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Research Article

Clinical Profile of Parapneumonic Effusion and Empyema at a Tertiary Center in Western India -"Changing Behavior of Microorganisms in Superbug Era"

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Abbreviations CAP: Community Acquired Pneumonia; HAP: Hospital Acquired Pneumonia; VAP: Ventilator Acquired Pneumonia; MRSA: Methicillin-Resistant Staphylococcus Aureus; ICD: Intercostal Drain; ICU: Intensive Care Unit; AFB: Acid Fast Bacilli; ACCP: American College Of Chest Physician; COPD: Chronic Obstructive Pulmonary Disease; MICU: Medical Intensive Care Unit; HIV: Human Immunodeficiency Virus; GPC: Gram Positive Cocci; GNB: Gram Negative Bacteria; WHO: World Health Organization; TPA: Tissue Plasminogen Activator

Abstract

Pleural effusion associated with bacterial pneumonia, lung abscess, or bronchiectasis is a parapneumonic effusion. An empyema is pus in the pleural space. The morbidity and mortality in patients with parapneumonic effusion are higher than in patients with pneumonia alone.

It is a cross-sectional observational study of 50 cases with parapneumonic effusion and empyema coming to tertiary care center, previously diagnosed outside or diagnosed on arrival over a period of 2 years (August 2014 - September 2016) with the aim to study their clinical profile.

In the present study, we found that patients have varied clinical symptoms mimicking pneumonia. Among cases from all age group studied, 66% (n-33) had CAP, 30% (n-15) had HAP and 4% (n-2) had VAP. Patients with comorbidities, tobacco and alcohol intake were more prone for developing the disease. 42% (n-21) had complicated parapneumonic effusion and 10% (n-5) had empyema. The overall cure rate was 80% (n-40); surgery was required in 4% (n-2) of patients while 12% (n-6) succumbed during the disease course. We found that 9.1% deaths incurred in patients of CAP whereas death amongst HAP were up to 13.3%. Mortality was highest amongst patients of VAP with parapneumonic effusion. Culture positive pleural fluid grew the following microorganisms- Acinetobacter baumannii (2%), Escherichia coli (2%), Methicillin-resistant Staphylococcus aureus (4%), Pseudomonas aeruginosa (4%), Peptostreptococcus (2%) with multidrug resistance pattern.

The important factors related to poor outcome amongst complicated pleural effusions were mixed bacterial infection with multidrug resistance, poor response to higher antibiotics, presence of bacteraemia and septic shock.

Introduction

Pleural effusion associated with bacterial pneumonia, lung abscess, or bronchiectasis is a parapneumonic effusion [1]. An empyema, by definition is pus in the pleural space. Approximately 60% of empyemas are parapneumonic, whereas 20% arise after thoracic surgical procedures, and the remaining 20% arise as complications of various conditions, such as thoracic trauma, esophageal perforation, thoracentesis, and sub-diaphragmatic infection [2]. The term complicated parapneumonic effusion was developed to refer to parapneumonic effusions that require tube thoracostomy for their resolution [3].

The annual incidence of bacterial pneumonia in the United States is estimated to be 4 million [4]. Approximately 20% to 40% of patients hospitalized with bacterial pneumonia have an accompanying pleural effusion [5,6]. The morbidity and mortality in patients with pneumonia and pleural effusion are higher than in patients with pneumonia alone. In one study of patients with community-acquired pneumonia, the relative risk of mortality was 7.0 times higher for patients with bilateral pleural effusions and 3.4 times higher for patients with unilateral pleural effusions of moderate or greater size than for those without effusions [7].

The most recent comprehensive report on the bacteriology of complicated parapneumonic effusions comes from the large trial of intrapleural streptokinase in the United Kingdom. Overall, a microbiologic diagnosis was obtained in 320 patients (74%). In patients with community-acquired pneumonia, the organisms most commonly responsible were Streptococcus intermedius-anginosus-constellatus (milleri) group (80), *S.pneumoniae* (71), other streptococcus species (25), *S.aureus* (34) (7 Methicillin-Resistant Staphylococcus Aureus (MRSA)), gram-negatives (29), and anaerobes (67). In patients with hospital-acquired parapneumonic effusions, the most common organism was *S.aureus* (21) of which 15 were MRSA [8].

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Patients with aerobic bacterial pneumonia and pleural effusion present as acute febrile illness consisting of chest pain, sputum production, and leukocytosis. The incidence of pleuritic chest pain and the degree of leukocytosis are comparable whether or not there is an accompanying pleural effusion [9]. Patients with anaerobic bacterial infections involving the pleural space usually present with a subacute illness, appear more ill and usually have a history of aspirations, alcoholism, and poor oral hygiene.

Due to highly variable environmental factors, diagnostic approach, population density, microbiological variants and emerging drug resistance pattern this study was being taken up to analyze the clinical profile in Indian population diagnosed with parapneumonic effusion and empyema.

Material and methods

Study subjects

It is a cross-sectional observational study of 50 cases of parapneumonic effusion and empyema coming to Bharati Hospital, Pune (Maharashtra), India previously diagnosed outside or diagnosed on arrival irrespective of their treatment status. We excluded all cases of effusions and empyema which stained or grew acid fast bacilli and patients below age of the 18 years. Informed written consent was obtained from the patient/relatives prior to enrolling in the study and this study was approved by the institutional ethical committee.

Study design

50 cases of parapneumonic effusion and empyema were studied over 2 years (August 2014 - September 2016). 2 cases were excluded from final analysis as they were discharged against medical advice. Our aim was to analyze the clinical profile of parapneumonic effusion and empyema at our tertiary care center. In the present study, we tried to correlate between microbiological, histopathological (if done) reports with clinical features and find the outcome of the disease. Use of adjunctive therapy as an Intercostal Drain (ICD) and intrapleural fibrinolytic in the management of parapneumonic effusion and empyema were also studied.

Methods

The information of all cases was collected using a structured questionnaire and information entered in computer software for analysis. The demographic details of patients, clinical symptoms, comorbidities, ICD insertion, Intensive Care Unit (ICU) stay and surgeries were also recorded. Biochemical testing of pleural fluid was used to distinguish between exudative and transudative fluid using Light's criteria [10] and all the pleural fluid samples were stained with gram stain, AFB (Acid Fast Bacilli) stain and were subjected to cultural isolation.

We classified and graded parapneumonic effusion and empyema based on Light's [11] and American College of Chest Physician (ACCP) [12] criteria.

Parapneumonic effusions were graded and grouped into three groups namely:-

1. Uncomplicated parapneumonic effusion
2. Complicated parapneumonic effusion
3. Empyema Thoracis.

Various forms of pneumonia were classified and grouped as below:

1. Community Acquired Pneumonia (CAP)
2. Hospital Acquired Pneumonia (HAP)
3. Ventilator Acquired Pneumonia (VAP)

Severity scoring of CAP was done using CURB-65: Confusion (based upon a specific mental test or new disorientation to person, place, or time), Urea (blood urea nitrogen in the United States) >7 mmol/L (20 mg/dL), Respiratory rate ≥30 breaths/minute, Blood pressure (BP; systolic <90 mmHg or diastolic ≤60 mmHg), Age ≥65 years.

Bedside ultrasound was used to guide thoracentesis whenever required. Intrapleural fibrinolysis was done using streptokinase instillation whenever indicated. Surgical drainage and decortication was done whenever required.

Lastly, various variables in this study were ultimately correlated with the outcome of the study.

We grouped the outcome of the study in three groups namely:

1. Cured
2. Patients requiring surgery
3. Death.

Statistical Analysis

The type of data is quantitative and qualitative. The relevant clinical, microbiology and long-term outcome data collected was summarized into tables and graphs and was analyzed using Microsoft Excel and SPSS (Version 20.0) software with help of biostatician whenever required. Nominal data such as demographic data and symptoms were presented as frequency (n) and percentage (%). Bivariate analyses were conducted using the Chi-squared or Fisher's exact test where appropriate. A p-value <0.05 was considered statistically significant in all analyses.

Results

50 cases of parapneumonic effusion were included in this study; however, only 48 cases were included in the final analysis as 2 were discharged against medical advice. In the present study, the overall cure rate was 80% (n-40), surgery was required in 4% (n-2) of patients while 12% (n-6) succumbed during the disease course.

In the present study we found that the occurrence of parapneumonic effusion was observed in all the adult age groups without any gender preference as shown in (Figure 1).

Patients with parapneumonic effusion had a fever as the most common presenting symptom followed by dyspnoea as occurs in the case of pneumonia. Chest pain as presenting feature was observed in only 14% (n-7) of patients as shown in (Figure 2).

Commonly associated comorbidities with parapneumonic effusion and empyema were diabetes, hypertension, kidney diseases, old pulmonary tuberculosis, COPD (Chronic Obstructive Pulmonary Disease), ischemic heart diseases. In the present study, 60% (n-30) of the patients had multiple comorbidities associated with parapneumonic effusion.

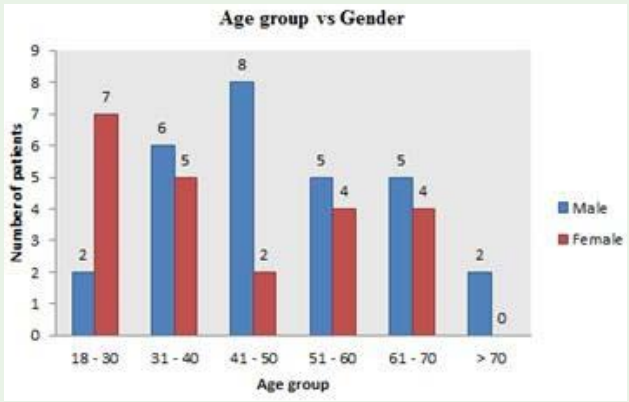

Figure 1: Age and gender distribution of parapneumonic effusion and empyema.

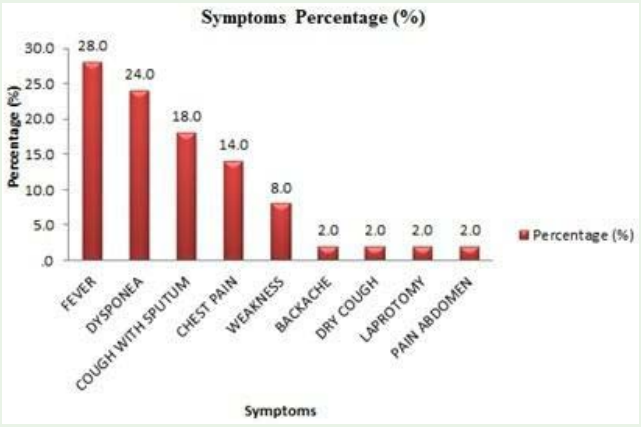

Figure 2: Distribution of clinical symptoms in parapneumonic effusion and empyema.

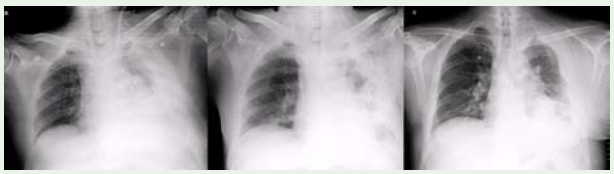

Figure 3: The sequelae of empyema with decortication and resolution in a patient.

Table 1: CAP/HAP/VAP associated pleural effusions and outcome.

Types of Pneumonia	Outcome			Total
	Cured	Death	Surgery	
CAP	87.50% (n-28)	9.38% (n-3)	3.13% (n-1)	n-32
HAP	78.57% (n-11)	13.3% (n-2)	6.7% (n-1)	n-14
VAP	50.0% (n-1)	50.0% (n-1)	0.0% (n-0)	n-2
Total	n-40	n-6	n-2	n-48

CAP: Community Acquired Pneumonia; HAP: Hospital Acquired Pneumonia; VAP: Ventilator Acquired Pneumonia; n: Number in frequency

Fisher's extract test used, *p*-value: 0.0331

Table 2: Grades of pleural effusion and outcome.

Grades of Pleural effusion	Outcome			Total
	Cured	Death	Surgery	
Complicated	65.0% (n-13)	25% (n-5)	10% (n-2)	n-20
Empyema	80.0% (n-4)	20% (n-1)	0.0% (n-0)	n-5
Uncomplicated	100% (n-23)	0.0% (n-0)	0.0% (n-0)	n-23
Total	n-40	n-6	n-2	n-48

n: Number in frequency.

Fisher's extract test used, *p*-value: 0.011

We found that amongst patients of parapneumonic effusion and empyema, 66% (n-33) had Community-Acquired Pneumonia (CAP), 30% (n-15) had Hospital-Acquired Pneumonia (HAP) and 4% (n-2) had Ventilator Associated Pneumonia (VAP). The outcome of the study related to the type of pneumonia and associated effusions is shown in (Table 1).

In the present study, we found that there were 42% (n-21) cases of complicated parapneumonic effusion, 48% (n-24) of uncomplicated and 10% (n-5) of empyema cases. The outcome was best amongst patients suffering from uncomplicated effusion. The cure rate was 100% (n-23) in our study amongst uncomplicated effusion group. 25% (n-5) of patients among complicated effusion group died though cure rate was observed in up to 65% (n-13) in this group. The same group also required surgery in 10% (n-2) of patients as treatment. Patients with empyema had a cure rate of 80% (n-4) while the mortality was noticed in up to 20 % (n-1) as shown in (Table 2) below.

Patients with complicated effusion (n-11) and empyema (n-5) required ICD insertion. Longer ICU hospitalization was required in patients with complicated effusion (n-10) and empyema (n-4.) The disease outcome amongst patients who required ICD insertion and longer ICU stay is summarized in (Table 3) and (Table 4) below.

CURB-65 scoring remains a good tool for severity scoring in CAP higher scoring was associated with worse outcome (Surgery and death) in the present study.

In present study, the sequelae of empyema with decortication and resolution in a patient is illustrated in (Figure 3).

The microbiological yield obtained in our study from various body fluids and sputum sample are summarized in (Table 5).

Table 3: ICD insertion and outcome.

ICD insertion		Outcome			Total
		Cured	Death	Surgery	
ICD	Yes	68.75% (n-11)	25.0% (n-4)	6.25% (n-1)	n-16
	No	90.63% (n-30)	6.25% (n-2)	0.00% (n-0)	n-32
Total		n-41	n-6	n-1	n-48

ICD: Intercostal Drain; n: Number in frequency

Fisher's extract test used, *p*-value: 0.107

Table 4: ICU stay and outcomes.

ICU Stay		Outcome			Total
		Cured	Death	Surgery	
ICU Stay	Yes	60.0% (n-9)	26.67% (n-4)	13.33% (n-2)	n-15
	No	93.94% (n-31)	6.06% (n-2)	0.00% (n-0)	n-33
Total		n-40	n-6	n-2	n-48

ICU: Intensive Care Unit; n: Number in frequency

Fisher's extract test used, *p*-value: 0.008

Table 5: Distribution of microorganisms isolated from various body fluids.

Microorganism grown	Pleural Fluid	Sputum	Blood	Urine	Bronchoalveolar Lavage (BAL)
Acinetobacter baumannii	1	0	1	0	1
Escherichia coli	1	1	0	4	1
MRSA	3	1	2	0	0
Pseudomonas aeruginosa	2	1	2	0	0
Peptostreptococcus	1	0	0	0	1
Klebsiella pneumoniae	0	2	0	0	1
Streptococcus pneumoniae	0	1	0	0	0
Enterococcus	0	0	2	0	0
Trichosporon	0	0	0	1	0

Among CAP-Most common organism isolated - *Streptococcus Pneumoniae*

Among HAP-Most common organism isolated- *Methicillin-Resistant Staphylococcus Aureus (*MRSA)

Among VAP-Most common organism isolated- *Pseudomonas Aeruginosa*

MRSA was commonest with associated Bacteremia and Sepsis.

Discussion

A prospective observational study was carried out in the department of Pulmonary Medicine, Bharati hospital and research center, Pune, Maharashtra, India to study the clinical profile of patients with parapneumonic effusion and empyema.

In this study, age and sex distribution is varied and has no predilection for the parapneumonic effusion and empyema. No recent studies have been conducted that relate age and sex with the patients of parapneumonic effusion and empyema though pneumonia in elderly is commonly found worldwide.

In this study it was observed that fever (28%) and dyspnoea (24%) are the most common clinical manifestations followed by cough (18%), chest pain (14%) and generalized weakness (8%).These were often found in combinations.

In the present study, it was found that around 30 percent of patients had various comorbidities. We observed that the comorbidities associated with parapneumonic effusion were often times present as combinations of diabetes, hypertension, kidney diseases, old pulmonary tuberculosis, COPD. Diabetes (18%) and hypertension (26%) were found to be most common comorbidities in our study. There were 8% of neoplasm and 4% of HIV associated parapneumonic effusion and empyemas. We also observed in our study that around 21% of patients had addictions in mixed form as alcohol (28%), tobacco chewing (16%) and smoking (8%) though we could not associate these addictions with the disease outcome.

Falguera M et al [13] in 2011 conducted a similar study about predictive factors, microbiology, and outcomes of patients with parapneumonic effusions and found that smoking (68%) and alcoholism (40%) was associated with patients of parapneumonic effusion and empyema secondary to community-acquired pneumonia (p-value <0.001). In comparison, it was about 8% of smoking and 28% of alcoholism in the present study. In the same study, he related diabetes, COPD, chronic renal disease, neoplasm, HIV as associated comorbidities which were also found in our study.

In the present study, among various types of pneumonia associated with parapneumonic effusion and empyema the number patients with community-acquired pneumonias were highest (66%). On relating it to the outcomes of the study, we found that 9.1% deaths incurred in patients of CAP whereas death amongst HAP were up to 13.3%. Mortality was highest amongst patients with VAP and parapneumonic effusion. There were 2% patients with post-abdominal surgery for acute pancreatitis, who developed HAP and subsequent septicemia had a poor outcome.

We related the types of parapneumonic effusion and empyema with disease outcome and observed that mortality is highest amongst complicated parapneumonic effusion and empyema 23% (n-6/26) as compared to uncomplicated parapneumonic effusion (0%). The mortality rate in patients with complicated parapneumonic effusion and empyema who required ICU stay in our study was 28.3%. In a similar study by Chih-Yen Tu et al [14] the infection-related mortality rate of complicated parapneumonic effusions or empyemic patients in the MICU was 41% (n-32/78).

Microbiology

In the present study, the mixed infection with Gram-Positive Cocci (GPC) and Gram-Negative Bacteria (GNB) was found quite high in our study which stained sputum (50%) as well pleural fluid smears (16%). We found that pleural fluid positivity on gram staining was less compared to sputum. On relating the sputum and pleural fluid Gram stains with the outcome of the present study, we found that mortality in patients with mixed infections of GPC and GNB was statistically significant (p<0.05).

In the present study, the culture positive pleural fluid grew the following microorganisms - Acinetobacter Baumannii (2%), Escherichia Coli (2%), Methicillin-Resistant Staphylococcus Aureus (4%), Pseudomonas Aeruginosa (4%), Peptostreptococcus (2%) with multidrug resistance pattern which falls in high and critical categories of the WHO latest list of antibiotic-resistant "priority pathogens" that pose the greatest threat to human health. These organisms pose a particular threat in hospitals, nursing homes, and among patients whose care requires devices such as ventilators and blood catheters. They can cause severe and often deadly infections such as bloodstream infections and pneumonia. These bacteria have become resistant to a large number of antibiotics, including Carbapenems and third-generation Cephalosporins - The best available antibiotics for treating multidrug-resistant bacteria [15].

In most series of patients with community-acquired empyema, aerobic bacteria predominate which includes Streptococcus Pneumoniae and Staphylococcus Aureus. Aerobic organisms also include Gram-negative bacteria such as Escherichia coli, Haemophilus Influenza and Klebsiella Pneumonia [16]. Mixed aerobic and anaerobic bacteria are commonly isolated from empyema. The commonest anaerobes are Bacteroides Fragilis [17]. In the United Kingdom bacteria commonly isolated from hospital-acquired empyema include Staphylococci, Enterobacteria, Enterococci and Pseudomonus Aeruginosa [18].

Our microbiological yield was less as compared to a similar microbiological study by Brook I et al [19] which focused on empyema stated that mixed aerobic and anaerobic bacteria are commonly isolated from empyema.

The low yield of pleural fluid and sputum culture positivity is one of the limitations of this study. This could be attributed to prior antibiotic use as this study was conducted in a tertiary care hospital. Mortality was high amongst patients with bacteremia/septicemia 50% (n-3/6).

Management

In the present study, it was found that 58% of all patients required combinations of higher antibiotics during the course of treatment. Mortality was also high (n-6/6) in this group of patients, which is statistically significant (p-value <0.05). The choice of antibiotics was in accordance with our hospital antibiotic policy.

We found that patients with parapneumonic effusion and empyema who required ICD insertion 34% (n-17) and patients who had streptokinase instillation as adjunctive treatment along with ICD 14% (n-7) had better outcomes which were statistically significant ($p<0.05$).

In a similar study by Davies RJO et al [20], it was shown that streptokinase improves the catheter drainage of such pleural collections in terms of increased pleural fluid flow and improvement in the chest radiograph by discharge from the hospital. This benefit was achieved without significant systemic fibrinolysis and was not associated with local or systemic hemorrhage.

We encountered fever and pain as systemic and local adverse effect of streptokinase instillation which was managed conservatively. Hemorrhage either in local or systemic form was not encountered in the present study.

Studies of Jerjes-Sánchez C et al [21] and Temes RT et al [22] in 1996 showed the improved outcomes of chest drainage with intrapleural fibrinolytics (eg: Streptokinase, Urokinase, and Tissue Plasminogen Activator (TPA)).

Conclusions

Parapneumonic effusions can complicate the course of pneumonia with variable disease outcomes. Newer rapid microbiological diagnostic testing for better yield from respiratory samples are required with a multidisciplinary approach for early diagnosis and prevention of morbidity and mortality associated with parapneumonic effusions and empyema.

Larger epidemiological studies can aid to study in detail about the demographic factors and microbiological profile of cases with parapneumonic effusion and disease outcome with changing behavior of the deadly microorganisms in the present world.

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