INTRODUCTION

Pleural effusion is an abnormal accumulation of fluid in the pleural space. Pleural effusion is not a specific disease, but rather a reflection of an underlying pathology. It is categorized as transudate or exudate based on laboratory characteristics of the pleural fluid ***(Joshi, 2014).***

In pediatrics, pulmonary infection is the most common cause of pleural effusion, such as bacterial, viral pneumonia, pulmonary tuberculosis and fungal infections. *Streptococcus pneumoniae* and *Staphylococcus aureus* remain the leading organisms causing para pneumonic effusions and empyema in pediatrics ***(Afsharpaiman et al., 2016).***

Other causes of pleural effusion include congestive heart failure, neoplastic diseases, hepatic cirrhosis, collagen vascular diseases, acute respiratory distress syndrome, hypoalbuminemia, parasitic infestations, intra-abdominal abscess, post abdominal surgery, hemothorax, chylothorax and pancreatitis ***(Light, 2011).*** Moreover, renal diseases such as nephrosis and chronic kidney disease may be complicated with pleural effusion ***(Ahluwalia, 2015).***

A chest radiograph remains the gold standard investigation for identification of pleural effusion, it is considered to be the least expensive and the simplest way to identify a pleural effusion in the current clinical practice ***(NA, 2014).***

Yet, emerging investigations, such as ultrasonography has proven to be more effective in identification of pleural effusion in comparison to supine chest radiograph as it allows detection of pleural fluid as small as 3 to 5 ml, while chest radiograph can only detect volumes of fluid above 50 ml ***(Chichra et al., 2016).***

Also, chest ultrasonography, contrary to the radiological method, allows differentiation between free and loculated pleural effusion ***(Soni et al., 2015).***

In addition, bedside ultrasound, compared to the chest radiograph, offers a safe modality for follow up of pleural effusion with reduced risk of radiation exposure ***(Inglis et al., 2016).***

Thoracic ultrasound is a rapid, safe tool that aids in diagnosis of pleural effusion as well as monitoring the effect of therapy. It has been said that the thoracic ultrasound has become the "stethoscope" of the twenty-first century ***(Koenig et al., 2011).***

AIM OF THE WORK

The aim of this study is to assess the value of Transthoracic Ultrasound in the early diagnosis of pleural effusion among clinically anticipated cases compared to physical examination and chest X-ray (AP & lateral views).

PLEURAL EFFUSION

Physiology of the pleural space

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, serves as a lubricant to facilitate movement of the pleural surfaces against each other in the course of respirations. It minimizes the friction and it allows better lung expansion during the respiration ***(Noppen, 2001).***

The pleural fluid filters through the capillaries of the parietal pleura, while drainage is mostly provided by the lymphatic stomata of the parietal pleura which directly connects the pleural space with the parietal lymphatic draining system; and a minor share of pleural fluid (<15%) is drained through the visceral pleura **(Figure 1)** ***(Porcel and Light, 2013).***

This small volume of pleural fluid is maintained through the balance of hydrostatic and oncotic pressure and lymphatic drainage, any disturbance in these forces may lead to pleural effusion ***(Diaz-Guzman and Dweik, 2007).***

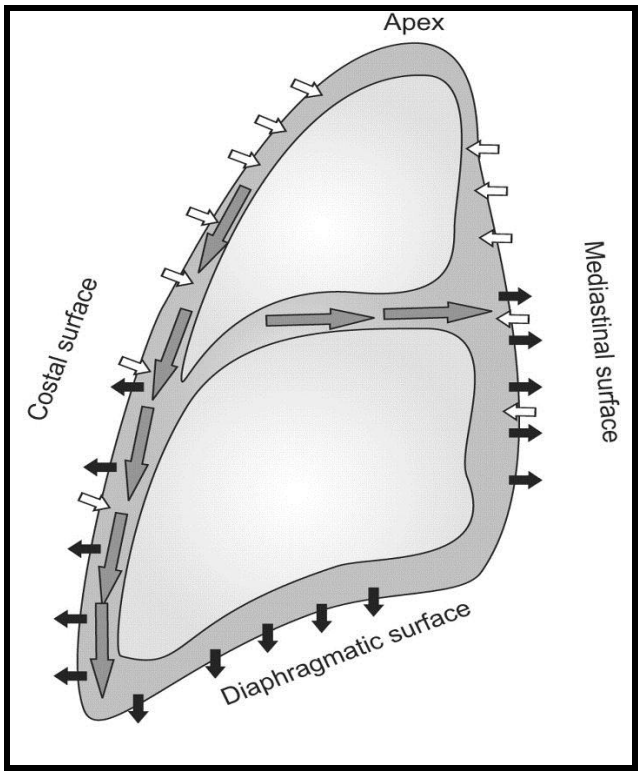

Figure (1): Filtration/drainage processes of the pleural fluid in the pleural cavity and intrapleural fluxes. White arrow: filtration; black arrow: lymphatic drainage; grey arrow: intrapleural fluxes ***(Miserocchi, 2010).***

Definition of pleural effusion

Pleural effusion is an abnormal accumulation of fluid in the pleural space and it results from an imbalance between pleural fluid production and pleural fluid absorption. It is the most prevalent manifestation of pleural diseases ***(Diaz-Guzman and Dweik, 2007).***

Differential diagnosis of pleural effusion

In pediatrics, Pleural effusion is the most common pleural disorder, and it is usually secondary to an underlying

pleural or systemic disease. By far, the most common disease that causes pleural effusion in the developing countries is bacterial pneumonia. Accurate and prompt diagnosis and treatment of para pneumonic effusion is necessary to provide effective treatment, as pleural effusion & subsequent empyema may lead to an increase in the morbidity, mortality and prolonged hospital stay ***(Afsharpaiman et al., 2016).***

The pleural effusion is divided into 2 main categories according to the pleural fluid analysis, transudates and exudates.

Transudative effusions

Transudates result from imbalances in hydrostatic and oncotic forces and are caused by a limited number of recognized clinical conditions such as heart failure and cirrhosis. Other causes include nephrotic syndrome, atelectasis, peritoneal dialysis, constrictive pericarditis, superior vena caval obstruction, and urinothorax. Transudative effusions usually respond to treatment of the underlying condition (e.g., diuretic therapy) ***(Light, 2011).***

Exudative effusions

Exudative pleural effusion usually results from a rise in the capillary permeability and or impairment in the lymphatic drainage, It occurs with inflammatory conditions such as bronchopneumonia or proliferative diseases such as tumors pneumonia and malignancy account for most exudative effusions in pediatrics ***(Porcel and Light, 2013).***

Table (1): Differential Diagnosis of Pleural Effusion ***(Light, 2011).***

Differential diagnoses of pleural effusion:

1. Transudative pleural effusions

a. Congestive heart failure (CHF)
b. Cirrhosis
c. Nephrotic syndrome
d. Superior vena caval obstruction
e. Urinothorax
f. Peritoneal dialysis
g. Glomerulonephritis
h. Myxedema
i. Cerebrospinal fluid leak to the pleura
j. Hypoalbuminemia

2. Exudative pleural effusions

a. Neoplastic diseases
   i. Metastatic disease
   ii. Mesothelioma
   iii. Lymphoma
b. Infectious diseases
   i. Bacterial infections
   ii. Tuberculosis
   iii. Fungal infections
   iv. Parasitic infections
   v. Viral infections
c. Pulmonary embolism
d. Gastrointestinal disease
   i. Pancreatic disease
   ii. Subphrenic abscess
   iii. Intrahepatic abscess
   iv. Intrasplenic abscess
   v. Esophageal perforation
   vi. Postabdominal surgery
   vii. Diaphragmatic hernia
   viii. Endoscopic variceal sclerosis
   ix. Post liver transplant
e. Heart diseases
   i. Pericardial disease
   ii. Fetal pleural effusion
f. Collagen vascular diseases
   i. Rheumatoid pleuritis

ii. Systemic lupus erythematosus
iii. Drug-induced lupus
iv. Immunoblastic lymphadenopathy
v. Sjo¨ gren syndrome
vi. Familial Mediterranean fever
vii. Churg-Strauss syndrome
viii. Wegener granulomatosis

g. Drug-induced pleural disease
i. Nitrofurantoin
ii. Dantrolene
iii. Methysergide
iv. Ergot drugs
v. Amiodarone
vi. Interleukin 2
vii. Procarbazine
viii. Methotrexate
ix. Clozapine

h. Miscellaneous diseases and conditions
i. Asbestos exposure
ii. Post lung transplant
iii. Post bone marrow transplant
iv. Yellow nail syndrome
v. Sarcoidosis
vi. Uremia
vii. Trapped lung
viii. Therapeutic radiation exposure
ix. Drowning
x. Amyloidosis
xi. Milk of calcium pleural effusion
xii. Electrical burns
xiii. Extra medullary hematopoiesis
xiv. Rupture of mediastinal cyst
xv. Acute respiratory distress syndrome
xvi. Whipple disease
xvii. Iatrogenic pleural effusions

i. Hemothorax
j. Chylothorax
k. Pseudochylothorax

In clinical practice, exudative effusions can be separated effectively from transudative effusions using Light's criteria. These criteria classify an effusion as exudate if one or more of the following are present: (1) the ratio of pleural fluid protein to serum protein is greater than 0.5, (2) the ratio of pleural fluid lactate dehydrogenase (LDH) to serum LDH is greater than 0.6, or (3) the pleural fluid LDH level is greater than two thirds of the upper limit of normal for serum LDH ***(Light, 2011).***

Light's criteria are nearly 100 percent sensitive at identifying exudates, but approximately 20 percent of patients with pleural effusion caused by heart failure may fulfill the criteria for an exudative effusion after receiving diuretics. In these circumstances, if the difference between protein levels in the serum and the pleural fluid is greater than 3.1 g per dL, the patient should be classified as having a transudative effusion ***(Papakala et al., 2015).***

A serum effusion albumin gradient greater than 1.2 g per dL also can indicate that the pleural effusion is most likely a true transudative effusion. However, neither protein nor albumin gradients alone should be the primary test used to distinguish transudative effusions from exudative effusions because they result in the incorrect classification of a significant number of exudates ***(Porcel and Light, 2013).***

Pleural fluid tests for pleural effusion are highlighted in **tables 2 & 3.**

Table (2): Routine pleural fluid tests for pleural effusion ***(Porcel and Light, 2006).***

Test	Test value	Suggested diagnosis	Comments
Adenosine deaminase (ADA)	>410 U per L (667 nkat per L)	Tubercubosis (>90 percent), complicated parapneumonic effusion (30 percent), malignancy (5 percent), rheumatoid arthritis	In the united states, ADA is not routinely requested because of the low prevalence of tuberculous pleurisy.
Cytology	Present	Malignancy	Actively dividing mesothelial cells can mimic an adenocarcinoma
Glucose	<60 mg per dL (3.3 mmol per L)	Complicated parapneumonic effusion or empyema, tuberculosis (20 percent, malignancy (<10 percent), rheumatoid arthritis	In general, pleural fluids with a low glucose level also have low pH and high LDH levels.
Lactate dehydrogenase (LDH)	> Two thirds of upper limits of normal for serum LDH	Any condition causing an exudates	Very high levels of pleural fluid LDH (>1.000 U per L) typically are found in patients with complicated parapneumonic pleural effusion and in about 40 percent of those with tuberculous pleurisy.
LDH fluid to serum ratio	>0.6	Any condition causing an exudates	Most patients who meet the criteria for an exudative effusion with LDH but not with protein levels have either parapneumonic effusions or malignancy
Protein fluid to serum ratio	>0.5	Any condition causing an exudates	A pleural fluid protein level >3 mg per dL suggests an exudates, but when taken alone this parameter misclassifies more than 10 percent to exudates and 15 percent of transudates
Red blood cell count	>100.000 per mm^3 (100 x 10^6 per L)	Malignancy, trauma, parapneumonic effusion , pulmonary embolism	A fluid hematocrit <1 percent is nonsignificant
White blood cell count and differential	>10.000 per mm^3 (10 x 10^6 per L)	Empyema, other exudates (uncommon)	In purulent fluids, leukocyte count is commonly much lower than expected because dead cells or other debris account for much of the turbidity
Eosinophils	>10 percent	Not diagnostic	The presence of air or blood in the pleura space is a common cause. No diagnosis is ever obtained in as many as one third of patients with eosinophilic pleural effusion
Lymphocytes	>50 percent	Malignancy, tuberculosis, pulmonary embolism, coronary artery bypass surgery	Pleural fluid lymphocytosis >90 percent suggests tuberculsosis or lymphoma.
Neutrophils	>50 percent	Parapneumonic effusion, pulmonary embolism, abdominal diseases	In about 70 percent of acute tuberculous pleurisy and 20 percent of malignant pleural effusions, a neutrophilic fluid predominance can be seen.

Table (3): Optional pleural fluid tests for pleural effusion ***(Porcel and Light, 2006).***

Tests	Tests value	Suggested diagnosis	Comments
Amylase	> Upper limit of normal	Malignancy (<20 percent), pancreatic disease esophageal rupture	Obtain when esophageal rupture or pancreatic disease is suspected. The amylase in malignancy and esophageal rupture is of the salivary type
Cholesterol	> 45 to 60 mg per dL (1.16 to 1.55 mmol per L)	Any condition causing an exudates	Measure if chylothorax or pesudochylothrorax is suspected. This parameter taken alone misclassifies 10 percent to exudates and 20 percent of transudates
Culture	Positive	Infection	Obtain in all parapneumonic pleural effusions because a positive gram stain or culture should lead to prompt chest tube drainage
Hematocrit fluid to blood ratio	≥ 0.5	Hemothorax	Obtain when pleural fluid is bloody. Hemothorax most often originates from blunt or penetrating chest trauma
Interferon	Different cutoff points	Hemothorax	Obtain when pleural fluid is bloody. Hemothorax most often originates from blunt or penetrating chest trauma
Interferon	Different cutoff points	Tuberculosis	Consider when ADA is unavailable or nondiagnostic and tuberculosis is suspected
NT-pro8NP	>1.500 pg per mL	Heart failure	If available, consider testing when heart failure is suspected and exudates criteria are met
pH	<7.20	Complicated parapneumonic effusion or empyema, malignancy (<10 percent), tuberculosis (<10 percent), esophageal rupture	Obtain in all nonpurulent effusions is suspected a low pleural fluid pH indicates the need for tube drainage only for parapneumonic pleural effusions.
Polymerase chain reaction	Positive	Infection	Consider when infection is suspected. Sensitivity of polymerase chain reaction to detect mycobacterium tuberculosis in pleural fluid varies from 40 to 80 percent and is lower in patients with negative mycobacterial cultures
Triglycerides	>110 mg per dL (1.24 mmol per L)	Chylothorax	Obtain when pleural fluid is cloudy or miky. Chylothorax is caused by lymphoma or trauma. Not all chylous pleural effusions appear milky white or whitish.
Tumor markers;	Different cut of points	Malignancy	Consider when malignancy is suspected and thoracoscopy is being considered. Except for telomerase activity. Individual tests tend to have low sensitivity (<30 percent) when looking for the utmost specificity

The most common causes of bilateral pleural effusion are heart failure, malignancy and bronchopneumonia. Usually the characteristic radiological sign in heart failure is enlarged cardiac silhouette. Around 60% of massive effusions are caused by malignancies followed by para pneumonic effusions (20%). Other causes of massive pleural effusion include tuberculosis, hepatic hydrothoraces and lupus pleuritis ***(Porcel and Light, 2013).***

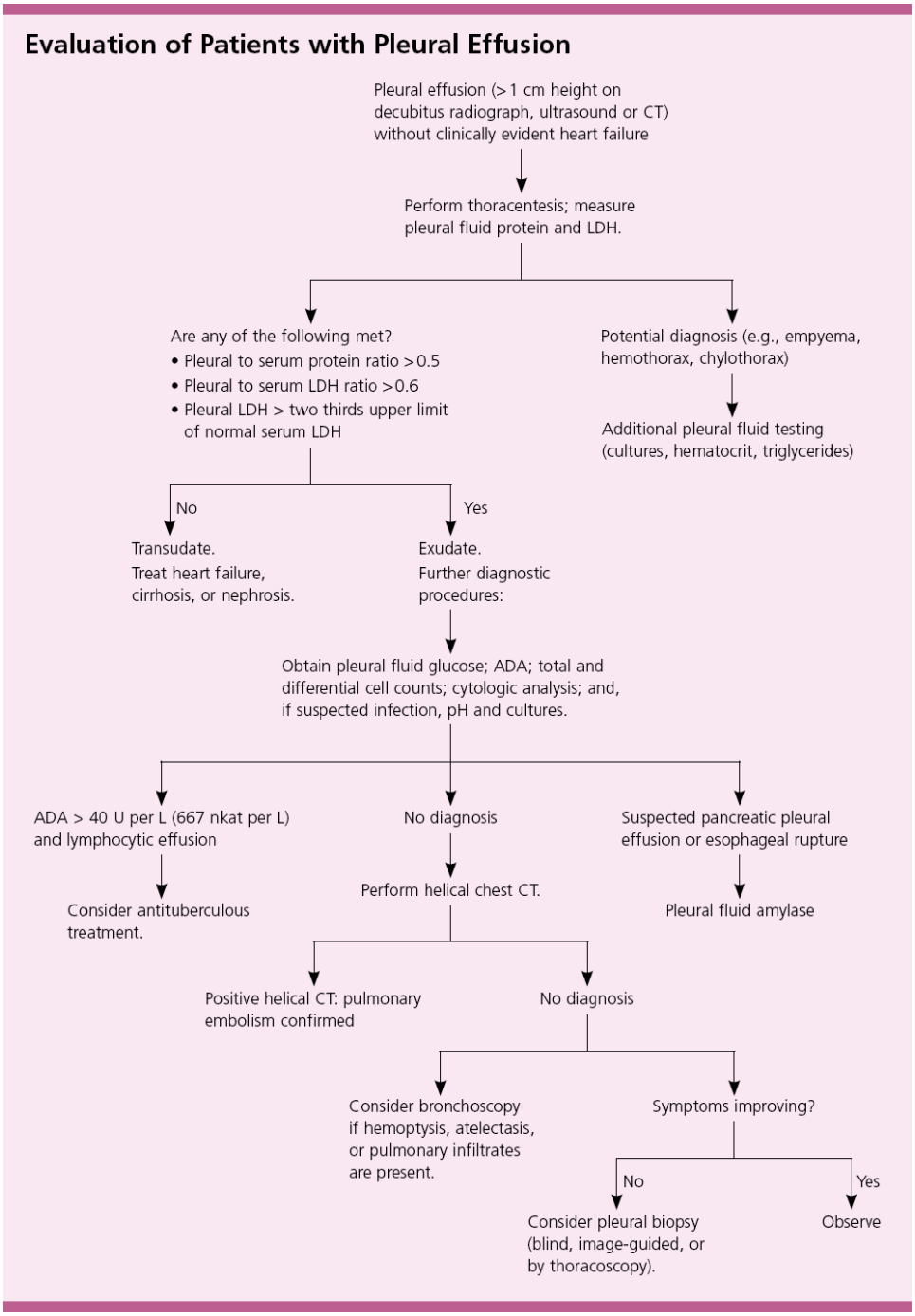

Figure (2): Algorithm for the evaluation of patients with pleural effusion ***(Porcel and Light, 2006).***

Symptoms of the pleural effusion

Chest pain

The most common presenting symptom of pleural effusion in children is chest pain, which could be shooting or dull aching, and it occurs due to the irritation of the parietal pleura ***(Porcel and Light, 2013).***

Shooting chest pain usually occurs with bronchopneumonia & pulmonary embolism, and the pain is often exaggerated by deep inspiration or by coughing. The pain is usually referred to the abdomen or the ipsilateral shoulder if the central diaphragmatic pleura is involved ***(Light, 2011).***

Dyspnea

Larger pleural effusions are usually accompanied with dyspnea, and trepopnea. Usually the larger the effusion the more the symptoms but this not always the case in all the patients, if there is an underlying lung disease, small to moderate effusion may lead to marked dyspnea. On the other hand, if the pleural effusion is minimal, the patient may be completely asymptomatic ***(NA, 2014).***

Cough

Pleural effusions are usually associated with dry, nonproductive cough ***(Karkhanis and Joshi, 2012).***

Vomiting & abdominal pain

Vomiting and abdominal pain occur with PE due to the presence of fluid in the pleural space or the presence of fluid near the diaphragm causing diaphragmatic irritation ***(Light, 2011).***

Fever

PE could be presented with fever in many pulmonary and extra pulmonary diseases. The most common are Pneumonia, empyema and tuberculosis ***(Porcel and Light, 2013).***

Other symptoms

Weight loss could be associated with Malignancy, tuberculosis and anaerobic bacterial pneumonia ***(Light, 2011).***

Signs of the pleural effusion

The physical findings are related to the volume of fluid in the pleural effusion and its effects on the chest wall, diaphragm, and lungs. Physical findings are generally normal if less than 300 mL of fluid is present, whereas large effusions (> 1,500 mL) can be associated with significant asymmetry of chest expansion and bulging of intercostal spaces ***(Soni et al., 2015).***