International Journal of Clinical Trials
Arivudainambi VP. Int J Clin Trials. 2017 Nov;4(4):176-183
http://www.ijclinicaltrials.com
pISSN 2349-3240 | eISSN 2349-3259
DOI: http://dx.doi.org/10.18203/2349-3259.ijct20174208

Original Research Article

Outcome and mortality analysis in complicated parapneumonic effusion and empyema

Arivudainambi Veerappan Periasamy*

KAPV and MGM Medical College Hospital, Trichy, Tamil Nadu, India

Received: 28 August 2017
Revised: 16 September 2017
Accepted: 18 September 2017

***Correspondence:**
Dr. Arivudainambi Veerappan Periasamy,
E-mail: arivudain@yahoo.com

ABSTRACT

Background: Pleural infection is a clinical problem with high mortality and morbidity; 20% of patients with empyema die and approximately 20% require surgery to recover within 12 months of their infection. Studies on pleural infection and their outcome are relevant in developing a scoring system by which failing cases and cases at risk of death can be identified.
Methods: The study is retrospective analysis of patient cohort admitted to the tertiary care institute from the period of July 2014 to July 2016 to determine the prognostic factors in the outcome of pleural space infection. The study included all complex, complicated parapneumonic effusion and empyema including tuberculosis above the age of fifteen years. The primary end of the present study was the success or failure. Possible predicting factors for the success or failure of therapy were assessed against this end. Pearson chi square test, $\chi 2$ (Fisher's exact test when needed) test was used for discrete data. Logistic regression analysis was applied to adjust for confounding variables to assess the possible predicting factors. Survival plot and analysis using Kaplan Meier method was used.
Results: 220 with parapneumonic effusion and empyema were analyzed. Successful outcome was seen in 107 and 113 had failed outcome. Mortality was 30.50%. By logistic regression method the odds of failed outcome were high with diabetes, hypoalbuminemia, loculation, tuberculosis which can predict the outcome especially complicated and complex parapneumonic effusion, empyema ($p<0.05$).
Conclusions: Diabetes, hypoalbuminemia, loculation, tuberculosis should be used in the prediction scoring system.

Keywords: Empyema, Complicated parapneumonic effusion, mortality, Outcome, Diabetes, Loculation

INTRODUCTION

Pleural infection is a clinical problem with annual incidence of up to 80,000 cases in the western world. Mortality and morbidity is high; 20% of patients with empyema die and approximately 20% require surgery to recover within 12 months of their infection.[1,2]

Despite the advent of effective antibiotics, bacterial pneumonia still results in significant morbidity and mortality in the population. In one study of 1,424 patients hospitalized with community-acquired pneumonia, patients with pleural effusions were 2.7 times more likely to be treatment failures than were those without pleural effusions.[3]

In another study, the relative risk of mortality in patients with community-acquired pneumonia was 7.0 times higher for patients with bilateral pleural effusions and 3.4 times higher for patients with unilateral pleural effusion of moderate or greater size as compared with other patients with community acquired pneumonia alone.[4]

Most pleural effusions associated with pneumonia resolve without any specific therapy directed toward the pleural fluid, but approximately 10% of patients require

operative intervention. Delay in instituting proper therapy for these effusions is responsible for some of the morbidity associated with parapneumonic effusions.[5]

For a simple parapneumonic effusion antibiotics according to culture and sensitivity will suffice. In complicated parapneumonic effusion and empyema intervention in the form of thoracentesis, tube thoracostomy, thoracoscopic intervention, surgery will be needed accordingly. Studies on pleural infection and their outcome are relevant in developing a scoring system by which failing cases and cases at risk of death can be identified.

Empyema thoracis (ET) or pyothorax is the inflammatory process of infection in pleural space causing the accumulation and organization of purulent material in the pleural space1; first reported by Hippocrates approximately 2400 years ago.[6] According to the American Thoracic Society, the ET process can be divided into three phases: (1) exudative (acute or Stage I), where exudative fluid accumulates without loculation; (2) fibrinopurulent (Stage II), where pleural fluid becomes turbid or purulent with loculation; and (3) organizing (chronic or Stage III), where thickened pus or fibrin peels begin to form, and granulation tissue replacement of the pleural space occurs.[1,2] The most common form of ET both in adults and children is attributable to parapneumonic effusion followed by complications of thoracic surgical procedures, such as esophageal surgery, cardiovascular surgery, and pulmonary surgery.[7-10] ET incidence is gradually increasing despite the advancements in the antibiotic treatment era. Mortality and morbidity varies between 3% and 33%.[10-13] The most important issue to prevent morbidity or mortality is the prevention of disease progression and adequate aggressive treatment. ET carries many complications such as sepsis, respiratory failure, lung collapse, broncho-pleural fistula (BPF), or gastropleural fistula. These complications should be a concern for prognosis as well as quality of life.[14]

Aim of the study

To determine the prognostic factors implied in the outcome of pleural space infection chiefly complicated and complex parapneumonic effusion and empyema admitted from period of June 2014 to June 2016 in tertiary care respiratory institute Trichy KAPV medical college and MGM Hospital, Trichy. It was hypothesized that there could be clinical, laboratory and biochemical prognostic factors determining the outcome of parapneumonic effusion that if identified at the optimal period would result in reduction in morbidity and mortality associated with parapneumonic effusion. This study was aimed at identification of such determinants which could form a model for scoring system in the outcome and mortality analysis.

METHODS

The study is retrospective analysis of patient cohort admitted to the tertiary care institute from the period of July 2014 to July 2016.

Inclusion criteria

Inclusion criteria were all patients with parapneumonic effusion admitted to the institute above age of fifteen years; all complicated parapneumonic effusion; all complex parapneumonic effusion; all patients diagnosed as empyema; tuberculous pleural effusion included (drug susceptible cases only included).

Exclusion criteria

Exclusion criteria were all patients with effusion of other causes like trauma, iatrogenic causes, pediatric parapneumonic effusion, all patients with HIV coinfection, all fungal and viral, unknown, malignant effusion and effusion due to connective tissue disorders.

Definitions

1. *Parapneumonic effusion*

Any pleural effusion associated with bacterial pneumonia, lung abscess, or bronchiectasis is a parapneumonic effusion.[15]

2. *Empyema*

An empyema, by definition, is pus in the pleural space.

Empyema as pleural fluid with a specific gravity greater than 1.018, a WBC count greater than 500 cells/mm^3, or a protein level greater than 2.5 g/dl- weese.16 Vianna 17 defined an empyema as pleural fluid on which the bacterial cultures are positive or the WBC is greater than 15,000/mm^3 and the protein level is above 3.0 g/dl.

The term empyema- pleural effusions with thick, purulent appearing pleural fluid. Successful closed-tube drainage of a complicated parapneumonic effusion is associated with improvement in the clinical and radiologic status of the patient within 24 to 48 hours.

3. *Tuberculous empyema*

Empyema with diagnosis of TB by pleural biopsy of caseating granuloma or ADA level >40 units or lymphocytes to polymorph ratio greater than 0.75.

Outcome definition

Success: In complicated parapneumonic effusion it is defined as absolute drainage of the effusion or improvement in sepsis syndrome (fever and leukocytosis)

after 2 weeks of appropriate antibiotics in accordance with culture and sensitivity.

Failure: Defined as incomplete drainage with failure of resolution of septic symptoms (fever, leukocytosis) or a fatal outcome.

Patients characteristics studied such as

1) Age.
2) Sex.
3) Co-morbid illness like diabetes mellitus, alcoholic liver diseases.
4) Blood glucose.
5) Pleural fluid biochemical parameters such as pH, glucose, culture and staining characteristics, leukocyte count.
6) Symptoms such as fever.
7) Other characteristics such as fibrin peel on thoracoscopy and imaging evidence of loculation, serum protein (albumin), total WBC count were taken up for analysis.
8) Time to death in days recorded in cases died of empyema.

Chest tube was inserted fulfilling the above criteria by surgeon/pulmonary physician. pH was measured using blood gas analyzer. Hypoalbuminemia first appearing after 2 weeks of antibiotic was considered for analysis. The patients were followed for the period of 28 weeks from their admission to the hospital.

For the empyema, all patients were admitted to the hospital. Pus or exudative fluid culture was done in all cases at the date of admission. Empirical antibiotic was administered to all cases while waiting for culture results, and then adjusted according to antibiotic sensitivity. Intercostal tube drainage was performed in all cases. If signs and symptoms did not improve, and if loculated empyema was suspected by CXR or CT after chest tube insertion, a surgical procedure was indicated, either video-assisted thoracoscopic surgery (VATS) or open thoracotomy for drainage or decortication, depending on the stage of the disease. Intrapleural fibrinolytic therapy was not performed in this cohort. A persistent pleural space was evaluated either intraoperatively or postoperatively using CXR. If pleural space was still seen in postoperative CXR 1 week after the procedures, or if the lung was not fully expanded when applying positive pressure via the endotracheal tube in the perioperative period, it was defined as persistent pleural space. The duration of antibiotic administration depended on the primary source of disease. Chest drain was removed if the content drainage was clear, had no pus, no fresh blood, no air leak, and <100 ml/d of fluid was recorded. All patients were followed and evaluated for clinical symptoms, and had a CXR at the thoracic surgery clinic 2 weeks and 3 months after surgery, and then every 6 months. Pus or exudative pleural fluid was taken by ultrasound or CT- guided thoracentesis. Empirical antibiotic was administered while waiting for culture results, and then adjusted according to antibiotic sensitivity. Thoracotomy for decortication or thoraco-plasty was performed depending on the stage of the disease, the thickness of pleural peel, and the size of remaining persistent pleural space.

Statistical analysis

Determinants (clinical, laboratory, and physical) of outcome in pleural space infection especially complicated and complex parapneumonic effusion, empyema was determined. Outcome was defined as success and failure.

Univariate analysis of the variables done using Chi-square test and likelihood ratio, Fisher exact test.

The primary end of the present study was the success or failure of CPE and empyema treatment. Possible predicting factors for the success or failure of therapy were assessed against this end. Pearson chi square test, $\chi 2$ (Fisher's exact test when needed) test was used for discrete data. Logistic regression analysis was applied to adjust for confounding variables to assess the possible predicting factors. All reported p values are two tailed, and a $p<0.05$ was statistically significant. SPSS 21 was used for analysis. Survival plot and analysis using Kaplan Meier method was done. We had done analysis of variables with respect to outcome and mortality so that study can also be viewed as variables predicting the outcome and mortality.

RESULTS

Two hundred and twenty patients (N=220) with parapneumonic effusion and empyema were analyzed during the study period.in the study. The Mean age in the study was 46.26, the mean pleural fluid pH was 6.7, mean pleural fluid protein was 3.587, mean WBC count in pleural fluid is 9058.56 (Table 1). Mean time to death in days was 13.554 (Table 1).

Mortality was sixty-seven (N=67). Mortality was 30.50%, alive patients at the end of the study were one hundred and fifty-three (N=153). Various causes of parapneumonic effusion in the study were pneumonia-105, lung abscess-14, bronchietasis-16, tuberculosis-85 (Table 2).

Results with outcome predictors

In two hundred and twenty patients with complicated and complex parapneumonic effusion, empyema under tube thoracostomy there was successful outcome in one hundred and seven patients (N=107). One hundred and thirteen (N=113) patients with CPE had failed outcome (Table 2). The cross tabulation showed that successful outcome in 107 cases (48.6%) and failed outcome in 113 cases (51.4%). The finding of 67 deaths in 113 failed cases of complicated parapneumonic effusion and empyema showed the lethality of the disease (Table 2).

Table 1: Descriptive analysis of continuous data.

Variables	N	Range	Minimum	Maximum	Mean	Standard deviation
Age	220	46.00	24	70	46.26	10.71
pH	220	6.7	3.1	9.8	6.70	1.21
Pleural fluid protein	220	5	2.9	7.9	3.5870	0.708
Time to death days	67	71	1	72	13.554	11.03
Pleural fluid WBC count	220	16710	1330	18040	9058	3623.724

Table 2: Cross tabulation of outcome and mortality.

Outcome	Death		Total [%]	P value
	Alive [%]	Death [%]		
Failure	46 [20.9]	67 [30.5]	113 [51.4]	0.000
Success	107 [48.6]	0 [0]	107 [48.6]	0.000

Table 3: Univariate analysis of variable in the outcome of complicated parapneumonic effusion and empyema.

Variables	Outcome		P value; Chi square value	P value (Fischer exact test)
	Success	Failure		
Pus (N=93)	32	61	0.00; 13.054	0.00
Diabetes mellitus (N=44)	3	41	0.00; 38.501	0.00
Serum albumin <3 gm (N=126)	33	93	0.00; 59.477	0.00
Tuberculosis (N=85)	31	54	0.004; 8.277	0.006
Male (N=175)	83	92	0.48	0.52
Female (N=45)	24	21	0.48	0.52
Loculation present (N=119)	32	87	0.00; 49.065	0.00
Liver failure/cirrhosis (N=15)	1	14	0.002; 16.361	0.003
Fever after first week (N=134)	49	85	0.00	0.00
Stain/culture positive(N=95)	49	46	0.44	0.49
pH <7.2 (N=91)	22	69	0.00; 31.170	0.00

Chi-square test: The values of p=0.000 for diabetes mellitus, p=0.000 for pus, p=0.000for hypoalbuminemia, p=0.004 for tuberculosis, p=0.00 for loculation, p=0.002 for liver failure, p=0.000 for pH <7.0. Univariate analysis of factors by Chi-square test showed significant results for the above variables with respect to outcome (Table 3).

Results with mortality predictors

The following are the significant results of Univariate analysis of factors by Chi-square test with respect to death in complicated parapneumonic effusion and empyema.

Chi-square test: Significant p values for variables with respect to death were p=0.000 for diabetes, p=0.000 for hypoalbuminemia, p=0.000 for loculation, p=0.000 for liver failure, p=0.000 for pH<7.0 (Table 4).

Binary logistic regression analysis using enter and backward conditional methods was applied for significant variables found in univariate analysis for outcome and mortality. The mortality model did not have a good fit and hence not reported. The following are discussion of the binary logistic regression of the outcome variables.

Overall percentage of prediction of the model is 78.2, hence the binary logistic results in this study could be considered valid (Table 5).

These values show good fitness of the model. Hosmer and Lemeshow test had value of p=0.145 establishing a good model (Table 6).

Cox and Snell R^2 and Nagelkerke R^2: These are pseudo R^2 their values were 0.434 and 0.579 showing good model and fit (Table 7).

Binominal logistic regression: Binary logistic regression was used upon data obtained from univariate analysis. By binary logistic regression (enter) method and backward conditional method the odds of failure were derived for variables. The odds of failure for diabetes was 88.30 with p=0.000. The odds of failure for loculation was 21.79 with p=0.000. The odds of failure for tuberculosis was 3.178 with p=0.019. The odds of failure for hypoalbuminemia was 7.843 with p=0.000. Other variables such as cirrhosis did not have significant p value. The results of binary logistic regression was given in Table 8).

Table 4: Univariate analysis of variable in the mortality of complicated parapneumonic effusion and empyema.

Variables	Mortality		P value; Chi square value	P value (Fischer exact test)
	Alive	Death		
Pus (N=93)	60	33	0.165	0.184
Diabetes (N=44)	21	23	0.00; 12.312	0.001
Serum albumin <3 gm (N=126)	72	54	0.00; 21.418	0.00
Tuberculosis (N=85)	58	27	0.73	0.78
Male (N=175)	121	54	0.79	0.85
Female (N=45)	32	13	0.79	0.85
Loculation present (N=119)	69	50	0.00; 16.361	0.00
Liver failure/cirrhosis (N=15)	2	13	0.00; 24.016	0.00
Stain/culture positive(N=95)	64	31	0.541	0.557
PH <7.0 (N=91)	45	46	0.00; 29.589	0.00

Table 5: Prediction of overall correct percentage.

Outcome	Predicted		
	Failure	Success	Percentage correct
Failure	93	20	82.3
Success	28	79	73.8
			78.2

Table 6: Hosmer Lemeshow test (goodness of fit test).

Step 1	Chi-square	df	Significance
1	9.547	6	0.145

Table 7: Model summary (pseudo R square test).

Step	-2 log likelihood	Cox and Snell R Square	Nagelkerke R Square
1	179.563	0.434	0.579

Table 8: Binary logistic regression analysis.

Binary logistic	Enter method				Backward conditional method			
Variables	B	EXP B/Odds	P value	Confidence interval	B	EXP B/Odds	P value	Confidence interval
Diabetes	4.481	88.30	0.000	12.556-620.54	4.116	61.3	0.000	10.16-38.231
Loculation	3.08	21.79	0.000	6.004-79.144	3.047	21.06	0.000	5.878-75.459
Tuberculosis	1.156	3.178	0.019	1.124-8.323	1.202	3.32	0.013	1.285-8.614
Cirrhosis	-2.235	0.107	0.276	0.002-5.979	-2.215	0.107	0.276	0.002-5.979
Hypoalbuminemia (<3 gm)	2.20	7.843	0.000	3.888-24.947	2.287	9.843	0.000	3.884-24.947

Kaplan Meier survival plot and analysis

This showed mean survival days of 28.94 and median survival of 30.00 days for tuberculous empyema. This showed mean survival days of 10.593 and median of 100 days for non-tuberculous empyema. The odds of death with tuberculous empyema were longer than with complicated parapneumonic effusion with a significant p value (Table 9).

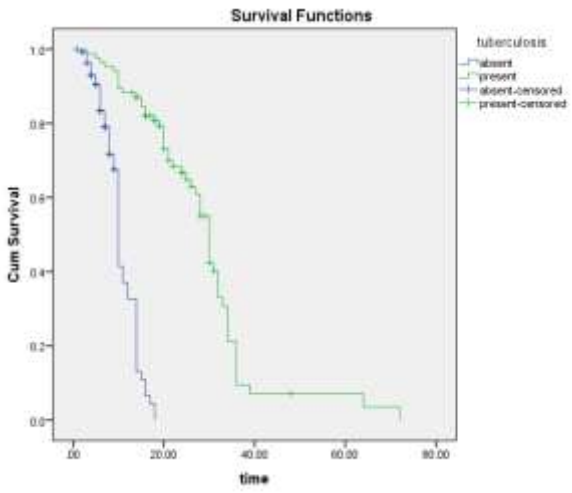

Figure 1: Plot 1 Kaplan Meier survival with and without tuberculosis (time versus percentage).

DISCUSSION

Univariate analysis was done with independent variables for outcome and mortality.

Univariate analysis showed mean age of the study was 46.26, the mean pH of the all effusion was 6.7, the mean time to death was 13.554.

The values of p=0.000 for diabetes mellitus, p=0.000 for pus, p=0.000 for hypoalbuminemia, p=0.004 for tuberculosis, p=0.00 for loculation, p=0.002 for liver failure, p=0.000 for pH <7.0. Univariate analysis of factors by Chi-square test showed significant results for the above variables with respect to outcome.

As stated a sub-analysis with mortality as endpoint was attempted along with the endpoint outcome. The following were observed.

The following are the significant results of univariate analysis of factors by Chi-square test with respect to death in complicated parapneumonic effusion and empyema. Significant p values for variables with respect to death were p=0.000 for diabetes, p=0.000 for hypoalbuminemia, p=0.000 for loculation, p=0.000 for liver failure, p=0.000 for pH<7.0.

Binary logistic regression analysis using enter and backward conditional methods was applied for significant variables found in univariate analysis for outcome and mortality. The mortality model did not have a good fit and hence not reported. The following are discussion of the binary logistic regression of the outcome variables. Overall percentage of prediction of the model is 78.2, hence the binary logistic results in this study could be considered valid. These values show good fitness of the model. Hosmer and Lemeshow test establishing a good model.

Important variables such diabetes, tuberculosis, loculation, hypoalbuminemia was found to be predictors of outcome.

The odds of failure for diabetes was 88.30with p=0.000 and a confidence interval of 12.556-620.54. The odds of failure for tuberculosis was 3.178 with p=0.019 and a confidence interval of 1.124-8.323. The odds of failure for loculation was 21.79 with p=0.000 and a confidence interval of 6.004-79.144. The odds of failure for hypo-albuminemia (<3 gms) was 7.843 with p value of 0.00 and a confidence interval of 3.888-24.942.

All the DM patients had HbA1c level above 8 during the study period.

The Kaplan Meier analysis in the study points to optimal time of intervention to prevent death. In the tuberculous empyema, the mean time to death is 28 days and median time is 30 days hence poor outcome cases if identified early can be treated efficiently and the mortality can be reduced. The principle can be applied to complicated parapneumonic effusion whose mean and time survival was 10.5 and 10 days respectively.

Several hypotheses have been postulated to explain mechanisms that could lead to increased risk of TB in patients with DM, and increased risk of mortality in TB-DM patients. Both mouse and human models have demonstrated that DM alters adaptive and cell-mediated immune responses.[18-20] Impaired alveolar macrophage activation due to glycation of binding sites may inhibit subsequent granuloma formation in TB-DM patients.[21]

Chronic hyperglycemia may disrupt the regulation of key cytokines, such as interferon-gamma, which in turn may increase the *M. tuberculosis* bacterial burden and subsequent risk of death in TB-DM patients.[22] In addition, altered T-helper (Th) 1, Th 2, and Th 17 cytokine responses have been demonstrated among patients with TB-DM.[23]

Diabetes mellitus (DM) is an increasingly recognized comorbidity that can both accelerate TB disease and complicate TB treatment. The prevalence of DM among TB patients around the world varies according to different regions that range from 12 to 44% and tended to increase in the past decade.[24] It increases the risk of TB disease, complicates TB treatment, and increases the risk of a poor TB outcome.[25]

LeMense et al, no difference in procedure success rates or hospital stay was observed between multiloculated and uniloculated empyema, parapneumonic and non-parapneumonic empyema, and culture proved and biochemically proved empyema.[26] Their success rate of tube thoracostomy drainage was only 11%, because all patients had loculated pleural fluid at presentation.

Success rate of tube thoracostomy without loculation in our study was around 86.7%. Patients should be considered for surgery if they have ongoing signs of sepsis in association with a persistent pleural collection despite drainage and antibiotics. Failure of sepsis to resolve within 5-7 days is suggested as an appropriate period following which a surgical opinion should be sought.[27,28] Discussion with a thoracic surgeon should be considered in all cases failing to respond.

Hypoalbuminemia, the presence of loculated fluid and anaerobic infections have been related to adverse outcome in previous studies although not in recent reports.[29-30] Long-term sequelae of pleural empyema may include residual pleural thickening (up to 13% of patients). This is not usually associated with functional impairment although, rarely, extensive incapacitating pleural fibrosis may develop (fibrothorax).[31,32] Surgical decortication may occasionally provide symptomatic benefit for patients with a fibrothorax. Pleural calcification, bronchopleural fistula formation and development of empyema necessitans (disruption of the parietal pleura with spontaneous discharge of pleural contents evident under the chest wall) are other rare complications. Early thoracotomy has the additional advantage that if decortications are accomplished within 2 weeks of pleural infection, the visceral pleural rind usually is easily extricated from the lung.[33] Hence early referral of failing cases will benefit from surgery.

The success rate for conventional tube thoracostomy drainage is 32 to 71%.[34] Success rate reported from other studies is comparable to that of 48.6% in our study.[34-36] High mortality rates from empyema have been reported, ranging from 1 to 61%.[37] In the present study, the overall mortality rate was 30.5%. The duration of the pleural infection, the characteristics of the pleural fluid, the presence or absence of loculations the overall condition of the patient are the four critical important factors to be considered in the selection of a pleural drainage method. These four factors also influence the tube thoracostomy drainage outcome according to the review of Moran.[38]

Prognosis in pleural infection

The long-term survival of patients with pleural infection is good if prompt treatment is initiated. In a series of 85 patients followed for up to 4 years, the mortality was 14% and all deaths occurred within the first 400 days after drainage.[39] Death was due to comorbid condition and not directly due to sepsis from the empyema. No reliable clinical, radiological or pleural fluid characteristics accurately determine patient's prognosis at initial presentation.

Determinants such as tuberculosis, loculation, serum albumin falling after a week of management and diabetes can successfully predict the failing cases according to our study which have proved statistically by using logistic regression model.

CONCLUSION

To conclude determinants such tuberculosis, pleural loculation, serum albumin and diabetes can predict the outcome of pleural space infection especially complicated and complex parapneumonic effusion. Such predictors can help to reduce the morbidity and mortality associated with complicated parapneumonic effusion by identification of failing cases and early referral for definite management.

Recommendations

A prediction scoring system with each of this variable as predictors can develop along with other variables identified in other studies. This system should be evaluated and validated for future use in pleural space infection.

Limitations of the study

It is a retrospective study. Data such as glycemic control prior to diagnosis of tuberculous and complicated parapneumonic with DM could not be accurately known. There are important limitations to note in our study. First, we relied on self-report and medical chart abstraction to determine whether TB patients had DM, and therefore the primary exposure of interest was subject to misclassification due to TB patients who did not know they had DM or who had never been screened. Intra pleural fibrinolytic therapy was not used to high cost of the therapy.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Ferguson AD, Prescott RJ, Selkon JB, Watson D, Swinburn CR. The clinical course and management of thoracic empyema. Q J Med. 1996;89:285-9.
2. Maskell NA, Batt S, Hedley EL, Davies CW, Gillespie SH, Davies RJ. The bacteriology of pleural infection by genetic and standard methods and its mortality significance. Am J Respir Crit Care Med. 2006;174:817-23.
3. Menendez R, Torres A, Zalacain R, Aspa J, Martín Villasclaras JJ, Borderías L, et al. Risk factors of treatment failure in community acquired pneumonia:implications for disease outcome. Thorax. 2004;59:960-5.
4. Hasley PB, Albaum MN, Li Y-H, Fuhrman CR, Britton CA, Marrie TJ, et al. Do pulmonary radiographic findings at presentation predict mortality in patients with community-acquired pneumonia? Arch Intern Med. 1996;156:2206-12.
5. Light RW, Girard WM, Jenkinson SG, George RB.. Parapneumonic effusions. Am J Med. 1980;69:507-11.

6. Taylor MD, Kozower BD. Surgical spectrum in the management of empyemas. Thorac Surg Clin. 2012;22:431-40.
7. Tsai CH, Lai YC, Chang SC, Chang CY, Wang WS, Yuan MK, et al. Video-assisted thoracoscopic surgical decortication in the elderly with thoracic empyema:five years' experience. J Chin Med Assoc. 2016;79:25-8.
8. Ferreiro L, San Jose ME, Valdes L. Management of parapneumonic pleural effusion in adults. Arch Bronconeumol. 2015;51:637-46.
9. Strange C, Sahn SA. The definitions and epidemiology of pleural space infection. Semin Respir Infect. 1999;14:3-8.
10. Molnar TF. Current surgical treatment of thoracic empyema in adults. Eur J Cardiothoracic Surg. 2007;32:422-30.
11. Herrera-Kiengelher L, Baez-Saldana R, Salas-Hernandez J, Avalos-Bracho A, Pérez-Padilla R, Torre-Bouscoulet L. Frequency of adverse events and mortality in patients with pleural empyema in a public referral hospital in Mexico City. Int J Tuberc Lung Dis. 2010;14:1187-92.
12. Ashbaugh DG. Empyema thoracis. Factors influencing morbidity and mortality. Chest. 1991;99:1162-5.
13. Ahmed AE, Yacoub TE. Empyema thoracis. Clin Med Insights Circ Respir Pulm Med. 2010;4:1-8.
14. Davies CW, Gleeson FV, Davies RJ. BTS guidelines for the management of pleural infection. Thorax. 2003;58:18-28.
15. Light RW, MacGregor Ml, Ball WC Jr, Luchsinger PC. Diagnostic significance of pleural fluid pH and Pco2. Chest. 1973;64:591-6.
16. Weese WC, Shindler ER, Smith IM. Empyema of the thorax then and now. Arch Intern Med. 1973;13:516-20.
17. Vianna NJ. Nontuberculous bacterial empyema in patients with and without underlying diseases. J Am Med Associat. 1971;215:69-75.
18. Pieters J. Mycobacterium tuberculosis and the macrophage: maintaining a balance. Cell Host Microbe. 2008;3(6):399–407.
19. Restrepo BI, Fisher-Hoch SP, Pino PA, Salinas A, Rahbar MH, Mora F, et al. Tuberculosis in poorly controlled type 2 diabetes: altered cytokine expression in peripheral white blood cells. Clin Infect Dis. 2008;47(5):634–41.
20. Stalenhoef JE, Alisjahbana B, Nelwan EJ, van der Ven-Jongekrijg J, Ottenhoff TH, van der Meer JW, et al. The role of interferon-gamma in the increased tuberculosis risk in type 2 diabetes mellitus. Eur J Clin Microbiol Infect Dis. 2008;27(2):97–103.
21. Banerjee D, Bhattacharyya R, Kaul D, Sharma P. Diabetes and tuberculosis: analysis of a paradox. Adv Clin Chem. 2011;53:139–53.
22. Kumar NP, Sridhar R, Banurekha VV, Jawahar MS, Nutman TB, Babu S. Expansion of pathogen-specific T-helper 1 and T-helper 17 cells in pulmonary tuberculosis with coincident type 2 diabetes mellitus. J Infect Dis. 2013;208(5):739–48.
23. Kourbatova EV, Leonard MK, Jr, Romero J, Kraft C, del Rio C, Blumberg HM. Risk factors for mortality among patients with extrapulmonary tuberculosis at an academic inner-city hospital in the U.S. Eur J Epidemiol. 2006;21(9):715–21.
24. Porkert MT, Sotir M, Parrott-Moore P, Blumberg HM. Tuberculous meningitis at a large inner-city medical center. Am J Med Sci. 1997;313(6):325–31.
25. Sterling TR, Zhao Z, Khan A, Chaisson RE, Schluger N, Mangura B, et al. Mortality in a large tuberculosis treatment trial: modifiable and non-modifiable risk factors. Int J Tuberc Lung Dis. 2006;10(5):542–9.
26. LeMense GP, Strange C, Sahn SA. Empyema thoracic:therapeutic management and outcome. Chest. 1995;107:1532–7.
27. Pothula V, Krellenstein DJ. Early aggressive surgical management of parapneumonic empyemas. Chest. 1994;105:832-6.
28. Cham CW, Haq SM, Rahamim J. Empyema thoracis:a problem with late referral? Thorax 1993;48:925-7.
29. Chen KY, Liaw YS, Wang HC, Luh KT, Yang PC. Sonographic septation:a useful prognostic indicator of acute thoracic empyema. J Ultrasound Med. 2000;19:837-43.
30. Himelman RB, Callen PW. The prognostic value of loculations in parapneumonic pleural effusions. Chest. 1986;90:852-6.
31. Sahn SA. Management of complicated parapneumonic effusions. Am Rev Respir Dis. 1993;148:813-7.
32. Jimenez CD, Diaz G, Pérez-Rodríguez E, Light RW. Prognostic features of residual pleural thickening in parapneumonic pleural effusions. Eur Respir J. 2003;21:952-5.
33. Sahn SA. Diagnosis and management of parapneumonic effusions and empyema. Clin Infect Dis. 2007;45:1480–6.
34. Mandal AK, Thadepalli H. Treatment of spontaneous bacterial empyema thoracic. J Thorac Cardiovasc Surg. 1987;94:414–8.
35. Lemmer JH, Botham MJ, Orringer MB. Modern management of adult thoracic empyema. J Thorac Cardiovasc Surg. 1985;90:849–55.
36. Lee-Chiong TL Jr, Matthay RA. Current diagnostic methods and medical management of thoracic empyemas. Chest Surg Clin North Am. 1996;6:419–38.
37. Bartlett JG, Finegold SM. Anaerobic infections of the lung and pleural space. Am Rev Respir Dis. 1974;110:56–77.
38. Mavroudis C, Symmonds JB, Minagi H, et al. Improved survival in management of empyema thoracis. J Thorac Cardiovasc Surg 1981;82:49–57.
39. 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):1682-7.

Cite this article as: Arivudainambi VP. Outcome and mortality analysis in complicated parapneumonic effusion and empyema. Int J Clin Trials 2017;4(4):176-83.