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Study of pattern of Tuberculosis patients admitted to Intensive Care Unit in GGH, Kadapa.

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Abstract
Background: *India is one of the highest Tuberculosis (TB) burdened countries in the world. Death due to TB crosses 1.6 million every year out of which one third is from India. This study aims at evaluating the pattern of TB patients getting admitted to Intensive Care Unit (ICU) in GGH, Kadapa.*
Methods and materials: *A prospective observational study was done from May 2019 to October 2019.*
Inclusion criteria: This study includes all newly diagnosed TB patients, treatment defaulters, patients with relapse and patients currently on treatment of TB(pulmonary and extra pulmonary) who were admitted to ICU.
Exclusion criteria: patients below 18 years were excluded from the study.
Results: *Atotal of 50 patients were admitted to ICU during this period. The mean age of patients admitted is 47.5 ±1.56 years. Mortality rate was 34 %. Males were significantly more than females. 14 patients presented with extra pulmonary TB. Overall median length of ICU stay is 5.28±1.15 days. The Respiratory failure is the most common cause of admission. Mechanical ventilation is predictor of ICU mortality.*
Conclusion: *The present study found high mortality rate in TB patients requiring ICU admission and mechanical ventilation.*
Key word: *Tuberculosis, ICU, Mechanical ventilation, mortality, respiratory failure.*

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I. Introduction

Tuberculosis(TB) remains major public health problem in world. India is one of the highest TB burdened countries in the world.In 2018, the global incidence of TB is 10 million out of which 2.69 million were from India according to 2018 TB report by WHO. The incidence of TB in HIV infected patients is 0.09 million in 2018. Although there is study decline in incidence of TB cases in India, there is slight increase in new and relapsed TB cases notified from 2009 to 2018. WHO attributed the TB incidence to five risk factors. They are diabetes, HIV, smoking, harmful use of alcohol and improper nutrition. India has about 0.6 million of TB cases attributed to improper nutrition.(1)

Death due to TB crosses 1.2 million worldwide. The death due to TB in India account for 0.4 million(one third of the global deaths). India still remains the highest TB burdened country in the world.(1) Delay in diagnosis and treatment can lead to severe form of disease. Poor accesses to health care, delay in diagnosis and treatment, improper nutrition, non-adherence to treatment, secondary infections are some of the major causes playing a important role in TB related mortality in India.

The most common cause of admission of TB patients into Intensive Care Unit(ICU) is respiratory failure. The presence of Extra pulmonary TB ranges from 19 to 64% of the cases in previous studies.(2) Co-morbidities such as HIV infection are considered risk factor for developing respiratory failure and requiring mechanical ventilation(MV).Gram negative pneumonia or sepsis, chronic obstructive pulmonary disease, history of poor compliance with TB treatment and cancer were predictors of respiratory failure(3). The mortality in Extra pulmonary tuberculosis patients ranges from 19 to 64% in various studies(2,14).

Limited studies reported a few factors that contributed to the mortality among critically ill patients with TB especially from India. This study aims to describe the clinical presentation, socio economic status, risk factors associated with mortality in TB patients requiring ICU admission.

II. Materials And Methods

This is a prospective observational study done in Government General Hospital, Kadapa from May 2019 to October 2019.
Study duration: 6 months.

Aims and objectives: To determine the risk factors associated with mortality in TB patients admitted to ICU.

Inclusion criteria:

1. All the patients with pulmonary TB admitted to ICU.
2. All the patients with extrapulmonary TB admitted to ICU were included in the study.

Exclusion criteria:

1. All patients below 18 years of age were excluded from the study.

A total of 50 cases were admitted to GGH, kadapa during this period of 6 months.

Definitions:

Active TB was defined as

i. Sputum or cerebrospinal fluid(CSF) or pleural fluid positive for CBNAAT .
ii. Mycobacterium tuberculosis culture positive.
iii. Histological clinical response to treatment.
iv. Pleural fluid for CBNAAT positive.
v. Pleural fluid for ADA positive response to treatment.
vi. CSF for ADA positive response to treatment.
vii. MRI showing tuberculoma with response to treatment.
viii. Presence of clinical or radiological lesions.

The diagnosis of respiratory failure was made after determination of PaO_2 <60 mm hg or arterial saturation SpO_2 on room air.

Anemia was defined as mild to no anemia (HB≥11 gms/dl), moderate to severe anemia(HB< 11 gms/dl) according to WHO classification.

The following data were collected in a standardized questionnaire

Demographic data(age, sex, socioeconomic status) smoking and alcoholic status, presence of co morbidities(diabetes mellitus, hypertension), clinical form of TB(patients with pulmonary involvement, pulmonary and extrapulmonary involvement, isolated extra pulmonary involvement, symptoms at the time of admission, methods of diagnosis, prior treatment for TB, duration from Hospital to MICU admission, reasons for ICU admission, presence of other disease during admission, need for ventilator support, laboratory investigations on admission(Hemoglobin, total count, differential count), survival at ICU discharge .

Samples for TB diagnosis includes sputum, tracheal nasogastric aspiration, CSF, pleural fluid. Drug resistance was defined as single/ poly drug resistance to 2 or more anti- TB drugs.

The protocol was submitted to the ethics committee of our hospital and an approval was obtained.

The ICU has 6 beds and a ventilator isolated for PTB patients.

Statistical analysis:

Data was analysis using Excel 2007 and Jamovi version 1.0.Continuous variable were expressed as mean. Categorical variables were expressed as proportion and compared using Chi-Square test. Data were compared between survivors and patients who died during hospital stay. A P value of <0.05 was considered statistically significant for all analysis.

III. Results

After 6 months of study thecharacteristics of 50 patients admitted to MICU were given in Table 1.

Table 1: Characteristics of patients in the study

Charecteristics	Survivors n=33(66%)	Non survivors n=17(34%)	Total	p-value [b]0.024
Age	47.4±13.3	48±13.7	47.5±1.56	[a]1.00
Sex				[b]0.01*
Male	29(65)	15(34)	44(88)	
Female	4 (66)	2(33)	6(12)	
Socio economic status				[b]0.396
Low				
Middle	14(63)	8(36)	22(44)	
	19(67)	9(32)	28(56)	
Co- morbidities				
HIV				
Diabetes	1(25)	3(75)	4(8)	[b]<0.01*
	12(70)	5(30)	17(34)	[b]0.024*
Smoker	16(53)	14(46)	30(60)	[b]0.157
Alcohol abuse	20(67)	10(33)	30(60)	[b]0.157

Data are represented as n (%). [a] Mann Whitney U test, [b] Chi Square test.* significant

Disease presentation and diagnosis:

The mean age of the patients was 47.5 years. Out of 50 patients, 44(88%) were male and 6(12%) were female. 22(44%) of the patients were from low socio economic status, 28(66%) were from middle socio economic group. The most common presenting complaint was breathlessness followed by evening rise of temperature. Cough with sputum was complained by 27(54%) patients. 42(84%) of them had previous history of TB. The mean treatment time of TB in the past was 2.91±0.35 months. 30(60%) patients were smokers and all of them were male. 30(60%) patient have history of alcoholic abuse. 17(34%) patients had diabetes, 7(14%) patients had hypertension and 4(8%) patients had HIV as co- morbidities. 14(28%) patients were admitted with extrapulmonary TB. Out of 14 members, 6 patients(12%) had pleural TB, 5(10%) patients had TB meningitis, 2(4%) had tuberculoma, 1(2%) patient had both TB spine and pleural TB. 24(48%) patients were defaulters.The most common cause for admission into ICU was respiratory failure(0.66%) followed by seizures(12%). The diagnosis was confirmed by subjecting sputum/ CSF/ pleural fluid samples to CBNAAT. The patients who have shown radiological signs of TB in chest X ray, MRI brain and spine were with clinical response to treatment were included. The patients who had positive Adenosine deaminase levels(ADA) levels in pleural fluid or CSF and clinically responding to treatment were also included.

ICU admission and outcome:

The mean duration of hospital to MICU admission was 0.84 ±0.26 days.The mean duration of ICU stay was 5.28±1.15 days. The mean hemoglobin of the patients was 9.48±0.26 gms/dL. The mean total count of the patients was 9976±379 cells/ dL. 32(64%) patients needed ventilator support. Table 2 shows data regarding hemoglobin, total count, need for ventilator support. The mortality rate of the study was 34%(17) patients.

Table 2: Clinical variables

Variable	Survivor n=33(67)	Non survivor n=17(33)	Total n=50(100)	p-value
Anemia				
Moderate to Severe Anemia	13(39)	16(94)	29(58)	0.258
Mild to no anemia	20(60)	1(14)	21(0.14)	
Total count				
Normal	25(73)	9(26)	34(68)	0.011*
High	8(50)	8(50)	16(32)	
Ventilator support				
Yes	17(53)	15(47)	32(64)	0.048
No	16(88)	2(12)	18(36)	
Defaulter				
Yes	14(59)	10(41)	24(48)	0.777
No	19(73)	7(27)	26(52)	

Data is presented as n(%). p-value is calculated by chi-square test. * significant.

Association with poor outcome:

Chi square test was performed to know the association between various parameters and outcome of the patient. Table 3 shows results of chi square test between outcome and various parameters.

Table 3: Association between various variables and mortality.

Parameter	**p-value(<0.05)**
Sex	0.97
Socio economic status	0.754
Smoking	0.021*
Alcohol abuse	0.903
Diabetes	0.623
HIV status	0.071
Moderate to severe anemia	<0.01*
Total count	0.101
Defaulter	0.27
Ventilator support	0.01*

p- value is determined by chi- square test. * significant.

There was significant association between the outcome of TB patients admitted to ICU and smoking history, hemoglobin level and need for ventilatory support of the the patient.

The patients who had history of smoking, who had moderate to severe anemia and who needed ventilator support had poor more mortality rate when compared to counterparts.

IV. Discussion

The prospective observational analysis of 50 patients requiring intensive care found a high mortality rate(34%). The mortality rate in other similar studies ranged from 21.5% to 90%.[2,3,4,5,6,7,8]Our aim was to evaluate the factors associated with mortality of these patients.

In this study the mean age was 47.5 years higher than many of the published studies where it ranged from 38 to 63 years[2,9,10,12,13]. TB remains an important public health problem especially in India.In previous studies also, males were more than females. This disparity is due to more exposure of men to droplet infections and other risk factors like smoking and alcohol abuse. There is no significant association between survival and sex similar to study done by Erbes*et al*.[8] Although there is no significant association between socio economic status of the patients, it is important to note that more than half of the patients(56%) were of middle socio economic group. This is in contrast to the usual trend of TB being a disease of poor. This can be due to lack of awareness regarding TB symptoms and treatment in middle socio economic group also. Another reason could be people from socio economic group not being affordable to stay in the hospital. In our study, there is significant association found with history of smoking and mortality of the patients. Other co morbidities such as diabetes, chronic alcoholism, HIV status didn't show any statistical significance.This may be due to the small sample size of the patients. 48% of the patients were treatment defaulters.

The clinical presentation was similar to other studies. Acute respiratory distress was the main cause of ICU admission in few previous studies [2,3]. Moderate to severe anemia is associated with higher mortality rates .Anemia was found as a risk factor for mortality of TB patients in study done by Alavi-naini R *et al*[15]. There is no significant association between total count of the patient and mortality rate. The need Mechanical ventilation was associated with high mortality rate. This is similar to studies done by Lee et al and Erbes et al.[7,8]. The mortality rate of patients requiring ventilator support was 34%.

V. Conclusion

The present study found high mortality rate in patients with tuberculosis requiring ICU admission. Moderate to severe anemia, smoking and need for ventilator support are associated with high mortality. There is high incidence of defaulters in the population. Proper measures should be taken to educate the general public about the need to complete the treatment, good nutrition during TB treatment, cessation of smoking. Measures should be taken for correction of anemia in TB patients.

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