificity 92.5%.[18] Oliver et-al,[7] in their study reported that CT imaging had poor sensitivity for the diagnosis of pleural malignancy. In their study,[7] five patients (7.7%) with pleural malignancy exhibited CT imaging characteri-

Table 2. Clinical characteristics of study cases

Procedure	Frequency	Percentage
Diagnosis Established		
Yes	43	74
No	6	10
Referred	9	16
Types of Procedures		
VATS	6	66.6
Thoracotomy	3	33.4
Other	0	0.0
Diagnosis Established (n=9)		
Yes	7	22
No	2	78
Causes of Pleural Effusion		
Lift Ventricular Failure	6	10.3
Malignancy	31	53.4
Benign Asbestos related	3	5.1
Parapneumonic	8	13.7
Tuberculosis	5	8.6
Others	5	8.6
No. of Pleurodesis for effusion (n=20)		
Single Pleurodesis	15	75
Second/Double Pleurodesis	5	25
Complications with Intercostal Drains (n=21)		
Drain fell out/dislodged	8	38.0
Surgical Emphysema	5	23.8
Other	8	38.0

stics that were only considered to be indicative of benign illness. A CT examination revealed some questionable signs in 18 (27%) patients with pleural malignancy, but they were not labelled as having probable or certain malignancy. This finding should serve as a reminder of the need for caution when utilizing radiography alone for diagnosis as well as the importance of interval imaging and close clinical follow-up in situations where the diagnosis is in doubt.

Most common cause of unilateral pleural effusion in our study group turned out to be malignant effusions (54%) followed by parapneumonic effusion and less commonly we came across LVF, TB, asbestos related effusions. Malignant effusions were diagnosed on the basis of cytology and/or biopsy. These findings are in contrast with the findings of Adeoye et al.[6] and Abbas et al,[25] who reported tuberculosis (TB) as responsible for approximately 32.9% of effusion cases, making it the primary contributor to pleural effusion. Malignancy, on the other hand, accounted for 18.7% of cases and was the second most common cause of pleural effusion.[6] TB has previously been identified as a common cause of large unilateral pleural effusion in several developing nations including Pakistan.[12,25] Abbas et al from Pakistan reported tuberculous pleural effusion as the commonest cause of effusion followed by malignancy and left ventricular failure.[25] Golshan et al,[19] reported congestive heart failure as the most common cause of pleural effusion followed by the malignancy. The observed variations in the etiology of pleural effusion causes may be attributed to the high prevalence of tuberculosis (TB), HIV endemicity, and low socioeconomic status of developing nations, as compared to industrialized countries. The observed discrepancies in certain research can be attributed to the epidemiological shift from communicable diseases to non-communicable diseases, specifically cancer.

Blind, image-guided needle biopsy, medical thoracoscopy (MT), video-assisted thoracic surgery (VATS) and pleuroscopy are procedures that provide access to the pleural space, but with unequal invasive injury.[17,18,19] Microbiological identification of a pathogenic organism can confirm infective pleural effusions, only 25% of the underlying pathogen is identified by Gram staining of a non-purulent parapneumonic effusion.[22] The yield of effusion culture has a sensitivity of 10–20%.[23] However, in this cohort only 3 patients had positive microbiological cultures requiring antibiotic therapy and follow-ups. When there is suspicion of tuberculous pleuritis, it is recommended to conduct microbiological investigation, AFB smear and culture and tissue biopsy.[21] Ideally, a volume ranging from 30 to 50 mL of untreated puncture fluid should be collected and submitted for diagnostic testing of mycobacterial infections.[24]

Life threatening complications may be observed with the procedure of intercostal drains. There is no organ in the thoracic and abodominal cavity that has not been pierced. Reported complications include haemothorax usually from laceration of intercostal vessel, lung laceration, diaphragm / abdominal cavity penetration, stomach / colon injury, tube placement in subcutaneous tissue instead of thoracic cavity and tube falling out /dislodging particularly if not secured appropriately.[25] In this study Seldinger technique was used to insert Thal-Quick chest drain tubes, mostly under ultrasound guidance as per guidelines from the British Thoracic Society. Drain falling out and surgical emphysema were the two commonest complications noted in our study. Luckily, there were no life threatening complications probably due to maximal utilization of bed side ultrasound.

Conclusion

Unilateral pleural effusion may pose diagnostic challenge. Reaching a firm diagnosis may need various investigations including certain invasive tests. The frequency of etiology may vary from one region to other across the globe. Malignancy was found to be the most common cause of unilateral pleural effusion in this study. Management of effusion may require hospital admission and this may be prolonged particularly if intercostal drains are to be placed, the etiology if infective or pleurodesis is required for recurrent pleural effusions. The intercostal tube insertion may lead to life threatening complication which may potentially be avoided with the use of bed side ultrasound imaging.

References

1. Jany B, Welte T. Pleural Effusion in Adults-Etiology, Diagnosis, and Treatment. Dtsch Arztebl Int. 2019; 116(21):377-86. DOI: 10.3238/arztebl. 2019.0377.
2. Beaudoin S, Gonzalez AV. Evaluation of the patient with pleural effusion. CMAJ. 2018;190(10):E291-5. DOI: 10.1503/cmaj.170420.
3. Skok K, Hladnik G, Grm A, Crnjac A. Malignant Pleural Effusion and Its Current Management: A Review. Medicina (Kaunas). 2019;55(8):55080490. DOI: 10.3390/medicina55080490.
4. Kulandaisamy PC, Kulandaisamy S, Kramer D, Mcgrath C. Malignant Pleural Effusions-A Review of Current Guidelines and Practices. J Clin Med. 2021 Nov 26;10(23).10235535. DOI: 10.3390/jcm10-235535.
5. Zarogoulidis K, Zarogoulidis P, Darwiche K, Tsakiridis K, Machairiotis N, Kougioumtzi. Malignant pleural effusion and algorithm management. J Thorac Dis.

2013;5 Suppl 4:S413-9. DOI: 10.3978/j.issn.2072-1439.2013.09.04.

6. Adeoye P, Johnson W, Desalu O, Ofoegbu C, Fawibe A, Salami A, et al. Etiology, clinical characteristics, and management of pleural effusion in Ilorin, Nigeria. Niger Med J. 2017;58(2):76-80.
7. Bintcliffe OJ, Hooper CE, Rider I, Finn RS, Morley AJ, Zahan-Evans NJ, et al. Unilateral Pleural Effusions with More Than One Apparent Etiology. A Prospective Observational Study. Ann Am Thorac Soc. 2016;13 7:1050-6.
8. Ogunleye E, Thomas MO, Olusoji O. Aetiology and Demographic Attributes of Common Pleural Collections in an African Population. Surg Sci. 2013;04: 332-8.
9. Valdés L, Alvarez D, Valle JM, Pose A, San José E. The etiology of pleural effusions in an area with high incidence of tuberculosis. Chest. 1996;109(1):158-62.
10. Khan FY, Alsamawi M, Yasin M, Ibrahim AS, Hamza M, Lingawi M, et al. Etiology of pleural effusion among adults in the state of Qatar: a l-year hospital-based study. East Mediterr Health J. 2011;17(7):611-8.
11. Soriano T, Alegre J, Alemán C, Ruiz E, Vázquez A, Carrasco JL, et al. Factors Influencing Length of Hospital Stay in Patients with Bacterial Pleural Effusion. Respirol. 2005;72(6):587-93.
12. Ferguson AD, Prescott RJ, Selkon JB, Watson D, Swinburn CR. The clinical course and management of thoracic empyema. Qjm. 1996;89(4):285-9.
13. Lindstrom ST, Kolbe J. Community acquired parapneumonic thoracic empyema: predictors of outcome. Respirol. 1999;4(2):173-9.
14. Alfageme I, Muñoz F, Peña N, Umbría S. Empyema of the thorax in adults. Etiology, microbiologic findings, and management. Chest. 1993;103(3):839-43.
15. Davies CW, Kearney SE, Gleeson FV, Davies RJ. Predictors of outcome and long-term survival in patients with pleural infection. Am J Respir Crit Care Med. 1999;160(5 Pt 1):1682-7.
16. Wickbom A, Cha SO, Ahlsson A. Thoracocentesis in cardiac surgery patients. Multimed Man Cardiothorac Surg. 2015. DOI:10.1093/mmcts/mmv002.
17. Ferreiro L, Toubes ME, San José ME, Suárez-Antelo J, Golpe A, Valdés L. Advances in pleural effusion diagnostics. Expert Rev Respir Med. 2020;14(1):51-66.
18. Bintcliffe OJ, Hooper CE, Rider IJ, Finn RS, Morley AJ, Zahan-Evans N, et al. Unilateral Pleural Effusions with More Than One Apparent Etiology. A Prospective Observational Study. Ann Am Thorac Soc. 2016;13(7):1050-6.
19. Golshan M, Faghihi M, Ghanbarian K, Ghanei M. Common causes of pleural effusion in referral hospital in Isfahan, Iran 1997-1998. Asian Cardiovasc Thorac Ann. 2002;10(1):43-6.
20. Lee P, Folch E, editors. Thoracoscopy: advances and increasing role for interventional pulmonologists. Seminars in Respiratory and Critical Care Medicine; 2018: Thieme Medical Publishers.
21. Koegelenberg CFN, Irusen EM, von Groote-Bidlingmaier F, Bruwer JW, Batubara EMA, Diacon AH. The utility of ultrasound-guided thoracentesis and pleural biopsy in undiagnosed pleural exudates. Thorax. 2015;70(10):995-7.
22. Jany B, Welte T. Pleural effusion in adults—etiology, diagnosis, and treatment. Dtsch Arztebl Int. 2019; 116(21):377.
23. Hooper C, Lee YC, Maskell N. Investigation of a unilateral pleural effusion in adults: British Thoracic Society Pleural Disease Guideline 2010. Thorax. 2010;65 Suppl 2:ii4-17.
24. Schaberg T, Bauer T, Brinkmann F, Diel R, Feiterna-Sperling C, Haas W, et al. S2k-Leitlinie: Tuberkulose im Erwachsenenalter. Pneumologie. 2017;71(06): 325-97.
25. Abbas SA, Bajwa M, Ahmed Z. Etiologies of Unilateral Pleural Effusion and Complications of intercostal drains. Pak J Chest Med. 2017; 23(1): 08-14