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Risk Factors and Outcomes for Tuberculosis Patients Requiring Hospital Admission

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ABSTRACT

Objectives: To identify the factors associated with outcomes including mortality in hospitalized tuberculosis patients at a tertiary care Hospital.

Methodology: This retrospective-prospective observational study was conducted at Indus Hospital and Health Network (IHHN), Karachi from June 2024-May 2025. All admitted patients aged 14 to 70 years; both genders with diagnosis of tuberculosis (pulmonary and extra-pulmonary) were included. Enrolled patients were prospectively assessed at admission and followed throughout hospitalization, while data for retrospectively identified patients were obtained from the Hospital medical records, using a structured proforma. Outcomes were assessed for risk factors and outcomes in terms of death or survival to discharge. All the relevant data were analyzed by using SPSS version 26.

Results: Overall, 202 hospitalized patients were enrolled, the cohort was predominantly young (32% aged 15–25 years) with a slight predominance of females (54.5%), most cases had microbiologically confirmed TB (82.2%), with 41% having disseminated TB, 27% PTB, and 32.5% EPTB. Fever was the most common presenting symptom (77.7%). Overall, in hospital mortality was 15.3%, but was significantly higher among ICU patients (86.7%). The demographic factors such as age, gender and BMI did not show significant association with mortality (p>0.05). Comorbidities included diabetes (14.4%), hypertension (9.4%), CKD (7.9%), and HIV (5%). Disseminated TB was strongly linked to mortality, approximately 77.4% of non-survivors compared to 34.5% of survivors (p<0.0001). Non-survivors also had significantly higher rates of in-hospital complications, including mechanical ventilation (80% vs. 7.1%), vasopressor requirement (80% vs. 6.5%), AKI (73.3% vs. 8.3%), and disseminated intravascular complications (40% vs. 5.3%) (p=0.001). Moreover, the non-survivors also had significantly higher WBC counts, lower count platelets and significantly lower serum albumin (p=0.0001).

Conclusions: Morality rate was observed 15.3%, with delayed presentation, disseminated tuberculosis and the development of in-hospital complications, particularly mechanical ventilation, vasopressor requirement, AKI, disseminated intravascular complications, and decreased albumin level as key determinants of the in-hospital mortality.

Keywords: Adults; Hospitalization; Mortality; Tuberculosis, Predictors.

Introduction

Tuberculosis (TB) remains the leading cause globally of death from a single infectious agent, regardless of being both preventable and curable through effective anti-tuberculosis therapy. According to estimates for 2024, approximately 10.7 million people fell ill with TB, including 5.8 million men, 3.7 million women and 1.2 million children.[1,2] Of these, approximately 1.23 million died from the disease, including 150,000 deaths among people living with HIV. The disease is present throughout the world, while its burden is excessively concentrated in specific countries and vulnerable populations, emphasizing ongoing disparities associated to social conditions, economic challenges, and healthcare systems limitations.[1] According to the WHO Global tuberculosis report issued in 2024, Pakistan has an tuberculosis incidence of 373 cases per 100,000 individuals, and an HIV-negative TB mortality rate of 38 deaths per 100,000, placing it among the 35 countries with the highest TB burden and mortality throughout the world.[3]

Although the majority of TB individuals are managed successfully as outpatients, a substantial subset requires hospital admission, because of more severe forms of disease, resulting in poor clinical outcomes and considerable mortality. The in-hospital mortality remains high among hospitalized patients during the hospital stay itself with an estimated range from approximately 2% to 12%, and continues to remain elevated even after discharge, with the greatest risk concentrated in the initial months of the treatment.[4,5.] Studies have reported that approximately 1–3% of all tuberculosis individuals require intensive care (ICU), most frequently due to acute respiratory distress syndrome (ARDS) or severe organ failure like as renal impairment, and the mortality rate among those needing ICU care for acute respiratory failure has been specified approximately 60%.[6,7]

The most significantly reported risk factors for TB-associated mortality comprise delays in diagnosis, the presence of comorbid conditions, smoking, substance

use, a prior tuberculosis history, male gender, advanced age and co-infection with the HIV. Furthermore, within the first year following TB diagnosis, mortality has also been independently associated to receiving care from a private provider rather than the public TB program and not being managed under directly observed therapy, poor adherence to the treatment, and belonging to an indigenous ethnic group.[4,5] According to a hospital-based cohort Chinese study, a tuberculosis related mortality rate was 1.6% during treatment, with male gender, advance age, lower BMI, anemia, presence of tumor, poor treatment adherence, and progression of underlying chronic disease emerging as the independent risk factors for mortality, particularly even within a well-resourced urban setting.[8] On the other hand it is reported that the among TB patients particularly, diabetes mellitus comorbidity (OR 8, 95% CI 2–26) and concomitant pulmonary tuberculosis (OR 4, 95% CI 1–14) carried higher crude odds of mortality, with all lethal TB cases presenting with two or more systemic symptoms at presentation.[9]Furthermore, a systematic review and meta-analysis comprising 11 cohort studies comprising 5,468 hospitalized TB cases noted only moderate-quality evidence relating comorbid malignancy to increase in-hospital mortality, while the evidence remains insufficient to establish positive sputum smear status, male gender, DM, or a prior TB history as reliable predictors of in-hospital mortality.[10]

Regardless of the clear clinical importance of this problem, the existing evidence on determinants of in-hospital TB mortality remains divided, inconsistent, and limited by small event numbers, retrospective designs, and a lack of standardized severity of disease. This gap is more pronounced in the context of local level, where locally available TB mortality data are drawn predominantly from drug-resistant TB registers or community-based and socio-demographic surveys, rather than from prospective, hospital-based cohorts that consistently evaluate severity using standardized measures indices together with routine clinical and treatment-related factors. Consequently, due to local specific, hospital-based prospective data addressing this exact question remain very limited, this study was aimed to identify the factors associated with mortality in tuberculosis patients admitted to hospital; by examining these determinants prospectively, the study provides crucial insights into patient management, allowing for tailored interventions to improve the outcomes in this population.

Methodology

This was a retrospective-prospective observational study conducted at the Indus Hospital and Health Network (IHHN), Karachi. Study was done after taken Institutional Review Board approval, (reference number IHHN_IRB_2024_09_018). Duration of study was one year from June 2024 to May 2025. The patients who were admitted with diagnosis of tuberculosis (pulmonary or extra-pulmonary) diagnosed through microbiological confirmation (smear microscopy, GeneXpert, or culture), or compatible clinical and radiological findings, between age 14 to 70 years of age and of either gender were included. On the other hand, patients with incomplete medical records, those who had been on anti-tuberculosis therapy (ATT) for less than two months were excluded, patients without confirmed tuberculosis diagnosis, patient. The informed consent was obtained from each prospectively enrolled patient prior to enrollment, while the data for the retrospective component were extracted from medical records after approval by Ethics Committee and following the institutional policies. Data were kept confidential to ensure the privacy of patients. The consecutive sampling technique was used for both the prospective and retrospective cohorts. All the patients patient meeting the eligibility criteria underwent baseline assessment was including socio-demographic characteristics like age and gender, along with detailed clinical history covering the duration and nature of symptoms prior to admission, history of tuberculosis treatment, prior tuberculosis history, history of contact with a tuberculosis case, smoking status, intravenous drug use, and known comorbid conditions. A thorough clinical examination was conducted at the time of enrollment, with qSOFA score at presentation, vital signs, oxygen saturation, and level of consciousness recorded, and baseline investigations, including hemoglobin, total leukocyte count, serum albumin, renal and liver function tests, sputum smear grading, culture and drug susceptibility testing, and chest radiography, were obtained and documented on a structured case record form developed specifically for the study. Additionally, the APACHE score and comorbidity index were measured for each patient using data gathered at admission, providing a standardized measure comorbid burden and severity of disease respectively. Subsequent baseline assessment, all the enrolled patients were followed prospectively throughout the course of hospitalization, working in coordination with the treating clinical staff. Regularly patients were monitored for clinical progression, any complications, hospital-acquired infections or admission to the intensive care unit (ICU), initiation of mechanical ventilation, or use of vasopressor support. The anti-tuberculosis treatment regimen administered, the timing of treatment initiation relative to admission, and the total duration of hospital stay were recorded as they occurred. Patients were followed until one of the predefined study endpoints was reached, namely discharge from

the hospital, transfer to another facility, or in-hospital mortality. All the data were recorded under code rather than by personal identifications, in order to preserve confidentiality throughout the follow-up period. All the relevant data were analyzed by using Statistical Package for the Social Sciences version 26. Chi-square test/Fisher exact test were applied to see the significant association between the categorical variables, taking a p-value of ≤0.05 as statistically significant.

Results

A total of 202 patients were enrolled in the study, close to a third were young adults with mean age of 37.0 ± 16.8 years. Females slightly predominated (54.5), but gender showed no association with outcome (p = 0.963). Over half of the patients had no comorbidities ((51.5%), whereas approximately one in ten had a high comorbidity burden, with four or more comorbid conditions. The most frequent comorbidity was diabetes mellitus (14.4%), followed by hypertension (19.4%), chronic renal disease (7.9%), and chronic lung disease (3.5%). Ten (5.0%) were HIV-positive, of whom nine had unsuppressed viral loads. Fever noted to be a most common symptom, affecting around 8 in 10 patients, followed by weight loss and cough in around 4 in 10 each, whereas around a third proportion had shortness of breath.

Individuals typically waited about two months between symptom onset and treatment initiation, reflecting considerable diagnostic delay. Majority, over 80%, had microbiologically confirmed TB and were started on standard first-line HREZ therapy. Pulmonary infiltrates and pleural effusion were the leading findings by chest imaging,

Sepsis (qSOFA ≥ 2) was present in 45 (22.3%), reflecting severe systemic involvement at admission. The disease was often severe enough at presentation that 45% of patients needed high-dependency care and a further quarter needed ICU admission, with only about 3 in 10 managed on a general ward, as presented in table i.

Out of all, approximately two-thirds (64.9%) required airborne isolation, reflecting the infectious burden of the cohort and around 1 in 6 patients faced serious complications, with (17.8%) requiring invasive ventilation and an equal proportion developing AKI, while roughly 1 in 10 had disseminated intravascular complications. Additionally, the Hospital-acquired infections were relatively uncommon, with hospital-acquired pneumonia being the most frequent (5.4%). The median hospital length of stay was approximately 6 days, with a similar median ICU stay among patients requiring intensive care. Ultimately, in-Hospital mortality rate around (15.3%), indicating the serious risk tuberculosis still carries once it becomes severe enough to require inpatient care, as presented in table II.

Table I: Demographic and clinical characteristics of recruited patients. (n=202)

Variable		Statistics
Age groups of the patients	15-25	66(32%)
	26-35	46(22.8%)
	36-45	33(16.3%)
	46-55	22(10.9%)
	56-66	21(10.4%)
	>65	14(6.9)
Gender	Males	92(45.5%)
	Females	110(54.5%)
Comorbidity	No comorbid	104(51.5%)
	Mild (1)	61(30.2%)
	Moderate (2-3)	17(8.4%)
	Severe (≥4)	20(9.9%)
Smokers		31(15.3%)
IV Drug Abuse		5(2.5%)
History of Previous TB		22(10.9%)
Contact history of TB		62(30.7%)
Duration between symptom onset and treatment initiation in days (median (IQR)		64(32-115)
Clinical Symptoms	Fever	157(77.7%)
	Cough	88(43.6%)
	Weight Loss	94(46.5%)
	Headache	17(8.4%)
	Diarrhea	45(22.3%)
	Abdominal Distention	26(12.9%)
	Fits	3(1.5%)
	Neck nodal Swellings	7(3.5%)
	Shortness of breath	64(31.7%)
	Others	110(54.5%)
Type Of Tuberculosis	Presumptive TB	36(17.8%)
	Microbiologically proven TB	166(82.2%)
X-ray findings	Normal	34(16.8%)
	Infiltrates	40(19.8%)
	Cavitation	5(2.5%)
	Consolidation	17(8.4%)
	Pneumothorax	2(1%)
	Hydropneumothorax	6(3%)
	Miliary pattern	11(5.4%)
	Pleural effusion	26(12.9%)
	Mediastinal/Hilar lymphadenopathy	2(1%)
	Others	4(2%)
Treatment given	HREZ	165(81.7%)
	Other drugs	48(23.8%)
In Hospital placement	ICU	52(25.7%)
	HDU	91(45%)
	Ward	59(29.2%)

According to the stratification analysis-based survival rate, age, gender, BMI, comorbidity burden and history of smoking showed higher mortality rate while findings were statically insignificant between the two groups (p>0.05). Type of tuberculosis was

significantly associated with mortality ($p < 0.001$). Disseminated TB was markedly overrepresented among non-survivors, accounting for approximately three-quarters (77.4%) of deaths compared to just over a third of survivors, making it the single most notable distinguishing factor. Additionally, the non-survivors' individuals were far more likely to develop serious complications: 80% required mechanical ventilation and vasopressor support, and about 73% developed AKI, compared to only around 7–8% among survivors. Diabetes and CKD also impact significantly along with disseminated intravascular complications were more common in those who died (40% vs. 5.3%), as were hospital-acquired pneumonia (16.1% vs. 3.5%), as presented in table III.

Moreover, the laboratory findings further underscored disease severity as non-survivors had notably higher WBC counts, lower counts of platelet, significantly lower serum albumin, and elevated liver enzyme (SGPT) levels compared to the survivors ($p<0.05$). However, the hemoglobin level, CRP, and APACHE II scores, did not showed significant difference across the groups. Table III

Table II: Outcomes of recruited patients. (n=202)

Outcomes		Statistics
Required Air Borne isolation room		131(64.9%)
Required Invasive Ventilation		36 (17.8%)
Developed AKI		36(17.8%)
Disseminated intravascular complications		21(10.4%)
Developed Hospital Acquired Infection	CLABSI	5(2.5%)
	HAP	11(5.4%)
	VAP	2(1%)
Length of ICU stay in days Median (IQR)		6 (3-9)
Hospital stay in days Median (IQR)		6(3-9)
Mortality	Yes	31(15.3%)
	No	171(84.7%)

Discussion

Even with effective treatment accessible, tuberculosis can still turn adverse outcomes, and this study was undertaken to elucidate the factors associated with mortality among hospitalized patients. Our study identified that young individuals were disproportionally affected, with the mean age of 37.0 ± 16.8 years, highlighting that tuberculosis predominantly affects the economically productive age group, However, they showed better recovery compared to advanced aged individual who have an inclination toward higher mortality. Interestingly, females predominated (54.5%), but overall association of age and gender was not reflected in mortality. TB generally exhibit male predominance globally and TB related mortality is 30% higher in males older than 65 years compared to females. [11] In contrast, regional studies have reported that pulmonary TB was more frequent among women compared to men (p=0.001), with an overall mean

Table II: Post stratification of demographic and clinical parameters for in-hospital mortality.

Clinical Characteristics		Survivors	Non-Survivors	p-value
Age Median (IQR)		33 (23-4)	43 (20-64)	0.134
Gender	Male Female	78 (45.6) 93 (54.4)	14 (45.2) 17 (54.8)	0.963
Comorbidity Index	No (0 score) Mild (1-2) Moderate (3-4) Severe (>5)	92 (53.8) 50 (29.2) 11 (6.4) 18 (10.5)	12 (38.7) 11 (35.5) 6 (19.4) 2 (6.5)	0.080
BMI (kg/m²) Median (IQR)		18 (16-21)	19.5 (16.3-25)	0.661
History of smoking		24 (14%)	7 (22.6)	0.276
Diabetes		22 (12.9)	11 (35.5)	0.001
Chronic Renal Disease		13 (7.6)	6 (19.4)	0.001
Type of tuberculosis	Disseminated TB Pulmonary TB Extra-pulmonary TB	59 (34.5) 50 (29.2) 62 (36.3)	24 (77.4) 4 (12.9) 3 (9.7)	<0.0001
In-hospital complications	DIC	9 (5.3)	12 (40)	< 0.001
	Required Mechanical Ventilation	12 (7.1)	24 (80)	<0.001
	Required Vasopressors	11 (6.5)	24 (80)	<0.001
	Developed AKI	14 (8.3)	22 (73.3)	<0.001
	Developed HAI – HAP	6 (3.5)	5 (16.1)	0.015
Laboratory parameters at baseline				
Hb, Median (IQR)		10 (8.8-11.7)	9.5 (8.2-10.3)	0.152
WBC count (×10⁹/L), median (IQR)		8.8 (6-12)	12.4 (7.2-21)	0.001
Platelets (×10⁹/L), median (IQR)		306.5 (169.3-404.8)	214 (132-286)	0.012
Serum albumin (g/dL), median (IQR)		2.8 (2.4-3.3)	2.3 (1.8-2.8)	<0.0001
SGPT (U/L), Median (IQR)		19 (14-33.3)	25 (20-109)	0.004
CRP (mg/l), Median (IQR)		67.5 (20-134)	67.5 (20-134)	0.078
APACHE II score (ICU patients) Median (IQR)		18 (14.5-23.5)	18.5(13.8-23.5)	0.599

age of patients was 30.16 ± 9.47 years,[12] indicating a female-predominant distribution, like our findings. Notably, a systematic review and meta-analysis reported that the evidence remains insufficient to prove male gender as a reliable predictor of in-hospital mortality among patients of TB.[10]

In our cohort, the in-hospital mortality was 15.3%, which fell well within the spectrum reported internationally for hospitalized TB cases. Previous studies have reported the in hospital mortality rates among patients admitted to non ICU settings ranges from 2-12 %, with significantly higher among patients requiring intensive care.[6,7] Our finding are comparable to 16.1% in-hospital mortality in a tertiary hospital cohort of Brazil with newly diagnosed TB patients,[13] The observed mortality was slightly lower than the multicenter prospective cohort in Taiwan where reported mortality rate around 19.7%,[14] and with the 19.7% early mortality recorded by a Ugandan case-control study among hospitalized patients with TB.[15] Such comparative positioning proposes that as mortality in the present cohort remains significant for patients admitted in non ICU settings, it is broadly consistent with rather than an exceptional observation from the pattern seen across similarly resourced health facilities internationally. However, mortality among patients requiring ICU admission was substantially higher at 86.7%, exceeding that reported in large ICU TB cohorts (41.1%).[8]

In this cohort, we found that Diabetes mellitus emerged as the most frequent comorbidity among hospitalized tuberculosis patients, consistent with global trends that identify diabetes as a major driver of TB incidence, yet comorbidity index failed to reach statistical significance (p=0.080), even though a trend toward higher mortality was found in cases with moderate scores of comorbidities. The findings were consistent with the meta-analysis, which reported only very low-quality evidence linking diabetes mellitus to in-hospital death rate (OR 1.31, 95% CI 0.38–4.46) and no significant link to previous history of TB,[10] indicating that the individual comorbidities, taken in isolation, may carry weak prognostic significance.

In the present study a strong association is observed between delayed presentation of symptoms, disseminated TB and in-hospital mortality (p=0.0001), with disseminated disease accounting for over three-quarters of deaths compared to approximately a third of survivors, which aligns closely with a prospective cohort study of hospitalized HIV-associated TB patients where disseminated tuberculosis, was significantly more common among those who died compared to the survivors (79.6% vs. 60.7%), p=0.001.[16] Compounding this, a large retrospective cohort conducted on non-HIV TB patients reported that the markers of disease dissemination and severity, including low BMI, immunosuppressive therapy, end-stage renal disease, pulmonary cavitation, and meningeal involvement, were independently linked to the mortality, with nearly one-fifth of patients with disseminated TB died during twelve months.[17] Collectively, these findings support disseminated disease as one of the most consistent and biologically plausible predictor of mortality across diverse clinical settings among TB patients.

Our study also identified that the development of in-hospital complications, like the need for mechanical ventilation, vasopressor support, acute kidney injury, disseminated intravascular complications and hospital-acquired pneumonia were strongly related to mortality p=0.001, these findings are aligned with the previous literature where patients with TB requiring mechanical ventilation for acute respiratory failure had markedly raised mortality (60%) [10] and requirement for ventilator support as a strong independent predictor of in-hospital mortality among patients with pulmonary TB.[18] Likewise, the relationship between AKI and increase mortality is supported by a cohort study form Uganda, where AKI developed in approximately a third of patients with drug-susceptible TB and was independently linked to the increased risk of mortality regardless of HIV status.[19] Collectively these findings suggest that it is the subsequent progressive pathophysiological process of organ failure, rather than any single baseline patient characteristic that directly determines survival once TB has progressed to the point requiring hospitalization. Furthermore, with respect to laboratory parameters, non-survivors in this cohort had significantly higher WBC counts, lower platelet counts, significantly decreased level of serum albumin and raised hepatic enzyme concentrations than survivors (p=0.004). Keeping with this, the albumin findings are well demonstrated in the literature, reporting that low serum albumin at admission serve as predictive risk factors for in-hospital mortality among TB patients.[18,20, 21] Notably, 64.9% of our admitted patients needed air-borne isolation, which has significant public health implications. AIIR rooms are a scarce resource in LMIC; most public sector hospitals lack them and hence patients suspected to have infectious TB are usually referred out from most facilities adding to critical delays in initiation of timely therapeutic and supportive care and also posing a risk of transmission with in the community. It also underscores the need for adequate negative-pressure rooms and strengthened infection control infrastructure in healthcare facilities.

Finally, our study has several limitations. It is a single-center design and a relatively, limited sample

size, the findings cannot yet be considered representative to the wider national population. Therefore, future larger, multi-center studies involving more diverse cases groups are therefore very important and recommended to further confirm this evidence before it can meaningfully guide broader clinical practice and healthcare policies.

Conclusion

This study concluded that mortality in hospitalized tuberculosis patients is primarily driven by disseminated infection due to delayed presentation and the development of in-hospital complications, including mechanical ventilation, vasopressors, AKI, disseminated intravascular complications, raised WBC and decreased albumin level, whereas demographic characteristics were not significantly associated with death likely reflecting delayed healthcare seeking and extensive disease at presentation rather than comorbidities or drug resistance alone.

Overall, findings indicate the need for early diagnosis and prompt initiation of anti-tuberculosis therapy, along with vigilant monitoring for organ-threatening complications particularly in critically ill patients to prevent in-hospital complications and mortality. Efforts should also be directed towards earlier identification of tuberculosis at the community level, both to prevent disease progression in affected individuals and to reduce ongoing transmission in the community. However, based on a single-center study with a limited sample size, the findings cannot be considered conclusive enough to generalize to the broader national population. Hence to prove the findings and evidence implementation, further large scale studies across the different regions of country are very important.

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