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Time to Recovery from Undernutrition and Its Predictors among Patients with Multi-drug-Resistant Tuberculosis in Addis Ababa, Ethiopia

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Abstract

Background: *Multidrug-resistant/rifampin-resistant tuberculosis is an emerging epidemic disease worldwide. Estimating the duration of recovery from malnutrition and identifying its determinants are crucial for practical and evidence-based public health decision-making among patients with multidrug-resistant tuberculosis who are experiencing non-nutrition. This study aimed to assess the time to recovery from undernutrition and its predictors among multidrug-resistant/rifampin-resistant tuberculosis patients in Addis Ababa.*

Methods: *We conducted a retrospective analysis of patients who received MDR-TB treatment in Addis Ababa, Ethiopia, from June 1, 2017, to July 30, 2022. The records of 381 MDR-TB patients were randomly selected using a simple random sampling technique. The data were collected using a pretested and structured data extraction checklist. Descriptive statistics were performed using graphs and frequencies. We constructed bivariable and multivariable Cox regression models to identify predictors of undernutrition among patients with multidrug-resistant tuberculosis.*

Results: *The undernutrition recovery rate was 8.353 per 1000 person-days. The median nutritional recovery time of the entire cohort of the study was 86 days, with an interquartile range of ±57.12 days. Age ≥ 55 years (AHR = 0.33, 95% CI = 0.15 - 0.75), living in a single room (AHR = 1.49, 95% CI =1.09 - 2.03), low household income (AHR = 0.62, 95% CI = 0.44 - 0.88), and co-infection with HIV (AHR = 0.28, 95% CI = 0.17 – 0.46) were found to be significant predictors of nutritional recovery time.*

Conclusion: *In this study, we found that approximately 77% of the malnourished patients recovered, with a median recovery time of 86 days. Age, housing condition, HIV status, and household income were found to be predictors of nutritional recovery time. Health care providers should place special emphasis on patients who are HIV positive, are old and have a low household income to improve nutritional recovery time.*

Introduction

Tuberculosis (TB) is a deadly communicable disease and was one of the top 10 causes of death in 2019 [1]. Multidrug-resistant tuberculosis (MDR-TB), which is characterized by resistance to at least two first-line ant-TB medications (isoniazid and rifampicin), has become a serious concern for global public health [2]. Globally, Multidrug-resistant/ rifampin-resistant (MDR/RR) tuberculosis infection is on the rise, which has brought its diagnosis and treatment under intense scrutiny [3]. Over the past 2 decades, it has become clear that widespread MDR/RR TB infection will continue to complicate attempts to treat patients and achieve the challenging goals of the End TB Strategy [3]. Malnutrition and MDR-TB are both problems of considerable magnitude in most underdeveloped regions of the world [4, 5]. Malnutrition can result from tuberculosis (TB), which in turn increases the risk of undernutrition [5, 6]. One major factor influencing the morbidity and death rate from MDR tuberculosis is nutritional condition [6, 7]. The extent and burden of undernutrition and MDR-TB vary greatly, but the burden is most severe in limited-resource countries [8-10]. Patients who have previously undergone TB treatment are more likely to develop MDR-TB and weight loss, which highlights the ineffectiveness of TB control programs [11-13]. Early detection of malnutrition and nutritional therapy can help patients recover from illness more quickly and efficiently [14, 15]. According to the study, nutritional supplementation with dietary counseling is desirable in addition to treatment, especially for malnourished patients (BMI < 18.5 kg/m2) [16, 17]. Correcting malnutrition can result in weight gain and a decrease in suffering, expenses, and fatalities among patients with MDR TB [17, 18]. In the majority of developing countries, including Ethiopia, undernutrition and tuberculosis are closely related. A poor nutritional status increases the likelihood of poor clinical outcomes, including mortality, and increases the spread of tuberculosis in the community, particularly in patients with multidrug-resistant tuberculosis [19, 20]. Several studies have reported that malnourished people are more prone to developing MDR/ RR TB, are at risk of having advanced disease, and are at greater risk of developing complications and deaths than are patients with a normal body mass index (BMI) [21]. Weight gain over time during therapy can serve as a biomarker for treatment efficacy and improved treatment outcomes [22]. Nutritional improvements are necessary to reduce the risk of MDR/RR TB disease, but they also increase the risk of relapse and mortality from the disease [23]. Undernutrition is a nutritional condition characterized by a deficiency in nutrients that has a variety of clinical manifestations. Various diagnostic criteria are mentioned, and undernutrition is defined as a situation that includes losing weight (low weight-to-height ratio), having a body mass index (BMI, kg/m2) below 18.5 in adults, and having micronutrient deficiencies [24]. Therefore, it is crucial to explore the risk factors for malnutrition in patients with MDR TB to improve prognosis and quality of life [25]. Hence, early detection of the possible risk factors for a protracted recovery from malnourishment in MDR-TB patients should improve the population's prognosis. Currently, there are no studies on the risk of malnutrition recovery among patients with MDR TB in Ethiopia. Therefore, the aim of this study was to identify determinants of nutritional recovery time among MDR-TB patients in Ethiopia. The results of this investigation may provide a foundation for clinical research on malnutrition detection and prevention.

Method and Material

Study design and setting

An institution-based retrospective follow-up study was conducted among patients treated for MDR/RR/TB from June 1, 2017, to July 30, 2022. The study was conducted in two selected treatment-initiated center hospitals in Addis Ababa, i.e., St. Peter and ALERT, which are comprehensive specialized hospitals. The city administration has a total population of 5,228,000. It has 11 sub-cities and 123 woredas with 13 public and more than 25 private hospitals. St. Peter Specialized Hospital and ALERT Comprehensive Specialized Hospital are among the public hospitals in Addis Ababa. The hospitals have a catchment area population of more than 3 000 000 people living in Addis Ababa and a nearby Oromia region.

Population and Sampling Procedure

All MDR-TB patients who initiated treatment at the two treatment-initiated centers found in Addis Ababa were the source population for this study. All MDR-TB patients who were identified at the two treatment centers and enrolled between June 1, 2017, and July 2022 were the study population. All MDR-TB patients enrolled in Addis Ababa from 2017 to

2022 were included in the study. All patients with incomplete data on entry, exit, or treatment outcomes were excluded from the study. The sample size was estimated by considering all available assumptions of the single population proportion formula; the prevalence of undernutrition 64%, a margin of error of 5%, a 95% confidence level, and a 10% nonresponse rate, and the final sample size we obtained was 389 study subjects. To select the study participants, we applied a stratified random sampling technique using proportional allocation.

Inclusion and exclusion criteria

This study included all adult patients aged 15 years or older who were diagnosed with MDR-TB either clinically or bacteriologically and who were receiving treatment between June 1, 2017, and July 2022. We excluded patients whose data were incomplete at the time of entry, whose data were missing, or who had no final treatment outcome (those who were transferred out or still on treatment or whose treatment outcome was missing from the data source).

Variables of the study

The dependent variable should be time to recovery from undernutrition, which is defined as patients gaining the ideal body weight (BMI > 18.5 kg/m^2). Body mass index was computed for each patient using their height and weight at the time of therapy initiation, and patients were deemed underweight if their BMI was less than 18.5 kg/m2. The independent variables included socio-demographic characteristics, including baseline age, sex, residence, occupation, marital status, and educational status; behavioral characteristics, including alcohol consumption, smoking, and chat chewing history; and clinical characteristics, including duration of illness, treatment delay, body mass index (BMI), treatment support and adherence.

Operational definitions of variables

Time to nutritional recovery: The length of time from the initiation of nutritional therapy (start of RTUF daily) to the time at which the patient reached their ideal weight (BMI>18.5 kg/m^2).

Nutrition therapy: is the treatment used to treat the medical condition of patients with tuberculosis through changes in diet by adjusting the quantity, quality and methods of nutrition intake.

Previous TB treatment: Patients who took standard anti-TB drugs for ≥ 1 month.

Recovered – Participants reached a BMI of ≥18.5 kg/m^2 for two consecutive visits after starting the therapeutic feeding programme (TFP).

Not recovered – Participants who did not reach a BMI of ≥18.5 kg/m^2 for two consecutive visits within three (MAM) or six (SAM) months.

Censored: All patients who failed to recover due to reasons such as defaulting from treatment, loss to follow-up, death, transfer, or nutritional therapy during the data collection time.

HIV-MDR/RRTB patients who tested positive for HIV during treatment initiation or were on ART.

Treatment regimen- Treatment group: MDR/RR TB patients who were receiving long-term regimens (18-24 months) or short-term regimens (9-12 months) [26]

Adherence levels were measured using pill counts.

Good adherence >= 95% or ≤2 missed 30 doses or <3 missed 60 doses.

Fair adherence-Drug adherence of 85–94% or 3–5 missed drug doses of 30 doses or 4–9 missed drug doses of 60 doses.

Poor Adherence-Drug adherence of <85% or ≥6 doses of missed ART drug doses of 30 doses or >9 doses missed ART drug doses of 60 doses.

Smear grade- Accordingly, sputum smears were graded as scant, 1+, 2+, or 3+. The sputum contained 1–9 AFB in 100 fields, grade 1+ for 10–99 AFB in 100 fields, grade 2+ for 1–10 AFB per field, and grade 3+ for more than 10 AFB per field.

Data collection and Measurement

The data were collected from patient medical charts and registration books using a standardized checklist. This was prepared in English after reviewing the treatment registration logbook and patient follow-up charts as well as a computer database. One supervisor (senior BSc nurse) and two data collectors (base nurses) were enrolled in the selected treatment center in the data collection process. To ensure the quality of the data, each checklist was reviewed for completeness of the data during the data collection procedure and was pretested at a different hospital that was not part of the study. Two days of training on how to extract data from patients' medical charts and registration books were given to the data collectors and supervisors. The principal investigator provided close site

supervision during the entire data collection period, and the collected data were checked for completeness, consistency, accuracy, and clarity on a daily basis.

Data Management and Analysis

The collected data were entered by using an epi data manager and exported to STATA for analysis. Depending on the nature of the variables, summary statistics are performed to describe the demographic, behavioral, and clinical characteristics of patients in general, specifically MDR-TB cases. The incidence rate was calculated by dividing the number of total nutritional recoveries by the total person-years of the follow-ups. The life table and Kaplan–Meier curves were used to estimate the overall survival time, and a log-rank test was used to compare the survival curves of different exposure groups. Both the bivariable and multivariable Cox regression models were fitted to identify predictors of the time to nutritional recovery. Variables with a p value < 0.2 in the bivariable analysis were included in the multivariable analysis, and variables with a p value < 0.05 in the multivariable Cox regression model were considered to be statistically significant. The findings are presented as the adjusted hazard ratio (AHR) and 95% confidence interval (CI). The Cox proportional hazard assumption was assessed graphically using log-log survival curves and Schoenfeld residual statistical tests. The goodness of fit of the final model was checked by Nelson Aalen's cumulative hazard function against the Cox-Snell residual.

Result

Socio-demographic Characteristics of the Study Participants

The study included records of 381 MDR/RR TB patients who had complete data, for a response rate of 97.94%. Among all participants, 53% were males, and nearly two-thirds (72.18%) were urban residents. The ages of the patients ranged from 18 to 75 years, with a median age of 30 years (IQR = 25, 40), and more than half (63.25%) of the study participants were aged less than 34 years. Nearly half (49.87) of the study participants were orthodox Christian followers. More than fifty (55.38%) of the participants were married. Regarding educational status, 23.10% of individuals were diploma holders. With respect to occupational status, 131 (34.38%) individuals worked at government offices, and 153 (40.2%) of the study participants had an average monthly household income of <5000 ETB **(Table 1).**

The behavioral and clinical characteristics of the study participants

Overall, 6% of the study participants were smokers. Nearly half (49%) of the participants were cured, 24.5% completed treatment, 13% were on treatment, 9% died, 3% were lost to follow-up, and 1.5% failed to recover from their MDR/RR/TB treatment. Among those patients, 119 (31%) study participants developed severe acute malnourishment, whereas 262 were moderately malnourished **(Table 2).**

Treatment Outcomes for MDR-TB Patients in Addis Ababa

Among the 381 study participants, 292 (76.6%) patients recovered from undernutrition **(Figure 1).** Nearly one-fourth (89, 23.4%) were censored; among those, 34 (9%) died, 28 (7.4%) did not recover, 21 (5.5%) were lost to follow-up, and 6 (1.5%) were receiving nutritional treatment. Among patients who were followed up at St. Peter Hospital, 161 (74.2%) recovered from malnutrition, whereas at ALERT Hospital, 131 (80%) of patients who were followed up recovered. The recovery rate for severe acute malnutrition (SAM) patients was 69.5%, whereas that for moderate acute malnutrition (MAM) patients was 79.5% **(Table 2).**

Kaplan–Meier Survival Estimates of Recovery Time from Undernutrition

The undernutrition recovery rate was 8.353 per 1000 person-days (CI = 0.007, 0.009) among the entire study participants in the cohort. There were 6.655 per 1000 person-days (CI = 0.005, 0.008) for severe acute malnutrition and 9.294 per 1000 person-days (CI = 0.008, 0.10) for moderate acute malnutrition. The overall median nutritional recovery time of the entire cohort was 86 days (IQR: 57.118) **(Figure 2).**

The age of the study participants was a significant risk factor for nutritional recovery time. Patients whose nutritional recovery time was >55 years had a median nutritional recovery time of 118 days, while patients aged 35-44 and < 34 years had median recovery times of 86 and 84 days, respectively **(Figure 3).** In addition, there was substantial variation in nutritional recovery time with HIV status. Patients who tested positive for HIV had a median recovery duration of 181 days from malnutrition, whereas patients who tested negative for HIV had a median recovery time of 84 days from malnutrition. Patients who lived in a house with a single room had an average recovery time of 85 days, which was shorter than that of people who lived in a house with two or more rooms. Severely malnourished participants recovered within 90 days, whereas moderately malnourished patients recovered within 65 days **(Table 3).**

Table 1: Socio-demographic characteristics of MDR/RR-TB patients in Addis Ababa, Ethiopia, from July 1, 2017, to June 30, 2022.

Variable	Category	Frequency	Percentage
Age	18 – 34	237	62.2
	35 – 54	119	31.2
	≥55	25	6.6
Sex	Male	202	53
	Female	179	47
Residency	Urban	275	72.3
	Rural	106	27.82
Occupation	Farmer	29	7.61
	House Wife	67	17.59
	Daily Laborer	40	10.50
	Government	131	34.38
	Nongovernment	2	0.52
	Private	73	19.16
	Other (specify)	39	10.24
Religion	Orthodox	190	49.87
	Muslim	108	28.35
	Protestant	82	21.52
	Catholic	1	0.26
	Others(specify)	0	0
Educational status	Un educated	66	17.33
	Primary	79	20.73
	Secondary	62	16.27
	Diploma+	174	45.67
Marital status	Single	170	44.63
	Married	211	55.38
Housing Condition	One room	170	44.62
	Two rooms	211	55.38
Family size	Less than five	341	89.50
	More than five	40	10.50

Table 2: Behavioral and clinical characteristics of the study participants

Variables	Category	Frequency	Percentage
Smoking	Smoker	23	6.0%
	None-smoker	358	94
khat chewing	Yes	22	5.77
	No	359	94.23
Alcohol drinking	Yes	64	16.8
	No	317	83.2
Hx of first line anti TB drugs Rx	Yes	260	68.24
	No	121	31.76
Hx of first second anti TB drugs Rx	Yes	10	2.62
	No	371	97.38
MDR/RR TB Rx adherence	Good	322	84.51
	Fair	45	11.81
	Poor	14	3.678
TB Type	Only pulmonary	364	95.54
	E/pulmonary	10	2.62
	Disseminated	7	1.84
Baseline sputum smear result	Positive	196	51.44
	Negative	185	48.56
DR/RR/TB registration group	New	111	29.13
	Relapse	43	11.29
	After lost to follow up	4	1.05
	After failure of FLD regimen	215	56.43
	After failure of SLD regimen	7	1.84
	Transfer in	1	0.26
Treatment interruption Hx	Yes	43	11.29
	No	338	88.71
Clinical complication during MDR/RR-TB treatment	No complication	187	49.08
	Pneumothorax	5	1.31
	Pneumonia	79	20.73
	Hemoptysis	75	19.69
	Pleural effusion	33	8.66
	Others	2	0.52
X-ray finding	Normal	83	21.78
	Consolidation	92	24.15
	Cavitation	129	33.86
	Pleural effusion	53	13.91
	Fibrosis	2	0.52
	Infiltration	22	5.77
Outcome	Cured	188	49.34
	Died	35	9.19
	Failure to recover	4	1.05
	Completed	93	24.41
	LTFU	12	3.15
	still on Rx	49	12.86
Comorbid conditions	Yes	340	89.24
	No	41	10.76
HIV test result	Positive	59	13.49
	Negative	322	84.51
BMI during Rx Initiation	<16.49 kg/m^2	119	31.23
	16.5-18.49 kg/m^2	262	68.77
Another outcome	Died.	34	9
	LTFU	21	5.5
	Still on Rx	6	1.5
	Rx Completed	28	7.4

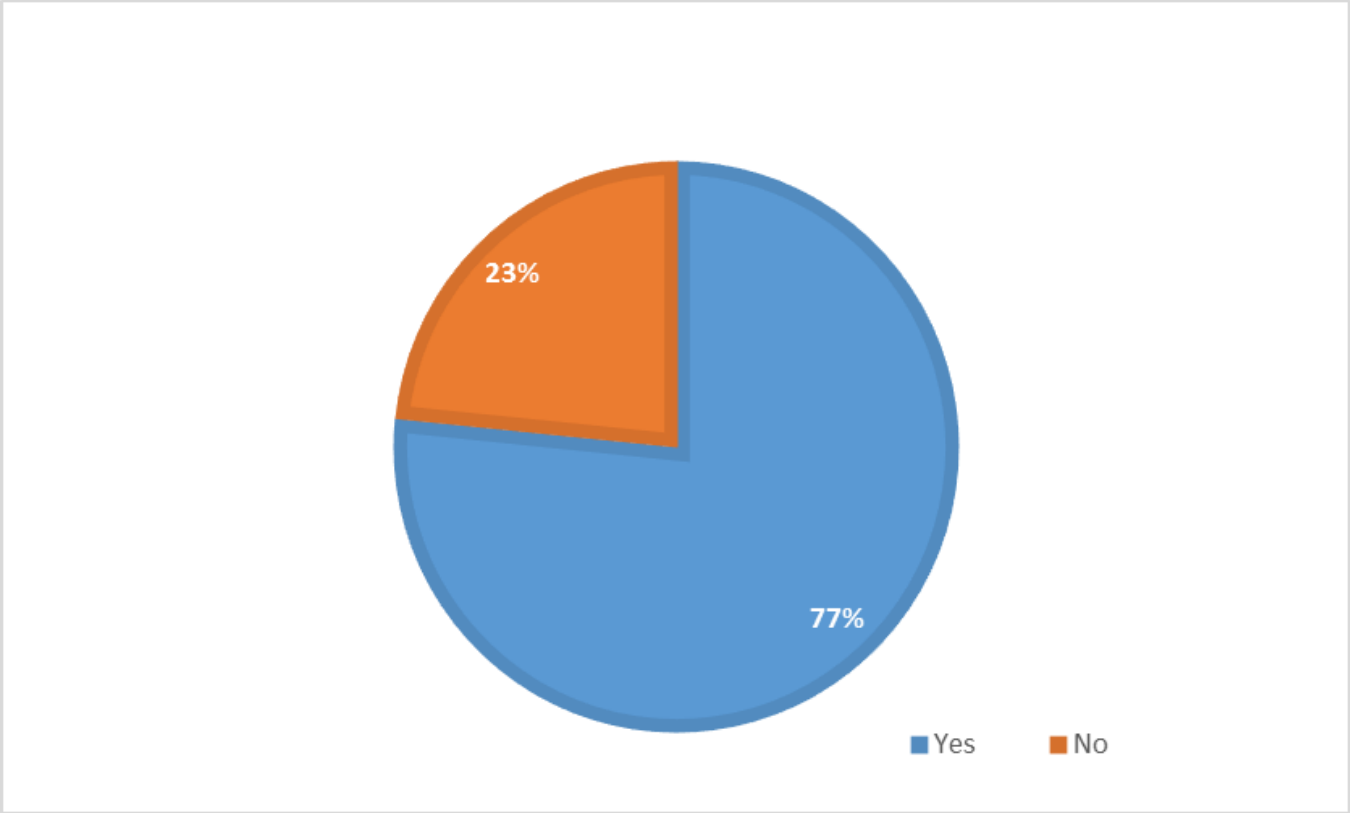

Figure 1: *Outcomes of the recovery rate from malnurtion among MDR-TB patients in Addis Ababa from 2017 to 2022*

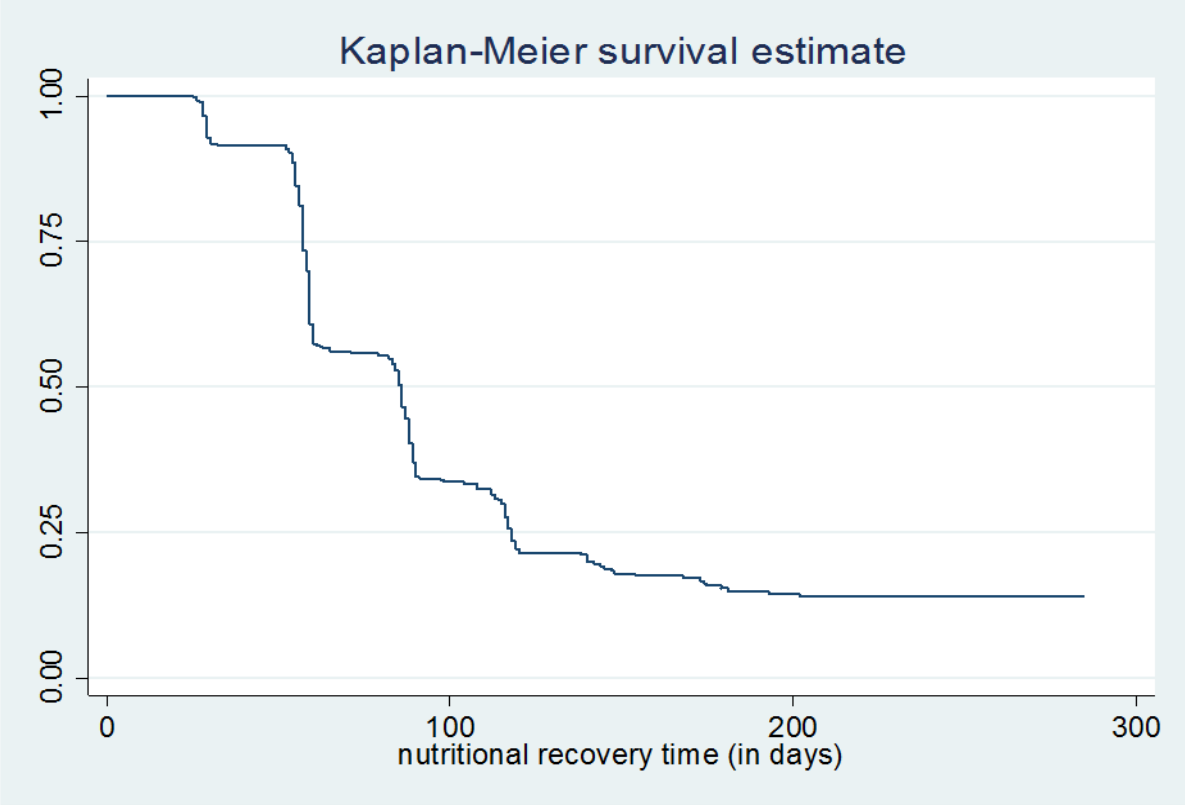

Figure 2: *Overall Kaplan–Meier estimation of survival time to recover from undernutrition among adult MDR/RR TB patients at Specialized Hospitals in Addis Ababa, Ethiopia, from July 1, 2017, to June 2022.*

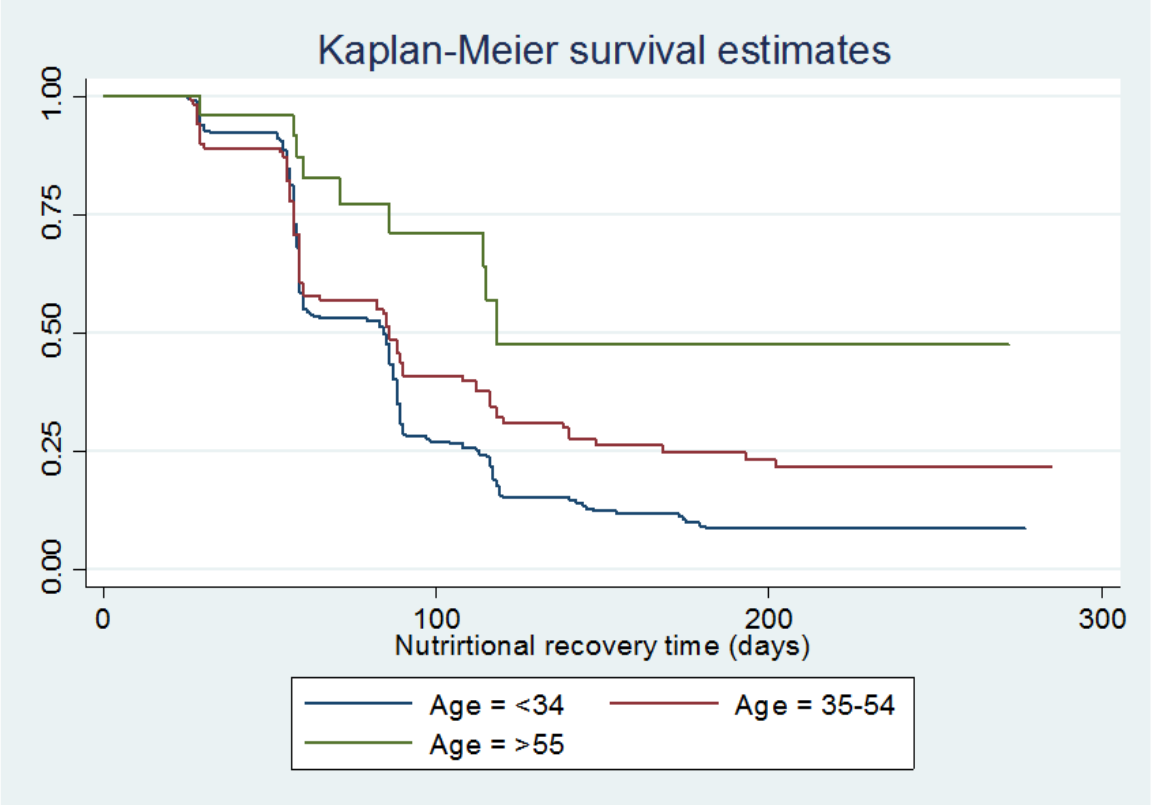

Figure 3: *Cumulative estimation of the recovery time among adult undernourished MDR/RR TB patients by age in patients at Specialized Hospitals in Addis Ababa, Ethiopia, from July 1, 2017, to June 30, 2022.*

Table 3: Kaplan–Meier Survival Estimates of the Recovery Time for Undernourished Adult MDR/RR TB Patients with Different Covariates in Addis Ababa, Ethiopia, from July 1, 2017, to June 30, 2022.

Variables	Categories	Time to recovery		Long-Rank X_2 value	P value
		Days	95% CI		
Age	18 – 34	84	60, 86	15.78	0.0004
	35 – 54	86	60,90		
	≥55	118	86.-		
Housing Condition	One room	85	60,88	4.06	0.1313
	Two rooms	86	60,88		
Household income	<5000	87	60,89	3.82	0.1484
	5000-10000	86	60,88		
	>10000	84	59,88		
HIV status	Positive	181	117, 193	28.59	0.0000
	Negative	84	60,86		
Undernutrition type	SAM	90	88, 116	11.47	0.0007
	MAM	65	57,113		

Factors associated with time to Recovery

The proportional hazards assumption was assessed by using both statistical and graphic tests **(Figure 4).** All of the covariates and the full model satisfied the proportional hazard assumption according to the global test (p value = 0.1384).

Bivariable and multivariable cox-regression analysis were computed. Variables that had a p value < 0.2 in the bivariable Cox regression analyses were entered into the multivariable Cox regression analysis. According to the multivariate Cox regression analysis, age, housing condition, household income, HIV status, and type of undernutrition were predictors of the time to recovery from undernutrition. Patients aged >55 years were 67% (AHR=0.33, CI=0.15, 0.75) less likely to recover from undernutrition than younger patients. Patients who lived in a house with one room had a 49% increased chance of recovery than patients who lived in a house with two or more rooms (AHR=1.49, CI=1.09, 2.03). Compared to patients with household incomes of more than ten thousand ETB during the treatment period, the likelihood of nutritional recovery for patients with incomes of less than five thousand ETB per month was reduced by 38% (AHR=0.62, CI=0.44, 0.88). Patients with positive HIV test results had a 72% lower chance of recovering than those with negative results (AHR=0.28, CI=0.17, 0.46). Patients who developed severe acute malnutrition (SAM) were 50% less likely to recover from undernutrition than were moderately malnourished (MAM) patients (AHR = 0.50, CI = 0.38, 0.67) **(Table 4)**.

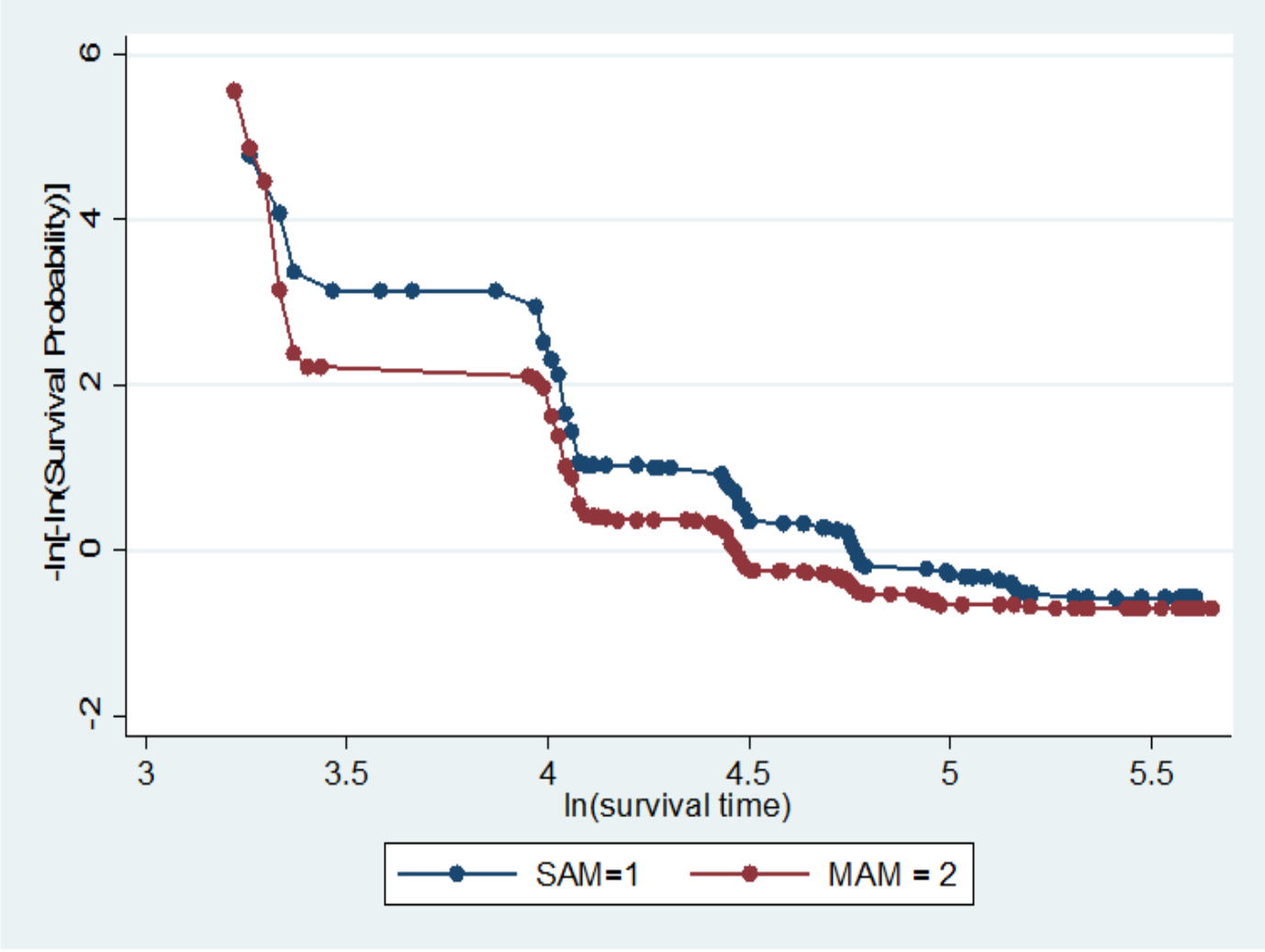

Figure 4: *Proportional hazard assumption test by type of malnutrition (severe acute malnutrition vs moderate acute malnutrition)*

Table 4: Predictors of recovery time among undernourished MDR/RR TB patient centers at specialized hospitals in Addis Ababa, Ethiopia, from July 1, 2017, to June 30, 2022.

Variables	Category	Status		CHR(95%CI)	AHR(95%CI)	p value
		Recovered	Censored			
Age	18 – 34	201(84.8%)	36(15.2%)	Ref.	Ref.	
	35 – 54	82(69%)	37(31%)	0.73(.56, 0 .94)	1.16(0.83,1.16)	0.89
	≥55	**9 (36%)**	**16 (64%)**	**0.34(0.18, 0.67)**	**0.33(0.15,0.75)**	**0.008***
Sex	Male	145 (71.8%)	57 (28.2%)	Ref.	Ref.	
	Female	147(82%)	32 (18%)	1.36(1.088, 1.72)	1.01(0.78,1.30)	0..11
Educational Status	Can't read and write	7 (63.6%)	4 (36.4%)	0.63(0.23,1.37)	0.78(0.31,1.72)	0.481
	Not formally educated	35(63.6%)	20 (36.4%)	0.82(0.54,1.23)	1.23(0.78,2.05)	0.336
	Primary	60(78%)	19(22%)	0.92(0.64,1.3)	0.95(0.65,1.40)	0.796
	Secondary	47(75.8%)	15(24.2%)	0.97(0.68,1,40)	0.92(0.62,1.36)	0.666
	Diploma	76(86.4%)	12 (13.6%)	1.85(0.85,1.47)	1.08(0.76,1.53)	0.668
	Degree and above	67(78%)	19 (22%)	Ref.	Ref.	
Housing Condition	One room	140(82.4%)	30(17.6%)	1.09(0.56,1.42)	**1.49(1.09, 2.03).**	**0.012***
	Two and more rooms	103(77%)	31(23%)	Ref.	Ref.)	
	Other(specify)	49(63%)	28(37%)	0.79(0.56,1.12)	0.93(0.40,0.97)	0.739
Household income ETB	<5000	113(69.8%)	49(30.2%)	0.75(0.56,1.01)	**0.62(0.44,0.88)**	0.007*
	5001-10000	106 (76.3%)	33(23.7%)	0.83(0.61,1.11)	0.73(0.52,1.02)	0.062
	>10000	73(91.3%)	7(8.7%)	Ref.	Ref.	
Smoking	Daily smoker	4 (30%)	9(70%)	0.24(0.09,0.64)	0.33(0.12,0.95)	0.41
	Former smoker	7(70%)	3(30%)	0.86(0.40,1.83)	1.60(0.68,3.77)	0.276
	Never smoke	281(78.5%)	77(21.5%)	Ref	Ref.	
Depression	Yes	242(78.3%)	67 (21.7%)	0.78(0.57,1.06)	0.98(0.68,1.41)	0.934
	No	50(69.4.4%)	22 (30.5%	Ref.	Ref.	
Alcohol drinking	Yes	37 (58%)	27(42%)	0.55(0.38,0.78)	0.77(0.50,1.18)	0.237
	No	255(80.5%)	62(19.5%)	Ref.	Ref.	
Rx supporter	Yes	287(78%)	80(20%)	Ref.	Ref.	
	No	5(35.7)	9(64.3%)	0.32(0.13,0,78)	0.62(0.23,1.61)	0.327
MDR/RR	Good	259(80.5%)	63(19.5%)	Ref.	Ref.	
TB Rx adherence	Fair	29(64.5. %)	16(35.5%)	0.60(0.41,0.88)	1.25(0.78,2.00)	0.345
	Poor	5 (36%)	9(64%)	0.31(.13,0.75)	0.49(0.18,1.29)	0.148
Clinical complication during	No	155(83%)	32(17%)	Ref.	Ref.	
MDR/RR-TB treatment	Pneumothorax	3(60%)	2(40%)	0.38(0.12,1.18)	0.31(0.83,1.16)	0.082
	Pneumonia	66(83.5%)	13(16.5)	0.93(0.69,1.24)	1.14(0.84,1.55)	0.404
	Hemoptysis	49(65%)	26(35%)	0.56(0.41,0.79)	0.73(0.52,1.04)	0.086
	P.effusion	18(54.5%)	15(45.5%)	0.51(0.31,0.84)	0.89(0.52,1.51)	0.667
	Others	1(50%)	1(50%)	0.40(0.06,2.86)	0.68(0.86,5.36)	0.716
Comorbid conditions	Yes	19(46%)	22 (53%)	0.41(0.26,0.66)	0.76(0.43, 1.34).	0.349
	No	273(80%)	67(20%)	Ref.	Ref	
HIV test result	Positive	20 (41.5%)	28(58.5%)	0.32(0.20,0,50)	**0.28 (0.17,0.46)**	0.001*
	Negative	264(82%)	58 (18%)	Ref.	Ref.	
	Unknown	8((73%)	3(27%)	0.86(0.43,1.74)	**1.00(0.44, 2.33)**	0.007*
Undernutrition type	SAM	83(69.5%)	35(29.5%	0.65(0.50,0.84)	**0.50(0.38, 0.67)**	0.001*
	MAM	209(79.5%)	54(19.5)	Ref	Ref.	

*(Variables with * signs are significant variables with p values <0.05)*

Discussion

MDR/RR TB patients frequently suffer from undernutrition. The provision of supplementary foods for a considerable duration of time along with MDR/RR/TB therapy is thought to cause weight gain and improve patients' functioning [23]. As a result, we aimed to assess nutritional recovery time and its predictors among undernourished MDR/RR/TB patients treated with regular therapeutic feeding at two treatment centers in Addis Ababa. In this study, we found that 292 (76.6%) MDR-TB/RR patients recovered from undernutrition. The undernutrition recovery rate was 8.353 per 1000 person-days (CI = 0.007, 0.009) among the entire study participants in the cohort. The overall median recovery time from undernutrition was 86 days (IQR: 57.118). The results of this study also revealed a median recovery time that met the goals of the World Health Organization (WHO) and the Ministry of Health Ethiopia MDR/RR TB treatment guidelines (90 days for MAM and 180 days for SAM) [26, 27]. This outcome may be attributable to the fact that the study sites were located in the capital city, which has well-organized staff, and continuous therapeutic and supplementary feeding programs, which are different from those used in the clinics in rural regions of Ethiopia. The results of this study revealed that the age of the patient, HIV test status during treatment initiation, MDR/RR/TB treatment outcome, housing condition, monthly household income and type of undernutrition were predictors of the time to nutritional recovery for MDR/RR/TB patients. The median recovery time for patients with moderate acute malnutrition was 65 days, but for severely malnourished patients, the median time to recovery from undernutrition was 90 days. This might be because patients who are severely malnourished are more likely to contract an infection, exhibit some clinical symptoms such as appetite loss and physical weakness, and suffer from decreased immunity, which delays recovery time.

This study revealed that individuals aged > 55 years had a lower rate of recovery time from malnutrition than did patients aged 18-34 years, which is in line with the findings of studies conducted in Guinea and Ethiopia [28, 29]. This difference between age groups could be because patients between the ages of 35 and 54 will perform tasks such as buying food by themselves without the need for permission and financial support from their family members. Patients can also enter treatment centers and start treatment early before the disease becomes more severe. The severity of the disease may be greater among aged patients than among young patients and may cause a longer recovery time.

In addition, the findings of this study revealed that individuals with a lower monthly income have a lower rate of recovery from undernutrition than individuals with a higher monthly income. This finding may be explained by the possibility that patients who come from families with low socioeconomic status experience food insecurity and financial instability, which lengthens the time it takes for nutritional therapy to be effective.

Additionally, in this study, we found that the housing conditions of MDR-TB patients were an independent predictor of the time to recover from undernutrition. This finding indicates that individuals with a single-room house had a quick recovery rate compared with other patients who had more than two rooms in the house. This result could be indirectly related to family size. Most of the time, single men or women will live in a single room, which might decrease food insecurity and ensure quicker healing time. In contrast, patients who lived in a residence with two or more rooms could experience parallel increases in family size, which could result in longer recovery times secondary to food insecurity and plate sharing.

Moreover, MDR/RR-TB patients who were HIV positive at the beginning of treatment had a lower recovery rate than did HIV-negative MDR-/RR-TB patients, which is in line with other studies conducted in Guinea [30]. This is because people infected with human immunodeficiency virus (PLWHIV) experience direct weight loss, and viral infection has already suppressed their immunity [29]. The clinical manifestations of HIV and opportunistic infections, along with social stigma, make patients sense hopelessness, decreased self-care, and low food intake, which results in a longer recovery time from undernutrition.

Limitations of the Study

The analysis of factors related to nutritional recovery time was limited by the data obtained from the patients' charts because of the retrospective nature of the study. Some socio-demographic factors, such as food insecurity and other clinical -related factors, were not included in the study due to a lack of information on patient charts and registration books. This study was conducted in specialized hospitals in the capital city, which has well-trained staff with continuous feeding programs.

Conclusion

In this study, about 77% of the malnourished patients recovered after the therapeutic feeding program. Age, housing condition, HIV test status, type of malnutrition, outcome of MDR RR/TB therapy, and household income were found to be statistically significant predictors of nutritional recovery time. The findings of this study showed that to increase the recovery rate for undernutrition cases, nutritional interventions and support must be given top priority. In addition, health care providers should provide special emphasis on patients who are HIV positive and have a low household income to improve nutritional recovery time. Further research should include additional clinical measurements that could not be included in this study for further improvement of the evidence.

Abbreviations/Acronym

AHR: adjusted hazard ratio; CI: confidence interval; CHR: crude hazard ratio; IQR: interquartile range, SAM: severe acute malnutrition. MAM: Moderate Malnutrition; A**IDS**: Acquired Immunodeficiency Disease Syndrome, **ALT**: Alanine Amino Transferase, **AST**: Aspartate Transaminase, **BMI**: Body Mass Index, **KG**: Kilogram, **LTFU:** Lost to Follow-up, **MDR/RR TB**: Multidrug Resistance/Rifampin Resistant Tuberculosis, **MoHE**: Ministry of Health Ethiopia, **PLHIV**: People Live with HIV Virus, **RUSF:** Ready to Use Supplementary Food, **RUTF**: Ready to Use Therapeutic Food, T**B:** Tuberculosis, **WHO:** World Health Organization.

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Ethical approval and consent to publication

Ethical approval and a letter of cooperation were obtained from the Institutional Review Committee of the University of Gondar, College of Medicine and Health Sciences, Institute of Public Health. St. Peter and ALERT Hospital were informed about the study objective through a written letter. Permission was obtained from the medical directors of each hospital. Confidentiality was maintained at all stages of the study. All methods were carried out following relevant guidelines and regulations (Declaration of Helsinki).

Availability of data and materials

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

Consent for publication

Not applicable

Authors' contributions

MYB and **TYB** conceptualized the research, developed the proposal, wrote the results, and discussion. The **AZA** guide proposal writing system participated in data collection tool development and result writing with **MG**. In general, all the authors approved the drafting and preparation of the manuscript.

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Competing Interests

The authors declare that they have no competing interests.

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