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Survival and Its Predictors among Tuberculosis Patients on Treatment in Selected Health Centers of Addis Ababa, Ethiopia: A Retrospective Cohort Study

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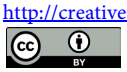

Abstract

Tuberculosis is one of the leading causes of morbidity and mortality globally. Although different strategies have been designed and implemented to combat it, it has continuously increased in the past five years, resulting in 10 million new cases and 1.6 million deaths. This study aims to estimate survival and predictors among tuberculosis patients on treatment in selected health centers in Addis Ababa, Ethiopia. The study employed a retrospective cohort design where data were collected by reviewing medical records of tuberculosis patients who were registered from May 2016 to May 2017 on treatment in 20 selected health centers in Addis Ababa. Independent predictors were identified, and the strength of association between dependent and independent predictors was determined using the Weibull regression model. Before computing Weibull regression analysis, Cox proportional assumption, model diagnosis, and fitness were checked. The hazard ratio was calculated to indicate the strength of association. Of 371 TB patients, about 136 (36.7%) died during the treatment period. Most TB deaths occurred during the intensive phase, and the overall estimated median survival time was 157 days. In the multivariable Weibull model, age (HR = 0.98), baseline weight (HR = 0.96, P = 0.03), tuberculosis treatment phase (continuation phase, HR = 0.48), and tuberculosis type (pulmonary negative TB, HR = 19.92) were found to be independent predictors of time to death of tuberculosis patients. Finally, the study concluded that the survival time to death of the patients is high. The health care providers should give special attention and follow up for pulmonary negative

and underweight TB patients.

Keywords

Mortality, Predictors, Survival Model, Survival Time, Tuberculosis

1. Introduction

In 2017, about 10 million TB incidence and 1.6 million deaths were reported worldwide. Among these developing countries taking the highest percent, the South-East Asian accounts for 44%, and the African Region accounts for 25%. The above-reported number should befall to 10% by 2020 to reach the first milestones of the End TB Strategy [1].

The significant primary predictors that aggravate the time to death of TB patients include irregular or inadequate treatment, late diagnosis of the disease, MDR-TB, advanced age [2], co-morbidities, baseline smear result [3]. HIV infection is also the primary driving cause for the progress of active TB infection, where the risk is 20 - 30 times higher compared to patients with negative HIV infection [4]. The catastrophic collision of TB and HIV has yielded an extraordinary burden of suffering and death [5].

Globally, Africa is the first in total TB incidence which was 237 with the estimated mortality of 39 and 24 in HIV positive and HIV negative patients respectively [1].

Cameroon had prevalence of 69,000 TB and 14100 TB deaths [6]. In Zimbabwe, the estimated TB death was 50 cases per 100,000 populations [7]. A retrospective cohort study conducted in Nigeria has found that the overall case fatality rate of 16.6% has crude mortality rate of 3.68 per 100 PMO of follow-up [8]. A study conducted in Kenya has shown that the crude mortality rate during anti-tuberculosis treatment was 18.0 per 100 PYO [9]. In another cohort study on 5685 patients in Democratic Republic of Congo, 390 deaths occurred during anti-tuberculosis treatment. The study also showed that, more than half (52%) died during intensive phase of anti-tuberculosis treatment and overall, death occurred after a median of 59 days (interquartile range [IQR] 27 - 108) of treatment [10]. Another study came across with a result of 60 (7.4%) death with the overall mortality rate of 12.8/1000 PMO. A majority of deaths (56.7%) occurred during the intensive phase of the treatment with the median time of two months [11].

Ethiopia is among the 30 high TB burden countries with ranking the 7th worldwide and 2nd in Africa [1]. In 2015, Ethiopia adopted a new post-2015 Global TB Strategy called "END TB strategy", which was launched to reduce TB incidence and deaths by 90% and 95% between 2015 and 2035, respectively [1] [12]. Despite this plan, the annual estimated TB incidence accounted for about 177/100,000 populations and a death rate of 25 per 100,000 populations for 2016 [12].

The previous study findings from the study setting were shown that 3.7% of patients died from tuberculosis [13], and the unpublished report from the health Bureau of the city showed that, among TB patients who were on treatment in one year, there is about 11.6% [14] death percentage, which is higher as compared to the previous study in the same setting. Despite different studies investigating mortality and its predictors conducted in different parts of the country [11] [15] [16], so far, there is no sufficient data about survival and predictors of mortality of a cohort of TB patients in Ethiopia, and similar information is lacking in Addis Ababa city. Therefore, the current study aims to estimate the survival status of the patients and investigate potential risk factors that influence their survival time during the treatment period in twenty public health centers of Addis Ababa, Ethiopia. This will be used to generate evidence that could be utilized to the better TB treatment service and improve the outcome.

2. Methods

2.1. Study Setting

The study was conducted in twenty selected health centers of Addis Ababa, the capital city of Ethiopia, which has an area of 540 sq. km [17]. The city's administration is organized into ten sub-cities and 116 WOREDAS (an administrative division of Ethiopia, managed by a local government). In the year 2017, the city's projected population was about 3,433,999, of which 52.7% were females [18]. During the study period, the city had 12 public hospitals, 25 private hospitals, and 96 health centers managed by the City Administration's health bureau [12]. All the health centers were providing TB diagnosis and treatment services. Trained nurses were running TB clinics, all of them provided the service based on revised TB guidelines [1], and generally, almost all facilities record the patient information as per logbook found at each health center.

2.2. Study Design and Participants

A retrospective cohort study was conducted in Addis Ababa health centers from April 1 to August 30, 2018, to assess survival time to death and its predictors among tuberculosis patients. Data were extracted from the document of TB patients enrolled for anti-TB treatment from May 2016 to May 2017 in 20 randomly selected health centers of the study setting. The health centers' selection was made using a simple random sampling technique and the total sample size determined for the study was then proportionally allocated to these health centers. The proportionally allocated participants were selected from each health center using systematic sampling technique (**Table 1**).

2.3. Data Collection Procedure

The document of the patient consists of pertinent information such as age, sex, residence (sub-cities), initial weight (kg), TB type, TB category (new, relapse, failure defaulter), baseline smear result, TB treatment phase, previous TB status,

Table 1. Sample size allocation to each health center of Addis Ababa, Ethiopia, May 2016 to May 2017.

Health Centers	Total number of patients in each health center	Total patients included
Addis Ketema Health Center	127	17
Felege Meles Health Center	75	10
Akaki Health Center	173	23
Kality Health Center	172	23
Woreda 8 Health Center	45	6
Woreda 1 Health Center	68	9
Kotebe Health Center	187	25
Yeka Health center	285	38
Kazanchis Health Center	105	14
Meshwalkiya Health Center	120	16
Hiwot Amba Health Center	127	17
Alem Bank Health Center	180	24
Mikyliland Health Center	97	13
Woreda 3 Health Center	180	24
Tekelehaymanot Health Center	210	28
Woreda 1 Health Center	60	8
Beletshachew Health Center	97	13
Nifas Silk No2 Health Center	142	19
Woreda 2 Health Center	232	31
Woreda 8 Amoraw Metasebia HC	97	13
Total	**2779**	**371**

presence of co-morbidity (diabetes mellitus, cancer, anemia), HIV infection. A structured data abstraction format was used to collect information from patients' medical records. Data were collected by nurses (one nurse from each health center) working at TB clinic in each health center. After getting approval, the principal investigator gave two-day training for all data collectors (one nurse from each TB clinic) in four cycles. Each cycle consists of five trainees. The data quality was ensured by continuous and supportive supervision throughout the data collection process, coding, checking completeness, and consistency daily.

2.4. Analysis of Variables

Age, sex, residence, initial weight (kg), TB type, TB category (new, relapse, failure defaulter), baseline smear result, TB treatment phase, previous TB status, presence of co-morbidity (diabetes mellitus, cancer, anemia) and HIV infection were independent predictors and time to death from TB treatment initiation until the occurrence of an event (death) or end of the treatment was dependent va-

riables considered for the analysis. Survival time was determined from the date of treatment initiation to the date of event occurrence, where days were used as a time scale to calculate survival time.

2.5. Statistical Analysis

Data entry was by SPSS version 25 and analyzed using STATA version 14. Descriptive statistics summarized the socio-demographic characteristics of the study participants. Kaplan-Meier survival estimates and the log-rank test were employed to investigate the significance of the difference in survival experience among different categories. Cox proportional hazard model was used to identify factors that affect the time to death of the patients. Model-checking was done by checking Cox proportional assumption: the test was checked based on Schoenfeld residuals, visual assessment, and plot of martingale residual used. The model was also diagnosed using cox Snell residual plots (cumulative hazard function). Finally, the Cox proportional hazard model failed (violated) to fit the data, and an alternative model, AFT parametric regression model, was used to fit the data. With AFT parametric regression model, a comparison of each distribution (exponential, lognormal, Weibull, and log-logistic) was made based on AIC and BIC. The Weibull model was selected to fit the data set among the AFT distribution assessed. The final significant predictors were identified using the backward stepwise technique and after checking for the interaction ($P < 0.05$). Finally, diagnosis of the Weibull model was assessed to measure the overall goodness of fit by using likelihood ratio, coefficient of determination R^2, and Cox-Snell residuals. The hazard ratio was used as a measure of association.

3. Results

3.1 Demographic Characteristics

Data on 371 TB patients from 20 selected public health centers were analyzed. Among the total study participants, 189 (50.9%) were females, 74 (19.9%) had a previous history of TB treatment, 220 (59.3%) had positive baseline smear results, 156 (42%) had TB/HIV co-infection, and 137 (36.9%) were pulmonary positives. Most of the study participants (80.1%) were new TB cases. Cancer, anemia, and diabetes mellitus were found to be the most common comorbid diseases. Of the study participants with these co-morbidities, 7 (38.9%) with cancer, 17 (48.6%) with anemia, and 19 (45.2%) with diabetes died during the entire study period (**Table 2**).

3.2. Survival Analysis of TB Patients

Of the 371 registered patients, 235 (63.3%) survived the entire follow-up period, and the remaining 136 (36.7%) died in the course of TB treatment. Out of the total deaths, 63 (58.3%) occurred in negative pulmonary patients, 82 (40%) in the continuation phase of the treatment phase, 59 (37.8%) in HIV positive patients, 82 (38.1%) in patients who had no co-morbidity and 32 (43.2%) occurred

Table 2. Demographic and health factors of categorical covariate by TB in Addis Ababa, Ethiopia, May 2016 to May 2017.

Covariate	Covariate Categories	Death	Censored	Total (%)	Median survival days
Sex	Male	63 (34.6)	119 (65.4)	182 (49.1)	155 (140, 161)
	Female	73 (38.6)	116 (61.4)	189 (50.9)	159 (143, 161)
TB treatment phase	Intensive phase	54 (32.5)	112 (67.5)	166 (44.7)	70 (56, 139)
	Continuation phase	82 (40)	123 (60)	205 (55.3)	162 (159, 166)
TB type	Pulmonary positive	6 (4.4)	131 (95.6)	137 (36.9)	161 (157, 163)
	Pulmonary negative	63 (58.3)	45 (41.7)	108 (29.1)	147 (131, 161)
	Extra pulmonary	67 (53.2)	59 (46.8)	126 (34)	148 (130, 160)
TB category	New	109 (36.7)	188 (63.3)	297 (80.1)	157 (150, 161)
	Relapse	22 (38.6)	35 (61.4)	57 (15.4)	167 (125, 185)
	Failure	3 (33.3)	6 (66.7)	9 (2.4)	121 (49, 169)
	Defaulter	2 (25)	6 (75)	8 (2.2)	158 (1, 169)
Previous TB status	Yes	32 (43.2)	42 (56.8)	74 (19.9)	169 (148,180)
	No	104 (35.0)	193 (65)	297 (80.1)	155 (143,160)
Baseline smear results	Positive	48 (21.8)	172 (78.2)	220 (59.3)	159 (154, 161)
	Negative	88 (58.3)	63 (41.7)	151 (40.7)	153 (132, 162)
HIV infection	Positive	59 (37.8)	97 (62.2)	156 (42)	154 (137, 161)
	Negative	77 (35.8)	138 (64.2)	215 (58)	159 (153, 161)
Presence of co-morbidity	Yes	54 (34.6)	102 (65.4)	156 (42)	140 (132, 155)
	No	82 (38.1)	133 (61.9)	215 (58)	160 (156, 162)
Presence DM	Yes	19 (45.2)	23 (54.8)	42 (11.3)	161 (136, 180)
	No	117 (35.6)	212 (64.4)	329 (88.7)	156 (146, 160)
Presence cancer	Yes	7 (38.9)	11 (61.1)	18 (4.9)	167 (75, 180)
	No	129 (36.5)	224 (63.5)	353 (95.1)	156 (146, 160)
Presence anemia	Yes	17 (48.6)	18 (51.4)	35 (9.4)	180 (139, 180)
	No	119 (35.4)	217 (64.6)	336 (90.6)	155 (144, 160)
Total		136 (36.7)	235 (63.3)	371 (100)	157 (148, 160)

in patients who had no previous TB treatment history. The Kaplan-Meier survival curve estimates: the overall estimated median survival time was 157 days, and the median survival time for those who died was 168 days and for those that censored was 112 days, respectively. Most of the deaths occurred in the first 60 days (during the intensive phase) of treatment initiation, *i.e.*, relatively, a large number of patients died at the earlier days of TB treatment initiation (**Figure 1**).

The survival plot decreases at an increasing rate at the beginning and decreases later. This indicated significant differences between the survival probabilities of the patients. Using log-rank test the existence of a significant difference between the survivals of a patient by covariates checked, there was a significant survival difference between patients during the different TB treatment phases,

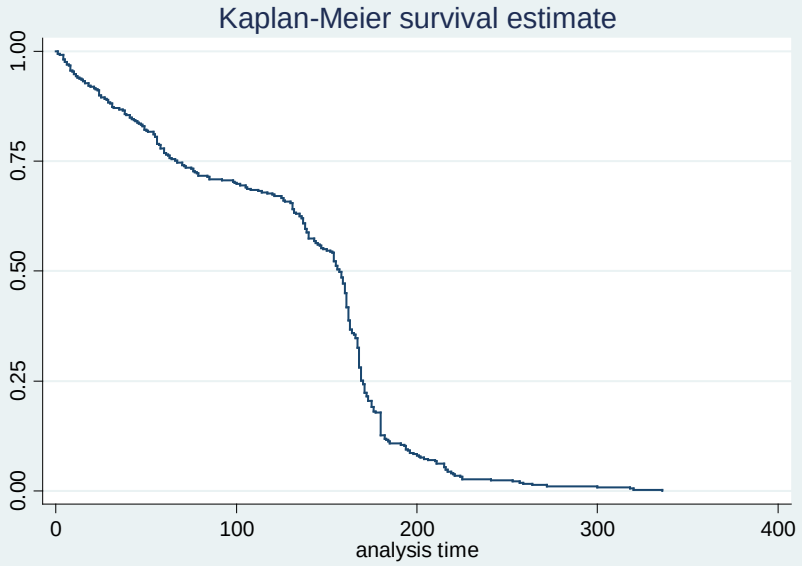

Figure 1. The Kaplan-Meier survival curve of the overall TB patients, in Addis Ababa, Ethiopia, May 2016 to May 2017.

previous TB status, TB category, and presence of anemia concerning survival time (**Table 3**).

The model was diagnosed, and the model with the best adherence to the model assumptions (cumulative hazard closer to the reference line; the plot for Weibull baseline distribution makes straight line better than exponential, lognormal, and Log-logistic baseline distribution) was selected for the analysis as illustrated in the Cox-Snell residuals plots (**Figure 2**).

In the multivariable AFT Weibull regression model, the patient's age, baseline body weight, TB treatment phase, and TB type were significantly associated with the time to TB-related mortality ($P \leq 0.05$). Baseline smear result, TB category, previous TB status, presence of co-morbidity, HIV infection, presence of DM, presence of cancer, and presence of anemia, were not significant predictors associated with the time to death. There was 2% decrease in rate of death for every year increase in age of TB patients; (HR = 0.98, 95% CI = [0.97, 0.99], P = 0.04). For every one unit decrease in weight of TB patients, there was 4% increase exposure to death; (HR = 0.96, 95% CI [0.91, 0.98], P = 0.03). Patients in the continuation phase at any time point during the study period were 52% less likely to die than patients in the intensive phase (there was higher death at the early stage of treatment initiation, meaning during intensive phase); (HR = 0.48, 95% CI [0.33, 0.69], $P \leq 0.001$). Similarly, the hazard rate of patients who had ETB and SNTB TB was respectively 9.49 and 19.92 times greater than those patients with SPTB TB type, which means patients with smear-negative TB patients died at a rate 19.92 times higher compared to smear-positive TB and Extra TB patients; (HR = 19.92, 95% CI [7.49, 52.96], $P \leq 0.001$). The 95% CI of independent predictors for the Weibull AFT model did not include one. This shows the statistical significance of the association of the covariates with the death of TB patients (**Table 4**).

Table 3. Comparison of survival experience of TB patients using log-rank test in Addis Ababa, Ethiopia, May 2016 to May 2017.

Covariates	Degree of freedom	Log-rank test	
		Chi-square	P-value
Sex	1	0.02	0.89
Residence	7	11.71	0.11
TB treatment phase	1	28.65	≤0.01
TB type	2	0.65	0.72
TB category	3	15.17	0.02
Previous TB status	1	20.36	≤0.01
Baseline smear results	1	0.02	0.88
HIV infection	1	0.34	0.56
Co-morbidity	1	1.44	0.23
Diabetic mellitus	1	0.80	0.37
Cancer	1	1.14	0.29
Anemia	1	7.07	0.01

Table 4. Summary result multivariable parameter estimate of Weibull AFT model in Addis Ababa, Ethiopia, May 2016 to May 2017.

Covariates	Category	β	P-value	HR	95% CI of HR
Age		−0.02	0.04*	0.98	[0.97, 0.99]
Baseline weight		−0.04	0.03*	0.96	[0.91, 0.98]
Baseline smear result	Positive	Ref			
	Negative	−0.19	0.45	0.82	[0.50, 1.36]
TB treatment phase	Intensive phase	Ref			
	Continuation phase	−0.74	≤0.01*	0.48	[0.33, 0.69]
TB type	Pulmonary positive	Ref			
	Pulmonary negative	2.99	≤0.01*	19.92	[7.49, 52.96]
	Extra pulmonary	2.25	≤0.01*	9.49	[3.99, 22.62]
TB category	New	Ref			
	Relapse	−0.52	0.28	0.59	[0.23, 1.51]
	Failure	0.10	0.89	1.11	[0.24, 5.15]
	Defaulter	−0.25	0.73	0.78	[0.19, 3.23]
Previous TB status	No	Ref			
	Yes	−0.38	0.37	0.68	[0.29, 1.56]
Presence of Comorbidity	No	Ref			
	Yes	0.48	0.09	1.62	[0.93, 2.83]
HIV infection	No	Ref			
	Yes	−0.15	0.59	0.86	[0.49, 1.49]
Presence of DM	No	Ref			
	Yes	−0.05	0.87	0.95	[0.55, 1.65]

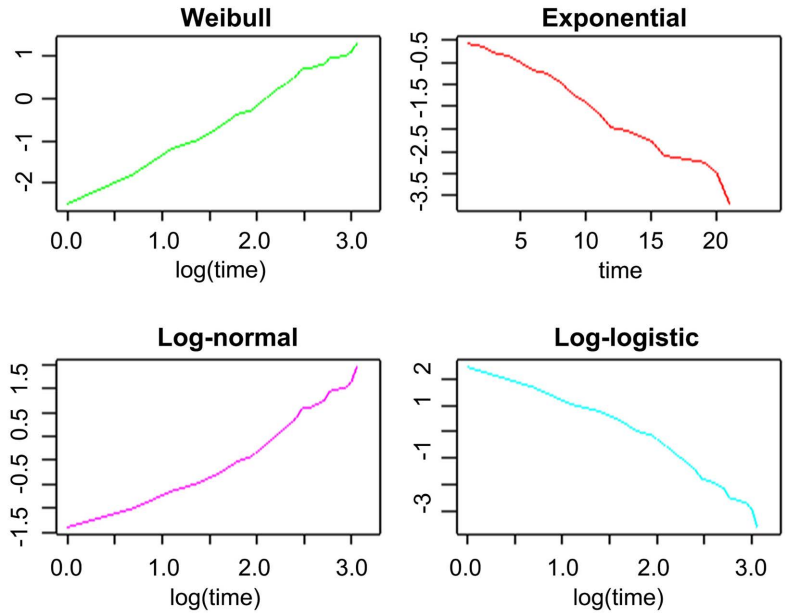

Figure 2. The graph of Weibull, exponential, log logistic and lognormal base line distribution of survival analysis of TB patients.

4. Discussion

This study was conducted to estimate survival time to death and identify its predictors among tuberculosis patients on treatment in 20 selected health centers in Addis Ababa, Ethiopia. In this study, a higher proportion of TB death was documented. Age, baseline weight, TB treatment phase, and TB type were significantly associated with survival time. The overall estimated median survival time was also found to be 157 days.

Among the 371 registered patients in this study, the proportion who died during the study period was 36.7%. This is much higher than what was documented by previous studies in Ethiopia, which ranged from 3.7% to 12.7% [14] [15] [19] [20] [21] [22]. This discrepancy might be due to differences in the study setting and subjects, the number of facilities included in the study (this study encompasses about twenty prominent health centers compared to the previous studies), and crowded settlements and poorly ventilated transportation systems. The proportion was also higher than previous findings out of Ethiopia, which ranged from 6.5% to 25% [6] [8] [23] [24]. On the other hand, the current finding is in agreement with the studies done in Cameroon (29.4%), China (30.7%), and the Philippines (37.5%) [25] [26] [27].

Our study indicated that, for every additional year of patients on treatment, the risk of death falls by 2%; meaning, the occurrence of death is increased in younger age (HR = 0.98 CI at 95% (0.97, 0.99), P = 0.04) of the study participants. Inconsistent with this finding, the result of previous studies in Ethiopia and elsewhere in the world showed that the risk of death increases as the patient gets older [11] [14] [20] [25] [27] [28] [29] [30] [31]. The lower number of geriatric participants might explain this variation compared to the other age cate-

gory (6.2%) in this study. On the other hand, in other studies, it was indicated that age difference had no risk with survival time to death of TB patients [6] [8] [22] [24] [31] [32] [33] [34] [35].

Results of this study showed that patients attending their treatment in the continuation phase were 52% less likely to die than patients in the intensive phase, *i.e.*, exposure to death (developing risk of death) was higher within two months of anti-TB treatment initiation (HR = 0.48, 95% CI [0.33, 0.69], P ≤ 0.001). This might be because of, decreased immunity and late diagnosis due to advanced disease during early-stage [3], decreased patient knowledge about their treatment (they may miss daily drug collection from health facilities), the difficulty of making a daily visit to health facilities for DOT due to distance of facilities from their residence. Furthermore, it may imply their work and social life. Additionally, in some health facilities, unavailability of facilities in support of TB care (lack of water) [35]. This finding is comparable with the study done in Ethiopia and elsewhere in the world, where the majority of death recorded within the two months of anti-TB treatment initiation [6] [14] [20] [25] [31] [36] [37]. In contrast to the current finding, the previous studies in Addis Ababa (75%) and Spain (51.7%) revealed that the continuation phase was a TB treatment stage in which higher death was observed [14] [31]. On the other hand, studies in the United States and Canada [28] indicated a similar occurrence of mortality throughout the study period, *i.e.*, during both TB treatment phases.

The current study demonstrated that, as the weight decreases by one unit, the occurrence of death increases by 4% [AHR = 0.96 CI at 95% (0.91, 0.98)], which is relatively concordant with previous studies conducted in Dangila and Addis Ababa [14] [15]. This may be assumed that being underweight is due to malnutrition, resulting in deterioration of immunity and increased severity of the disease [38] [39] [40] [41].

In this study, it is found that pulmonary negative TB patients had 19.92 times [AHR = 19.92 CI at 95% (7.49, 52.96)] and extrapulmonary TB patients had 9.49 times [AHR = 9.49 CI at 95% (3.99, 22.62)] higher rate of death than positive pulmonary patients, implicating the effect of a negative pulmonary result on the survival time to death during TB treatment. The reasons might be due to delays in the diagnosis and treatment since it requires assessing the response to antibiotic therapy as well reviewing radiological investigations and the disease being active and in progress due to longer interval of clinical and health care system [42] [43] [44]. On top of this, the possibility that persons diagnosed with culture-negative TB may not have had TB and died of other causes [28]. Eastern Ethiopian researcher and of Gondar University found consistent findings where patients with pulmonary negative had 3.2 times [AHR = 3.204 CI at 95% (2.277 - 4.509) and extrapulmonary had 3.18 ([AHR = 3.175 CI at 95% (2.201 - 4.581)] higher rate of death [32] [45]. However, a study in northern Ethiopia identified that positive pulmonary patients were 58.3% more likely to die than patients with pulmonary negative [11], which may be due to differences in the study setting, study population and survival model used in the studies. On the other

hand, a study in China revealed similar survival among all TB type cases [27], and other studies in Ethiopia identified that TB type had no association with survival of the patients [14] [15] [19].

In this study, it was ascertained that the overall median survival time to death was 157 days, which is shorter as compared to study done in Northeast Ethiopia (210 days) [11], Northwest Ethiopia (231 days) [15], and Vietnam (240 days) [46]. The contributing factors might be differences in the study setting, health facilities, study population, and study time gap. On the other hand, the finding is higher than the study done in Taiwan (20 days [47], Ireland (51 days) [48], Democratic Republic of Congo (59 days) [10] as well as study in Ethiopia (60 days) [15] and relatively similar to the study in Iran (168 days) [24].

Our study has some limitations. It was conducted retrospectively and relied on each health facility's patients' medical records. Hence, data on some demographic characteristics (religion, height, economic status) and behavioral characteristics (drinking alcohol, smoking cigarettes, chewing khat) could not be available in the patient's record, and these variables were not integrated into the study. Mortality might be overestimated since any death during TB treatment was considered TB-related.

As a strength, this study was conducted in multi-center facilities, and both Cox: the proportional hazard model and Weibull accelerated failure time model, applied for the data analysis.

As a limitation, this study was conducted retrospectively; data on some demographic characteristics, economic status, and behavioral characteristics could not be available in the patient's record, and these variables were not integrated into the study.

5. Conclusion

The finding of this study indicated that a higher proportion of the patients (36.7%) died. Most of the death occurred within the first two months of anti-TB initiation, and the patients' overall median survival time was 157 days. Pulmonary negative TB type, intensive phase of TB treatment, being underweight, and younger age of the patients were found to be probable predictors for the survival time to death of the patients. The study also demonstrated that the Weibull model best fits the current data to predict the survival time of TB patients.

Availability of Data and Materials

All data are available and can be shared upon reasonable request.

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Author's Contribution

All authors contributed to conceptualization and proposal development, data

collection and analysis, writing original draft, preparing and reviewing the manuscript, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

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Ethical Consideration

Ethical approval was obtained from the Research and Ethics Review Committees of the School of Pharmacy, Addis Ababa University, and Addis Ababa Regional Health Bureau. A support letter was obtained from Addis Ababa Health Bureau and given to each health center administrator's office. Confidentiality was assured by using data collector nurses from the TB program clinic of the selected health facilities.

Consent for Publication

Not applicable.

Conflicts of Interest

The authors declare that they have no competing interests.

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Abbreviation

AIC: Akaike Information Criterion, DOTS: Directed Observed Therapy Strategy, ETB: Extrapulmonary Tuberculosis, FMOH: Federal Ministry of Health, HIV: Human Immune Virus, HR: Hazard Ratio, PTB: Pulmonary Tuberculosis, SNTB: Smear negative Tuberculosis, SPTB: Smear positive Tuberculosis, WHO: World Health Organization.