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TUBERCULOSIS IN ICU PATIENTS

Dr. Uzm. İrem Akin Şen* and Prof. Dr. Hülya Sungurtekin

Pamukkale University Hospital Anesthesia Intensive Care Unit, Denizli, Türkiye.

***Corresponding Author: Dr. Uzm. İrem Akin Şen**

Pamukkale University Hospital Anesthesia Intensive Care Unit, Denizli, Türkiye.

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ABSTRACT

Introduction: Tuberculosis (TB) is an infectious disease that causes significant mortality and morbidity worldwide.There are still many questions about the diagnosis of TB. In this study, we evaluated the clinical and laboratory finidings of patients with TB who require intensive-care unit (ICU) support. **Methodology:** Patients of the University Hospital Anesthesia Intensive Care Unit who received inpatinet treatment for active TB between 2012-2017 were retrospectively evaluted. Demographic characteristics, medical history, as well as clinical and laboratory findings were analyzed statistically from the patient files. Data were given as mean ± SD or %. **Results:** Twelve patients with active TB, of which nine (75%) were male, and three (25%) were female, were included in the study.The mean age was 55.67 ± 20.1 years.The Acute Physiology and Chronic health Assesment (APACHE II), the Simplified Acute Physiology Score (SAPS 2) and the Sequential Organ Failure Assesment Score (SOFA) were significantly higher (p; 0.002, 0.0001 and 0.041 respectively). The mean duration of ICU admission was 30.4 days. Nine patients were diagnosed with pulmonary TB (75%) and three patients with suspected TB meningitis (25%). Ten patients (83.3%) died in the ICU. **Conclusions:** TB is a serious health problem of international significance and remains one of the deadliest infectious diseases. It may be the major cause of death among patients hospitalized in intensive care. Early and effective treatment may decrease mortality in TB patients .TB should always be remembered and considered as a possibility.

KEYWORDS: Tuberculosis; intensive care unit; critical illness; acute disease.

INTRODUCTION

Tuberculosis (TB) is an important public health problem. It is the second most common infectious disease in the world after human immunodeficiency virus (HIV).[1] Globally, TB has been detected in 9 million people, and more than 1.5 million people (360,000 HIV-positive) died from the disease, according to the World Health Organizations (WHO) 2013 data.[2] In 2002, the prevalence of TB in Turkey was 38/100,000, while in 2010, it caused the death of 24/100,000. In 2009, the mortality rate associated with TB was 3,1% in all patients; 3,0% were newly diagnosed, and 3,3% were previously treated patients.[3] TB can affect all organs of the body, especially, with the frequent pulmonary involvement. The most common form in adults is postprimer TB, which can occur with various clinical findings and radiological images in places with high prevalence. TB may mimic non-infectious disease or any infectious disease and may begin acutely. The most common acute forms are miliary, meningeal, abdominal and pulmonary TB.[4,5]

The development of acute TB is a serious issue and 1-3% of the cases require follow-up and treatment in intensive care units (ICUs). Pulmonary TB is the most common acute form requiring intensive care follow-up. It has been reported to cause 25-33% of in-hospital mortality. The mortality rate is increase up to 70% in patient requiring intensive care follow-up and provided with mechanical ventilator support.[5] It was aimed determined the characteristics of patients with TB requiring ICU support, by considering clinical, laboratory and radiological findings in our ICU in this study.

MATERİAL AND METHODS

This study was done on a retrospective review of patients with acute TB who were hospitalized in University Hospital Anesthesiology ICU between the years of 2012 and 2017. The investigation was approved by the University Ethics Committee (no:60116787-020/55450). Only new TB cases have been included in the study. Patients, whose TB treatment was initiated before 30 days, were excluded from the study. Clinical data and radiological findings were obtained from medical records. The clinical data consisted of age, gender, the Acute Physiology and Chronic Health Assessment (APACHE II) score, the Simplified Acute Physiology Score (SAPS 2) and the Sequential Organ Failure Assessment Score (SOFA), as well as the presence of comorbidity, length of stay in ICU, nosocomial infection,

radiological involvement, biochemical data and complete blood count. IBM SPSS Statistics 23 program was used for statistical analysis. A- Chi a square test was performed for comparison with $p<0.05$ was significant.

RESULTS

In our study, 12 patients with acute TB were followed up in the ICU over a 5-year period. Clinical and characteristic features of the patients are summarized in Tables 1 and 2.

The median age of the patients was 58,5 (min-max, 22-83) years. There were 9 males and 3 females. Intensive care admission was due to respiratory failure in 9 patients (75%) and seizures in the remaining 3 patients (25%). There was pulmonary involvement in 6 (50%) of 12 patients, miliary involvement in 3 (25%) patients and extrapulmonary involvement in 3 (25%) patients. Six (50%) patients had comorbid diseases. The other patients had no additional illnesses. Only 2 (16.6%) patients were receiving immunosuppressive therapy; while the remaining 10 (83.3%) patients did not have any immunosuppressive treatment. All patients received mechanical ventilator support. .Eight (66.6%) patients had nosocomial infections, such as bacteremia and ventilator-associated pneumonia.

The median APACHE II score was 29.5 (min-max, 22-39), median SOFA score of 14 (min-max, 8-21) and median SAPS 2 score of 74 (min-max, 49-105). The median partial pressure of oxygen/fraction of inspired oxygen (PaO_2/FiO_2) was 204 (min-max, 33-442). The average length of stay in ICU was 30,4 days. Seven patients required intensive care during the service follow-up. The other 5 patients were directly admitted to the ICU. The average length of stay in hospital was found to be 23,8 days in the service. In total, 11/12 patients died during follow-up in intensive care. During the follow-up 1 patient, was referred to the other center upon request from his relatives. Five (45,4%) patients had septic shock, and the remaining 6 (54,5%) patients died due to acute respiratory distress syndrome. Demographic data, disease severity scores and laboratory values were shown in Table 3.

Table 1: Disease severity score and demographic characteristics of patients.

Patient no.	Age	Gender	APACHE II	SOFA	SAPS 2	Lenght of stay (ward/ICU) (day)
1	82	M	25	10	42	31/50
2	53	M	13	11	38	7/14
3	65	M	27	14	47	-/31
4	34	F	10	4	24	-/17
5	67	M	20	79	31	44/50
6	68	M	11	6	24	9/12
7	24	M	19	11	30	-/8
8	83	F	13	4	24	19/25
9	59	M	29	14	62	13/58
10	58	F	16	6	19	-/32
11	22	M	22	11	43	44/65
12	53	M	31	10	55	-/3

APACHE II: The Acute Physiology and Chronic Health Assessment; ICU: intensive care unit; SAPS 2: the Simplified Acute Physiology Score; SOFA: the Sequential Organ Failure Assessment Score.

Table 2: Clinical data and characteristics of the diseases.

No	MY/ NIMV	Nosocomial infection	Comorbidity	Immunosuppression	TB form	Radiology	Reason for admission
1	MV	resp. culture *Acinetobacter*	DM, CHF	None	Pulmonary	Nodular	Resp. failure
2	MV	resp. culture *Acinetobacter*	None	None	Pulmonary	Nodular	Resp. failure
3	MV	None	None	None	Extra-pulmonary (CNS)	Leptomeningeal	Seizure
4	MV	None	None	None	Pulmonary	Left upper lobe	Resp. failure
5	MV	Resp. culture *Escherichia coli*	CRF	None	Pulmonary	Left upper lobe	Resp. failure
6	MV	Resp. culture *Escherichia coli*	Renal transplantation	+	Pulmonary	Nodular	Resp. failure
7	MV	Resp. culture *Escherichia coli*	None	None	Miliary	Miliary	Resp. failure

8	MV	None	None	None	Miliary	Miliary	Resp. failure
9	MV	Resp. culture *Serratia*	HT	None	Miliary	Miliary	Resp. failure
10	MV	Resp. culture *Pseudomonas*	None	None	Extra-pulmonary (CNS)	Leptomeningeal	Seizure
11	MV	Resp. culture *Acinetobacter*	Allogenic bone marrow transplant-ation	+	Extra-pulmonary (CNS)	Leptomeningeal	Seizure
12	MV	None	COPD	None	Pulmonary	Nodular	Resp. failure

CHF: chronic heart failure; CNS: central nervous system; COPD: chronic obstructive pulmonary disease; CRF: chronic renal failure; DM: diabetes mellitus; HT: hypertension; MV: mechanical ventilation; NIMV: non-invasive mechanical ventilation; Resp: respiratory; TB:tuberculosis.

Table 3: Demographic data, disease severity scores and laboratory values.

Parameter	Mean ± SD	Median (min-max)
Age	55.67 ± 20.1	58.5 (22-83)
APACHE II	19.67 ± 7.23	19.5 (10-31)
SAPS 2	36,58 ± 13,57	34,5 (19-62)
SOFA	15 ± 20,45	10,5 (4-79)
PaO_2/FiO_2	197,83 ± 145,55	137,5 (31-467)
Sodium	139 ± 3,44	138 (134-147)
Potassium	3,98 ± 0,91	3,9 (2,9-5,4)
WBC	11,71 ± 8,34	11,05 (3,07-34,12)
Lymphocytes	0,68 ± 0,5	0,53 (0,18-2,05)
Creatine	0,93 ± 0,77	0,7 (0,36-3,18)
CRP	13,81 ± 6,3	15,29 (2,44-27)
AST	29 ± 16,78	28,5 (8-63)
ALT	18,92 ± 15,95	13 (2-47)
Albumin	2,85 ± 0,46	2,73 (2,2-3,7)

ALT: alanine aminotransferase; APACHE II: the Acute Physiology and Chronic Health Assessment; AST: aspartate aminotransferase; CRP: C-reactive protein; FiO_2: fraction of inspired oxygen; PaO_2: partial pressure of oxygen; SAPS 2: the Simplified Acute Physiology Score; SOFA: the Sequential Organ Failure Assessment Score; WBC: white blood cells.

DISCUSSION

Although TB is a treatable disease, mortality rates of active TB cases in the ICU are very high. Pulmonary and miliary TB, presenting as acute hypoxic respiratory failure, rarely cause acute distress syndrome.[6,7] Central nervous system TB, the most serious form of extrapulmonary TB, follows three progressive stages: stage I, normal consciousness; stage II, unconsciousness or confusion and stage III, stupor or coma.

The most common organs affected are the spleen, liver and lungs, although the bone marrow, kidneys, central nervous system, adrenal gland and peritoneum may also be involved. Symptoms may be acute or chronic. Fever, sweating, fatigue, weight loss, loss of appetite and lung symptoms may also be present, and the disease may be accompanied by hepatosplenomegaly and pancytopenia. Equally large, round interstitial nodular involvement is typically seen on chest X-ray. While the diameter of the nodules is initially 0.5 mm, if the disease not treated, they can reach up to 3 mm. Notably, serum alanine aminotransferase and aspartate aminotransferase levels usually 2-5 times above normal.[8]

In several previous studies, acute respiratory failure and pulmonary TB were predominantly responsible for admission of patients to the ICU.[9-12] In our research, pulmonary involvement was present in 6 patients (50%), miliary involvement in 3 (25%) patients and extrapulmonary involvement in the remaining 3 (25%) patients.

Central nervous system TB has an important place among indications for intensive care hospitalization in cases of TB. The most severe form of central nervous system TB is meningitis. The mortality rate of TB meningitis was reported between 17% and 27% in Turkey.[13,14] Consciousness-related changes are more frequent in the central nervous system meningoencephalitis cases than meningitis.[5] Central nervous system TB can develop following eruption of the cerebral tuberculoma into the subarachnoid space or the bacillus can spread to the bloodstream directly. There may be cranial nerve paralysis. Tuberculomas and vascular occlusions may cause local neurological deficits and seizures. Obstructive hydrocephalus may develop. The cerebrospinal fluid is clear or cloudy, white blood cells: 500 mm^{-3}, leukocytes first, then lymphocytes are dominant. Protein has increased. Glucose is low. The number of bacteria is low. Smear positivity; 5-37% and culture positivity is 40-80%. A fast and sensitive culture system is needed. Computed tomography and magnetic resonance imaging findings strongly suggest TB meningitis.[15] In the current study, we followed TB meningitis suspected cases. Three patients were followed up for intensive care because of the possibility of seizures, and mechanical ventilator support was provided.

TB rarely causes sepsis or septic shock, also known as Landouzy septicemia. This process is usually seen in immunosuppressed patients.[16-18] However, for TB-associated sepsis or septic shock diagnosis,

microorganisms other than Mycobacterium tuberculosis must be excluded. In our study, two patients were immunosuppressed (One of the two patients was allogenic bone marrow transplantation and the other with renal transplantation. Two patients were also died.) and six were not immunosuppressive. In patients with septic shock, blood and other body fluids were isolated from microorganisms outside of TB. These microorganisms included Acinetobacter, Escherichia coli, Serratia and Pseudomonas.

Ryu et al.[19] considered APACHE II scores above 20 in patients with active TB requiring intensive care follow-up, as a poor prognosis. In our study, the APACHE II score was 29,5 (22-39). In several studies, SAPS II was found to be high in this group of patients[11,20,21] in agreement with our result (median, 74; min-max, 49 - 105). Furthermore, the SOFA value (median, 14; min-max, 8 - 21) was also high in our study, which is consistent with the literature.[7,22]

In TB cases followed up in the ICU, prior studies observed no significant change in the serum albumin[22-24] and creatinine levels of patients.[21,24] In our study, serum albumin (median, 2,73; min-max: 2.2-3.7) and creatinine (median, 0,7; min-max: 0,36-3,18). Laboratory values such as albumin and creatinine were normal in agreement with the literature.

ICU mortality has been significantly associated with age, a low Glasgow score, SAPS II, a high SOFA Score, mechanical ventilation, ARDS, MOF, sepsis, lymphopenia, hypoproteinemia, low serum albumin levels, vasoactive drugs, renal replacement therapy, and two concomitant non-tuberculous infections.[10,11,19,24] Failure of any organ can negatively affect the TB prognosis, and it is associated with increased mortality. However, among all potential organ dysfunctions, neurological dysfunction occurred more frequently in non-survivors than in survivors, even after excluding patients with primary CNS involvement.[11] In patients with TB requiring intensive care follow-up, Frame et al.[4] documented a mortality rate of 67% in 43 patients and Erbes et al.[10] found a mortality rate 22,4 % in 58 patients. In our study, the mortality rate of patients with acute TB in the ICU was 91,6 %. Our work is a single centered study of very small sample size. Therefore, it may not be reliable in determine the mortality rate.

CONCLUSION

TB remains an important disease, despite considerable improvement in the diagnosis and treatment procedures in recent years. Prospective studies will help to identify new parameters and treatment strategies that can be used in TB cases in ICUs.

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