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Different Infective and Non-Infective Etiology of Exudative Pleural Fluid Effusion: Experience of 50 Cases in Bangladesh

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Abstract

Background: Several diseases are responsible for the causation of exudative pleural fluid effusion among patients. **Objective:** The purpose of the present study was to identify the etiologies of exudative pleural fluid effusion. **Methodology:** This cross-sectional study was carried out at medicine indoor department of Sylhet MAG Osmani Medical College Hospital, Sylhet over a period of six month from October 2009 to March 2010. Patients who were admitted with pleural effusion were selected as the study population. Pleural fluid was collected by a physician. The laboratory tests were performed in the Department of Laboratory medicine of the Hospital. The different etiologies were determined by the different diagnostic tests. **Results:** A total of 50 cases were selected consecutively in the study. Out of 50 patients, 28.0% was in the range of 41 to 50 years followed by 26.0% between 31 to 40 years. Tuberculosis was the most common cause of exudative pleural effusion and among 50 cases of effusion 30 were due to tuberculosis (60%). Malignancy was found as the 2nd common cause of exudative pleural effusion (24.0%). Pneumonia was found as the 3rd common cause of exudative pleural effusion (10.0%). **Conclusion:** In conclusion tuberculosis is the most common cause of exudative pleural effusion followed by malignancy.

Keywords: Etiology; exudative; pleural fluid effusion

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Introduction

The leading causes of exudative effusion are pneumonia, tuberculosis, malignant disease, connective tissue disease particularly SLE, rheumatoid arthritis, pulmonary infarction, acute rheumatic fever and many more[1]. Pleural space normally contains a very thin layer of fluid which serves as a coupling system. Accumulation of pleural fluid occurs when it is formed in excess of absorption. Disease affecting any structure of thorax like pleura itself, lungs, thoracic wall or mediastinal structure can lead to development of pleural effusion[2-3]. However, some extra thoracic sources like subphrenic structures or some systemic disease also cause it[4].

Pleural effusion is not a diagnosis but describes the underlying pathological process involving the pleura either primarily or secondarily and it can be either unilateral or bilateral[5]. Pleural effusions arise as a complication of many different diseases. Basically they could be divided into: nonmalignant, malignant and paramalignant effusions. In another way, it may be classified by differential diagnosis or by pathophysiology[6].

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The causes of the majority of pleural effusions can usually be identified through history, examinations and relevant investigations[7]. When a patient is found to have a pleural effusion, an effort should be made to determine the cause. The 1st step is to determine whether the effusion is a transudate or an exudate[2]. The leading, causes of transduative pleural effusion are left ventricular failure, hepatic failure, nephrotic syndrome, malnutrition and so one[4].

The principal function of pleural fluid is to provide a frictionless surface between the two pleurae in response to changes in lung volume with respiration[7]. The following mechanisms play a role in the formation of pleural effusion like altered permeability of the pleural membrane like inflammatory process, neoplastic disease, pulmonary embolus, reduction in intravascular oncotic pressure like hypoalbuminemia, hepatic cirrhosis, increased capillary permeability or vascular disruption like trauma, neoplastic disease, inflammatory process, infection, pulmonary infarction, drug hypersensitivity, uremia, pancreatitis, Increased capillary hydrostatic pressure in the systemic and/or pulmonary circulation like congestive heart failure, superior vena caval syndrome, reduction of pressure in pleural space; lung unable to expand like extensive atelectasis, mesothelioma and inability of the lung to expand like extensive atelectasis, mesothelioma[8-10]. Decreased lymphatic drainage or complete blockage, including thoracic duct obstruction or rupture like malignancy, trauma, increased fluid in peritoneal cavity, with migration across the diaphragm via the lympatics like hepatic cirrhosis, movement of fluid from pulmonary edema across the visceral pleura, persistent increase in pleural fluid oncotic pressure from an existing pleural effusion[11-12], causing accumulation of further fluid and iatrogenic causes like central line misplacement are also reported. The purpose of the present study was to identify the etiologies of exudative pleural fluid effusion.

Methodology

Study Settings & Population: This comparative cross-sectional study was carried out at medicine indoor department of Sylhet MAG Osmani Medical College Hospital, Sylhet, Bangladesh over a period of six months from October 2009 to March 2010. Patients who were admitted with pleural effusion were selected as the study population. Patients who were presented with clinically and radiologicaly detected pleural effusion with exudative pleural effusion were included in this study. Exclusion criteria were transudative pleural effusion, traumatic pleural effusion or haemothorax, effusion due to chest surgery and chylothorax. The variables studied were demographic characteristics like age, sex and clinical presentation.

Study Procedure: Pleural fluid was collected by a physician. The laboratory tests were performed in the Department of Laboratory medicine of the Hospital. Chest X-ray was performed to all patients. Data were collected using a structured questionnaire (research instrument) containing all the key variables.

Statistical Analysis: Statistical analyses were performed with SPSS software, versions 22.0 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Continuous data were summarized in terms of the mean, standard deviation, median, minimum, maximum and number of observations. Categorical or discrete data were summarized in terms of frequency counts and percentages. For end points analysis, Fisher's exact test was used for categorical variables and an analysis of variance (Student t Test) was applied for continuous outcomes. A two-sided P value of less than 0.05 was considered to indicate statistical significance.

Ethical Considerations: Ethical clearance was taken from the appropriate authority and ethics was maintained strictly through the study. Ethical clearance was obtained from Ethical Review Committee of local Institute. All the participants were given an explanation about the objectives of the study and their right to participate or not. An information sheet for participants in Bengali was also given to each subject to read and it was also explained by the investigator to the participants. All questionnaire and ethical documents were translated into Bengali before interview.

Results

A total of 50 cases were selected consecutively in the study. Out of 50 patients, 28.0% was in the range of 41 to 50 years followed by 26.0% between 31 to 40 years.

Table 1: Distribution of bacteria isolated from blood sample (n=483)

Age Group	Frequency	Percent
Less Than 20 Years	1	2.0
21 to 30 Years	6	12.0
31 to 40 Years	13	26.0
41 to 50 Years	14	28.0
51 to 60 Years	9	18.0
More Than 60 Years	7	14.0
Total	**50**	**100.0**

Table 2: Distribution of Patients by Result of Pleural Fluid Analysis

Disease	Cytology	Gram Staining	Z-N Staining	Malignant Cell
Tubercular (n=30)	Plenty Lymphocyte (28) Occasional cell (2)	No organism found	AFB seen-2(6.6%)	Not found
Malignant (n=12)	Plenty RBC & Lymphocytes (8) Mesothelial cell & polymorph (4)	No organism found	No AFB seen	Found in1 (8.5%)
Pneumonia (n=5)	Plenty PMN with few lymphocyte (4)	Gram+ve cocci-2(40%)	No AFB seen	Not found
Others (n=3)	Some lymphocyte (3)	No organism found	No AFB seen	Not found

18.0% was in the range of 51 to 60 years and 14.0% was above 60 years. Very few (2%) were below 20 years of age. The mean age of the patients was 44.5 ± 12.86 years with age range 16 to 70 years (Table 1).

AFB was found in the pleural fluid in 2 cases of tubercular pleural effusion. Malignant cell was found in the pleural fluid in 1(8.5%) case of malignant pleural effusion. Gram positive organism was found in 40.0% cases of pneumonic pleural effusion (Table 2).

Tuberculosis was the most common cause of exudative pleural effusion and among 50 cases of effusion 30 were due to tuberculosis (60%). Malignancy was found as the 2nd common cause of exudative pleural effusion (24%). Of the malignant cases, 11 had bronchial carcinoma & 1 lymphoma. Pneumonia was found as the 3rd common cause of exudative pleural effusion (10%). The remaining 3 patients had other causes of exudative pleural effusion which included Rheumatoid arthritis (01) and non-specific (02) (Figure I).

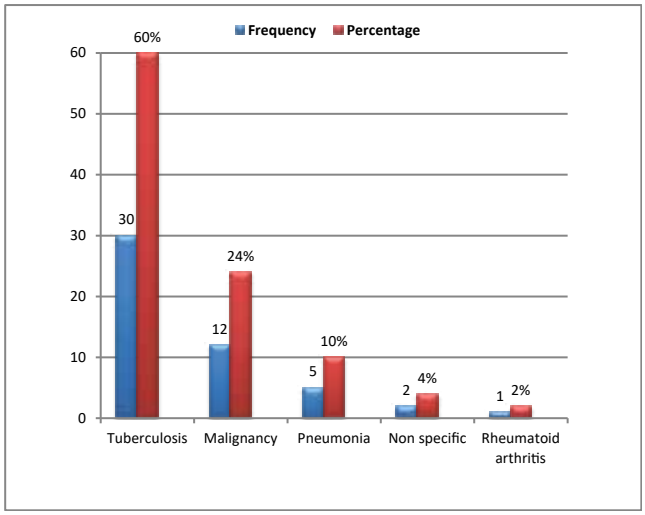

Figure I: Etiology of Exudative Pleural Effusion (n=50)

Discussion

Parapneumonic effusion are associated with bacterial pneumonia, lung abscess or bronchiectasis and are one of the common causes of exudative pleural effusion[13]. Empyema refers to a grossly purulent effusion. Initially the effusion may be amber-colored, containing predominantly polymorphs, but it may progress to increasing turbidity with a high white cell count empyema. Patients with aerobic bacterial pneumonia and pleural effusion present with an acute febrile illness consisting of chest pain, sputum production and leucocytosis[14]. Patient with anaerobic infection present with a subacute illness with weight loss, a brisk leucocytosis and mild anemia.

The possibility of parapneumonic effusion should always be suspected if fever persists despite the appropriate antimicrobial therapy.[15] The presence of free fluid in the pleural space can be demonstrated with a lateral decubitus radiograph. If the free fluid separates the lung from the chest wall by more than 10mm on the decubitus radiograph, a therapeutic thoracentesis should be performed.

The mean age of the patients was 44.5± 12.86 years and the lowest and highest ages were 16 and 70 years respectively. Majority (68%) of the patients was male and 32% female giving a male-to-female ratio roughly of 2.1:1. Valdes et al[3] reported that pleural effusion patients aged 57.1 ± 21.1 years. More than three quarter (82%) of the patients exhibited decreased chest movement and expansion and 64% had mediastinal shifting. The chest was stony dull on percussion (98.0%). twenty percent of the patients exhibited signs of tenderness. In this study maximum number of patients belonged to 31 to 60 years of age (72.0%). Incidence was found lower before 20 years (2%) which is more or less similar to another study.[11] In 74.0% of cases breath sound was absent and vocal resonance decreased while in 18.0% of the cases added sound was heard. Around 54.0% of the patients had right-sided pleural effusion, 40.0% left-sided and 6% had bilateral. Patchy opacities with cavitary lesions was found in 16.0%, and mass lesion with irregular

margin in 14.0% 0f patients.

AFB was found in the pleural fluid in 2 cases of tubercular pleural effusion. Malignant cell was found in the pleural fluid in 1(8.5%) case of malignant pleural effusion. Gram positive organism was found in 40% cases of pneumonic pleural effusion.[11] Pleural effusion may occur in any pulmonary fungal infection and it usually mimics tuberculosis clinically, radiologically and in the features of the pleural fluid. It may occur as a usually self-limiting process together with fever and malaise, in the primary infection or as a more intractable illness in association with rupture of a lung focus in post primary or disseminated disease. Pleural effusion may occur in association with coccidiodomycosis, blastomycosis and rarely in histoplasmosis, cryptococcosis and other fungal infection. It is an occasional complication of invasive or disseminated aspergillosis and has been described very rarely in allergic aspergillosis.[18]

Tuberculosis was the most common cause of exudative pleural effusion and among 50 cases of effusion 30 were due to tuberculosis (60.0%). Malignancy was found as the 2nd common cause of exudative pleural effusion (24.0%). Of the malignant cases, 11 had bronchial carcinoma & 1 lymphoma. Pneumonia was found as the 3rd common cause of exudative pleural effusion (10.0%). The remaining 3 patients had other causes of exudative pleural effusion which included Rheumatoid arthritis (01) and non-specific (02). Subphrenic infection, usually due to a perforated abdominal viscus, may spread up through the diaphragm. The effusion initially contains polymorphs but no organism. If untreated it may progress to empyema. Diagnosis is aided by the presence radiologically of gas under the diaphragm. The usual organisms are coliforms, *Streptococci* and *clostridia*[8]. When pleural effusion occurs with an episode of acute pancreatitis, it is usually small and self-limited14. Although the effusion may be bilateral or right sided, the majority is left sided. The predilection for the left side is described to the fact that pancreatic lymphatics are just apposed to the left hemidaphragm[15]. Acute pancreatitis may lead to pleural exudate, probably by transmission of the inflammation through the adjacent diaphragm and of the fluid through diaphragmatic lymphatics. The fluid is characterized by high amylase levels, often higher than in the serum. A pancreatic pleural effusion is defined as fluid accumulation in the thorax with a high amylase content resulting from a disrupted pancreatic duct. It is said that in adult the cause of most pancreatic duct disruption is chronic relapsing pancreatitis. It may also result from trauma[13]. Alcohol is the most common cause of chronic relapsing pancreatitis. Effusion is mainly left sided in pancreatitis. The pleural effusion is bloody in many cases with a very high amylase level always exceeding the serum amylase level, the protein content also increases. Here it is also associated with increased incidence of pseudocyst formation.

Although the list of causes of exudative pleural effusion is extensive, the great majority of the cases are caused by pneumonia malignancy and tuberculosis in developed countries in contrast to developing countries like Bangladesh, where tuberculosis is a major cause. Analysis of aspirated pleural fluid and pleural biopsy is essential for diagnosis the etiology of exudative pleural effusion.

Conclusion

Tuberculosis is the commonest etiology of exudative pleural effusion in this series and malignancy being the second leading cause. Some effusions remain unexplained despite extensive tests. Pleural effusion is found more common in male. Haemorrhagic pleural effusion may occur in tuberculosis. So by observing the colour of pleural fluid only, we cannot gaze the etiology of exudative pleural effusion. A systemic approach to pleural effusion will generally results in a specific diagnosis and help to guide therapy. In the light of the findings of the present study and discussion thereof, the following recommendations are put forward. All those interested in pleural diseases should determine the etiologic pattern of exudative pleural effusion using as less invasive diagnostic aids as possible. Further studies are needed to evaluate the utility of the procedures presently being used to come to a diagnosis of pleural effusion.

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Conflict Of Interest
The authors have no conflicts of interest to disclose.

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Authors' contributions
Mohith MT, Rahman MZ conceived and designed the study, analyzed the data, interpreted the results, and wrote up the draft manuscript. Zannat T, Ansary AMAA contributed to the analysis of the data, interpretation of the results and critically reviewing the manuscript. Syed M, Kamal M involved in the manuscript review and editing. All authors read and approved the final manuscript.

Data Availability
Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the

corresponding author on reasonable request.

Ethics Approval and Consent to Participate
Ethical approval for the study was obtained from the Institutional Review Board. As this was a prospective study the written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

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