Outcome of active pulmonary tuberculosis patients requiring respiratory intensive care admission

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Introduction There are limited data regarding active pulmonary tuberculosis (APTB) patients requiring ICU admission.

Aim This study aimed to determine the mortality rate and risk factors associated with mortality in patients with APTB requiring respiratory intensive care unit (RICU) admission.

Patients and methods A combined retrospective–prospective study was conducted during the period between January 2009 and December 2010 (retrospective part) and between January and December 2011 (prospective part) on adult patients with APTB admitted to the RICU of Abbassia Chest Hospital for a period of more than 24 h. Demographic, clinical, and therapeutics characteristics as well as outcome (RICU morality) were obtained from the medical records.

Results A total of 100 patients (median age 38 years) were included (60 retrospective and 40 prospective). The RICU morality rate was 74%. The overall median length of stay in RICU was 5 days. Respiratory failure was the most common cause of admission. Mechanical ventilation (MV) was needed in 65% of patients. Complications occurred in 45% of cases. Female sex, lower diastolic blood pressure, far advanced lesion, respiratory failure type II, higher Acute Physiology and Chronic Health Evaluation II score, lower Glasgow Coma Scale score, increased need for MV, and electrolytes disturbances were significantly more frequent in nonsurvivors than in survivors in the RICU. Risk factors identified for nonsurvival were pneumonia pattern and far advanced lesion by radiology, female sex, and renal impairment. MV was the only predictor of RICU mortality.

Conclusion The present study found a very high mortality rate among APTB patients requiring RICU admission and identified associated risk factors and a predictor of RICU mortality. *Egypt J Broncho* 2014 8:79–86

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Keywords: active pulmonary tuberculosis, mortality, respiratory intensive care unit, risk factors

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Introduction

Across the world, tuberculosis (TB) remains an important public health problem, especially in developing countries. One-third of the world's population is infected with *Mycobacterium tuberculosis*. Every year almost two million people die from TB, most of them in low-income and middle-income countries [1].

Among hospitalized patients with active TB, the most common symptoms include fever, night sweats, weight loss, and cough [2]. In only one study, dyspnea was the most commonly reported symptom [3]. The mean symptom duration before hospital admission was ~30 days in most of the studies. The presence of extrapulmonary TB ranged from 19 to 64% of the cases. Comorbidities, especially those related to immunosuppression, such as HIV infection, are considered risk factors for developing respiratory failure and requiring mechanical ventilation (MV). The most common radiological findings are reticular infiltrates and consolidation, and cavitations can occur in 27–50% of cases [2].

The leading cause of respiratory intensive care unit (RICU) admission was respiratory failure, and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores ranged from 13 to 23 in most of the studies [4]. Frame *et al.* [5] evaluated the factors associated with the development of respiratory failure and the need for MV. Gram-negative pneumonia or sepsis, chronic obstructive pulmonary disease, history of poor compliance with TB treatment, and cancer were predictors of respiratory failure. However, despite their high mortality rate, the TB-related critical conditions are rarely reported. The cases of TB requiring intensive care represent 1–3% of all patients with TB [5–7].

Limited studies reported a few factors that contribute to mortality among critically ill patients with TB, such as extensive fibrocavitary disease and consolidations on chest radiographs, acute respiratory distress syndrome, sepsis, and multiple organ failure (MOF) also carry a very high mortality [3,8,9]. Appropriate anti-TB treatment is an important factor that can affect patient outcome. Higher mortality is found among patients who do not receive optimal treatment [10].

There are limited data regarding patients with active pulmonary tuberculosis (APTB) requiring ICU admission, especially when reported from developing countries. To our knowledge, this has never been

studied before in Egypt. This study aims to describe and determine the clinical presentation, mortality rate, and risk factors associated with mortality in patients with APTB requiring RICU admission.

Patients and methods

This was a retrospective–prospective study design initiated in January 2011 in which adult patients (>16 years) with APTB previously or subsequently admitted to the RICU of Abbassia Chest Hospital between January 2009 and December 2010 (retrospective part) and between January 2011 and December 2011 (prospective part), respectively, were included.

Patients who stay or stayed at RICU for less than 24 h or presenting with inactive pulmonary TB or extrapulmonary TB were excluded.

The Abbassia Chest Hospital is a special, tertiary care hospital with 600-bed occupancy in which 100 of them are for TB, 32 ICU beds; three of them are isolated for APTB. TB treatment in the hospital is according to the Egyptian national guidelines [11].

The following data were obtained from the medical records:

Demographic characteristics

It included age, sex, special habits of medical importance, and comorbidities.

Clinical characteristics

(1) Pulmonary TB presentations: symptoms included the presence or absence of the following presenting symptoms: fever, cough, dyspnea, hemoptysis, loss of body weight, and symptoms more than 30 days. Signs included blood pressure, temperature, and heart rate.
(2) Pattern of pulmonary TB: whether it is miliary or pneumonic TB type.
(3) Radiological features: chest radiographic findings commenting on extent of lesion(s) whether minimal, moderate, or far advanced lesions as previously prescribed in details [12].
(4) Respiratory failure and MOF occurrences.
(5) Scores: APACHE II score and Glasgow Coma Scale (GCS) score.
(6) RICU stay: causes, type of admission (early or late), length of stay, and recorded complications during RICU stay.

Laboratory investigations on admission

This included white cell count, hemoglobin, coagulation profile, liver and renal function tests, electrolytes, and arterial blood gases analysis.

Therapeutic characteristics

This included anti-TB drug regimen, oxygen therapy, and MV.

Outcomes

This included RICU outcome (survivors and nonsurvivors).

Definitions

Case definitions of active pulmonary tuberculosis

(1) Smear and/or culture-positive pulmonary TB patient in one of three ways: patient with at least two sputum specimens positive for acid fast bacilli (AFB) by microscopy or patient with at least one sputum, bronchial aspirates, or bronchoalveolar lavage fluid positive for AFB by microscopy and radiographic abnormalities consistent with pulmonary TB and decision by a physician to treat with a full course of anti-TB chemotherapy or patient with at least one sputum specimen positive for AFB by microscopy, which is culture positive for *M. tuberculosis* [11].
(2) Histopathological diagnosis of computed tomography-guided biopsy or transbronchial samples showing caseating granulomatous reaction.

Drug-resistant tuberculosis

Drug-resistant TB is defined as multidrug resistant tuberculosis (MDR-TB) in which colonies are resistant to at least isoniazid and rifampicin [11].

Extensive drug-resistant tuberculosis

Extensive drug-resistant tuberculosis (XDR-TB) is defined as TB in which in addition to being resistant to rifampicin and isoniazid, colonies are resistant to one of the fluoroquinolones and one or more than one of the injectable drugs (kanamycin, amikacin, and capreomycin) [11].

Respiratory failure

Respiratory failure was defined as a PaO_2, measured at rest at sea level, of less than 60 mmHg or a $PaCO_2$ above 49 mmHg. Type I respiratory failure was defined as hypoxemia without hypercapnia, but type II respiratory failure is associated with hypercapnia [13,14].

Multiple organ failure

MOF was defined as the failure of more than one organ.

Acute respiratory distress syndrome

Acute respiratory distress syndrome was diagnosed based on the criteria defined in the American–European consensus conference [15].

Early/late intensive care unit admission

Early ICU admission was defined as admitted directly or transferred to an ICU within 4 days of admission.

Late ICU admission was defined as transferred to an ICU after more than 4 days of admission to TB ward.

Glasgow Coma Scale

GCS score was calculated as previously stated in details using medical calculator available on the internet [16].

Acute Physiology and Chronic Health Evaluation II

APACHE II score was calculated using medical calculator available on the internet [17].

Statistical analysis

The collected data were coded, tabulated, and statistically analyzed using statistical package for social sciences software (SPSS, version 18.0; SPSS Inc., Chicago, Illinois, USA).

Descriptive statistics were presented for numerical parametric data as mean ± SD, minimum and maximum of the range, and for numerical nonparametric data as median and first and third interquartile range, whereas they were presented for categorical data as number and percentage.

Analysis was performed for quantitative variables using independent *t*-test in cases of two independent groups with parametric data and using the Mann–Whitney *U*-test in cases of two independent groups with nonparametric data. Inferential analysis was performed for qualitative data using the χ^2-test for independent variables.

Receiver–operator characteristic curve was used to evaluate the performance of different tests and to differentiate between certain groups. Logistic regression model was used to find out independent factors affecting nonsurvival.

The level of significance was considered at *P* value less than 0.05 as significant, otherwise nonsignificant.

Results

A total of 100 patients were included during the study period from January 2009 to December 2011 (retrospective part included 60 patients and prospective part included 40 patients). Of 100 patients studied, 74 (74%) died in the ICU.

Demographic characteristics

The baseline demographic characteristics of both survivor and nonsurvivor patients are shown in Table 1. The median age of all patients was 38 years. Men outnumbered women. Female frequency was significantly higher in nonsurvivors than in survivors. Liver impairment (48%) was the most common comorbidity. Four of the 100 patients were positive for HIV infection.

Clinical characteristics

The clinical characteristics including causes of RICU admission and complications of studied cases are illustrated in Tables 2 and 3. Fever was the most common symptom. Pneumonic pattern of pulmonary TB represented the majority of cases than miliary pattern. The majority of radiographic findings were moderate to far advanced lesions. The median length of stay in RICU for all patients was 5 days (range 2–60 days). Sixty-five percent of studied patients needed MV. Respiratory failure was the most common cause of admission in the RICU. Complications occurred in 45% of cases in which electrolyte disturbance was the most common complication recorded. Lower diastolic

Table 1 Comparison between survivors and nonsurvivors with respect to demographic characteristics

Variables	Patients (*N* = 100)	Nonsurvivors (*N* = 74)	Survivors (*N* = 26)	*P*
Age (years)				
Median (IQR)	38.0 (27.3–53.8)	37.0 (27.0–53.5)	39.0 (27.8–54.0)	0.651[a]
Range	17.0–73.0	17.0–73.0	22.0–63.0	
Sex				
Female	20 (20.0)	19 (25.7)	1 (3.8)	0.017[b,*]
Male	80 (80.0)	55 (74.3)	25 (96.2)	
Current smoking	70 (70.0)	44 (59.5)	16 (61.5)	0.852[b]
Addiction	25 (25.0)	18 (24.3)	7 (26.9)	0.792[b]
Comorbidities				
Any comorbidity	75 (75.0)	59 (79.7)	16 (61.5)	0.065[a]
Diabetes mellitus	20 (20.0)	14 (18.9)	6 (23.1)	0.648[a]
Renal impairment	20 (20.0)	18 (24.3)	2 (7.7)	0.068[a]
Previous IST	7 (7.0)	7 (9.5)	0 (0.0)	0.104[a]
Liver impairment	48 (48.0)	37 (50.0)	11 (42.3)	0.499[a]
Pre-existing PD	10 (10.0)	8 (10.8)	2 (7.7)	0.648[a]
HIV	4 (4.0)	4 (5.4)	0 (0.0)	0.226[a]
Hypertension	5 (5.0)	(6.7)	0 (0.0)	0.174[a]
Cardiac	1 (1.0)	1 (1.4)	0 (0.0)	0.551[a]

Data are presented as *n* (%), unless otherwise indicated; IQR, interquartile range; IST, immunosuppressive therapy; PD, pulmonary disease. [a]Mann–Whitney *U*-test; [b]χ^2-Test; *Significant.

Table 2 Comparison between survivors and nonsurvivors with respect to clinical characteristics

Variables	Total patients	Nonsurvivors	Survivors	*P*
Presenting symptoms				
Fever	100 (100)	74 (100.0)	26 (100)	–
Cough	98 (98)	72 (97.3)	26 (100)	0.397[d]
Dyspnea	99 (99)	73 (98.6)	26 (100)	0.551[d]
Hemoptysis	27 (27)	17 (23.0)	10 (38.5)	0.126[d]
Body weight loss	93 (93)	69 (93.2)	24 (92.3)	0.872[d]
Symptoms >30 days	100 (100)	74 (100.0)	26 (100)	–
Signs (mean ± SD)				
SBP (mmHg)	99.2 ± 25.3	97.5 ± 26.9	103.8 ± 20.0	0.211[d]
DBP (mmHg)	62.4 ± 18.5	60.2 ± 18.5	68.5 ± 17.4	0.046[d]*
Temperature (°C)	37.5 ± 0.9	37.4 ± 0.7	37.9 ± 1.1	0.053[d]
Heart rate (BPM)	109.1 ± 15.1	110.1 ± 15.2	106.3 ± 14.7	0.275[d]
Pattern of PTB				
Miliary	8 (8.0)	4 (5.4)	4 (15.4)	0.107[c]
Pneumonia	92 (92.0)	70 (94.6)	22 (84.6)	
Radiological features				
Minimal lesion	17 (17.0)	11 (14.9)	6 (23.1)	0.024[c]*
Moderate advanced	26 (17.0)	15 (20.3)	11 (42.3)	
Far advanced	57 (57.0)	48 (64.9)	9 (34.6)	
Respiratory failure[a]	74 (74.0)	56 (75.7)	18 (69.2)	0.519[c]
Type I	47 (63.5)	32 (57.1)	15 (83.3)	0.045[c]*
Type II	27 (36.5)	24 (42.9)	3 (16.7)	
APACHE II score				
Mean ± SD	20.5 ± 5.9	21.4 ± 6.2	17.7 ± 3.9	0.005*
Range	9.0–39.0	9.0–39.0	9.0–25.0	
GCS				
Mean ± SD	13.0 ± 3.6	12.3 ± 3.9	14.7 ± 0.7	<0.001*
Range	3.0–15.0	3.0–15.0	13.0–15.0	
Time of RICU admission				
Early	26 (26.0)	22 (29.7)	4 (15.4)	0.151[d]
Late	74 (74.0)	52 (70.3)	22 (84.6)	
Length of stay in RICU (days)				
Median (IQR)	5.0 (3–7)	4.0 (3–7)	5.0 (4–7)	0.258[c]
Range	2–60	2–60	2–12	
Mechanical ventilation	65 (65.0)	62 (83.3)	3 (11.5)	<0.001*[d]
Duration on MV (days)				
Median (IQR)	3.0 (2–5.5)	3.0 (2–6)	[b]	
Range	1–50	1–50		

Data are presented as *n* (%), unless otherwise indicated. APACHE II, Acute Physiology and Chronic Health Evaluation II; BPM, beats per minute; DBP, diastolic blood pressure; GCS, Glasgow Coma Scale; IQR, interquartile range; MV, mechanical ventilation; PTB, pulmonary tuberculosis; RICU, respiratory intensive care; SBP, systolic blood pressure; [a]Refer to text for respiratory failure definitions; [b]Median could not be calculated as only three patients survived MV and duration were 3, 3, and 1 days; [c]Mann–Whitney *U*-test; [d]χ^2-Test; *Significant.

blood pressure, far advanced lesion, type II respiratory failure, higher APACHE II score, lower GCS score, more need for MV, and electrolytes disturbances complication occurrence were significantly more frequent in nonsurvivors than in survivors in the RICU. Respiratory alkalosis was the cause of RICU admission in only two survivor cases, and hepatotoxicity was a recorded complication in also two survivor cases only. Thus, both were significantly more in survivors than in nonsurvivors.

Laboratory investigations on admission

The laboratory investigations on admission of studied cases are shown in Table 4. Albumin, pH, and O_2 saturation were significantly lower in nonsurvivors than in survivors. Total leukocytic count, international normalized ratio, urea, creatinine, and bilirubin were significantly higher in nonsurvivors than in survivors.

In nonsurvivors, 70 (94.5%) and four (5.4%) patients were diagnosed by positive acid-fast bacilli smears and positive TB culture, respectively. However, in survivors patients, 24 (92.3%), one (3.8%), and one (3.8%) were diagnosed by positive acid-fast bacilli smears, positive TB culture, and tissue biopsy, respectively. Four nonsurvivors cases were resistant to anti-TB drugs (two MDR-TB and two XDR-TB. MDR-TB and XDR-TB-positive findings were nonsignificantly present only in nonsurvivors ($P = 0.226$).

Table 3 Comparison between survivors and nonsurvivors with respect to causes of respiratory intensive care unit admission and complications

Variables	Patients (*N* = 100)	Nonsurvivors (*N* = 74)	Survivors (*N* = 26)	*P*
Causes of ICU admission				
RF	52 (52)	39 (52.7)	13 (50)	0.812[a]
Massive hemoptysis	1 (1.0)	1 (1.4)	0 (0)	0.551[a]
Pneumothorax	4 (4.0)	2 (2.7)	2 (7.7)	0.264[a]
Pulmonary edema	1 (1)	0 (0.0)	1 (3.8)	0.090[a]
DKA	9 (9)	5 (6.8)	4 (15.4)	0.186[a]
Respiratory alkalosis	2 (2)	0 (0.0)	2 (7.7)	0.016[a,*]
Hyperkalemia	4 (4)	4 (5.4)	0 (0)	0.226[a]
Hypokalemia	2 (2)	1 (1.4)	1 (3.8)	0.434[a]
DCL	7 (7)	5 (6.8)	2 (7.7)	0.872[a]
BGC	11 (11)	7 (9.5)	4 (15.4)	0.406[a]
Shock	30 (30)	25 (33.8)	5 (19.2)	0.164[a]
Severe anemia	8 (8)	5 (6.8)	3 (11.5)	0.439[a]
DVT	2 (2)	2 (2.7)	0 (0)	0.397[a]
Hematemesis	3 (3)	1 (1.4)	2 (7.7)	0.103[a]
TB meningitis	3 (3)	2 (2.7)	1 (3.8)	0.769[a]
MOF	2 (2)	2 (2.7)	0 (0)	0.397[a]
SVT	2 (2.0)	2 (2.7)	0 (0)	0.397[a]
Complications				
Any complication	45 (45)	33 (44.5)	12 (46.2)	0.891[a]
Electrolyte disturbances	40 (40)	35 (47.3)	5 (19.2)	0.012[a,*]
Shock	7 (7)	7 (9.5)	0 (0)	0.104
Anemia	3 (3)	3 (4.1)	0 (0)	0.297
Hepatotoxicity	2 (2)	0 (0)	2 (7.7)	0.016[a,*]
RF	22 (22)	17 (23)	5 (19.2)	0.692
Pyopneumothorax	1 (1)	0 (0.0)	1 (3.8)	0.090[a]
Pneumothorax	3 (3)	2 (2.7)	1 (3.8)	0.769[a]
Empyema	1 (1)	1 (1.4)	0 (0)	0.551[a]
VF	1 (1)	1 (1.4)	0 (0)	0.551[a]
AF	1 (1)	1 (1.4)	0 (0)	0.551[a]
MOF	1 (1)	1 (1.4)	0 (0)	0.551[a]

AF, atrial fibrillation; BGC, bad general condition; DCL, disturbed conscious level; DKA, diabetic ketoacidosis; DVT, deep venous thrombosis; MOF, multiple organ failure; RF, respiratory failure; SVT, supraventricular tachycardia; TB, tuberculosis; VF, ventricular fibrillation; [a]χ^2-Test; *Significant.

Therapeutic characteristics

Comparison between survivors and nonsurvivors with respect to treatment regimens was significantly different (Table 5).

Risk factors for nonsurvival

On studying different involved factors, pneumonia pattern, female sex, far advanced lesion (by radiology), and renal impairment were found to be a significant model for risk factors for nonsurvival (Table 6) using logistic regression model.

Predictive factors for respiratory intensive care unit mortality

On studying different involved factors to search for predictors of mortality, MV was the only predictor of mortality with diagnostic accuracy of 85%, whereas other factors such as female sex, far advanced lesion, electrolytes disturbance, and renal impairment on admission were nonpredictors of mortality with diagnostic accuracy less than 85% (Table 7). Albumin, O_2 saturation, GCS, urea, creatinine, and APACHE II score were nonpredictors for mortality as indicated by low area under curve (<0.9) (Table 8).

Discussion

Across the world, TB remains an important public health problem, especially in developing countries. Despite the availability of curative therapy, a large proportion of patients with TB are being hospitalized. In-hospital mortality rates remain high, particularly among patients with TB requiring ICU [8].

Pulmonary TB requiring ICU care is rare [5]. To our knowledge, this was the first Egyptian study to deal with APTB inside RICU. This study aimed to evaluate, on retrospective–prospective basis, the clinical presentation, mortality rate, and risk factors associated with mortality among RICU patients with APTB.

The mortality rate for ICU patients with TB is difficult to compare because of different definitions of estimation used (ICU morality, in-hospital morality, 30-day mortality, and 180-day mortality) by previous studies [3,10,18,19]. In addition, some studies included only cases of APTB [3,10,19], whereas others incorporated nonactive or extrapulmonary TB cases [19]. However, the mortality rate varies in the literature from 22.4 to 90%, with median values around 60% [3,10,18-20]. In the current study, the RICU mortality rate for the APTB population was 74%. Taking into consideration that 64.9, 75.7, 83.3, and 5.4% of current study nonsurvivor patients had far advanced TB lesion, respiratory failure, MV, and HIV-positive cases, respectively, the mortality rate may be judged comparable with previous TB ICU mortality rates.

The median age of the patients in this study was 38 years. However, the median age in different studies varies in the literature from 41 to 63 years [5,19,21]. Sex distribution was in line with data from previous studies, as men (80%) were seen more often than women (20%) [10,19]. One possible explanation for this disparity might be the higher exposure of men to droplet infections due to a greater prevalence of outdoor occupations. Aggravating factors such as smoking, exposure to air pollutants, and industrial exposure may also predispose men to TB [19]. However, women were significantly higher in nonsurvivor than in survivor patients, and it was one of the risk factor of mortality. In contrast, Erbes *et al.* [10] found no significant

Table 4 Comparison between survivors and nonsurvivors with respect to laboratory findings

Variables	Patients (*N* = 100)	Nonsurvivors (*N* = 74)	Survivors (*N* = 26)	*P*
Mean ± SD				
Hb (g/dl)	10.1 ± 2.4	10.0 ± 2.2	10.2 ± 2.9	0.817[b]
PT (s)	16.5 ± 4.3	16.8 ± 4.0	15.7 ± 5.0	0.274[b]
PTT (s)	35.8 ± 7.4	36.4 ± 7.2	34.1 ± 7.6	0.179[b]
Albumin (g/dl)	2.7 ± 0.7	2.6 ± 0.7	3.0 ± 0.5	<0.001[b,*]
K (mEq/l)	4.1 ± 0.8	4.2 ± 0.9	3.9 ± 0.6	0.221[b]
Na (mEq/l)	132.9 ± 7.1	132.8 ± 7.1	132.9 ± 7.1	0.957[b]
pH	7.41 ± 0.1	7.37 ± 0.1	7.45 ± 0.1	0.003[b,*]
O_2 saturation%	83.8 ± 15.0	81.3 ± 16.2	91.0 ± 7.0	<0.001[b,*]
Median (IQR), range				
TLC (×10^3/ml)	10.6 (7.2–13.7) 2.9–32	11.3 (7.8–14.0) 2.9–24.7	7.7 (5.6–11.6) 3.5–32	0.038[a,*]
INR	1.3 (1.1–1.5) 0.9–3.3	1.3 (1.2–1.6) 1.0–3.3	1.1 (1–1.4) 0.9–3.2	0.006[a,*]
Urea (mg/dl)	36.5 (22–64) 15–248	45 (25.8–78.3) 15–248	22 (20–35) 18–51	<0.001[a,*]
Creatinine (mg/dl)	1.0 (0.9–1.4) 0.5–4.2	1.1 (0.9–1.6) 0.6–4.2	0.9 (0.8–1) 0.5–1.4	<0.001[a,*]
SGOT (U/ml)	60.0 (40–128.8) 23–409	65.0 (40–136.3) 23–409	50.5 (35–101) 26–327	0.381[a]
SGPT (U/ml)	41.5 (25.3–84.8) 12–387	43.0 (27.5–85.1) 12.0–387.0	35.5 (20–79) 14–375	0.187[a]
Bilirubin (mg/dl)	1.1 (0.9–2.1) 0.6–12.9	1.3 (0.9–2.1) 0.6–12.9	0.9 (0.8–1.6) 0.6–4.8	0.028[a,*]
$PaCO_2$	29.0 (22–46.9) 9.8–115	29.4 (21.8–54.8) 9.8–115	29.0 (21.8–31.5) 14–80	0.381[a]
PaO_2	57.5 (46.6–79.5) 27–154	57.5 (40.9–80.3) 27–154	56.5 (51.5–76.3)47–154	0.187[a]

Hb, hemoglobin; INR, international normalized ratio; IQR, interquartile range; PT, prothrombin time; PTT, partial thromboplastin time; SGOT, serum glutamate oxaloacetate transaminase; SGPT, serum glutamate pyruvate transaminase; TLC, total leukocytic count; [a]Mann–Whitney *U*-test; [b]Independent *t*-test; *Significant.

Table 5 Comparison between survivors and nonsurvivors with respect to antituberculosis treatment regimens and its duration

Variables	Patients	Nonsurvivors	Survivors	*P*
Treatment regimens [*n* (%)]				
Cat I	81 (81)	55 (55)	26 (26)	0.041
Cat II	15 (15)	15 (15)	0 (0)	
MDR regimen	1 (1)	1 (1)	0 (0)	
No treatment	3 (3)	3 (3)	0 (0)	
Duration of treatment (days) [median (IQR), range]				
Cat I	15 (10–20) 3–25	10.0 (8–15) 5–20	5.0 (4–10) 3–25	0.532#
Cat II	30 (10–40) 10–60	30 (10–40) 10–60	–	–
MDR regimen	90	90	–	–

Antituberculosis treatment regimens were according to National Tuberculosis Control Program [11]. Cat I, category I: intensive phase 2HRZE (2 months), continuation phase 4HR (4 months); Cat II, category II: intensive phase 2HR2ES (1st 2 months), then HRZE (1 month), continuation phase 5HRE (5 months); E, Ethambutol; H, Isoniazid; R, Rifampicin; S, Streptomycin; Z, Pyrazinamide; MDR, multidrug resistant tuberculosis.

Table 6 Risk factors for nonsurvival (logistic regression model)

Factors	β	SE	*P*	OR (95% CI)
Pneumonic pattern	3.51	1.25	0.005	33.36 (2.88–386.39)
Female	3.06	1.29	0.018	21.42 (1.70–270.59)
Far advanced lesion	2.07	0.60	0.001	7.93 (2.44–25.77)
Renal impairment	1.52	0.85	0.043	4.58 (0.87–24.25)

CI, confidence interval; OR, odds ratio; SE, standard error; β, regression coefficient; Constant (represent other factors tested, other than those in the model): β = −16.60 and SE = 4.06.

Table 7 Performance of some suggested non-numerical value factors for prediction of nonsurvival

Characters (%)	Female	Renal impairment[a]	Far advanced lesion	Mechanical ventilation	Electrolytes disturbance[b]
Sensitivity	25.7	24.3	64.9	83.8	1.4
Specificity	96.2	92.3	65.4	88.5	92.3
PPV	95.0	90.0	84.2	95.4	33.3
PNV	31.2	30.0	39.5	65.7	24.7
DA	44.0	42.0	65.0	85.0	25.0

DA, diagnostic accuracy; PNV, predictive negative value; PPV, predictive positive value; [a]Serum creatinine above normal range; [b]Abnormal sodium and/or potassium levels.

Table 8 Performance of some suggested numerical value factors for prediction of nonsurvival

Factors	AUC	SE	*P*	95% CI
Albumin	0.67	0.06	0.012	0.56–0.78
O_2 saturation	0.65	0.06	0.020	0.54–0.77
GCS	0.66	0.05	0.017	0.55–0.77
Urea	0.75	0.05	<0.001	0.65–0.85
Creatinine	0.74	0.05	<0.001	0.65–0.84
APACHE II	0.67	0.06	0.008	0.56–0.79

APACHE, Acute Physiology and Chronic Health Evaluation; AUC, Area under curve; CI, confidence interval; GCS, Glasgow Coma Scale; SE, standard error.

difference between survivors and nonsurvivors with respect to patient sex. This discrepancy may be related to difference in disease severity, comorbidities, and need for MV between both studies.

In the present study, a history of renal impairment was found to be a risk factor for ICU mortality, similar to the

study by Silva *et al.* [18]. However, it did not influence the mortality rates significantly. Erbes *et al.* [10] identified a history of chronic pancreatitis as independent risk factor for mortality, which was related to chronic alcohol abuse. Other comorbidities such as diabetes or even coinfection with HIV encountered in the current study as well as in other studies [3,10,18] did not influence the mortality rates significantly in patients with TB requiring ICU. In fact, mortality in patients with TB–HIV coinfection seems to be related to the patient's overall degree of immunosuppression [22].

The clinical presentation of current study population was similar to previous studies [3,10,19]. Fever was the most common symptom observed upon presentation to the hospital and was seen in all (100%) patients. Fever was indicative of a high-grade of infection that required immediate attention [19]. Dyspnea, cough, hemoptysis, and loss of body weight were also frequent presenting symptoms, similar to other previous studies [3,10,19].

In the current study, nonsurvivor patients with far advanced lesion were significantly more than survivor patients, and far advanced lesion was significant risk factor of mortality. Other studies reported increased mortality among those with extensive bilateral infiltrates and cavitary lesions, but it did not reach a significant value [10]. This may be due to the increased number of studied patients with extensive lesions in current study in comparison with Erbes *et al.*'s [10] study.

APACHE II score was found to be significantly higher in nonsurvivor patients compared with survivor patients. It has been previously found that APACHE II score at ICU admission might underestimate the morality rate among TB patients requiring MV [23]. In the present study as well as in Silva *et al.*'s [23] study, the mean APACHE II score on admission was 20.5 ± 5.9 and 21.2 ± 6.5, respectively, indicating a mortality rate around 30%. However, the mortality rates were found to be 74 and 67.8%, respectively [19]. It is possible that the events occurring during hospitalization, such as respiratory failure or any other complications, contributed to the increased mortality rates [23].

There was a significant increase in electrolyte disturbances as a recorded ICU complication in nonsurvivors compared with survivor patients. Electrolytes disturbances in TB patients are likely multifactorial including disease chronicity, poor nutritional status, anti-TB treatment-induced diarrhea and vomiting, and aminoglycosides and capreomycin-induced hypokalemia, hypomagnesemia, and hypocalcemia, especially in MDTR-TB. Electrolyte disturbances may be manifested as subtle complaints up to lethal cardiac arrhythmias [24]. This may explain the cardiac complications such as atrial fibrillation and ventricular fibrillation that occurred in the current study.

Hypoalbuminemia was a common laboratory finding in previous studies dealing with TB patients requiring ICU admission similar to current study results [3,10,18]. Unlike previous studies, hypoalbuminemia had affected mortality among current study patients. However, it was not among the predictor of mortality.

Pulmonary TB is a rare primary cause of acute respiratory failure (ARF) [6]. However, high mortality rates have been reported in patients with ARF arising from TB [3]. In the present study, respiratory failure was clinically manifested in 74% of study population with a morality rate 75%, which lays in range with previous studies results [3,5,8,10].

Appropriate anti-TB treatment is an important factor affecting patient's outcome. It was found that a higher mortality is present in patients who did not receive an optimal treatment including isoniazid and rifampicin [10,23]. In the current study as well as in other studies, optimal treatment is difficult to achieve in those critically ill TB patients due to use of alternative regimens (without isoniazid and rifampicin) for maintenance therapy in patients with impaired liver function or organ dysfunction and with low serum concentrations of anti-TB drugs as results of uncertain enteral absorption of drugs and hypoalbuminemia [23,25–27]. The combined MDR-TB and XDR-TB rate in the present study reached 4% with its subsequent expected adverse outcomes such as treatment failure and death.

MV was the only predictive factor associated with ICU mortality in the current study, which is in accordance with Lee *et al.* [3] and Erbes *et al.*'s [10] studies. The mortality rate in patients with APTB requiring MV in the current study was high (83%). ARF caused by TB and requiring MV has been associated with morality rates ranging from 17.5 to 81% [3,5,10,23] and being 93% in one study [8].

In the ICU setting, a high clinical suspicion is mandatory in suspected cases, with smear microscopy for AFB and culture of respiratory secretions in suspected cases. Biosafety measures to suspected or diagnosed cases including individual isolated negative-pressure rooms, usage of endotracheal suctioning without disconnection (closed system), and a bacterial filter should be placed in the expiratory line of the

ventilator circuit. Healthcare professionals should wear N95 masks while performing the intubation/suctioning procedure and should also be periodically screened for TB [28].

The current study as any other study has its own limitations that should be noted. Part of the information was obtained retrospectively from patient records and probably was not as complete and accurate as when data collection was performed in the prospective part of study. Single-center study with relatively small sample size may have lacked sufficient statistical power to reveal an association with some of the factors. Despite these limitations, the present results provide important implications for similar demographic areas and clinical settings.

In conclusion, the present study found a very high mortality rate among APTB patients requiring RICU admission. Risk factors identified for nonsurvival were pneumonia pattern and far advanced lesion by radiology, female sex, and renal impairment. Only MV was a predictor of RICU mortality. Measures aimed at promoting appropriate management of these recognized risk factors and predictor of morality could contribute to improving outcome.

Acknowledgements

Conflicts of interest

None declared.

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