Section: Miscellaneous

Original Research Article

UNVEILING THE SILENT KILLERS: A MIXED-METHODS ANALYSIS OF RISK FACTORS IN TUBERCULOSIS MORTALITY AT TERTIARY CARE CENTRE BHAVNAGAR

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ABSTRACT

Background: Tuberculosis (TB) remains a significant cause of mortality in India despite ongoing public health efforts under the National Tuberculosis Elimination Programme (NTEP). This study aimed to identify risk factors contributing to TB-related deaths and explore the perceptions of caregivers and NTEP stakeholders to inform targeted interventions.

Materials and Methods: A convergent parallel mixed-methods study was conducted at the DOTS Plus Site of a tertiary care center in Bhavnagar, Gujarat. The quantitative component included retrospective analysis of all TB deaths recorded from July 2023 to June 2024 (n=97), using a pretested checklist capturing socio-demographic, clinical, and programmatic data. The qualitative component involved in-depth interviews with purposively selected caregivers of deceased TB patients and NTEP stakeholders. Data were analyzed using descriptive statistics and thematic content analysis.

Results: Most TB deaths occurred among males (73%), individuals aged 41–60 years and those with comorbidities such as diabetes or HIV (61%). Common clinical risk factors included delayed diagnosis, drug-resistant TB (15%) and treatment interruption. Behavioral issues such as substance abuse (67%) and poor nutritional status were prevalent. Qualitative analysis revealed themes including lack of awareness, stigma, emotional distress, financial barriers, and gaps in follow-up services. Stakeholders highlighted systemic issues such as workforce shortages, poor coordination, and insufficient counseling.

Conclusions: TB mortality results from a combination of clinical, behavioral and health system factors. A holistic, patient-centric approach addressing timely diagnosis, comorbidity management, psychosocial support and programmatic strengthening is critical to reducing preventable TB deaths in high-burden settings.

Keywords: Tuberculosis, Mortality, Mixed Methods Study, TB Death

INTRODUCTION

Tuberculosis (TB) continues to pose a formidable global health challenge despite concerted efforts toward its elimination. The World Health Organization (WHO) End TB Strategy ambitiously targets 95% reduction in deaths from TB by 2035, yet the disease remains one of the leading infectious causes of death worldwide.[1] India bears the highest TB burden globally, contributing significantly to the morbidity and mortality statistics, with approximately 2.7 million cases annually and an estimated 440,000 deaths.[2] Despite the implementation of comprehensive control programs, mortality rates remain stubbornly elevated, particularly among vulnerable populations and those with comorbidities.

Extensive literature indicates that TB mortality is influenced by a combination of clinical, biological, demographic and socio-behavioral factors. Key comorbidities, particularly HIV/AIDS and diabetes mellitus, significantly elevate the risk of mortality among TB patients.[1,2] A cohort study in Nigeria revealed that deaths among pediatric TB patients occurred predominantly in the early stages of treatment, suggesting the critical importance of early detection and prompt intervention.[1]

Clinical characteristics such as the presence of drug-resistant TB strains, extrapulmonary TB or coexisting pulmonary and extrapulmonary forms also play a substantial role in increasing mortality risk.[2,3] Multidrug-resistant TB (MDR-TB) patients face a markedly increased risk of poor outcomes. Research has shown that MDR-TB is associated with a more than sevenfold increase in the likelihood of death compared to drug-susceptible TB, highlighting the urgent need for robust drug resistance management protocols.[3]

Non-clinical factors further complicate the landscape of TB mortality. Sociodemographic characteristics such as age, gender and educational attainment significantly associated with patient outcomes. Older individuals, males and those with lower levels of education have been found to have higher mortality rates.[4] These association are reflective of broader structural inequalities and barriers to healthcare access, especially in resource-limited settings.

Moreover, behavioral and lifestyle factors such as alcohol use and smoking have been shown to contribute to adverse TB outcomes. A study conducted in Tomsk Oblast, Russia, identified alcohol dependence as one of the leading predictors of mortality among TB patients, underscoring the need for integrated interventions that address substance use alongside TB care.[5] Tobacco use, often co-occurring with alcohol consumption, has also been associated with delayed diagnosis and increased severity of disease.[4]

Treatment adherence represents another critical determinant of outcomes. Non-adherence to MDR-TB treatment regimens nearly doubles mortality risk.[6] Factors contributing to poor adherence include internalized stigma, prolonged waiting times at directly observed treatment (DOTS) centers and current smoking status.[7]

While previous research has identified various risk factors for TB mortality, significant knowledge gaps persist, particularly in understanding region-specific determinants in high-burden settings like Gujarat, India. Most existing studies employ purely quantitative methodologies, failing to capture the nuanced socio-behavioral and health system factors that influence mortality outcomes. Additionally, the perspectives of family members and healthcare providers remain insufficiently explored, despite their critical insights into the circumstances surrounding TB deaths.

The present study addresses these gaps through its innovative mixed-methods approach, combining rigorous quantitative analysis of clinical, demographic and radiological profiles with qualitative exploration of perceptions among patients' relatives and National Tuberculosis Elimination Program (NTEP) stakeholders. This comprehensive methodology will enable a holistic understanding of TB mortality risk factors in the specific context of Bhavnagar, potentially informing targeted interventions and differentiated care models.

By unraveling the complex interplay of biological, clinical, socioeconomic and health system factors contributing to TB mortality, this research aims to generate actionable evidence for improving survival outcomes. The findings will potentially inform the development of mortality risk prediction tools and guide the implementation of context-specific interventions to achieve the ambitious targets of the End TB Strategy in high-burden regions of India.

MATERIALS AND METHODS

Study Design and Setting

This mixed-methods study was conducted at Government Medical College, Bhavnagar—a tertiary care center in Gujarat, India. The quantitative component employed a cross-sectional, record-based design, while the qualitative component utilized in-depth interviews (IDIs). Data collection spanned July 2023 to June 2024.

Quantitative Component

The study population comprised all patients who succumbed to active tuberculosis (TB) at the tertiary care center during the defined study period. Data were extracted retrospectively from medical records maintained by the Department of Respiratory Medicine. Key variables collected included demographic details such as age, gender, residence, and occupation. Clinical information encompassed the presence of comorbidities, symptomatology of TB, radiological findings, bacteriological confirmation via sputum acid-fast bacilli (AFB)

smear, HIV serological status, history of prior TB infection, adherence to anti-tuberculosis treatment, and duration of hospital stay. Diagnosis of TB was confirmed based on either a positive sputum AFB smear for *Mycobacterium tuberculosis* and/or clinical or histopathological findings consistent with TB. Mortality was defined as death occurring from any cause during the course of TB treatment or prior to its initiation. Cases were classified in accordance with World Health Organization (WHO) guidelines as pulmonary TB (PTB), extrapulmonary TB (EPTB), or disseminated TB (involving two or more anatomical sites).

Qualitative Component

The qualitative strand of the study involved in-depth interviews (IDIs) with two distinct participant groups. The first included close relatives of deceased TB patients—spouses, siblings, adult children, or parents—who were directly involved in caregiving. The second group comprised stakeholders of the National Tuberculosis Elimination Programme (NTEP), including the District TB Officer, Medical Officers designated as TB In-charge, Senior Treatment Supervisors, and TB Health Visitors. IDIs were conducted at locations and times convenient to the participants and continued until thematic saturation was achieved. All interviews were audio-recorded following the provision of written informed consent.

Data Analysis

Data Analysis

Quantitative data were analyzed using JAMOVI statistical software. Descriptive statistics were employed to summarize the demographic and clinical characteristics of the study population. Additionally, potential risk factors associated with tuberculosis-related mortality were explored through appropriate statistical measures.

The qualitative data, derived from transcribed in-depth interviews, were analyzed using thematic analysis. A coding framework was developed and applied by a researcher trained in qualitative research methodology. Emerging themes were identified and organized to capture patterns and insights relevant to the experiences of caregivers and stakeholders involved in TB care.

Ethical Considerations

The study was approved by the Institutional Ethics Committee (Approval No. 1466/2024). All patient data were anonymized during extraction and stored securely to ensure confidentiality. In-depth interviews were conducted at locations and times convenient for participants, following ethical protocols that prioritized their comfort and autonomy. This structured and ethically grounded approach facilitated a comprehensive assessment of the biological, clinical, and socio-systemic determinants of tuberculosis mortality.

RESULTS

Between 1st July 2023 to 30th June 2024, a total of 97 patients died from active tuberculosis at the Department of Respiratory Medicine, Sir T Hospital, Bhavnagar; all were included in this analysis.

Table 1: Demographic, Nutritional and Treatment Profile (N = 97)

Variable	Category	n	%
Gender	Male	71	73.2
	Female	26	26.8
Age group (years)	≤ 20	6	6.2
	21–40	30	30.9
	41–60	39	40.2
	> 60	22	22.7
Weight (kg)	21–40	47	48.5
	41–60	40	41.2
	61–80	10	10.3
Current regimen	Drug-sensitive TB (DSTB)	83	85.6
	Mono-H resistance	2	2.1
	MDR-TB	12	12.4
Past ATT history	Yes	48	49.5
	No	49	50.5
Drug default	Defaulter	24	24.7
	Non-defaulter	73	75.3
Microbiological confirmation	Confirmed	79	81.4
	Clinically diagnosed	18	18.6
Phase of ATT at death	Intensive phase (IP)	87	89.7
	Continuation phase (CP)	10	10.3

Note: ATT: anti-tubercular treatment; MDR: multidrug-resistant; IP: intensive phase; CP: continuation phase.

Among the 97 deceased TB patients, a majority were males (73.2%) and aged between 41–60 years (40.2%). Nearly half had low body weight (48.5%) and a history of past ATT (49.5%). Most were on drug-sensitive TB treatment (85.6%) and 24.7% had defaulted treatment. Microbiological confirmation was present in 81.4% of cases and 89.7% died during the intensive phase of treatment. (Table:1)

Table 2: Behavioral Addictions, TB Site and Radiological Findings (N = 97)

Variable	Category	n	%
Addiction	Bidi smoking	38	39.2
	Alcohol consumption	24	24.7
	Tobacco chewing ("mava")	23	23.7
	Betel quid ("bajar")	3	3.1
	None	9	9.3
Site of TB	Pulmonary only	82	84.6
	Extrapulmonary only	7	7.2
	Both	8	8.2
Radiological	Infiltration	48	49.5
	Cavitary lesions	23	23.7
	Consolidation	14	14.4
	Pleural effusion	3	3.1
	Pyo pneumothorax	4	4.1
	Pneumothorax	4	4.1
	No abnormality detected	1	1.0

Substance use was common, with 39.2% reporting bidi smoking and 24.7% alcohol consumption. Pulmonary TB alone accounted for 84.6% of cases. Infiltrates and cavitary lesions were the most common radiological findings, seen in 49.5% and 23.7% respectively. (Table 2)

Table 3: Comorbidities and Contributory Causes of Death (N = 97)

Comorbidity	n	%	Contributory Cause	n	%
Chronic lung disease	43	44.3	Anaemia	41	42.3
Chronic liver disease	17	17.5	Sepsis	27	27.8
Diabetes mellitus	13	13.4	CO_2 narcosis	22	22.7
Hypertension	7	7.2	Electrolyte imbalance	17	17.5
Cardiovascular disorders	6	6.2	Acute kidney injury	15	15.5
HIV infection	5	5.2	Septic shock	13	13.4
Malignancy	3	3.1	Metabolic acidosis	10	10.3
CNS disorders	3	3.1	Myocardial infarction	7	7.2
Chronic kidney disease	2	2.1	Hepatic encephalopathy / liver injury	9	9.3
Connective tissue / psychiatric / hypothyroidism (combined)	6	6.2	Multi organ dysfunction syndrome	5	5.15
None	7	7.2	ARDS	3	3.1
			Diabetic ketoacidosis	4	4.1
			Cardiac arrhythmia / shock (combined)	10	10.3
			Cerebrovascular stroke	4	4.1
			DVT / pulmonary embolism (combined)	3	3.1
			None	14	14.4

Note: COPD: chronic obstructive pulmonary disease; OAD: obstructive airway disease; ILD: interstitial lung disease; ARDS: acute respiratory distress syndrome; DVT: deep vein thrombosis

Chronic lung disease (44.3%), chronic liver disease (17.5%) and diabetes (13.4%) were frequent comorbidities. Common contributory causes of death included anemia (42.3%), sepsis (27.8%), and CO_2 narcosis (22.7%). Multiple systemic complications were observed. (Table 3)

Table 4: Association Between Past ATT History and MDR-TB (N = 97)

Past ATT History	MDR-TB	Drug-sensitive TB	Total
Yes	10	38	48
No	2	47	49
χ^2= 6.28, DF= 1, p value= 0.012			

A statistically significant association was observed between past ATT history and MDR-TB status (p = 0.012), indicating that patients with prior TB treatment were more likely to develop drug resistance. (Table 4)

Table 5: Perspectives of Relatives of Deceased TB Patients on Risk Factors Associated with Tuberculosis Mortality

Theme	Category	Code	Explanation	Verbatim (English)
Behavioral & Lifestyle Factors	Substance Abuse	Alcohol dependence	Relatives attributed death to heavy alcohol use, which reduced treatment adherence.	"He drank heavily...that's why he died." (P1)
		Tobacco use (bidis)	Bidi smoking was seen as a direct cause of worsening TB	"Bidis are responsible...caused his death." (P3)

			and death.	
	Poor Treatment Adherence	Irregular medication intake	Patients skipped doses due to addiction or carelessness.	"He didn't take medicines regularly...we fought over it." (P1)
Healthcare System Challenges	Delayed Diagnosis	Ignoring early symptoms	Families delayed seeking care despite prolonged symptoms.	"He had a cough for 15 days but didn't see a doctor." (P3)
	Accessibility Barriers	Financial constraints	Poverty prevented access to private care or nutritional support.	"Costly medicines...no one can afford private care." (P8)
Socioeconomic Determinants	Occupational Hazards	Dust exposure	Occupations like diamond cutting exposed patients to lung irritants.	"He cut diamonds...maybe dust caused TB." (P1)
	Nutritional Deficiencies	Reduced appetite	Poor appetite during treatment worsened health.	"He ate very little...just a few bites." (P6)
Psychological Barriers	Stigma & Denial	Social isolation	Patients were isolated due to fear of contagion.	"They told us TB is contagious...stay away." (P6)
	Lack of Awareness	Misconceptions about TB	Relatives believed TB spread through alcohol or myths.	"TB spreads through alcohol." (P3)

It presents a thematic analysis of the perspectives of relatives of deceased TB patients, highlighting perceived risk factors associated with tuberculosis mortality. The themes that emerged from the qualitative interviews encompass behavioral and lifestyle factors, healthcare system challenges, socioeconomic determinants, and psychological barriers.

Under Behavioral & Lifestyle Factors, substance abuse—particularly alcohol dependence and bidi smoking—was frequently cited as a contributor to poor treatment outcomes, with relatives emphasizing the negative impact of addiction on medication adherence. Additionally, irregular medication intake was mentioned as a consequence of addiction or negligence, contributing directly to the progression of the disease.

Healthcare System Challenges were reflected in reports of delayed diagnosis due to ignoring early symptoms and accessibility barriers such as financial constraints, which limited access to private healthcare and nutritional support.

Socioeconomic Determinants included occupational hazards, such as exposure to dust in professions like diamond cutting and nutritional deficiencies, where reduced appetite and poor dietary intake were observed during the treatment period.

Finally, Psychological Barriers emerged through narratives around stigma and denial, with patients often facing social isolation and lack of awareness, where misconceptions about TB transmission (e.g., linking it to alcohol use) further hindered appropriate treatment-seeking behavior.

These insights underscore the multifaceted nature of TB mortality, where individual behaviors intersect with systemic, economic and cultural factors, indicating the need for a more integrated and context-sensitive approach to TB prevention and care. (Table 5)

Table 6: Perspectives of NTEP Stakeholders on Contributing Risk Factors in Tuberculosis Mortality

Theme	Category	Code	Explanation	Verbatim (English)
Systemic Challenges	Medication Stockouts	DR-TB drug shortages	Critical drugs like cycloserine were unavailable for a while, affecting treatment.	"Clofazimine and cycloserine are unavailable... slum patients can't afford them." (TBHV)
	Delayed Care-Seeking	Reliance on private clinics	Patients sought private care first, delaying TB diagnosis.	"Patients go to private clinics… leading to late diagnosis." (TBHV)
Patient-Related Factors	Comorbidities	HIV/diabetes co-infections	Comorbidities weakened immunity, increasing TB severity.	"…HIV weakens immunity." (MO)
	Addiction	Alcohol/tobacco dependency	Addiction reduced treatment efficacy and nutrition.	"Alcohol reduces treatment effectiveness." (DTO)
Socioeconomic Barriers	Poverty	Slum residence	Slum dwellers had higher exposure and poorer outcomes.	"Slums increase exposure risk." (TBHV)
	Stigma	Familial neglect	Families isolated elderly patients, worsening their condition.	"Elderly patients are neglected at home..." (MO)
Clinical Gaps	Treatment Monitoring	Defaulting	Patients stopped treatment midway, becoming defaulters.	"Patients stop treatment midway…." (TBHV)
	Awareness Deficits	Community misconceptions	Lack of awareness about TB's preventability delayed care-seeking.	"…People don't understand TB is preventable." (DTO)

It outlines the perspectives of National Tuberculosis Elimination Program (NTEP) stakeholders on key risk factors contributing to tuberculosis mortality, categorized into systemic, patient-related, socioeconomic and clinical dimensions. These findings, drawn from in-depth interviews with medical officers (MOs), district TB officers (DTOs) and TB health visitors (TBHVs), provide critical insights into operational and patient-level challenges impacting TB outcomes.

Among Systemic Challenges, medication stockouts were identified as a serious barrier, particularly for drug-resistant TB (DR-TB) treatment, with stakeholders citing the unavailability of essential medications like clofazimine and cycloserine. Additionally, delayed care-seeking due to patients' initial reliance on private healthcare providers was seen as a factor leading to late diagnosis and treatment initiation.

Patient-Related Factors included the presence of comorbidities, such as HIV and diabetes, which were believed to exacerbate TB progression due to weakened immune responses. Addiction to alcohol and tobacco was also frequently mentioned as a barrier that negatively affected both the efficacy of treatment and the patient's nutritional status.

Socioeconomic Barriers were prominently highlighted, with poverty and slum residence contributing to higher exposure to TB and reduced access to consistent care. Stigma within families—particularly the neglect of elderly TB patients—was seen as a compounding factor that led to poor home-based support and deteriorating health.

Within the theme of Clinical Gaps, treatment monitoring was a recurring concern, with instances of patients defaulting due to poor follow-up and lack of support. Awareness deficits within the community, including widespread misconceptions about TB's causes and preventability, were identified as deterrents to timely diagnosis and adherence.

Overall, these stakeholder narratives emphasize the need for systemic strengthening, improved patient education and targeted community-level interventions to reduce TB mortality, especially among vulnerable populations. (Table 6)

DISCUSSION

The complexity of TB mortality is rooted in an intricate mix of biological, behavioral, social and systemic factors.

In our study, among the deceased, 73.2% were male and most (40.2%) belonged to the 41–60-year age group, aligning with global evidence that middle-aged and older adults are at higher risk of TB mortality.8 Study from Brazil suggest that, factors strongly associated with probable TB deaths were male gender (sHR = 1.33, 95% CI: 1.26–1.40), age over 60 years (sHR = 9.29, 95% CI: 8.15–10.60).8 De Almeida et al. found that malignancy and older age were significant predictors of TB mortality in hospitals, while smear positivity and male gender showed no consistent association.[9] In our qualitative part, one of our health worker said that elder people are neglected one so there is delay in diagnosis and treatment. Generally, elderly patients encounter unfavorable living conditions, malnutrition, comorbidities and diminished access to healthcare, any of which may elevate the risk of mortality. It is conceivable that older tuberculosis cases exhibited a heightened mortality rate due to their propensity to present with nonspecific symptoms, potentially leading to delays in the diagnosis and treatment of tuberculosis and ultimately a greater risk of death.[10,11] More robust clinical management and preventive strategies, encompassing earlier suspicion, diagnosis and treatment of tuberculosis, may mitigate fatalities among the elderly population.[12]

Notably, 48.0% of patients weighed between 21–40 kg, indicating severe undernutrition—a well-documented risk factor for poor TB outcomes. Malnutrition plays a critical role in TB outcomes. In our study, nearly 90.0% of deceased patients were under 60 kg, with 48.0% below 40 kg. Shah et al.'s findings in Jamnagar stated nutritional supplementation significantly improved cure rates and reduced mortality from 5.7% to 1.1%.[13]

In our study 5.2% patients had HIV positive. HIV co-infection presents perhaps the most devastating synergy, with mortality rates reaching 90.3% in HIV-positive TB patients not receiving antiretroviral therapy, compared to 14.3% in those on appropriate HIV treatment.[20] Also, HIV positive serology was strongly associated with probable TB deaths (sHR = 62.78; 95% CI: 55.01–71.63).[8] Gaifer (2017) similarly reported that over half of TB deaths in Oman occurred within the first month of diagnosis, particularly among older, underweight individuals with HIV.[14]

Substance use was prevalent, with 39.2% of individuals reporting engagement in bidi smoking and 24.7% indicating alcohol consumption. In qualitative part Patient-related factors such as comorbidities like HIV and diabetes, as well as addiction to alcohol and tobacco, were highlighted as barriers that worsened TB progression by weakening immune responses and impacting treatment efficacy.

Bidi smoking is associated with chronic pulmonary ailments, including chronic obstructive pulmonary disease and lung carcinoma, leading to a markedly elevated mortality rate in comparison to non-smokers. Our qualitative part of study also suggests, addiction that Bidi smoking was seen as a direct cause of worsening TB and death. Smoking is associated with a nine-fold greater risk of death associated with TB.[15] Smokers are at much greater risk of delayed diagnosis of TB,[16] greater symptoms and bacterial load,[17] unfavorable TB treatment outcomes,[18] more severe disease progression,[19] An association between smoking and

drug-resistant TB has recently been identified.[20] In our examination of deceased individuals, 44.3% were diagnosed with chronic lung diseases, while 3.2% were afflicted with lung carcinoma that is related to smoking.

Alcohol consumption significantly compromises the immune system, thereby augmenting susceptibility to tuberculosis (TB) infection.[21] Furthermore, alcohol intake has been linked to malnutrition, hepatic disorders and social marginalization, all of which elevate the risk of TB infection and the propagation of Mycobacterium tuberculosis (Mtb).[22,23] Among individuals with alcoholism, there exists an elevated likelihood of antitubercular therapy (ATT)-induced hepatotoxicity, which further exacerbates the risk of mortality. In our study, 9.2% of patients succumbed to hepatic encephalopathy or acute liver injury attributable to alcoholism. Thus, alcoholism emerges as a significant risk factor for mortality related to TB.[5] Our qualitative analysis further indicated that alcoholism serves as a significant factor contributing to the non-adherence to tuberculosis treatment, which ultimately results in mortality.

A significant proportion of patients (49.5%) had a prior history of TB treatment. MDR-TB was detected in 12.4% of patients, with a statistically significant association between past treatment history and the development of drug resistance (p=0.012). The situation becomes markedly worse in drug-resistant TB cases, where global data indicate that approximately 20.0% of patients initiated on multidrug-resistant tuberculosis (MDR-TB) treatment succumb during the course of therapy.[24] Our cohort and Velavan et al.'s study both demonstrate that patients with a history of lost to follow up or treatment failure are more likely to develop MDR-TB and experience mortality.[25] Retreatment cases require personalized interventions such as hospital-based supervision, psychosocial counseling and targeted nutritional support. Balaji et al. further identified inappropriate past TB treatments and prior fluoroquinolone use as drivers of MDR and XDR-TB.[26]

In our study, 24.7% patients were treatment defaulters. Treatment adherence represents another critical determinant of outcomes. Non-adherence to MDR-TB treatment regimens nearly doubles mortality risk (aOR: 1.92; 95% CI: 1.02-4.83).[24] Factors contributing to poor adherence include internalized stigma, prolonged waiting times at directly observed treatment (DOTS) centers and current smoking status.[7] In the qualitative component of our study, inadequate adherence emerges because of addiction or negligence, which directly propels the progression of the disease.

Nearly 90.0% of deaths occurred during the intensive phase of treatment, suggesting vulnerabilities in early-stage care. A cohort study in Nigeria revealed that deaths among pediatric TB patients occurred predominantly in the early stages of treatment, suggesting the critical importance of early detection and prompt intervention.[1]

Lin et al,[27] propose that 82.7% of tuberculosis (TB) fatalities are attributed to non-TB-related causes, including malignancies, bacterial infections, cerebrovascular disorders, cerebrovascular accidents, hepatic failure, renal failure, chronic obstructive pulmonary disease (COPD), and human immunodeficiency virus (HIV). In our investigation, all these comorbidities were observed in 92.78% of TB-related deaths. It is imperative to implement interventions and collaborative care strategies to address both TB and its concomitant diseases to mitigate overall mortality.[28] In the qualitative segment, our stakeholders underscored that patient-related factors, particularly comorbidities such as HIV and diabetes, were identified as significant impediments that exacerbated the progression of tuberculosis by compromising immune responses and adversely affecting treatment efficacy.

In Lin et al,[27] final mode of death was septic shock in 46.5%, respiratory failure in 41.9%, and TB related cachexia in the remaining 11.6%. In our study immediate cause of death was sepsis (28.0%), CO2 narcosis (23%), electrolyte imbalances (17.5%), acute kidney injury (15.5%) and septic shock (13.4%). Only 14.4% of patients died solely from TB, while 85.6% had additional complications, underscoring the multi-systemic impact of TB.

Microbiologically confirmed TB was present in 81.4% of patients and pulmonary TB accounted for 84.6% of all cases. While pulmonary TB dominated in our study, extrapulmonary TB (EPTB) cases such as TB meningitis and abdominal Koch's disease were also present. Bjørgaas et al. reported that EPTB, particularly at non-lymphatic sites, increases the risk of hospitalization and death. Pediatric patients, although fewer in number, often face diagnostic challenges due to non-specific symptoms.[29]

In our study 49.5 % patients had infiltrations, 23.7% had cavitary lesion, 14.4% had consolidation and pleural effusion in 3.1% while in other study both cavity lung disease, upper lobe involvement and pleural effusion occur in half of the patients. Lower lobe involvement and nodular changes were less commonly present.[30] Comorbidity has previously been identified as a significant predictor of mortality during treatment among patients with tuberculosis (TB).[28,31,32] The most prevalent conditions associated with TB as a contributing factor to mortality include HIV/AIDS, renal disorders, hepatic diseases, cardiovascular ailments, malignancies, chronic obstructive pulmonary disease (COPD) and diabetes mellitus.[5,12,31–34] Nevertheless, the impact of underlying conditions, apart from HIV/AIDS, on the mortality risk attributed to TB remains inadequately explored. Certain ailments, such as renal and hepatic diseases, may alter the clinical presentation of TB, complicating both diagnosis and treatment and may also heighten the risk of adverse reactions to anti-

TB pharmacotherapy.35 In our investigation, comorbidities were evident in 92.78% of patients who succumbed to TB. While the precise etiology of death remains undetermined, implementing TB screening among individuals with conditions that elevate mortality risk could prove beneficial in facilitating early detection of TB and enhancing treatment outcomes.

Qualitative analysis

Qualitative interviews with relatives and healthcare providers highlighted behavioral factors such as alcohol dependence and poor medication adherence. Psychosocial stressors—like addiction and stigma—also contributed to poor outcomes, as supported by qualitative feedback from relatives and echoed in Velavan et al.'s Puducherry study on retreatment patients.[25]

Low community awareness of tuberculosis (TB) frequently serves as a barrier to seeking medical attention for cough, adherence to treatment regimens and the effective implementation of infection prevention and control measures. In the present study, a significant number of participants were unaware of the precise etiology of TB. A deficiency in adequate knowledge regarding TB was deemed a contributory factor to mortality associated with the disease. The findings indicate that TB patients often underestimate the severity of their symptoms during the initial stages and fail to associate them with any underlying health conditions.

In this study, families delayed seeking care due to financial constraints or low awareness. This is similar to other study in which healthcare-seeking behaviour of the community was found to be inadequate, primarily due to a lack of awareness regarding tuberculosis (TB) and the absence of coordinated interventions. Individuals demonstrated a preference for traditional medicine over conventional medical practices and this reluctance to seek timely medical attention exacerbates the severity of the disease.[36]

Participants in the study articulately expressed that the adherence to treatment among tuberculosis patients was significantly deficient, primarily attributable to limited awareness of tuberculosis, insufficient nutritional intake, financial constraint and apprehension regarding adverse drug reactions. In concordance with this, a qualitative investigation conducted in Southern Ethiopia revealed that a considerable number of tuberculosis patients failed to comply with their medication regimens due to financial constraints, food scarcity, reliance on traditional healing practices for tuberculosis treatment and a lack of familial and communal support.[37]

In our study, some individuals reported that numerous tuberculosis patients conceal their ailments out of fear of social stigma. A comprehensive survey on stigma conducted in Ethiopia revealed that over half of the respondents would be willing to disclose their condition; however, a quarter expressed concern that the community would shun them, and others indicated they would be asked to distance themselves from the community. The presence of stigma was found to correlate with educational attainment and awareness.

Stakeholders cited drug stockouts, stigma, reliance on private clinics and poor treatment monitoring as systemic barriers to effective TB control. Samudyatha et al. observed patient resistance, stigma and supply-side failures in drug availability. These issues were mirrored in our qualitative findings, where stockouts and delayed care-seeking due to cost were commonly reported.

Stakeholders also posit that socioeconomic impediments, including poverty, residence in slums and familial stigma, have exacerbated susceptibility to tuberculosis, curtailed access to healthcare, and diminished home-based support for elderly tuberculosis patients.

In our study according to stakeholder, clinical gaps were noted, particularly concerning treatment monitoring, patient follow-up and community awareness deficits regarding TB causes and prevention, all of which hindered timely diagnosis and adherence to treatment. That is substantiated by Shegaze et al,[36] who highlight that insufficient diagnostic facilities, inadequate infrastructure, suboptimal infection prevention measures within healthcare institutions, unavailability of medications, a shortage of adequately trained personnel and a lack of ongoing training and professional development for healthcare practitioners significantly contribute to the mortality of tuberculosis patients. Stakeholder narratives underscored the importance of systemic strengthening, enhanced patient education, and targeted community interventions to combat TB mortality, particularly focusing on vulnerable populations.

Strength: A limited mixed-method study was previously conducted to explore caregivers' perceptions of the risk factors associated with TB mortality. This study provides detailed insights into their knowledge and perceptions regarding these risk factors.

Limitation: The study group was patients who died from active TB and since no comparison group was included, inferential statistical tests could not be applied.

Recommendation: TB mortality is associated with multiple risk factors, which vary widely across different geographical and socioeconomic contexts. Therefore, further multicentric qualitative studies should be conducted to explore these factors in depth.

CONCLUSION

Tuberculosis (TB) mortality is influenced by a blend of clinical, behavioural and health system elements. In the context of effective chemotherapy for TB, we

have observed that a substantial proportion of mortality among elderly tuberculosis patients is attributable to preexisting comorbidities. Furthermore, inadequate adherence to treatment regimens, a lack of awareness regarding tuberculosis, pervasive social stigma, poor nutritional intake and limited healthcare-seeking behaviour have emerged as significant factors exacerbating mortality rates. The predominant cause of mortality in these individuals was sepsis. An integrative, patient-oriented strategy that includes prompt diagnosis, health education, nutritional support, management of comorbidities, psychosocial assistance and the enhancement of healthcare systems is vital for decreasing preventable TB fatalities in regions with a high disease burden.

Conflict of Interest

The authors affirm that there are no conflicts of interest, financial or otherwise, that could have influenced the conduct or outcomes of this study.

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REFERENCES

1. WHO. The end TB strategy by WHO [Internet]. 2015 [cited 2025 May 14]. Available from: https://www.who.int/publications/i/item/WHO-HTM-TB-2015.19
2. Indian Council of Medical Research CTD (CTD) and NTEPM of H and FWG of IWHOI. National TB Prevalence Survey in India 2019 - 2021, summary report. New Delhi; 2021.
3. Adamu AL, Aliyu MH, Galadanci NA, Musa BM, Gadanya MA, Gajida AU, et al. Deaths during tuberculosis treatment among paediatric patients in a large tertiary hospital in Nigeria. PLoS One. 2017 Aug 17;12(8): e0183270.
4. Lo HY, Suo J, Chang HJ, Yang SL, Chou P. Risk Factors Associated with Death in a 12-Month Cohort Analysis of Tuberculosis Patients. Asia Pacific Journal of Public Health. 2015 Mar 23;27(2):NP758–68.
5. Chung-Delgado K, Guillen-Bravo S, Revilla-Montag A, Bernabe-Ortiz A. Mortality among MDR-TB Cases: Comparison with Drug-Susceptible Tuberculosis and Associated Factors. PLoS One. 2015 Mar 19;10(3):e0119332.
6. Nahid P, Jarlsberg LG, Rudoy I, de Jong BC, Unger A, Kawamura LM, et al. Factors associated with mortality in patients with drug-susceptible pulmonary tuberculosis. BMC Infect Dis. 2011 Dec 3;11(1):1.
7. Mathew TA, Ovsyanikova TN, Shin SS, Gelmanova I, Balbuena DA, Atwood S, et al. Causes of death during tuberculosis treatment in Tomsk Oblast, Russia. Int J Tuberc Lung Dis. 2006 Aug;10(8):857–63.
8. Kizito E, Musaazi J, Mutesasira K, Twinomugisha F, Namwanje H, Kiyemba T, et al. Risk factors for mortality among patients diagnosed with multi-drug resistant tuberculosis in Uganda- a case-control study. BMC Infect Dis. 2021 Dec 22;21(1):292.
9. Suliman Q, Lim PY, Md. Said S, Tan KA, Mohd. Zulkefli NA. Risk factors for early TB treatment interruption among newly diagnosed patients in Malaysia. Sci Rep. 2022 Jan 14;12(1):745.
10. Viana PV de S, Paiva NS, Villela DAM, Bastos LS, de Souza Bierrenbach AL, Basta PC. Factors associated with death in patients with tuberculosis in Brazil: Competing risks analysis. PLoS One. 2020 Oct 8;15(10):e0240090.
11. 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 May 8;8(1):7230.
12. Pérez-Guzmán C, Vargas MH, Torres-Cruz A, Villarreal-Velarde H. Does Aging Modify Pulmonary Tuberculosis? Chest. 1999 Oct;116(4):961–7.
13. Doherty MJ, Spence DP, Davies PD. Trends in mortality from tuberculosis in England and Wales: effect of age on deaths from non-respiratory disease. Thorax. 1995 Sep 1;50(9):976–9.
14. Borgdorff M, Veen J, Kalisvaart N, Nagelkerke N. Mortality among tuberculosis patients in The Netherlands in the period 1993-1995. European Respiratory Journal. 1998 Apr 1;11(4):816–20.
15. Shah V, Murugan Y, Patel SS, Trivedi NS, Pithadiya D, Makwana N, et al. Nutritional Supplementation in Tuberculosis Treatment: A Mixed Methods Study of Clinical Outcomes and Patient Perceptions in Jamnagar, India. Cureus. 2024 Sep 27;
16. Gaifer Z. Risk factors for tuberculosis mortality in a tertiary care center in Oman, 2006–2016. Int J Mycobacteriol. 2017;6(4):356.
17. Wen CP, Chan TC, Chan HT, Tsai MK, Cheng TY, Tsai SP. The reduction of tuberculosis risks by smoking cessation. BMC Infect Dis. 2010 Dec 7;10(1):156.
18. Altet N, Latorre I, Jiménez-Fuentes MÁ, Maldonado J, Molina I, González-Díaz Y, et al. Assessment of the influence of direct tobacco smoke on infection and active TB management. PLoS One. 2017 Aug 24;12(8):e0182998.
19. Adegbite BR, Edoa JR, Achimi Agbo P, Dejon-Agobé JC, N Essone P, Lotola-Mougeni F, et al. Epidemiological, Mycobacteriological, and Clinical Characteristics of Smoking Pulmonary Tuberculosis Patients, in Lambaréné, Gabon: A Cross-Sectional Study. Am J Trop Med Hyg. 2020 Dec 2;103(6):2501–5.
20. Leung CC, Yew WW, Chan CK, Chang KC, Law WS, Lee SN, et al. Smoking adversely affects treatment response, outcome and relapse in tuberculosis. European Respiratory Journal. 2015 Mar;45(3):738–45.
21. Altet-Gómez MN, Alcaide J, Godoy P, Romero MA, Hernández del Rey I. Clinical and epidemiological aspects of smoking and tuberculosis: a study of 13,038 cases. Int J Tuberc Lung Dis. 2005 Apr;9(4):430–6.
22. Wang MG, Huang WW, Wang Y, Zhang YX, Zhang MM, Wu SQ, et al. Association between tobacco smoking and drug-resistant tuberculosis. Infect Drug Resist. 2018 Jun;Volume 11:873–87.
23. Yeligar SM, Harris FL, Hart CM, Brown LAS. Glutathione attenuates ethanol-induced alveolar macrophage oxidative stress and dysfunction by downregulating NADPH oxidases. American Journal of Physiology-Lung Cellular and Molecular Physiology. 2014 Mar 1;306(5):L429–41.
24. Wigger GW, Bouton TC, Jacobson KR, Auld SC, Yeligar SM, Staitieh BS. The Impact of Alcohol Use Disorder on Tuberculosis: A Review of the Epidemiology and Potential Immunologic Mechanisms. Front Immunol. 2022 Mar 31;13.
25. Ma Y, Che NY, Liu YH, Shu W, Du J, Xie SH, et al. The joint impact of smoking plus alcohol drinking on treatment of pulmonary tuberculosis. European Journal of Clinical Microbiology & Infectious Diseases. 2019 Apr 15;38(4):651–7.
26. van Rhijn P, Desair J, Vlassak K, Vanderleyden J. The NodD proteins of Rhizobium sp. strain BR816 differ in their interactions with coinducers and in their activities for

nodulation of different host plants. Appl Environ Microbiol. 1994 Oct;60(10):3615–23.
27. Velavan A, Purty AJ, Shringarpure K, Sagili KD, Mishra AK, Selvaraj KS, et al. Tuberculosis retreatment outcomes and associated factors: a mixed-methods study from Puducherry, India. Public Health Action. 2018 Dec 21;8(4):187–93.
28. Balaji V, Daley P, Anand AA, Sudarsanam T, Michael JS, Sahni RD, et al. Risk Factors for MDR and XDR-TB in a Tertiary Referral Hospital in India. PLoS One. 2010 Mar 4;5(3):e9527.
29. Lin CH, Lin CJ, Kuo YW, Wang JY, Hsu CL, Chen JM, et al. Tuberculosis mortality: patient characteristics and causes. BMC Infect Dis. 2014 Dec 3;14(1):5.
30. Hansel NN, Merriman B, Haponik EF, Diette GB. Hospitalizations for Tuberculosis in the United States in 2000. Chest. 2004 Oct;126(4):1079–86.
31. Helle OMB, Kanthali M, Grønningen E, Hassan S, Purohit MR, Mustafa T. Factors associated with hospitalization and mortality in adult and pediatric extrapulmonary tuberculosis at a tertiary care hospital in Central India. Infect Dis. 2024 Dec 24;56(12):1080–92.
32. Alsehali A, Alrajih H, Al-Jahdali H, Al-Safi E, Layqah L, Baharoon S. Clinical, Radiological Features and Treatment Outcomes of Tuberculosis in Patients Aged 75 Years and Older. J Epidemiol Glob Health. 2024 Dec;14(4):1591–601.
33. Walpola HC, Siskind V, Patel AM, Konstantinos A, Derhy P. Tuberculosis-related deaths in Queensland, Australia, 1989-1998: characteristics and risk factors. Int J Tuberc Lung Dis. 2003 Aug;7(8):742–50.
34. Oursler KK, Moore RD, Bishai WR, Harrington SM, Pope DS, Chaisson RE. Survival of Patients with Pulmonary Tuberculosis: Clinical and Molecular Epidemiologic Factors. Clinical Infectious Diseases. 2002 Mar 15;34(6):752–9.
35. Sterling TR, Zhao Z, Khan A, Chaisson RE, Schluger N, Mangura B, et al. Mortality in a large tuberculosis treatment trial: modifiable and non-modifiable risk factors. Int J Tuberc Lung Dis. 2006 May;10(5):542–9.
36. White MC, Portillo CJ. Tuberculosis mortality associated with AIDS and drug or alcohol abuse: analysis of multiple cause-of-death data. Public Health. 1996 May;110(3):185–9.
37. American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America. Am J Respir Crit Care Med. 2003 Feb 15;167(4):603–62.
38. Shegaze M, Boda B, Ayele G, Gebremeskel F, Tariku B, Gultie T. Why people die of active tuberculosis in the era of effective chemotherapy in Southern Ethiopia: A qualitative study. J Clin Tuberc Other Mycobact Dis. 2022 Dec; 29:100338.
39. Gugssa Boru C, Shimels T, Bilal AI. Factors contributing to non-adherence with treatment among TB patients in Sodo Woreda, Gurage Zone, Southern Ethiopia: A qualitative study. J Infect Public Health. 2017 Sep;10(5):527–33.