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Factors Associated with Mortality among Patients with Drug Sensitive Tuberculosis in Selected Counties, Kenya, 2021-2023

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Abstract

Background: Tuberculosis (TB) remains a significant public health challenge in Kenya, contributing to high mortality rates despite efforts to improve diagnosis and treatment. Understanding the factors associated with mortality among patients with drug-sensitive TB is crucial for enhancing TB control strategies and reducing deaths.

Methods: The study conducted a retrospective analysis of TB surveillance data from selected counties after validating it through annual performance review meetings. It included patients with drug-sensitive tuberculosis reported monthly through the TB Information Basic Unit (TIBU) electronic reporting system by sub-county coordinators. Sociodemographic and clinical data were collected at enrollment, including age, sex, type of TB, sputum and chest X-ray results, body weight, BMI, follow-up smears, treatment regimen, date of drug collection, HIV status, comorbidities, ART usage, nutritional assessment, and treatment outcomes. Data abstraction was performed from the national TB and Leprosy control program database on March 7, 2023.

Results: A total of 47,727 TB patients were included in the study. The majority were male (61.8%) and adults aged 15–34 years (41.1%). Overall, 6.1% had a mortality outcome. Mortality was higher among adults (92.1%) compared to children (7.9%), and among underweight TB patients (52.7%). HIV-positive TB patients accounted for 54.3% of reported deaths. Most deaths occurred among new TB cases (91.4%) and extra-pulmonary TB patients (76.7%). Significant predictors of TB outcomes included age (especially 55+), underweight BMI, HIV-positive status, extra-pulmonary TB, certain treatment regimens (2RHZ/4RH and 2RHZE/4RH), abnormal X-rays, and county of residence.

Conclusions: The study highlights that mortality among patients with drug-sensitive tuberculosis is a result of biological, clinical, and health-system factors. The high mortality rate signals a challenge to translate global advances into favorable patient outcomes. Addressing diagnostic accuracy and the interconnected social and health disparities is crucial to reducing preventable mortality.

Keywords: Factors, Mortality, Clinical diagnosis, Drug-Sensitive Tuberculosis, Kenya

Background

Tuberculosis (TB) remains a devastating global health crisis, with *Mycobacterium tuberculosis* infecting 10.8 million people and claiming 1.1 million lives in 2023 [1]. While primarily transmitted through airborne particles and targeting the lungs, TB mortality is driven not only by the pathogen but also by fractured health systems and social inequities [2]. This is starkly evident in Kenya, which remains among the 30 high TB/HIV burden countries, facing a disturbing paradox: despite a 40% decline in HIV incidence between 2010 and 2023, TB mortality persists at 15 deaths per 100,000 individuals [3]. This stagnation defies expectations, as TB deaths fell by a mere 21% from 2015 to 2022, far below the 75% reduction needed to meet the 2030 targets [4]. Current trajectories project that Kenya will only reach zero TB deaths by 2080, a devastating 45 years behind the global End TB target of 2035 [5].

In Kenya, 47% of TB cases lack bacteriological confirmation and are diagnosed clinically [3]. This aligns with global evidence consistently showing that mortality is substantially higher among patients with clinically diagnosed TB than among those with bacteriological confirmation [6]. This is a common necessity in low-resource settings, where persistent barriers limit diagnostic capacity and accuracy [7]. However, clinical diagnosis without definitive confirmation often results in substantial misdiagnosis, especially in conditions with overlapping symptoms [8].

Autopsy studies have revealed the grave consequences of this: nearly one-third (31%) of deaths attributed to clinically diagnosed TB were actually caused by cancer, fungal infections, or other conditions [9]. This diagnostic inaccuracy distorts our understanding of TB mortality and misdirects resources, leaving patients with true TB missed to be diagnosed, while others receive incorrect and delayed treatments [10].

Known risk factors only partially explain persistent mortality. Undernutrition impairs the immune responses needed to control *Mycobacterium tuberculosis*, significantly increasing the risk of developing active TB and raising mortality rates [11]. Furthermore, HIV-induced immunosuppression profoundly alters the clinical course of TB, resulting in more severe disease and an increased risk of death [12]. The synergistic relationship between TB and HIV significantly worsens patient outcomes. HIV-positive TB patients face a 2–3 times higher risk of death compared to their HIV-negative counterparts, a disparity largely driven by advanced immunosuppression and the absence of antiretroviral therapy (ART) [5]. This excess mortality is preventable, as initiating ART during TB treatment has been shown to drastically reduce the risk of death [13]. These factors, combined with extreme age and poverty, create a complex web of vulnerability.

Across multiple global studies, TB mortality rates rise significantly with advancing age [14,15]. Older TB patients frequently have multiple comorbidities. Diabetes, chronic kidney disease, liver disease, HIV, cancer, and chronic lung diseases (COPD) are repeatedly identified as major contributors to poor TB outcomes and increased mortality [16,17]. Males have higher all-cause and TB-related mortality compared to females, with meta-analyses showing a 26–31% increased odds of death for men [18,19].

Multidisciplinary teams (MDTs) are widely implemented in cancer care and increasingly in other complex diseases such as multidrug-resistant TB (MDR-TB) [20]. While MDTs are a standard of care for MDR-TB in many countries, they are not routinely used for evaluating difficult cases of presumed drug-sensitive TB, especially those based on clinical diagnosis alone.

However, a significant proportion of mortality remains unexplained. Preliminary analysis of routine data from high-burden counties in Kenya suggests that a significant proportion of patients diagnosed with TB also had a recorded comorbidity of cancer, an association that is not well characterized in such settings. This indicates that cancer may be a critical, overlooked factor masquerading as or coinciding with TB, leading to misdiagnosis and contributing to stagnant mortality rates. While Kenya has expanded diagnostics and integrated care, a new focus on improving the accuracy of clinical diagnosis is urgently needed to change the current trajectory and prevent unnecessary deaths. This study aimed to evaluate factors associated with mortality among patients with drug-sensitive tuberculosis in eleven high-burden counties in Kenya.

Methods

Study Design and Setting

Centre for Health Solutions-Kenya supports all 47 counties of Kenya in the implementation of TB control activities with additional support to the highly burdened counties. This support includes monthly supervision by sub-county and county TB coordinators, TB/HIV data review meetings, sample networking, capacity building, coordination meetings, and monthly clinical review meetings.

A cross-sectional analysis of routinely collected TB surveillance data from eleven high-burden counties was conducted after validation of data through annual performance review meetings.

Data Sources and Collection

Patients with drug-sensitive tuberculosis are notified monthly through an electronic case-based surveillance reporting system by sub-county coordinators on a monthly basis. During enrollment, sociodemographic and clinical data were collected, including age, sex, type of TB, initial sputum and CXR results, body weight, BMI, follow-up smears, treatment regimen, date of drug collections, HIV status, comorbidities, ART, nutritional assessment, type of TB patient, and treatment outcomes. Data were abstracted from the national TB and Leprosy Control program database on March 7, 2023. Data cleaning for the drug-sensitive register was done in 2021 through the support of the sub-county TB and Leprosy Coordinators. The data was validated through the annual performance review meeting conducted by the National TB and Leprosy Control Program, Kenya, in March 2023.

Variables

The primary outcome was all-cause mortality within six months of starting treatment for bacteriologically confirmed and clinically diagnosed cases. The patients with TB of the bones and spine were evaluated after 12 months. Survival time was retrospectively calculated from the date of starting treatment to the time of death, with those alive censored. The risk factors examined were age, sex, nutritional status, HIV status, types of TB, regions, sector, nutritional status, mode of diagnosis (clinical or bacteriological), CXR results, baseline smears, GeneXpert results, and ART status.

Study Sample

The study included 47,727 patients with drug-sensitive tuberculosis from eleven high-burdened counties in Kenya.

Data Analysis

Descriptive statistics using counts, proportions, and median (interquartile range) were used. Kaplan Meier plots were used to display the probability of mortality over time by age category and BMI status. Univariable and multivariable Cox Proportional Hazards regression analyses were done to assess factors associated with mortality among TB patients. Adjusted hazard ratios (aHR) and corresponding 95% confidence intervals, and p-values were reported. All statistical significance was evaluated at the 5% level of significance. All analyses were done using Stata version 17.1 (Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC. StataCorp. 2019).

Ethical Considerations

The AMREF Ethics and Scientific Review Committee, Nairobi, Kenya, approved the protocol for this analysis (protocol number: P2186/2026) and waived consent from study participants because the de-identified data were retrospective and drawn from the national TB surveillance database. The study followed the ethical principles outlined in the World Medical Association's Declaration of Helsinki, the Kenya government, the Ministry of Health, and AMREF ESRC guidelines for research involving human subjects.

Results

Patient Characteristics

A total of 47,727 patients were included in the study, with characteristics shown in Table 1. The results showed that most of the patients, 61.8%, were male. A majority, 90.9%, were adults, with most, 41.1%, aged between 15–34 years. Most of the patients had a healthy weight (44.3%) and were HIV negative (62.8%). Participants were mainly from Nyanza North, Nairobi, and Nyanza South regions.

Mortality Outcomes

Out of 47,727 patients, mortality was recorded for 6.1% as shown in Table 1. Significant bivariate differences were observed between those who survived and those who died. Age, BMI, HIV status, type of TB, diagnostic results, nutritional support, and geographical location were associated with

mortality. Results indicated a significantly higher proportion of elderly (55+ years) among those who died compared to those alive, 24.7% vs. 13.8%. There was a significantly higher proportion of underweight participants among those who died compared to those who were alive, 52.7% vs. 42.2%, respectively. Similarly, there was a higher proportion of HIV-positive patients among those who died compared to those alive, 54.3% vs. 35.9%, respectively. Results also showed a higher proportion of Extra-pulmonary TB patients among those who died compared to those alive, 23.3% vs 14.5%. There was a higher proportion of patients with an abnormal X-ray suggestive of TB among those who died compared to those alive, 70.1% vs. 58.8%, respectively. GeneXpert results indicated a higher proportion of individuals with no TB detected and those without results among those who died, compared to those alive. Regional and county analyses highlighted geographical disparities in mortality, with a higher proportion of patients from Nyanza North and Coast among those who died compared to those alive.

Table 1: Social demographic and clinical characteristics of Patients with Drug-Sensitive Tuberculosis in 11 Selected Counties in Kenya, 2021

Columns by: Mortality Outcome n (%)	**Total 47727 (100.0)**	**Not dead 44816 (93.9)**	**Dead 2911 (6.1)**	**P-value**
Sex, n (%)				0.982
Female	18241 (38.2)	17129 (38.2)	1112 (38.2)	
Male	29486 (61.8)	27687 (61.8)	1799 (61.8)	
Age Category, n (%)				0.027
Child	4333 (9.1)	4102 (9.2)	231 (7.9)	
Adult	43394 (90.9)	40714 (90.8)	2680 (92.1)	
Age Category, n (%)				<0.001
0-14	4333 (9.1)	4102 (9.2)	231 (7.9)	
15-34	19608 (41.1)	18763 (41.9)	845 (29.0)	
35-54	16894 (35.4)	15777 (35.2)	1117 (38.4)	
55+	6892 (14.4)	6174 (13.8)	718 (24.7)	
BMI Category (kg/m^2), n (%)				<0.001
Underweight	19776 (42.8)	18335 (42.2)	1441 (52.7)	
Normal	20432 (44.3)	19412 (44.7)	1020 (37.3)	
Overweight/Obese	5963 (12.9)	5690 (13.1)	273 (10.0)	
HIV Status, n (%)				<0.001
Unknown	51 (0.1)	50 (0.1)	1 (0.0)	
HIV exposed infant (HEI)	35 (0.1)	33 (0.1)	2 (0.1)	

Negative	29973 (62.8)	28647 (63.9)	1326 (45.6)	
Positive	17668 (37.0)	16086 (35.9)	1582 (54.3)	
Type of TB, n (%)				<0.001
Extra Pulmonary	7171 (15.0)	6492 (14.5)	679 (23.3)	
Pulmonary	40556 (85.0)	38324 (85.5)	2232 (76.7)	
Type of patient, n (%)				0.112
New	43994 (92.2)	41333 (92.2)	2661 (91.4)	
Relapse/Failure/LTFU	3733 (7.8)	3483 (7.8)	250 (8.6)	
Regimen, n (%)				0.192
2RHZ/4RH	447 (0.9)	415 (0.9)	32 (1.1)	
2RHZE/10RH	685 (1.4)	644 (1.4)	41 (1.4)	
2RHZE/4RH	46343 (97.1)	43529 (97.1)	2814 (96.7)	
Other	242 (0.5)	220 (0.5)	22 (0.8)	
Xray, n (%)				<0.001
Abnormal Other	1193 (3.4)	1106 (3.3)	87 (4.0)	
Abnormal suggestive of TB	21042 (59.5)	19517 (58.8)	1525 (70.1)	
Not Done	12930 (36.5)	12374 (37.3)	556 (25.6)	
Normal	218 (0.6)	211 (0.6)	7 (0.3)	
Sputum Smear Examination 0th Month Result, n (%)				<0.001
Not Done	28816 (60.4)	26874 (60.0)	1942 (66.7)	
Negative	7762 (16.3)	7257 (16.2)	505 (17.3)	
Positive	11149 (23.4)	10685 (23.8)	464 (15.9)	
Gen expert, n (%)				<0.001
Invalid/no result/error	405 (0.8)	361 (0.8)	44 (1.5)	
MTB detected, Rifampicin resistance detected	61 (0.1)	59 (0.1)	2 (0.1)	
MTB detected, Rifampicin resistance indeterminate	85 (0.2)	81 (0.2)	4 (0.1)	
MTB detected, Rifampicin resistance not detected	19124 (40.1)	18343 (41.0)	781 (26.9)	
MTB not detected	12671 (26.6)	11783 (26.3)	888 (30.6)	
Not Done	15312 (32.1)	14126 (31.6)	1186 (40.8)	
Genexpert, n (%)				<0.001
MTB not detected	12671 (26.6)	11783 (26.3)	888 (30.6)	
MTB detected	19270 (40.4)	18483 (41.3)	787 (27.1)	
Not done/No results	15717 (33.0)	14487 (32.4)	1230 (42.3)	
Directly Observed Therapy provided by, n (%)				0.108
Clinic (CHW/CV)	2867 (6.0)	2712 (6.1)	155 (5.3)	
Home	44771 (94.0)	42019 (93.9)	2752 (94.7)	
Nutritional Support, n (%)				<0.001

No	38 (0.1)	29 (0.1)	9 (0.3)	
Yes	47688 (99.9)	44786 (99.9)	2902 (99.7)	
Region, n (%)				<0.001
Coast	5671 (11.9)	5254 (11.7)	417 (14.3)	
Eastern North	585 (1.2)	567 (1.3)	18 (0.6)	
Eastern South	4730 (9.9)	4466 (10.0)	264 (9.1)	
Nairobi	10477 (22.0)	9878 (22.0)	599 (20.6)	
Nyanza North	18873 (39.5)	17573 (39.2)	1300 (44.7)	
Nyanza South	7391 (15.5)	7078 (15.8)	313 (10.8)	
County, n (%)				<0.001
Homa Bay	8702 (18.2)	8157 (18.2)	545 (18.7)	
Isiolo	585 (1.2)	567 (1.3)	18 (0.6)	
Kilifi	1317 (2.8)	1192 (2.7)	125 (4.3)	
Kwale	819 (1.7)	753 (1.7)	66 (2.3)	
Meru	3796 (8.0)	3585 (8.0)	211 (7.2)	
Migori	6540 (13.7)	6261 (14.0)	279 (9.6)	
Mombasa	3535 (7.4)	3309 (7.4)	226 (7.8)	
Nairobi	10477 (22.0)	9878 (22.0)	599 (20.6)	
Nyamira	851 (1.8)	817 (1.8)	34 (1.2)	
Siaya	10171 (21.3)	9416 (21.0)	755 (25.9)	
Tharaka Nithi	934 (2.0)	881 (2.0)	53 (1.8)	

TB Treatment Outcomes

The treatment outcomes shown in Table 2 indicate that the highest percentage of TB patients in 11 selected counties in Kenya underwent treatment up to the completion stage (47.41%), and 35.97% were cured. Those who died while undergoing treatment accounted for 6.1%, and the median time to death was 1.34 months (IQR: 0.46 - 2.79). 5.62% of the patients were not cured, 3.38% of the patient's discontinued treatment and did not attend follow-up appointments, and the median follow-up time to event was 5.97 months (IQR: 5.61 - 6.39). In addition, 0.59% of the patients stopped or interrupted treatment without medical advice or without completing the full course, 0.49% of the patient's conditions did not improve despite receiving the recommended treatment, and 0.43% of the patients were transferred to another healthcare facility or location.

Table 2: Treatment Outcomes for Drug-Sensitive Tuberculosis in 11 Selected Counties Kenya, 2021

Treatment Outcomes	Freq.	Percent
Cured	17,169	35.97
Dead	2,911	6.1
Failure	236	0.49

LTFU	1,615	3.38
MT4	280	0.59
NC	2,683	5.62
Treatment completed	22,627	47.41
Transferred out	206	0.43
Total	49,812	100

** Median follow-up time to event was 5.97 months (IQR: 5.61 - 6.39)*

** Median time to death was 1.34 months (IQR: 0.46 - 2.79)*

Factors Associated with Mortality

The univariable and multivariable Cox Proportional Hazards regression analysis of the factors associated with mortality among drug-sensitive TB patients in 11 selected counties in Kenya are shown in Table 3. The multivariate analysis results revealed a significantly higher risk of mortality among ages 55+ as compared to those aged between 0-14 years, aHR = 2.15 (95% CI: 1.34 - 3.45), p-value = 0.002. On the contrary, those aged 15-34 years had a significantly lower hazard of mortality compared to those aged between 0-14 years, aHR = 0.86 (95% CI: 0.84 - 0.88), p-value <0.001.

There was a significantly higher mortality risk in underweight TB patients compared to those with normal BMI, aHR = 1.40 (95% CI: 1.29 - 1.53), p-value <0.001. TB patients who were HIV positive had over two times higher and significant mortality hazard compared to those with negative HIV status, aHR = 2.04 (95% CI: 1.63 - 2.55), p-value <0.001.

The results also showed that there was a higher and significant mortality risk among extra-pulmonary TB patients as compared to those with pulmonary TB, aHR = 1.37 (95% CI: 1.01 - 1.86), p-value = 0.043. TB patients on the 2RHZ/4RH and 2RHZE/4RH treatment regimens had significantly higher mortality hazards compared to those on 2RHZE/10RH regimen, aHR = 1.62 (95% CI: 1.21 – 2.17), p-value = 0.001, and aHR = 1.31 (95% CI: 1.09 - 1.58), p-value = 0.005, respectively.

TB patients on the 2RHZ/4RH and 2RHZE/4RH treatment regimens had significantly higher mortality risk compared to those on the 2RHZE/10RH regimen, aHR = 1.62 (95% CI: 1.21 – 2.17), p-value = 0.001, and aHR = 1.31 (95% CI: 1.09 - 1.58), p-value = 0.005, respectively.

The X-ray tests indicating abnormal signs suggestive of TB or other abnormal signs showed a significantly higher mortality risk as compared to those with no X-ray tests done, aHR = 1.44 (95% CI: 1.21 - 1.72), p-value <0.001, and aHR = 1.35 (95% CI: 1.27 - 1.43), p-value <0.001. Patients without a sputum smear examination were also found to have a significantly higher mortality risk compared to those with positive sputum smear examination results, aHR = 1.34 (95% CI: 1.14 - 1.59), p-value 0.001. Patients without a GeneXpert done or no results had a significantly higher risk of mortality compared to those who had GeneXpert done and MTB detected, aHR = 1.60 (95% CI: 1.24 - 2.06), p-value <0.001.

The study also observed over two-fold significant risk of mortality in Kilifi, Meru, Tharaka Nithi, Mombasa, and Kwale counties compared to those reported in Isiolo county. Mortality hazard in Nairobi, Nyamira, and Siaya counties was also significantly higher but less than two-fold

compared to that reported in Isiolo county. However, there were no significant associations with sex, type of patient, DOT, and nutritional support.

The Kaplan-Meier curves in Figure 1 show a lower probability of survival among those who were underweight compared to overweight and normal BMI TB patients. Figure 2 shows a lower probability of survival among TB patients who were 35-54 years and 55 years and above compared to the under 0-14 years age group and 15-34 years age group.

Table 3: Factors Associated with Mortality among Drug-Sensitive TB Patients in 11 Selected Counties in Kenya 2021

Variables	Univariable Hazard Ratio (95% CI)	P value	Multivariable Hazard Ratio (95% CI)	P value
Sex				
Female	Reference		Reference	
Male	1.01 (0.73 - 1.38)	0.967	1.10 (0.81 - 1.48)	0.548
Age Category				
0-14	Reference		Reference	
15-34	0.80 (0.64 - 1.01)	0.065	0.86 (0.84 - 0.88)	<0.001
35-54	1.25 (1.13 - 1.38)	<0.001	1.15 (0.92 - 1.45)	0.225
55+	2.00 (1.45 - 2.76)	<0.001	2.15 (1.34 - 3.45)	0.002
BMI category				
Normal	Reference		Reference	
Underweight	1.49 (1.26 - 1.77)	<0.001	1.40 (1.29 - 1.53)	<0.001
Overweight/Obese	0.90 (0.79 - 1.02)	0.100	0.90 (0.79 - 1.02)	0.106
HIV Status				
Negative	Reference		Reference	
D	0.46 (0.05 - 4.39)	0.503	0.47 (0.05 - 4.53)	0.516
HIV Exposed Infant (HEI)	1.35 (0.17 - 11.00)	0.778	1.08 (0.11 - 10.70)	0.947
Positive	2.05 (1.75 - 2.39)	<0.001	2.04 (1.63 - 2.55)	<0.001
Type of TB				
Pulmonary	Reference		Reference	
Extra Pulmonary	1.67 (1.56 - 1.78)	<0.001	1.37 (1.01 - 1.86)	0.043
Type of patient				
New	Reference		Reference	
Relapse/Failure/LTFU	1.14 (1.00 - 1.30)	0.059	1.13 (0.92 - 1.40)	0.248

Regimen				
2RHZE/10RH	Reference		Reference	
2RHZ/4RH	1.27 (1.00 - 1.62)	0.048	1.62 (1.21 - 2.17)	0.001
2RHZE/4RH	1.07 (0.87 - 1.31)	0.533	1.31 (1.09 - 1.58)	0.005
Other	1.21 (0.40 - 3.66)	0.731	0.84 (0.33 - 2.15)	0.713
X-ray				
Not Done	Reference		Reference	
Abnormal Other	1.77 (1.30 - 2.40)	<0.001	1.44 (1.21 - 1.72)	<0.001
Abnormal suggestive of TB	1.71 (1.42 - 2.05)	<0.001	1.35 (1.27 - 1.43)	<0.001
Normal	0.77 (0.38 - 1.53)	0.452	0.72 (0.42 - 1.25)	0.240
Sputum Smear Exam				
Positive	Reference		Reference	
Not Done	1.63 (1.47 - 1.80)	<0.001	1.34 (1.14 - 1.59)	0.001
Negative	1.58 (1.28 - 1.96)	<0.001	1.06 (0.84 - 1.35)	0.608
Genexpert				
MTB detected	Reference		Reference	
MTB not detected	1.74 (1.25 - 2.41)	0.001	1.40 (0.88 - 2.24)	0.160
Not done/No results	1.93 (1.65 - 2.26)	<0.001	1.60 (1.24 - 2.06)	<0.001
DOT				
Clinic (CHW/CV)	Reference		Reference	
Home	1.12 (0.91 - 1.38)	0.270	1.08 (0.90 - 1.29)	0.400
Nutritional support				
Yes	Reference		Reference	
No	2.23 (0.98 - 5.06)	0.056	1.19 (0.49 - 2.90)	0.706
County				
Isiolo	Reference		Reference	
Homa Bay	1.97 (1.96 - 1.99)	<0.001	1.04 (0.91 - 1.18)	0.584
Kilifi	3.12 (3.10 - 3.14)	<0.001	2.72 (2.50 - 2.96)	<0.001
Kwale	2.62 (2.62 - 2.63)	<0.001	2.01 (1.86 - 2.17)	<0.001
Meru	1.81 (1.80 - 1.81)	<0.001	2.28 (1.91 - 2.72)	<0.001
Migori	1.31 (1.29 - 1.33)	<0.001	0.95 (0.91 - 1.00)	0.072
Mombasa	2.09 (2.09 - 2.10)	<0.001	2.11 (1.84 - 2.41)	<0.001
Nairobi	1.82 (1.82 - 1.83)	<0.001	1.73 (1.43 - 2.08)	<0.001
Nyamira	1.30 (1.29 - 1.30)	<0.001	1.24 (1.14 - 1.35)	<0.001

Siaya	2.34 (2.31 - 2.36)	<0.001	1.58 (1.36 - 1.83)	<0.001
Tharaka Nithi	1.81 (1.80 - 1.83)	<0.001	2.12 (1.83 - 2.46)	<0.001

Cluster adjusted for region

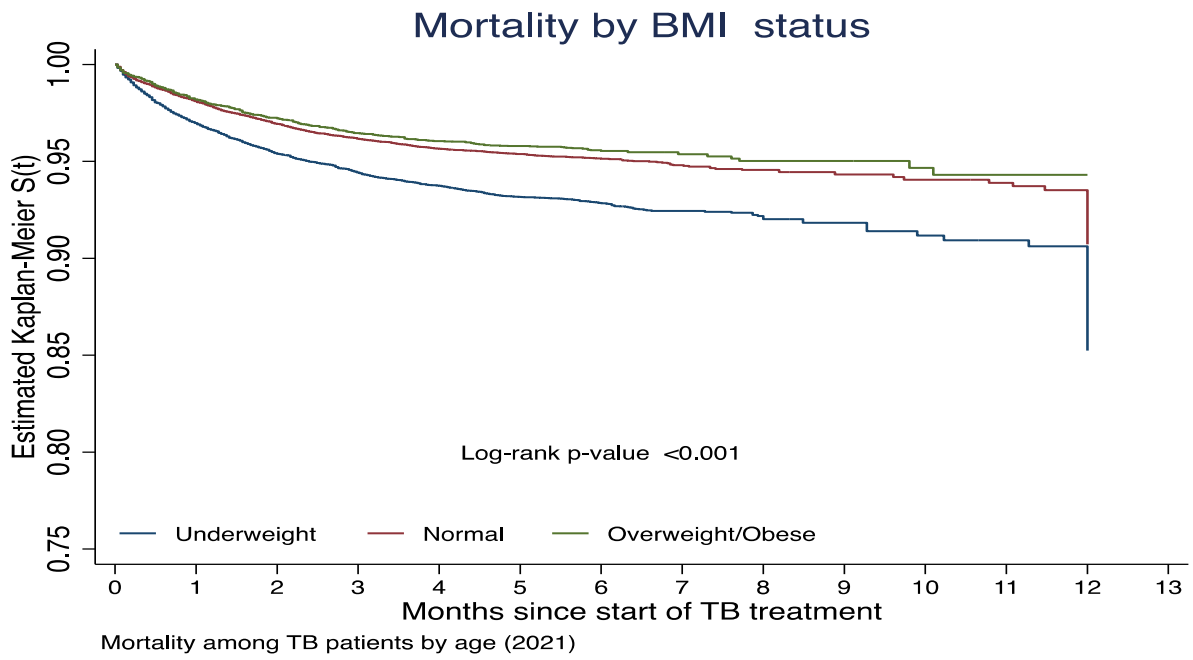


Figure 1: Mortality of TB patients by BMI status

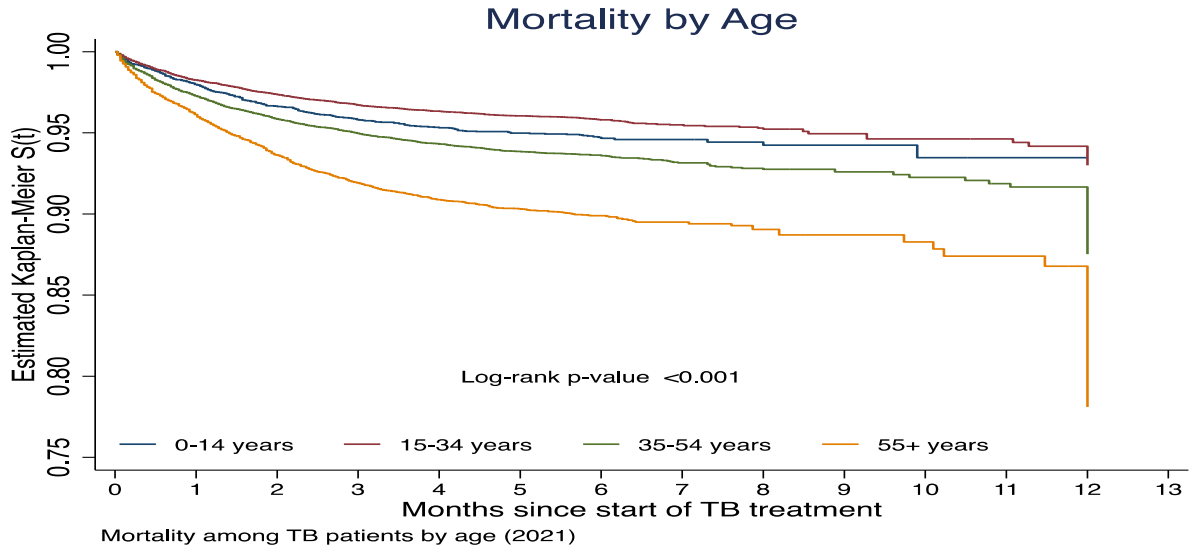


Figure 2: Mortality by Age

Mortality incidence rates (MIR)

The estimated mortality incidence rates (MIR) per 100 person-years of observation (pyo) in patients with drug-sensitive TB were reported to be highest in Coast (15.40 per 100 pyo) and lowest in Eastern North (6.41 per 100 pyo) as shown in Table 4. Similarly, among counties, Siaya county led with MIR (of 14.51 per 100 pyo) while Isiolo county had the lowest MIR (6.41 per 100 pyo). It was also observed that the MIR among adults was higher than in children (12.30 vs. 10.54 per 100 pyo). In addition, MIR among male TB patients was also found to be higher (12.21 per 100 pyo) than that of females (12.02 per 100 pyo). TB patients aged 55 years and above had the highest MIR (21.23 per 100 pyo) while patients aged between 15-34 years had the lowest MIR of 8.48 per 100 pyo. Underweight TB patients also had a higher MIR than overweight TB patients (14.85 vs. 8.76 per 100 pyo).

TB patients with positive HIV status had the highest MIR (17.91 per 100 pyo) as shown in Table 4. Extra-pulmonary TB patients were also observed to have a higher MIR (17.09 per 100 pyo) than pulmonary TB patients (11.15 per 100 pyo). Additionally, relapse/ failures/LTFU cases recorded higher MIR than new cases (13.95 vs. 11.99 per 100 pyo). MIR of patients under 2RHZ/4RH treatment regimen was reported to be the highest (14.67 per 100 pyo) while MIR of patients under other treatment regimens was the lowest (10.57 per 100 pyo).

Furthermore, MIR of patients whose X-ray tests showed abnormal suggestive TB was reported to be the highest (14.35 per 100 pyo) whereas, patients whose X-ray tests were normal had the lowest MIR (6.37 per 100 pyo MIR of patients whose sputum smear examination results were not done was also found to be the higher (13.35 per 100 pyo) while patients with positive sputum smear examination results were the lowest (8.31 per 100 pyo). In addition, MIR of patients whose MTB tests were not done was observed to be highest (15.32 per 100 pyo) while MIR of patients detected of MTB was the lowest (8.15 per 100 pyo).

On the other hand, the MIR of patients provided with DOT at home (12.23 per 100 pyo) was found to be higher than MIR of patients provided with DOT at clinic (10.84 per 100 pyo). MIR of patients that were not provided with nutritional support was also observed to be higher (29.02 per 100 pyo) than MIR of patients provided with nutritional support (12.13 per 100 pyo).

Table 4: Estimated person-time and mortality incidence rates of Patients with Drug Sensitive Tuberculosis in 11 Selected Counties in Kenya 2021.

Characteristics	Person-time	Failures	Rate (per 100 pyo)	[95% confidence interval]	
Region					
Coast	408	26.5	15.4	13.97	16.97
Eastern North	18	2.81	6.41	4.04	10.18
Eastern South	259	22.16	11.69	10.35	13.2
Nairobi	585	50.72	11.53	10.64	12.51
Nyanza North	1269	93.98	13.5	12.78	14.27
Nyanza South	308	38.45	8.01	7.16	8.96
County					

Homa Bay	535	43.39	12.33	11.33	13.42
Isiolo	18	2.81	6.41	4.04	10.18
Kilifi	122	6.16	19.81	16.59	23.65
Kwale	65	3.88	16.74	13.13	21.35
Meru	206	17.47	11.79	10.29	13.52
Migori	274	34.39	7.97	7.08	8.97
Mombasa	221	16.46	13.43	11.77	15.32
Nairobi	585	50.72	11.53	10.64	12.51
Nyamira	34	4.06	8.38	5.99	11.73
Siaya	734	50.58	14.51	13.5	15.6
Tharaka Nithi	53	4.69	11.3	8.63	14.79
Sex					
Female	1092	90.82	12.02	11.33	12.76
Male	1755	143.78	12.21	11.65	12.79
Child/Adult					
Child	226	21.44	10.54	9.25	12.01
Adult	2621	213.16	12.3	11.83	12.78
Age Category					
0-14	226	21.44	10.54	9.25	12.01
15-34	823	97.01	8.48	7.92	9.08
35-54	1092	82.9	13.17	12.41	13.98
55+	706	33.25	21.23	19.72	22.86
BMI Category					
Underweight	1413	95.14	14.85	14.1	15.65
Normal	1002	101.74	9.85	9.26	10.48
Overweight/Obese	265	30.26	8.76	7.76	9.88
HIV status					
HIV Exposed Infants	2	0.17	12.01	3	48.01
Negative	1300	147.99	8.78	8.32	9.28
Positive	1544	86.21	17.91	17.04	18.83
TB type					
Extra Pulmonary	664	38.86	17.09	15.84	18.44
Pulmonary	2183	195.75	11.15	10.69	11.63
Type of patient					
New	2604	217.19	11.99	11.54	12.46
Relapse/Failure/LTFU	243	17.42	13.95	12.31	15.82
Regimen Category					

2RHZ/4RH	31	2.11	14.67	10.32	20.86
2RHZE/10RH	40	3.75	10.65	7.81	14.52
2RHZE/4RH	2753	226.71	12.14	11.7	12.61
Other	21	1.99	10.57	6.89	16.21
Xray					
Abnormal Other	87	6.2	14.04	11.38	17.33
Abnormal suggestive of TB	1490	103.82	14.35	13.64	15.1
ND	538	63.8	8.43	7.75	9.18
Normal	7	1.1	6.37	3.04	13.36
Sputum					
Not Done	1897	142.07	13.35	12.77	13.97
Negative	499	38.28	13.04	11.94	14.23
Positive	451	54.26	8.31	7.58	9.11
Gene expert					
Invalid/no result/error	46	0	23366.6	17502.2	31195.9
MTB detected, Rifampicin resistance detected	2	0	10819	2705.8	43259.2
MTB detected, Rifampicin resistance indeterminate	4	0	9230.5	3464.4	24593.8
MTB detected, Rifampicin resistance not detected	780	0.1	7980.2	7439.4	8560.4
MTB not detected	898	0.06	14129	13234.4	15084
Not Done	1207	0.08	14877.6	14061.5	15741.1
Genexpert					
MTB not detected	871	61.85	14.08	13.18	15.05
MTB detected	763	93.64	8.15	7.59	8.75
Not done/No results	1207	78.78	15.32	14.48	16.21
DOT by					
Clinic (CHW/CV)	152	14.02	10.84	9.25	12.7096
Home	2692	220.17	12.23	11.77	12.6978
Nutritional Status					
No	4	0.14	29.02	10.89	77.31
Yes	2843	234.46	12.13	11.69	12.58

MTB - Mycobacterium

DISCUSSION

This study provides critical insights into the factors driving mortality among patients with drug-sensitive tuberculosis (DS-TB) in Kenya. Our findings align with global evidence, underscoring that TB mortality is a multifactorial outcome stemming from demographic, clinical, and health-system vulnerabilities.

The significantly elevated mortality risk among patients aged ≥55 years (aHR=2.15) is a consistent finding, attributable to immunosenescence, a higher burden of comorbidities like diabetes and cardiovascular disease, and increased drug intolerance, which complicates TB management in the elderly [21–23]. Furthermore, the strong association between undernutrition (aHR=1.40) and mortality reinforces the well-established role of malnutrition in weakening immune responses and compromising treatment efficacy [11,24]. The Kaplan-Meier curves, which show a clear survival disadvantage for underweight patients, provide visual confirmation of this relationship and compellingly argue for nutritional support as a core component of TB therapy.

As observed globally, HIV co-infection was a powerful driver of mortality, more than doubling the risk of death (aHR=2.04). This finding resonates with other studies from the region that attribute this to advanced immunosuppression and the lethal synergy between the two diseases [25,26]. The high mortality incidence rate (17.91 per 100 pyo) in this group signals an urgent need to optimize the integration of TB/HIV services and ensure timely initiation of antiretroviral therapy.

A crucial finding was the higher mortality risk among patients without bacteriological confirmation. The elevated hazards for those with extrapulmonary TB (aHR=1.37), abnormal chest X-rays, or no sputum/GeneXpert result point to critical health system challenges. This is a major public health concern, as autopsy studies have revealed that a significant proportion of deaths attributed to clinical TB are actually caused by other conditions, such as fungal infections or cancer [9,10]. This diagnostic ambiguity leads to a dual tragedy: patients with true TB present late, while those with alternative conditions are misdiagnosed.

The significant variation in mortality risk between counties highlights sub-national health system inequities, likely driven by disparities in diagnostic access and quality of care. Interestingly, the treatment regimen was associated with mortality, a finding that warrants further pharmacovigilance investigation. In contrast to other studies, this analysis found no significant independent association between mortality and sex, patient type, or DOT method, suggesting that in this cohort, biological and clinical factors were more powerful determinants of survival than these programmatic characteristics [25,26].

In conclusion, drug-sensitive DS-TB mortality in Kenya is driven by a confluence of factors: the vulnerability of older age, the compounding effects of HIV and undernutrition, and a health system strained by diagnostic inaccuracy and geographic inequities. The high death rate among clinically diagnosed patients is a particularly urgent concern. Addressing this burden requires a shift to a

precision public health approach that includes robust nutritional support, optimized TB/HIV care, and strengthened diagnostic pathways to ensure every patient receives a correct diagnosis and appropriate, life-saving treatment.

Limitations

This study has several limitations. First, the use of routinely collected surveillance data may be subject to underreporting and misclassification, particularly for clinical diagnoses. Second, the cross-sectional design limits causal inference. Third, data on important confounders such as socioeconomic status, diabetes, and other comorbidities were not consistently available. Fourth, the study period (2021) may not reflect current programmatic changes. Finally, the findings may not be generalizable to counties not included in the analysis.

Conclusions

In conclusion, this Kenyan cohort from eleven selected counties reveals that TB mortality is not a simple outcome but the result of a combination of biological and health-system failures. The potent synergy of HIV, undernutrition, and an aging population creates intersecting vulnerabilities that our current systems fail to address. Most importantly, mortality is concentrated in patients diagnosed on clinical grounds, which serves as an indication for a strained system characterized by late presentation and significant diagnostic inaccuracy. This reality risks a vicious cycle where resources are misdirected based on flawed data, and patients with TB or alternative conditions like cancer fail to receive correct, lifesaving treatment.

To counter this, we must shift from a generalized program to a precision public health approach. This requires a dual strategy: first, fortifying diagnostics by deploying rapid molecular tests to replace clinical suspicion with bacteriological certainty. Second, we must implement integrated care that proactively addresses key mortality drivers through seamless TB/HIV care, mandatory nutritional support, and critically the novel adoption of multidisciplinary teams (MDTs) for complex drug-sensitive TB cases. By confronting diagnostic inaccuracy and the overlapping social and medical risks with this targeted, collaborative model, TB programs can finally turn the tide against preventable mortality.

List of Abbreviations

Abbreviations	Full meaning
aHR	Adjusted Hazard Ration
ART	Antiretroviral Therapy
BMI	Body Mass Index
CHW	Community Health Worker
CI	Confidence Interval

COPD	Chronic Obstructive Pulmonary Disease
CPT	Co-trimoxazole Preventive Therapy
CXR	Chest X-Ray
DOT	Direct Observed Therapy
DR-TB	Drug-Resistant Tuberculosis
DS-TB	Drug Sensitive Tuberculosis
ESRC	Ethics and Scientific Review Committee
HEI	HIV Exposed Infant
HIV	Human Immunodeficiency Virus
IQR	Interquartile Range
LTFU	Lost to Follow-Up
MDT	Multidisciplinary Team
MDR-TB	Multidrug Resistant Tuberculosis
MIR	Mortality Incidence Rate
MTB	Mycobacterium Tuberculosis
NTP	National Tuberculosis Program
PYO	Person-Years of Observation
TB	Tuberculosis
Abbreviations	**Full meaning**
TIBU	TB Information Basic Unit
WHO	World Health Organization

Declarations

Ethics Approval and Consent to Participate

Ethical approval was obtained from the AMREF Ethics and Scientific Review Committee (ESRC). Data was extracted from the TIBU system onto a password-protected computer accessible only to authorized personnel. Patient identifiers were removed to ensure confidentiality.

Consent for Publication

We give full consent for publication

Availability of Data and Materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

GM conceptualized the study, designed the methodology, and drafted the original manuscript. KO and RM contributed to data interpretation, developed the summary tool, and assisted with visualization of results. SW, SO, and DB coordinated data collection and conducted the mortality audit reviews. NMN and SM provided clinical oversight, validated TB diagnosis classifications, and reviewed treatment outcomes. PW provided technical guidance on TB program indicators and critically revised the manuscript for intellectual content. All authors read and approved the final manuscript.

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Figures

Figure 1: Mortality of TB patients by BMI status

453 **Figure 2:** Mortality by Age

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