

Original Research Article

Reported high in hospital mortality among adult tuberculosis patients admitted to university of Gondar hospital, North-West Ethiopia

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Received: 26 January 2023

Revised: 12 March 2023

Accepted: 13 March 2023

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ABSTRACT

Background: Due to a single infectious pathogen, tuberculosis (TB) is the world's second-greatest cause of mortality. The majority of TB deaths happen during the intensive phase of treatment. The purpose of this study is to determine the incidence and predictors of in-hospital mortality in adult TB patients.

Method: A 4 year retrospective follow-up study was conducted among 200 admitted adult TB patients at the university of Gondar hospital from September 1, 2017 to September 30, 2021. The Cox proportional hazards model was used to calculate the hazard ratios (HR). The Kaplan-Meier method was used to compute survival rates. Cox regression models were used to determine the predictors of mortality.

Results: This study enrolled 200 adult TB patients. Among these 60 (30%) died, 140 (70%) censored with overall incidence of death rate of 165 (95 percent CI: 128, 213)/10,000 days of observation. A multivariate Cox regression analysis revealed that patients with a low WBC count at baseline (AHR=3.16, 95% CI: 1.55, 6.41) and bedridden patients (AHR=3.49, 95% CI: 1.83, 6.66) independent predictors of in-hospital mortality among adult TB patients.

Conclusions: This retrospective study found that hospital mortality among adult TB patients is high in public hospitals in northwest Ethiopia. Patients with a low WBC count and who were bedridden at the time of presentation were independent predictors of in-hospital mortality.

Keywords: TB, Incidence of in-hospital mortality, Predictors, Retrospective follow-up, Ethiopia

INTRODUCTION

Tuberculosis (TB), caused by the Mycobacterium TB complex, is the leading cause of infectious mortality globally, with an estimated 9.9 million people becoming infected and 1.3 million dying each year.¹ TB -related mortality ranks as one of the top ten reported causes of death among hospital admissions. If properly treated, TB is a curable disease in the vast majority of cases.^{1,2}

Geographically, Africa reported 24% of TB cases in WHO regions, ranking second only to South-East Asia (44%).³ Nearly 90% of all cases are accounted for by 30 high TB burden countries. Despite reducing yearly TB incidence by 42% from 369 cases per 100,000 people in 1990 to 140 cases per 100,000 people in 2020, Ethiopia remains among the 30 countries with a high burden of TB, TB/HIV, and DR-TB from 2015 to 2020.^{2,4}

A meta-analysis and systematic review of ten studies indicated that estimated in-hospital mortality ranged from 2% to 12%, while a Chinese retrospective cohort study of TB patients hospitalized for acute care found that 90-day all-cause death was 13.8%.⁴⁻⁶ Similarly, a research conducted in Saudi Arabia revealed a 14% mortality rate after a mean stay of 1.87 months.⁷ A 5-year retrospective study of Kenyan TB surveillance data found an overall 5.5% patient death rate; a mortality rate of 12.2 deaths per 100 person-years (PY), with the mortality rate increasing from 7.8 in 2012 to 17.7 in 2016.⁸

A research conducted in southern Ethiopia to establish total death rate of TB revealed 9.3% mortality rate throughout full follow-up period.⁹ Study of smear-positive TB patients in Dale district and Yirgalem town found a death rate of 27.1 per 1,000 person-years, with increasing risk after age 34.¹⁰ Despite fact that Ethiopia has already accomplished its millennium development goal of reducing TB incidence by 50%, fall in TB incidence and prevalence has been relatively slow.^{2,11}

Clinical characteristics and patient presentation were important predictors of early mortality in an Indian study, which found that SpO₂ 90%, tachypnea, hypotension, advanced disease at chest radiography, and tachycardia were predictors of early mortality with positive predictive value of 94.88% and negative predictive value of 19.90%.¹² Systematic review and meta-analysis of hospitalized pulmonary TB patients found that leukopenia and anemia (moderate/severe) significant predictors of mortality.⁵ Immobility, moderate/severe under nutrition, HIV status, and clinical diagnosis of community acquired pneumonia were also found as risk factors in research conducted in Philippines.¹³

This research article was the first of its kind in Ethiopia to determine the incidence of in-hospital mortality rates and further identify the predictors of mortality among adult hospitalized TB patients.

METHODS

Study design and setting

A hospital-based retrospective follow up study was conducted on bacteriologically confirmed adult TB patients admitted at the university of Gondar hospital TB isolation and treatment unit between September 2017 and

September 2021. The hospital is located in Northwest Ethiopia, which is 750 km away from the capital, Addis Ababa. The hospital had a catchment population of 7 million people. The TB treatment center has a total of 28 beds for admitted Tb patients, hospital also has 2 Gen-Xpert MTB/RIF assay machine and external quality assured TB culture with phenotypic DST, 1st and 2nd line LPA and acid-fast staining sites for TB diagnosis.

Study population and study subjects

Study population was all bacteriologically confirmed drug-susceptible TB patients by AFB, gene X-pert/culture who admitted and treated at university of Gondar hospital TB isolation and treatment unit in study period.

Inclusion criteria

Patients 18 years and older, bacteriologically confirmed TB patients who had been admitted and treated with first line anti-TB drugs.

Exclusion criteria

Patient charts, which are not available at time of data collection were excluded.

Study variables

Dependent variable: Time in days from admission to the hospital to death or censored.

Independent variable: Sociodemographic characteristics which includes Age, sex, residence, region and occupation; behavioral characteristics which includes cigarette smoking and alcohol drinking status; clinical characteristics HIV co-infection, function status, Comorbidities like diabetic mellitus, cardiovascular disease, chronic lung disease, malignancy, chronic liver disease. Symptoms and signs at baseline presentation, Shortness of breath requiring supplementary oxygen; TB and treatment characteristics; radiologic and laboratory tests characteristics complete blood count (hemoglobin, white blood cell, platelet count), creatinine, blood urea nitrogen, SGOT, SGPT, bilirubin total, bilirubin direct, serum albumin, alkaline phosphatase and chest radiologic findings (bilateral involvement, cavitory lesion, pleural effusion)

Table 1: Sample size calculation for the predictor variables of in-hospital mortality among bacteriological confirmed TB patients.

Predictor	Assumptions	Probability of event	CHR	Sample size
Age category of above 65	Significant level (α)=0.05, type II error rate (β)=0.2, allocation ratio=1, two sided	P=0.38	2.00	182
Comorbid malignancy	Significant level (α)=0.05, type II error rate (β)=0.2, allocation ratio=1, two sided	P=0.25	2.85	134
Renal insufficiency*	Significant level (α)=0.05, type II error rate (β)=0.2, allocation ratio=1, two sided	P=0.31	2.24	173

*Renal insufficiency- patients with elevated marker (serum creatinine and BUN) of kidney injury with/with decrease urine out.

Sample size and sampling procedure

Sample size calculation for the predictor variables of incidence of in-hospital mortality among TB patients.

The final sample size calculated was one hundred and eighty-two. Considering 10% chart attrition and incomplete data on the outcome variable the final sample size was 200 we had included all admitted TB patients (n=240) within the follow-up period to the study. A was consecutive sampling method to recruit 240 study subjects.

Data collection instrument and procedures

Data were collected through structured data extraction tool which was prepared in English language and relevant medical information was extracted from the participants' medical records. The records to be reviewed were identified using the patients identification number. The data was collected by bachelor degree graduate nurse working at the TB treatment center under close supervision of the principal investigator. Data collector was given training on the objective of the study as well as how to extract data from the medical records of the patients.

Data analysis

Data were entered into EPI Info version 4.4.1 and transported to Stata version 14.1 for analysis. For categorical variables, patient characteristics were reported as counts (percentages), and for continuous variables, as mean with standard deviation. The incidence rate was calculated by dividing the number of total death to the total person days of observation. A life table was used to estimate the cumulative failure at a different point in time. Kaplan-Meier cumulative hazard curve was done to estimate overall failure rate. The log-rank test was used to compare the survival experience between different exposure groups. Cox proportional hazard assumption was tested for each variable and globally by using Schoenfeld residuals. Kaplan-Meier cumulative hazard graph was used to test goodness of model fit. Bi-variable model was fitted first and variables with a p value less than or equal to 0.25 were used in the final multi-variable model to identify the predictor variables. Finally, adjusted hazard ratio (AHR) with 95 percent confidence interval (CI) in the multi-variable model was used to select variables which have a significant association with the dependent variable (in-hospital mortality).

Ethical considerations

The research protocol complied with the Declaration of Helsinki and ethical approval was granted by the institutional review board (IRB) of the college of medicine and health sciences, university of the Gondar

(02 June 2021; IRB No. 638/06/2021). All data obtained were treated confidentially. Those patients diagnosed with the TB was taken care of as per the recommendation of the Ethiopian national TB /HIV guideline 2016 (reference).

RESULT

Socio-demographic and behavioral characteristics of study participants

A total of 200 patients' charts were reviewed. Majority of studied patients were male, accounting for (58.00%) of the total sample, and (73%) of the patients were from the country's rural areas. Median age was 36 years, with an interquartile range (IQR) of 28-50 years (Table 2).

TB treatment and co morbid characteristics of study participants

Most of our research participants (55%) only had pulmonary TB. Among all patients tested for HIV, with (25.5%) of them were HIV positive. Other than HIV, 34.5% of patients had comorbid disease; among these comorbid diseases, 9% of patients had chronic lung diseases such as asthma, COPD, ILD, and bronchiectasis, followed by 3% of patients with CKD and 3% of patients with cardiac conditions (Table 3).

Baseline clinical and complication during hospital admission characteristics of study participants

TB showed constitutional signs and symptoms in all patients in the study, including productive cough, fever (99.5%), weight loss (99.50), night sweating (99.5%), and fatigue (99%). Most patients' chief complaints at admission were productive cough (88.5%) with duration more than 2 weeks, followed by shortness of breath (29%). Approximately (93%) of patients experienced additional clinical problems during their presentation and hospital stay, with pneumonia being the most common (88.2%), followed by severe adult malnutrition (23%), and drug-induced liver disease (10.2%) (Table 4).

Baseline laboratory and radiologic (plain chest X-ray) characteristics of study participants

At baseline, more than 2/3rd patients 157/200 (78.5%) had low hemoglobin levels (anemia), 163/200 (87.6%) had hypoalbuminemia, and 44/200 (22%) had low WBC count (leukopenia). Inflammatory marker ESR was considerably high in 138 (82%) of patients. One-third of patients, 67/200 (37%), had mild to moderate hypokalemia at start. Pleural effusion was most prevalent finding on plain chest X-ray imaging at baseline in 55/200 (27.5%) patients, followed by chronic changes (fibrosis, collapsed lobes, bullae/ bronchiectasis changes) in 44/200 (22%) patients, and bilateral nodular infiltrations in 44/200 (22%) patients (Table 5).

Incidence of death

The minimum hospital stay was 2 days and max 92 days with total follow up was 3634 days. Median follow-up time 12 (IQR: 6, 22) days. From those 200 admitted TB patients 60(30%) of them died, 135 (67.5%) discharged improved, and 5 (2.5%) went against medical advice. Incidence of death-165 (95% CI: 128, 213)/10,000 days of observation. Cumulative probability of death was 3.31% (95% CI: 2.60, 4.14), 4.32% (95% CI: 3.28, 5.52) and 7.57% (95% CI: 5.71, 9.06) at the end of 28, 56, and 84 days of observation respectively (Figure 1).

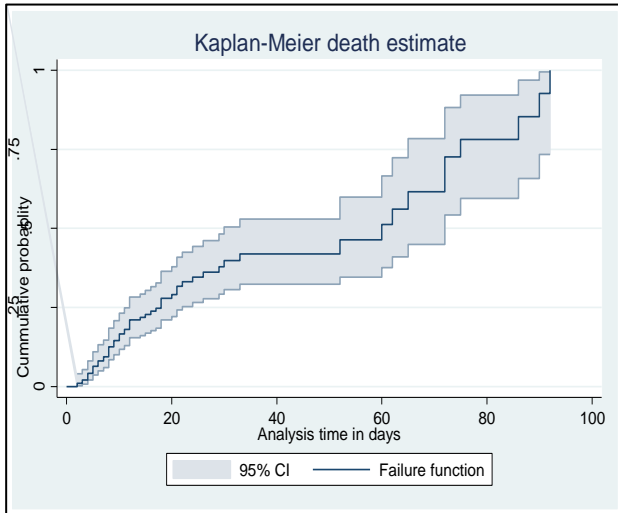


Figure 1: Kaplan-Meier cumulative hazard estimation of in-hospital mortality of TB patients.

Predictors of death

In the multivariable cox regression showed a significant

difference with incidence of mortality between patients who had low WBC count and normal WBC count. Risks of in-hospital mortality among bedridden patients 3 ½ times higher as compared to those who were ambulatory at baseline presentation (AHR=3.49, 95% CI: (1.83, 6.66)). Patients who had low WBC count (leukopenia) at hospital presentation had 3 times higher in-hospital mortality as compared to patients who had normal WBC count (AHR=3.16, 95%CI; (1.55, 6.41) (Table 6).

The proportional-hazards assumption based on the Schoenfeld residuals was done and it was found that all of covariates and full model satisfies proportional hazard assumption with the global test, $p=0.5769$ (Figure 2).

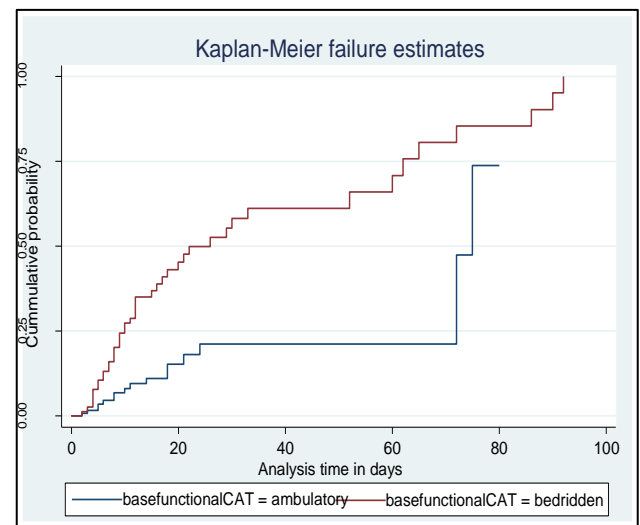


Figure 2: Kaplan-Meier cumulative hazard curve of in-hospital mortality by functional status on time to death.

Table 2: Socio-demographic and behavioral characteristics of bacteriological confirmed TB patients admitted to TB treatment unit, university of Gondar hospital, September 2017-September 2021, (n=200).

Variables	Categories	Death		Total, N (%)
		Yes (event), (n=60)	No (Censored), (n=140)	
Sex	Male	35	81	116 (58.00)
	Female	25	59	84 (42.00)
Age (Years)	15-24	5	21	26 (13.00)
	25-34	19	46	65 (32.00)
	35-44	14	31	45 (22.50)
	45-54	13	19	32 (16.00)
	≥55	9	23	32 (16.00)
Residency	Urban	18	36	54 (27.00)
	Rural	42	104	146 (73.00)
Cigarette smoking	Yes	3	4	7 (3.50)
	No	57	136	193 (96.50)
Drug abuse	Yes	1	0	1 (0.50)
	No	59	140	199 (99.50)
Alcohol history	Yes	19	44	63 (31.50)
	No	41	96	137 (68.50)
Khat chewing	Yes	3	1	4 (2.02)
	No	56	138	196 (97.88)

Table 3: TB treatment and comorbid characteristics of bacteriological confirmed TB patients admitted to TB treatment unit, university of Gondar hospital, September 2017-september 2021, (n=200).

Variables	Categories	Death		Total, N (%)
		Yes (event), (n=60)	No (Censored), (n=140)	
TB type	Only pulmonary TB	20	90	110 (55.00)
	Disseminated TB	40	50	90 (45.00)
Previous history of TB treatment	Yes	13	21	34 (17.00)
	No	47	119	166 (83.00)
Co-morbid conditions	Yes	25	44	69 (34.5)
	No	35	96	131 (65.5)
	CKD	1	5	6 (3.00)
	Pulmonary condition (Asthma, COPD, ILD, bronchiectasis)	5	13	18 (9.00)
	CLD	1	1	2 (1.00)
	HTN	1	2	3 (1.50)
	DM	1	2	3 (1.50)
	Cardiac	3	3	6 (3.00)
	Others	9	22	31 (15.50)
HIV status	Positive	17	34	51 (25.50)
	Negative	43	106	149 (74.50)

Table 4: Baseline clinical and complication of the patient during admission characteristics of bacteriological confirmed TB patients admitted to TB treatment unit, university of Gondar hospital, September 2017-September 2021, (n=200).

Variables	Categories	Death		Total, N (%)
		Yes (event), (n=60)	No (Censored), (n=140)	
Symptoms at presentation	Fever	60	139	199 (99.50)
	Weight loss	60	139	199 (99.50)
	Productive cough	60	140	200 (100.00)
	Night sweating	60	139	199 (99.50)
	Fatigue	59	139	198 (99.00)
	Shortness of breath with (PsO ₂ <90%)	36	45	81 (40.5)
	Hemoptysis	8	17	25 (12.50)
	Chest pain	47	63	110 (55.00)
	Others	21	55	76 (38.00)
Chief complaint at admission	Fever	9	8	17 (8.50)
	Shortness of breath	29	29	58 (29.00)
	Productive cough	52	125	177 (88.50)
	Hemoptysis	4	9	13 (6.50)
	Others*	10	17	27 (13.50)
Functional status	Ambulatory	16	107	123(61.50)
	Bedridden	33	44	77 (38.50)
Treatment interruption	Yes	16	14	30 (15.00)
	No	44	126	170 (85.00)

Table 5: Baseline laboratory finding and radiologic characteristics of bacteriological confirmed TB patients admitted to TB treatment unit, university of Gondar hospital, September 2017-September 2021, (n=200).

Lab* finding during admission		Death		Total, N (%)
		Yes (event), (n=60)	No (Censored), (n=140)	
Hemoglobin (Baseline)	Normal	12	31	43 (21.50)
	Mild anemia	4	21	25 (12.50)
	Moderate anemia	27	63	90 (45.00)
	Severe anemia	17	25	42 (21.00)

Continued.

Lab finding during admission		Death		Total, N (%)
		Yes (event), (n=60)	No (Censored), (n=140)	
WBC count (Baseline)	Low	19	25	44 (22.00)
	Normal	29	93	122 (61.00)
	High	12	22	34 (17.00)
Platelet count (Baseline)	Low	21	34	55 (27.50)
	Normal	30	82	112 (56.00)
	High	9	24	33 (16.50)
ESR (Baseline)	Normal	3	6	9 (5.39)
	Mildly elevated	6	14	20 (11.98)
	Markedly elevated	44	94	138 (82.63)
Serum albumin (Baseline)	Markedly low	44	63	107 (57.50)
	Mild low	14	42	56 (30.11)
	Normal	1	22	23 (12.37)
Total protein (baseline)	Low	42	55	97 (53.89)
	Normal	17	66	82 (46.12)
Serum creatinine (Baseline)	Low	33	104	137 (68.50)
	Normal	17	27	44 (22.00)
	High	10	9	19 (9.50)
BUN (Baseline)	low	1	2	3 (1.52)
	Normal	13	65	78 (39.59)
	high	44	72	116 (58.88)
S. sodium (Na+) (Baseline)	Sever low	2	3	5 (2.76)
	Moderate low	9	20	29 (16.02)
	Mild low	24	34	58 (32.04)
	Normal	24	65	89 (49.17)
S. potassium (K+) (Baseline)	Sever low	2	2	4 (2.21)
	Moderate low	5	8	13 (7.18)
	Mild low	26	28	54 (29.83)
	Normal	26	84	110 (60.78)
S. total Ca++ (Baseline)	Low	34	49	83 (49.40)
	Normal	23	64	87 (50.60)

Table 6: Bi-variable and multivariable cox-regression of bacteriological confirmed TB patients admitted to TB treatment unit, university of Gondar hospital, September 2017-september 2021, (n=200).

Variables	Categories	Death		CHR (95% CI)	AHR (95% CI)
		Yes (event)	No (Censored)		
Age (Years)	Mean \pm SD	40.77 \pm 15.12	38.46 \pm 15.56	1.01 (1.00, 1.03)	1.01 (0.99, 1.03)
TB type	Only pulmonary TB	20	91	Reference	
	Disseminated TB	40	49	1.88 (1.08, 3.25)	1.74 (0.92, 3.29)
Shortness of breath	Yes	36	45	1.72 (1.01, 2.93)	1.01 (0.53, 1.93)
	No	24	95	Reference	
Chest pain x-ray	Yes	47	63	2.53 (1.35, 4.72)	2.09 (0.97, 4.50)
	No	13	77	Reference	
Functional status	Ambulatory	16	107	Reference	
	Bed ridden	33	44	3.33 (1.86, 5.95)	3.49 (1.83, 6.66)
WBC count	Low	19	25	2.08 (1.14, 3.77)	3.16 (1.55, 6.41)
	Normal	29	93	Reference	
	High	12	22	1.11 (0.55, 2.25)	1.02 (0.46, 2.29)
Albumin	Markedly low	44	63	5.22 (0.72, 38.05)	2.28 (0.29, 17.91)
	Mild low	14	42	3.22 (0.42, 24.61)	2.24 (0.28, 18.17)
	normal	1	22	Reference	
Creatinine	Low	33	104	0.54 (0.29, 0.98)	0.61 (0.30, 1.25)
	Normal	17	27	Reference	
	High	10	9	1.10 (0.45, 2.43)	1.90 (0.75, 4.83)
Serum Ca++ T	Low	34	49	1.58 (0.91, 2.74)	1.24 (0.68, 2.89)
	Normal	23	62	Reference	

DISCUSSION

Despite the END-TB strategy's efforts to reduce TB mortality by 90% by 2030 and 95% by 2035, one of the problems is the high incidence of in-hospital mortality.^{1,2,14} The in-hospital mortality rate of TB patients in this study was 30%, which was higher than that of the 14% mortality rate in Saudi Arabia and Israel, as well as the 20.73%, 10% and 23% mortality rates in Japan, Papua New Guinea and Pakistan, respectively.^{6,15-18} The disparities in death rates across these nations may be attributable to variances in patient groups investigated, which may be impacted by socioeconomic characteristics, health care quality and coverage, and the burden of TB. On the other hand, a study from Brazil reported a mortality rate of 31.8%, which was complementary to our study, and a higher mortality rate of 37.5% was observed from study from the Philippines, as both the Philippines, Brazil, as well as Ethiopia are among the 30 high TB burden countries.^{1,19,20}

The cumulative probability of death was 3.31% (95% CI: 2.60, 4.14), 4.32% (95% CI: 3.28, 5.52) and 7.57% (95% CI: 5.71, 9.06) at the end of 28, 56, and 84 days of observation respectively, which suggests that the risk of death increases with the number of days the patient stayed in the hospital. More than half (56%) (n=34) of the deaths occurred during the first week of admission. As also mentioned from Saudi Arabia's, 78% of patients died in the first week of admission Brazil study shows mean time of death 3.7 ± 2.5 months and 39.5 days in Russia.^{16,21,22} The plausible explanation for this higher mortality rate seemed to be factors such as advancing age, limited availability of health care facilities nearby, low socio-economic status and delayed and progressed stage of illness at presentation to the emergency rooms as seen from the descriptive data close to half of the patients had disseminated TB that might be attributed with late presentation and contributed significantly to the mortality of TB patients.^{15,18,21}

In this study, patients who were bedridden by the time they presented to TB ward and those who had a low baseline WBC count at admission had a higher risk of in-hospital death. Other studies shows predictors of TB patients in hospital mortality comorbid disease like IHD, DM and COPD also other studies found advanced age, underlying immunocompromised conditions and hypoxia some shows also bilateral lung involvement, cavitary lesion, anemia and delay diagnosis.^{14,22,23}

The risk of in-hospital mortality was three and a half times higher in bedridden patients than that of ambulatory patients at baseline (AHR=3.49, 95% CI: (1.83, 6.66)). As evidenced by the Rwandan trial, inability to walk unassisted at hospital presentation had a low specificity (20%) but was 100% sensitive (CI 95%, 90-100%) to predict in-hospital death, recommending that it could be used as simple and reliable triage tool with a high sensitivity to predict in-hospital mortality.¹⁹

Patients with low WBC counts (leukopenia) at admission

to hospital had three times higher in-hospital mortality than those with normal WBC counts (AHR=3.16, 95% CI: (1.55, 6.41)). This finding was supported by the Japan study (OR: 0.28, 95% CI: 0.11-0.73) In addition, Uganda research found a high prevalence of low WBC count (leukopenia) with low CD4+ lymphocytes in TB patients with no HIV co-infection during inpatient treatment.^{24,25} Study suggested that TB patients may develop chronic immunosuppression, which potentially increase their risk of severity of illness and mortality further. Aside from the fact that a complete understanding of this mechanism is still lacking.²⁶ Another prospect from study was that hypoalbuminemia, prior steroid use, hyponatremia and severe malnutrition could result low WBC count (leukopenia) in TB patients.^{15,23} Our data shows more than half of patients had markedly low hypoalbuminemia at presentation, and more than 60% were clinically diagnosed with severe adult malnutrition as a clinical complication during hospitalization by treating physician, but patients' BMI and MUAC were not fully recorded.

In-hospital mortality rate is an important outcome indicator in determining treatment success of TB patients. Reducing in-hospital mortality can have significant impact on lowering health-care costs and improving patients' long term health status and prevent further transmission of the infection and help to eliminate the disease.

Strength and limitation

The major strength of this study was its prospective study design, which allowed collecting reliable data. The limitation of the study was selection bias as severely ill hospitalized patients were included as study subjects.

CONCLUSIONS

This study found that the incidence of in-hospital mortality of TB patients was high especially in the first week of treatment. Bedridden functional status and low WBC count at presentation were independent predictors of in-hospital mortality.

Recommendations

Targeted interventional and preventive measures that reduce and control the above-mentioned risk factors might substantially reduce mortality of TB patients.

ACKNOWLEDGEMENTS

Author would like to thanks to the study participants and their health personnel.

Funding: Funding sources by "Research and Publication Office" of the College of Medicine and Health Sciences, University of Gondar.

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Morphology TC. WHO Global TB Report 2021. 2021. Available at: <https://www.who.int/publications/i/item/9789240037021>. Accessed on 3 June 2022.
2. Ethiopian leprosy, TB and DRTB treatment guideline. 2018;7(2557):1-16.
3. World Health Organization. Are Updated Every Year for the Tuberculosis. 2020. Available at: <https://www.who.int/publications/i/item/9789240013131>. Accessed on 3 June 2022.
4. Eshetie S, Gizachew M, Alebel A, Van Soolingen D. Tuberculosis treatment outcomes in Ethiopia from 2003 to 2016, and impact of HIV co-infection and prior drug exposure: A systematic review and meta-analysis. *Plos One*. 2018;13(3):1-18.
5. De Almeida CPB, Ziegelmann PK, Couban R, Wang L, Busse JW, Silva DR. Predictors of In-Hospital Mortality among Patients with Pulmonary Tuberculosis: A Systematic Review and Meta-analysis. *Sci Rep*. 2018;8(1).
6. Hu D, Long Q, Chen J, Wang X, Huang F, Ji JS. Factors influencing hospitalization rates and inpatient cost of patients with tuberculosis in Jiangsu province, China: An uncontrolled before and after study. *Int J Environ Res Public Heal*. 2019;16(15).
7. Aljadani R, Ahmed AE, Al-Jahdali H. Tuberculosis mortality and associated factors at King Abdulaziz Medical City Hospital. *BMC Infect Dis*. 2019;19(1).
8. Id OAA, Ngari MM, Sanga D, Katana G, Willetts A. Mortality during treatment for tuberculosis ; a review of surveillance data in a rural county in Kenya. 2019;87:1-15.
9. Beyene Y, Geresu B, Mulu A. Mortality among tuberculosis patients under DOTS programme : a historical cohort study. *BMC Public Heal*. 2016;4-9.
10. Dangisso MH, Woldeamayrat EM, Datiko DG, Lindtj B. Long-term outcome of smear-positive tuberculosis patients after initiation and completion of treatment: A ten-year retrospective cohort study. *Plos One*. 2018;1-16.
11. Deribew A, Biadgilign S, Deribe K, Dejene T, Tessema GA, Melaku YA et al. The Burden of HIV/AIDS in Ethiopia from 1990 to 2016: Evidence from the Global Burden of Diseases 2016 Study. *Ethiop J Health Sci*. 2019;29(1):859-68.
12. Singla R, Raghu B, Gupta A, Caminero JA, Sethi P, Tayal D et al. Risk factors for early mortality in patients with pulmonary tuberculosis admitted to the emergency room. *Pulmonology*. 2021;27(1):35-42.
13. Id NL, White L V, Marin FP, Saludar NR, Solante B, Tactacan-abrenica RJC et al. Mid-upper arm circumference predicts death in adult patients admitted to a TB ward in the Philippines: A prospective cohort study. 2019;1-17.
14. World Health Organization. Global Tuberculosis Rep. 2019;283:1-7. Available at: <https://www.who.int/publications/i/item/9789241565714>. Accessed on 3 June 2022.
15. Lubart E, Lidgi M, Leibovitz A, Rabinovitz C, Segal R. Mortality of patients hospitalized for active tuberculosis in Israel. *Isr Med Assoc J*. 2007;9(12):870-3.
16. Aljohaney AA. Mortality of patients hospitalized for active tuberculosis in King Abdulaziz University Hospital, Jeddah, Saudi Arabia. *Saudi Med J*. 2018;39(3):267-72.
17. Vakadem K, Anota A, Sa'avu M, Ramoni C, Comrie-Thomson L, Gale M et al. A mortality review of adult inpatients with tuberculosis in Mendi, Papua New Guinea. *Public Heal Action*. 2019;9(1):S62-7.
18. Shimazaki T. Risk factors for death among hospitalised tuberculosis patients in poor urban areas in Manila, the Philippines. *Int J Tuberc Lung Dis*. 2013;17(11):1420-6.
19. Kwizera A, Urayenzeza O, Mujiyugamba P, Meier J, Patterson AJ, Harmon L et al. The inability to walk unassisted at hospital admission as a valuable triage tool to predict hospital mortality in Rwandese patients with suspected infection. *PLoS One*. 2020;15(2).
20. Rao VK, Iademarco EP, Fraser VJ, Kollef MH. The impact of comorbidity on mortality following in-hospital diagnosis of tuberculosis. *Chest*. 1998;114(5):1244-52.
21. Silva DR, Menegotto DM, Schulz LF, Gazzana MB, Dalcinv PTR. Mortality among patients with tuberculosis requiring intensive care: a retrospective cohort study. *BMC Infect Dis*. 2010;10:54
22. Kourbatova EV, Borodulin BE, Borodulina EA, Del Rio C, Blumberg HM, Leonard MK. Risk factors for mortality among adult patients with newly diagnosed tuberculosis in Samara, Russia. *Int J Tuberc Lung Dis*. 2006;10(11):1224-30.
23. Lui G, Wong RYK, Li F, Lee MKP, Lai R, Li TCM et al. High Mortality in Adults Hospitalized for Active Tuberculosis in a Low HIV Prevalence Setting *PLOS one*. 2014;3(4).
24. Okamura K, Nagata N, Wakamatsu K, Yonemoto K, Ikegame S, Kajiki A et al. Hypoalbuminemia and lymphocytopenia are predictive risk factors for in-hospital mortality in patients with tuberculosis. *Intern Med*. 2013;52(4):439-44.
25. Baluku JB, Musaaazi J, Mulwana R, Mugabo AR, Bongomin F, Katagira W. Prevalence and Predictors of CD4+ T-Lymphocytopenia Among HIV-Negative Tuberculosis Patients in Uganda. *Res Rep Trop Med*. 2020;11:45-51.
26. Cilloniz C, Peroni HJ, Gabarrús A, García-Vidal C, Pericàs JM, Bermejo-Martin J et al. Lymphopenia Is Associated With Poor Outcomes of Patients With Community-Acquired Pneumonia and Sepsis. *Open Forum Infect Dis*. 2021;8(6).

Cite this article as: Abegaz SH, Yimer TY, Ayalew DG, Kassa GM, Yferu ZA, Legese GL et al. Reported high in hospital mortality among adult tuberculosis patients admitted to university of Gondar hospital, North-West Ethiopia. *Int J Sci Rep* 2023;9(4):92-100.

ANNEXURE

Definition of terms

Survival time: was defined as a time difference in months from the start of treatment to the time the patient becomes an event or censored.

Event: In this study patient who died during hospitalization in their course of TB treatment was considered as an event. For the purpose of the analysis, the status was dichotomized by 1 (Yes i.e., Death) and 0 (No Death).

Censored: Patients when death occurs has not been observed during the follow up time.

Individuals that were discharged improved and went against medical advice at the end of study time were considered as right censored and there is no left censored.

Previously not treated for TB: A patient who denies having had any prior anti-TB treatment or taking anti TB less than one month.

Previously treated case: A patient who has been treated with anti TB for one month or more;

Cigarette smoking: was recorded by asking a respondent whether they ever smoke cigarette in life history. It was dichotomized by 1 (Yes i.e., smoke cigarettes) and 0 (No smoke cigarettes).

Alcohol consumption: was recorded by asking a respondent whether they ever drink alcohol or not. It was dichotomized by 1 (Yes i.e., drink alcohol) and 0 (No drink alcohol).

Laboratory reference and categories

Hemoglobin (Baseline): Normal (12 gm/dl-17 gm/dl), Mild anemia (10 gm/dl-11.9 gm/dl), Moderate anemia (8 gm/dl-9.9 gm/dl), Severe anemia (≤ 8 gm/dl).

WBC count (Baseline): Low ($<4,400$ micro/cell), Normal (4400-11000 micro/cell), High (>11000 micro/cell).

Platelet count (Baseline): Low ($<150,000$ micro/cell), Normal (150000 -450000 micro/cell), High (>450000 micro/cell).

ESR (Baseline): Normal (0-20 mm/hr), Mildly elevated (20-40 mm/hr), Markedly elevated (>40 mm/hr).

Serum albumin (Baseline): Markedly low (≤ 2.5 gm/dl), Mild low (2.5-3.4 gm/dl), Normal (≤ 3.5 gm/dl).

Total protein (baseline): Low (< 6 gm/dl), Normal (6-8.3 gm/dl).

Serum creatinine (Baseline): Low (0-0.49 mg/dl), Normal (0.5-1.25 mg/dl), High (>1.25 mg/dl).

BUN (Baseline): Low (0-8 mg/dl), Normal (8-20 mg/dl), High (>20 mg/dl).

Serum sodium Na^+ (Baseline): Sever low (<120 mmol/l), Moderate low (120-129 mmol/l), Mild low (130-135 mmol/l), Normal (136 – 147mmol/l).

Serum potassium K^+ (Baseline): Sever low (≤ 2.5 mmol/l), Moderate low (2.5-2.9 mmol/l), Mild low (3-3.49 mmol/l) Normal (3.5-5 mmol/l).

Serum total calcium Ca^{++} (Baseline): Low (<2.2 mmol/l), Normal (2.2-2.6 mmol/l).

SGOT (serum glutamic oxaloacetic): Normal (0-33 U/l, Mild elevation (33-165 U/l), Mild to moderate (165-330 U/l), Marked elevation (≥ 330 U/l).

SGPT (serum glutamic pyruvic): Normal (0-40 U/l, Mild elevation (40-200 U/l), Mild to moderate (200-400 U/l), Marked elevation (≥ 400 U/l).

Total bilirubin: Normal (0.3 to 1.2 mg/dl), Mild to moderate (1.2-4 mg/dl), Marked elevation (≥ 4 mg/dl).

Direct bilirubin: Normal (0.1 to 0.5 mg/dL), Mild to moderate (0.5-3 mg/dl), Marked elevation (≥ 3 mg/dl).

ALP (Alkaline phosphatase): Normal (30-120U/l), High (120-480U/l), Very high (>480 U/l).