Available online at www.sciencedirect.com

ScienceDirect

Journal of the Chinese Medical Association 81 (2018) 605−610

www.jcma-online.com

Original Article

Contributing factors to mortality rates of pulmonary tuberculosis in intensive care units

Dursun Tatar [a], Gunes Senol [b,*], Cenk Kirakli [a], Ozlem Edipoglu [a], Pinar Cimen [a]

[a] *Dr. Suat Seren Chest Diseases and Chest Surgery Teaching Hospital, Intensive Care Unit, Izmir, Turkey*
[b] *Dr. Suat Seren Chest Diseases and Chest Surgery Teaching Hospital, Infectious Diseases and Clinical Microbiology, Izmir, Turkey*

Received September 3, 2016; accepted February 23, 2017

Abstract

Background: Tuberculosis (TB) remains an important health problem worldwide. TB patients sometimes require intensive care unit (ICU) treatment. The aim of this study is to establish special features and mortality rates of pulmonary TB patients in ICUs and identify the factors contributing to ICU mortality.
Methods: Medical records of adult patients (>18 years) with a diagnosis of TB who were admitted to the ICU of a referral hospital for chest diseases between 2004 and 2010 were reviewed retrospectively. Demographic characteristics, comorbidities, APACHE II scores, symptoms, radiologic appearance of the disease, bacteriological and laboratory investigations, need and type of mechanical ventilation support (invasive, non-invasive), characteristics related to ICU stay, length of ICU stay, mortality and factors affecting mortality were recorded and analysed.
Results: Forty patients (33 male) with active pulmonary TB with a median age of 55 years (43−63 years) and a median APACHE II score of 22 (17−26) were followed up in the ICU. Patients who needed invasive mechanical ventilation had significantly longer ICU stays than patients who were treated with non-invasive ventilation or medical therapy (Log rank $p = 0.014$). Mortality was 72.5%. The only independent risk factor for mortality was having an APACHE II score ≥18.
Conclusion: The mortality of TB patients who needed ICU support remains high. This higher mortality rate seems related to multi-organ failure, requiring invasive mechanical ventilation and high APACHE II scores.

Keywords: Intensive care; Mechanical ventilation; Mortality; Tuberculosis

1. Introduction

Tuberculosis (TB) remains an important health problem, especially in developing countries, with high incidence and mortality rates worldwide. There were an estimated 9.6 million incident cases of TB globally in 2015, 1.4 million deaths among HIV-negative cases of TB and an additional 0.35 million deaths among people who were HIV-positive.[1]

Incidence and mortality rates of TB in Turkey were 15.8 cases/100.000 population per year and 5%, respectively.[2]

Despite the improvement in strategies such as directly observed therapy during recent years, some smear-positive TB patients still require hospitalisation. Mortality of these patients still exists, particularly among those who are admitted to the intensive care unit (ICU). The most common causes of ICU admission of TB patients are acute respiratory failure and other severe organ failures such as renal and hepatic failure.[3−6] Some studies performed in small patient groups also suggest that patients with miliary TB, HIV infection or both

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

* Corresponding author. Dr. Gunes Senol, Dr. Suat Seren Chest Diseases and Chest Surgery Teaching Hospital, Infectious Diseases and Clinical Microbiology, Izmir, Turkey.
E-mail address: drshenol@yahoo.com (G. Senol).

https://doi.org/10.1016/j.jcma.2018.02.003

commonly need ICU support.[7−9] Mortality, rates of TB patients requiring mechanical ventilation vary from 25% to 81% whereas this is around only 25% in patients with severe pneumonia.[10−14] According to our knowledge, there are no data regarding the outcomes of TB patients followed up in the ICU in Turkey.

The aim of this study was to establish mortality rates of TB patients who need ICU treatment and identify the factors contributing to ICU mortality in Izmir, which is one of the biggest cities of a developing country with intermediate TB endemicity.

2. Methods

2.1. Setting

Our institution is a regional referral and training hospital for chest diseases and chest surgery with 420 general and 29 ICU beds in Izmir, Turkey. Hospital also has a special 60 bed ward for TB patients. Annually, approximately 500 TB patients are hospitalised.

2.2. Study design

Medical records of adult patients (>18 years) hospitalised between 2004 and 2010 with a diagnosis of TB who were admitted to the ICU of the hospital were reviewed retrospectively. The study was approved by the local institutional review board.

2.3. Study population and criteria

The diagnosis of TB was based on the following: (1) positive cultures of sputum, bronchial aspirates or bronchoalveolar lavage fluid; and/or (2) positive, acid-fast bacilli smears; and/or (3) clinical and radiological findings with a histopathologic diagnosis on lung biopsy. Demographic characteristics, comorbidities, smoking history, alcoholism, reasons for ICU admission, acute physiology and chronic health evaluation (APACHE II) score (a severity-of-disease classification system applied within 24 h of admission of a patient to an ICU: an integer score from 0 to 71 is computed based on several measurements; higher scores correspond to more severe disease and a higher risk of death), symptoms, radiologic appearance of the disease, bacteriological and laboratory investigations (white cell count, haemoglobin, platelets, arterial blood gases), need and type of mechanical ventilation support (invasive, non-invasive), drug regimen used for anti-TB treatment, complications such as hepatotoxicity, acute renal failure, cardiovascular failure, central nervous system failure and other organ failures, length of stay (LOS) in the ICU and 28- day -mortality were recorded and analysed.

Clinical respiratory specimens were decontaminated and homogenized by the N-acetyl-l-cysteine-sodium hydroxide (NALC-NAOH) method. The MGIT 960 automated culture system (BD, Sparks, Maryland, USA) and Lowenstein-Jensen (LJ) medium were used for isolation of mycobacteria. Strains were identified by stain characterisation and the ProbeTech System (BD, Sparks, Maryland, USA). The susceptibility patterns of all isolates were studied with regard to first-line antituberculosis drugs (isoniazid, rifampin, streptomycin, and ethambutol and pyrazinamide) by MGIT 960 AST system (BD, Sparks, Maryland, USA) according to manufacturer instructions. Drug resistance patterns of the isolates are given in Table 1. Standard identification and susceptibility testing was applied according to Clinical and Laboratory Standards Institute (CLSI) standards.[10]

Chest radiographic patterns were classified according to the National TB and Respiratory Disease Association (NTRDA), with category 1 defined as minimal infiltration without cavities; category 2 as moderate expansion of infiltrates, category 2a as occasional infiltrates, unilateral or bilateral without cavities, category 2b as compact infiltrates with expansion to not more than one lung lobe, and cavities with a diameter < 4 cm,; category 3 as advanced with any expansion (with or without cavities) and category 4 as miliary forms.[15] Miliary TB was defined as the presence of micronodules on chest radiographs or high-resolution computed tomography (CT).

2.4. Statistics

Categorical data were presented as number of cases and percentages. Continuous data were presented as medians with

Table 1
Baseline demographic characteristics of TB patients requiring intensive care.

Patient characteristics	All	Survivors	Deceased	*p*
n (%)	40	11 (27.5)	29 (72.5)	
Age (years), mean ± SD	54 ± 15	55 ± 13	54 ± 16	0.84
Male gender, n (%)	33 (83)	9 (81)	24 (83)	0.94
Smoking history	22 (55)	7 (63)	15 (52)	0.72
APACHE II score	22 (15−26)	17 (15−22)	23 (20−26)	0.016
Symptoms				
Dyspnea	32 (80)	6 (54)	26 (89)	0.025
Cough	25 (63)	6 (54)	19 (65)	0.72
Sputum	16 (40)	5 (45)	11 (38)	0.73
Fever	7 (17)	3 (27)	4 (14)	0.36
Presence of comorbidity	25 (63)	6 (55)	19 (65)	0.71
Laboratory parameters				
WBC ($x10^3$/L)	12.5 (9.8−22.1)	11.1 (11.3−18.4)	12.8 (9.8−22.6)	0.80
Hb, g/dl	11 (9.4−13)	9.5 (9.2−9.5)	11 (9.6−13)	0.34
Htc, %	32.5 (28.3−35)	28.2 (28−28.3)	33 (29.3−36.3)	0.21
Plt ($x10^3$/L)	266 (148−426)	443 (181−550)	249 (114−403)	0.12
Arterial blood gases				
pH	7.29 (7.16−7.36)	7.30 (7.21−7.34)	7.27 (7.13−7.38)	0.83
$PaCO_2$, mmHg	58 (39−87)	58 (39−91)	59 (37−84)	0.98
PaO_2/FiO_2	166 (128−243)	161 (135−285)	171 (126−225)	0.83

Data are presented as median (IQR) or n (%) unless specified. WBC = white blood cell, Hb = haemoglobin, Htc = haematocrit, Plt = platelets, $PaCO_2$ = arterial carbon dioxide tension, PaO_2 = arterial oxygen tension, FiO_2 = inspiratory oxygen fraction.

interquartile ranges (IQRs) unless normally distributed. The normality of the data was evaluated by the Shapiro Wilk test. Categorical values were compared with the chi-square test and in cases of at least 25% of the expected cell counts <5 with Fisher's exact test. Continuous data were compared by the Mann−Whitney U test. Kaplan−Meier curves were used to analyse time-dependent variables. Factors that were significantly associated with survival in the univariate analysis were entered in a stepwise logistic regression analysis to assess the risk factors for mortality. Inclusion and exclusion criteria were 0.10 and 0.15, respectively. The best cut-off value for APACHE-II score was selected by Youden's index.[16] A two-sided p value < 0.05 was considered significant. Data analysis was performed using SPSS 17.0 (Statistical Package for the Social Sciences, Chicago, Illinois).

3. Results

During the 6-year period, a total of 40 patients (33 male, 83%) with active pulmonary TB, a median age of 55 years (43−63) and a median APACHE II score of 22 (17−26) were followed up in the ICU (Fig. 1). All the patients were admitted to the ICU because of respiratory failure. Only seven (17.5%) patients already diagnosed with TB were accepted to the ICU. Others were diagnosed during the ICU stay. Median time for new diagnosis was 7 days (4−18 days). During the study period, 3125 TB patients were diagnosed and treated in our hospital.

Twenty-two (55%) ICU-TB patients had smoking history. None of the patients were HIV-positive. Twenty-nine (72.5%) patients died during follow-up.

The mortality rate of TB patients was 72.5%, whereas the 28- day -mortality rate in our ICU during this 6-year period was 43%; the median APACHE II score was 24 in the deceased patients ($p < 0.001$).

The median APACHE II score was significantly higher in deceased patients ($p = 0.016$). The most common symptoms were dyspnea, cough and sputum production, respectively. Dyspnea was significantly more common in deceased patients ($p = 0.024$). Twenty-five patients (63%) had at least one comorbidity. The most common comorbidities were chronic obstructive pulmonary disease (COPD) in 12 patients (30%), diabetes mellitus (DM) in 7 patients (17.5%) and cardiovascular and psychiatric diseases in 3 patients each (7.5%). Three diabetic patients also had co-infections (two from pneumonia and one urinary infection). Fifteen patients (37.5%) had no comorbidity. The distribution of comorbidities did not indicate significant differences among the survivors and deceased patients. The baseline characteristics of both survivors and deceased patients are shown in Table 1.

Twenty-one (53%) patients had both positive, acid-fast bacilli smears and cultures, nine (23%) had only positive acid-fast bacilli smears and five (12.5%) had positive cultures for TB. In five patients (12.5%), diagnosis of TB was established based on histopathologic examination of the biopsy.

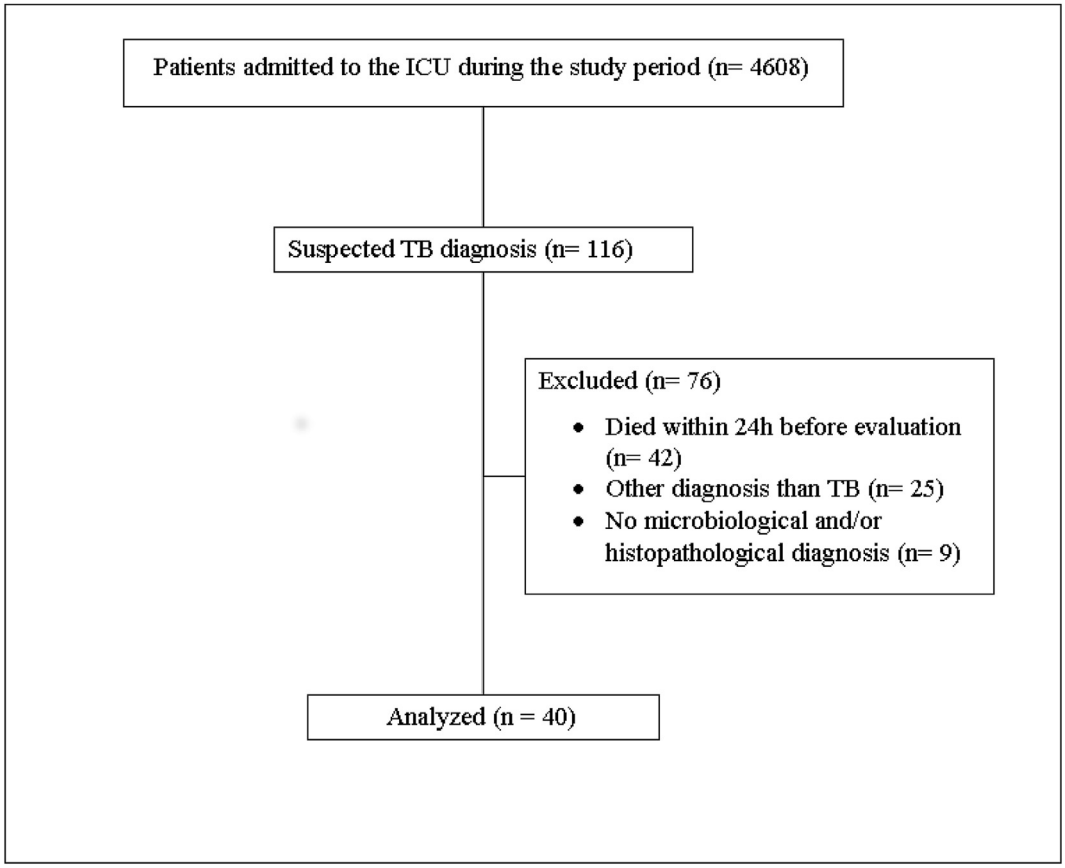

Fig. 1. Flow of patients throughout the study period.

More than half of the patients (65%) presented extensive infiltrates, according to category 3 NTRDA guidelines, on chest radiographs or thoracic CT. Three patients (7%) had miliary patterns. None of the patients were in category 1 according to the NTRDA (Table 3).

The most common choice of anti-TB treatment was a four-drug regimen including isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E) with 35 patients (88%). One patient received multi-drug resistant TB treatment, and 2 patients received a re-treatment regimen with 5 drugs, including HRZE plus streptomycin (S) (Table 3). Thirty patients (75%) required invasive mechanical ventilation and 6 patients (15%) required non-invasive mechanical ventilation support. The mortality rate was significantly higher, and survival was significantly shorter in patients who required mechanical ventilator support (invasive or non-invasive), compared to patients who had only medical therapy (Table 2 and Fig. 2).

Thirty-three patients (82.5%) took antibiotics other than specific anti-TB drugs. Those patients were hospitalised for pneumonia and exacerbation of COPD. The remaining seven patients who were known to have TB received specific anti-TB drugs, starting from their admission to the ICU. Levofloxacin were administered to 2 patients (5%); others were treated with beta-lactam antibiotics. Both patients treated with levofloxacin took their medications (7 days and 11 days duration) before the diagnosis of TB, and both of them survive. Antibiotic treatment was continued due to presence of pneumonia besides TB in two patients and urinary infections in one patient. Nonspecific antibiotic drugs were stopped in other patients.

Patients also took essential the medications according their comorbidities (COPD, DM, etc.).

Besides respiratory failure, 19 patients (48%) developed one more organ failure during their ICU stay. Twenty-one patients (52%) had no other organ failure besides respiratory failure. The mortality of patients who developed another organ failure besides respiratory failure was significantly higher than in the ones who did not ($p = 0.034$). The most common extra organ failure was cardiovascular failure, followed by acute renal failure and hepatotoxicity.

Overall LOS (length of stay) in the ICU was median 5 days (2−10 days), and LOS in the hospital was median 13 days (5−27 days). LOS in the ICU was comparable between survivors and deceased patients but significantly longer in patients who needed invasive mechanical ventilation than in patients treated with non-invasive ventilation or medical therapy alone (log rank $p = 0.014$, Fig. 3). High APACHE II score, presence of dyspnea, need for mechanical ventilation and presence of organ failure in addition to respiratory failure were introduced into a stepwise logistic regression model, which showed that only an APACHE II score of 18 or greater was significantly related to mortality (OR: 6.5, 95% CI: 1.19−35.39, $p = 0.03$).

Table 2
Characteristics of patients related to intensive care unit stay.

	All	Survivors	Deceased	p
Patients requiring MV	36 (90)	7 (63)	29 (100)	0.004
Initial type of ventilator support at admission to the ICU				
IMV	30	6	24	
NIV	6	1	5	
Patients with extra organ failure besides respiratory failure	19	2	17	0.034
Cardiac	8	0	8	
Renal	6	0	6	
Hepatic	4	1	3	
CNS	1	1	0	
Duration of MV, days	4 (2−18)	12 (5−18)	3 (2−6)	0.009
LOS in the ICU, days	5 (2−18)	9 (2−18)	3 (2−8)	0.07
LOS in the hospital, days	13 (5−27)	23 (18−27)	7 (5−24)	0.035

Data are presented as median (IQR) or n (%). MV = mechanical ventilation, IMV = invasive mechanical ventilation, NIV = noninvasive ventilation, CNS = central nervous system, LOS = length of stay, ICU = intensive care unit.

Table 3
Radiologic and bacteriologic characteristics and anti-TB drug combination choices of TB patients requiring intensive care.

Radiologic patterns according to NTRDA	All	Survivors	Deceased	p
Category 1	0 (0)	0	0	0.45
Category 2	11 (28)	4	7	
Category 3	26 (65)	7	19	
Category 4	3 (7)	0	3	
Bacteriologic characteristics				
Smear (+), culture (+)	21 (53)	8	13	0.12
Smear (+), culture (−)	9 (22)	1	8	
Smear (−), culture (+)	5 (13)	0	5	
Smear (−), culture (−)	5 (7)	2	3	
Anti-TB drug combination choices				
HRZE	35 (88)	10	25	0.24
HRZES	2 (5)	0	2	
HRZS	2 (5)	0	2	
MDR therapy	1 (2)	1	0	

TB = tuberculosis, NTRDA = National Tuberculosis and Respiratory Disease Association, H = isoniazid, R = rifampicin, E = ethambutol, Z = pyrazinamide, S = streptomycin, MDR = multidrug resistance.

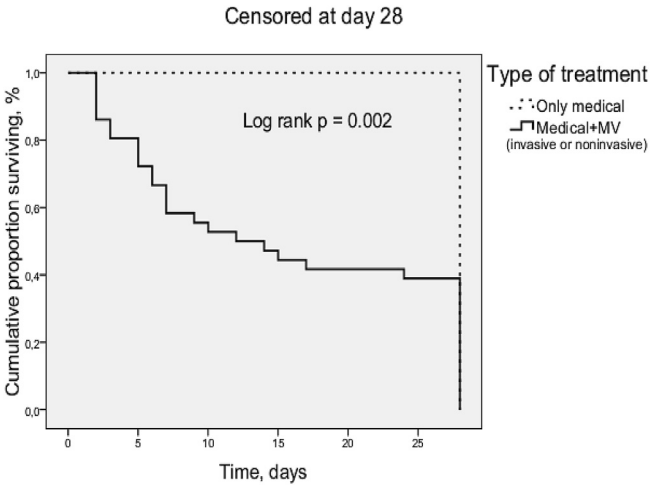

Fig. 2. Kaplan−Meier survival curves of tuberculosis patients needing mechanical ventilation support (invasive or noninvasive) and only medical therapy.

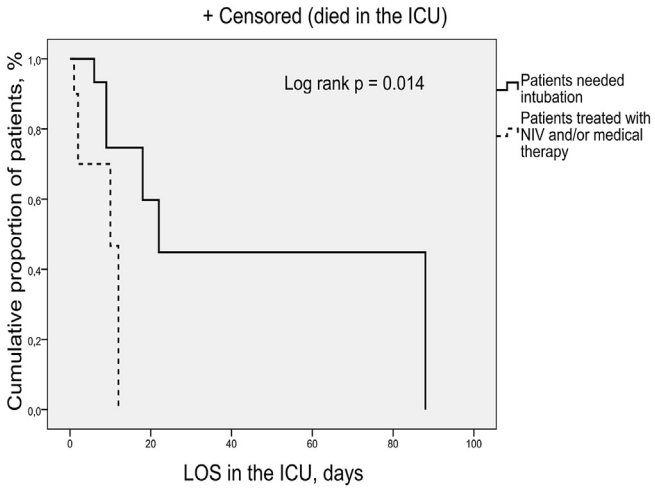

Fig. 3. Length of intensive care unit stay in patients who required intubation and invasive mechanical ventilation or not. NIV = non-invasive ventilation, LOS = length of stay, ICU = intensive care unit.

Details of clinical characteristics appear in Table 1. Immunosuppression or shock status did not occur. No nosocomial infection was detected in the patients. Mortality was mainly considered related to the severity of TB disease.

4. Discussion

The main finding of this study was a high mortality rate in active-TB patients requiring intensive care when compared to the overall mortality rate of our ICU during the study period. Factors such as dyspnea, need for mechanical ventilation and one or more organ failures accompanying respiratory failure seemed to be related to mortality, but the only independent risk factor predicting mortality was an APACHE II score of 18 or higher.

Despite the advances in pharmacologic treatments, diagnostic procedures and patient care in the medical field in recent years, TB remains a serious health problem around the globe. Mortality rates are still high, especially in older patients with comorbidities, who require mechanical ventilation and ICU support. Frame et al. reported a mortality rate of 81% in TB patients who had acute respiratory failure.[10] In another retrospective cohort, Silva et al. reported a mortality rate of 65.7%. Some studies also reported mortality rates of up to 90% in patients with miliary TB and acute respiratory distress syndrome (ARDS).[7,17] We found a mortality rate as high as 72.5% in this study. APACHE II scores from deceased patients were significantly higher. Some studies reported lower mortality rates, such as like 26%, but the subjects enrolled in these studies had relatively lower median APACHE II scores, below 18, showing that the patients were less severely ill.[11] Nevertheless, the median APACHE II score from deceased patients in the our study is 23, which related to a predicted mortality rate of around 40%, according to the scoring system. These findings suggest that the mortality rates of TB patients requiring ICU support remain higher than predicted.

Factors associated with mortality in TB patients requiring intensive care varied among studies. The most common predictive factors of mortality reported in the ICU were acute renal failure, need for mechanical ventilation, ARDS, delay in diagnosis, superinfections such as ventilator-associated pneumonia, low body weight and HIV infection.[11,12,18–20] We also found that the need for mechanical ventilation and having an additional organ failure were associated with mortality in the univariate analysis. Despite some studies reporting that acute renal failure was an important factor predicting mortality in TB patients,[11,21] we could not find any significant relationship between acute renal failure and mortality, which is consistent with some other studies in the literature.[6,10,18]

According to NTRDA classification, the most common radiologic presentations were category 3, category 2 and category 4. These findings were similar to other studies in the literature for TB disease.[11,12] Miliary pattern was reported as a protective factor in the study by Silva et al. but all three patients with military pattern on their X-rays at the study were lost. The mortality of patients with category 3 X-rays was greater than those in category 2 (73% vs. 63%, respectively), but that was not statistically significant. Other studies did not indicate a significant relationship between the radiologic pattern and mortality.[18]

Antibiotic uses other than anti-TB drugs might be considerable. Use of fluoroquinolones appeared to be especially important. They may reduce the mortality of ICU patients admitted for pulmonary TB-mimicking community-acquired pneumonia (CAP) due to the anti-mycobacterial effects. They also might weaken the symptoms for the same reason. Thus, possible delays in diagnosis might be associated with high mortality rates. In a study by, Tseng et al., empirical fluoroquinolone usage was independently associated with a better survival rate.[22] In our study, only two patients initiated treatment with fluoroquinolones. They both survived, but statistical evaluation is not possible due to the small number of cases.

The timing of diagnosis is an important issue for management of TB and is critical for both treatment success and public health. In our study, the time to diagnosis of TB was considered longer than expected (median time seven days after ICU admission [4–18 days]). Smear-negative patients have deceased more than smear-positive ones even though the difference is not statistically significant (80% vs. 42%). Silva et al. had noticed that smear positivity was associated with better survival rates due to rapid diagnosis.[18]

This study has some limitations. This is a single-centre study with a small sample size. Therefore, the results of the statistical analysis and the external validity of this study for other hospitals are questionable. A meta-analysis indicated that trials with fewer than 100 patients show higher mortality among patients with pulmonary TB than trials with more than 100 patients. Our results correlate with this hypothesis.[23]

Large, prospective, multicentre studies with bigger sample sizes are needed to establish the characteristics and predictors of mortality in TB patients requiring intensive care support.

In conclusion, despite the improvements in critical-care medicine and treatment modalities, TB is still a serious health problem with high mortality rates in ICU patients. The mortality of these patients seems especially related to multi-

organ failure, requiring invasive mechanical ventilation and high APACHE II scores.

However, large cooperative studies are required with sufficient numbers of patients.

Acknowledgments

The authors would like to thank those involved in the American Thoracic Society's Methods in Epidemiologic, Clinical and Operations Research (MECOR) program, and Ahmet Ugur Demir, MD, MSc (Epidemiology and Biostatistics) in particular for his invaluable time and help with the statistical analysis.

References

1. Organization, W.H. *Global tuberculosis control-WHO report*. 2015. p. 2011 [Geneva].
2. *Tuberculosis 2014 report in Turkey*. Ankara: Ministry of Health; 2015. Publication No: 1026, http://tuberkuloz.thsk.saglik.gov.tr.
3. Levy H, Kallenbach JM, Feldman C, Thorburn JR, Abramowitz JA. Acute respiratory failure in active tuberculosis. *Crit Care Med* 1987;**15**:221−5.
4. Lintin SN, Isaac PA. Miliary tuberculosis presenting as adult respiratory distress syndrome. *Intensive Care Med* 1988;**14**:672−4.
5. Sydow M, Schauer A, Crozier TA, Burchardi H. Multiple organ failure in generalized disseminated tuberculosis. *Respir Med* 1992;**86**:517−9.
6. Zahar JR, Azoulay E, Klement E, De Lassence A, Lucet JC, Regnier B, et al. Delayed treatment contributes to mortality in ICU patients with severe active pulmonary tuberculosis and acute respiratory failure. *Intensive Care Med* 2001;**27**:513−20.
7. Piqueras AR, Marruecos L, Artigas A, Rodriguez C. Miliary tuberculosis and adult respiratory distress syndrome. *Intensive Care Med* 1987;**13**:175−82.
8. Davaro R, Thirumalai A. Life-threatening complications of HIV infection. *J Intensive Care Med* 2007;**22**:73−81.
9. Rosen MJ, Clayton K, Schneider RF, Fulkerson W, Rao AV, Stansell J, et al. Intensive care of patients with HIV infection: utilization, critical illnesses, and outcomes. Pulmonary Complications of HIV Infection Study Group. *Am J Respir Crit Care Med* 1997;**155**:67−71.
10. Frame RN, Johnson MC, Eichenhorn MS, Bower GC, Popovich J. Active tuberculosis in the medical intensive care unit: a 15-year retrospective analysis. *Crit Care Med* 1987;**15**:1012−4.
11. Erbes R, Oettel K, Raffenberg M, Mauch H, Schmidt-Ioanas M, Lode H. Characteristics and outcome of patients with active pulmonary tuberculosis requiring intensive care. *Eur Respir J* 2006;**27**:1223−8.
12. Lee PL, Jerng JS, Chang YL, Chen CF, Hsueh PR, Yu CJ, et al. Patient mortality of active pulmonary tuberculosis requiring mechanical ventilation. *Eur Respir J* 2003;**22**:141−7.
13. Ryu YJ, Koh WJ, Kang EH, Suh GY, Chung MP, Kim H, et al. Prognostic factors in pulmonary tuberculosis requiring mechanical ventilation for acute respiratory failure. *Respirology* 2007;**12**:406−11.
14. Penner C, Roberts D, Kunimoto D, Manfreda J, Long F. Tuberculosis as a primary cause of respiratory failure requiring mechanical ventilation. *Am J Respir Crit Care Med* 1995;**151**:867−72.
15. Mass chest x-ray screening. Chest x-ray screening recommendations for TB-RD Associations. A statement by the NTRDA Committee for the guidance of the tuberculosis program. *Bull Natl Tuberc Respir Dis Assoc* 1971;**57**:3.
16. Fluss R, Faraggi D, Reiser B. Estimation of the Youden Index and its associated cutoff point. *Biom J* 2005;**47**:458−72.
17. Dyer RA, Chappell WA, Potgieter PD. Adult respiratory distress syndrome associated with miliary tuberculosis. *Crit Care Med* 1985;**13**:12−5.
18. Silva DR, Menegotto DM, Schulz LF, Gazzana MB, Dalcin PT. Mortality among patients with tuberculosis requiring intensive care: a retrospective cohort study. *BMC Infect Dis* 2010;**10**:54.
19. Rao VK, Iademarco EP, Fraser VJ, Kollef MH. The impact of comorbidity on mortality following in-hospital diagnosis of tuberculosis. *Chest* 1998; **114**:1244−52.
20. Al-Homrany M. Successful therapy of tuberculosis in hemodialysis patients. *Am J Nephrol* 1997;**17**:32−5.
21. Carroll GC. Review: noninvasive positive pressure ventilation reduces intubation and length of ICU stay in acute respiratory failure. *ACP J Club* 2005;**143**:19.
22. Tseng YT, Chuang YC, Shu CC, Hung CC, Hsu CF, Wang JY. Empirical use of fluoroquinolones improves the survival of critically ill patients with tuberculosis mimicking severe pneumonia. *Crit Care* 2012;**16**:R207.
23. de Almeida CPB, Couban R, Kallyth SM, Cabral VK, Craigie S, Busse JW, et al. Predictors of in-hospital mortality among patients with pulmonary tuberculosis: a protocol of systematic review and meta-analysis of observational studies. *BMJ Open* 2016;**6**. e011957.