Vol 2 | Issue 1 | Pages 21-29

Insights of Bioinformatics

Research Article

DOI: 10.36959/317/682

Retrospective Analysis of Drug Resistant Tuberculosis and the Associated Treatment Outcomes in Kenya

David Mutabari[1], Idah Orowe[2], Anthony Karanja[3] and Hillary Kipruto[4]*

[1]*Medical Statistics, University of Nairobi, Kenya*

[2]*Senior Lecturer, School of Mathematics, University of Nairobi, Kenya*

[3]*Senior Lecturer, Masai Mara University, Kenya*

[4]*Senior Statistician, World Health Organization, Kenya*

Abstract

Background: Tuberculosis is the world's deadliest infectious disease and kills up to 1.4 million people a year. The latest diagnostic tests can rapidly and accurately diagnose T.B. New medicines can help prevent and cure T.B. Yet two years after a United Nations High-Level Meeting on T.B. in 2018, people are still dying of a disease that should have been eliminated decades ago.

Drug resistance is a significant public health crisis thwarting the effective treatment and care of people living with tuberculosis (TB) - the world's leading infectious disease killer. But with the release of new curative medicines and patient-minded improvements of treatment guidelines, drug-resistant T.B. (DR-TB) no longer has to be a death sentence.

Methods: The analysis was based on a retrospective review of patients' data enrolled with drug-resistant tuberculosis treatment from 2014 to 2019. We included gender, County, resistance patterns, registration, group, type of tuberculosis, sector treatment, Model of care, H.I.V. status, and treatment outcomes. Categorical variables were reported as numbers and percentages and continuous variables as medians and interquartile range (IQR). Categorical variables were compared using χ^2 test and the exact fishers test. Treatment outcome was categorical with, Ongoing treatment, successful and unsuccessful. Multivariate logistic regression was used to explore further this association, having a variable included to assess the influence on the treatment outcomes. The associations were reported as odds ratio (OR) and 95% confidence interval (CI) $P < 0.05$ was considered as statistically significant.

Results: The clients included in the study comprised all patients confirmed of the treatment period for the period of 2014 to 2019, from which we had a total of 2674 patients, of which 64.7 were males while females were 34.3%. The distribution of DR-TB cases was even across the country in terms of geographic position, but Nairobi County had the most significant burden OF 16%. Pulmonary type carried the highest proportion of 98% of the total cases reported. New cases were 36% of the cases on enrollment, while those who had previously been treated the least at 0.71%. H.I.V. status had been done to 98% of the total and from which 39% reported being H.I.V. positive, of which 97% of all H.I.V. Positive clients had been initiated on A.R.V. medications.

Conclusion: Drug resistance to tuberculosis poses a significant challenge to the Kenyan population, with up to 36% of DR-TB cases diagnosed. Meaning these cases are within the community level. The people tested had up to 39% of them were H.I.V. positive, translating to a group of people who are already immunologically challenged hence a higher likelihood of getting the infection. Additionally, the disease patterns were seen more in urban towns, with Nairobi County leading with 16%, translating to the bigger population ling in Nairobi. From this, we see more action should be taken to tackle the burden of DR-TB, which needs more treatment periods, more expensive drugs, and a higher association of mortalities with the disease than the susceptible one.

Keywords

Drug resistant tuberculosis, Drug susceptibility testing, Multidrug resistant tuberculosis, National tuberculosis, Leprosy, Lung disease, World Health Organization

Abbreviations

DHIS: District Health Information System; DNTLD: Division of National Tuberculosis, Leprosy and Lung Disease; DRTB: Drug Resistant Tuberculosis; DST: Drug Susceptibility Testing; FL L.P.A: First Line Line Probe Assay; H.C.W: Health Care Workers; H.I.V.: Human Immunodeficiency Virus; I.P.C.: Infection Prevention and Control; MDR TB: Multidrug Resistant Tuberculosis; MTBC: Mycobacterial Tuberculosis Complex; N.S.P.: National Strategic Plan PMDT: Programmatic Management of Drug-Resistant Tuberculosis; Pre-XDR: Pre-Extensively Drug-Resistant Tuberculosis; RR TB:

***Corresponding author:** David Mutabari, PhD Student, Medical Statistics, University of Nairobi, Nairobi, Box 30197-00100, Kenya

Accepted: May 29, 2022

Published online: May 31, 2022

Citation: Mutabari D, Orowe I, Karanja A, et al. (2022) Retrospective Analysis of Drug Resistant Tuberculosis and the Associated Treatment Outcomes in Kenya. Insights Biomed Res 2(1):21-29

Rifampicin Resistant Tuberculosis; SL L.P.A. : Second Line Line Probe Assay; STR: Shorter Term Regimen; S.L.D.s: Second Line Drugs; T.B.: Tuberculosis; T.S.R.: Treatment Success Rate; WHO: World Health Organization; XDR TB: Extensively Drug Resistant Tuberculosis

Introduction

The emergence and spread of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) are significant medical and public health problems threatening global health [1]. The diagnostic and treatment complexity, morbidity, and mortality associated with drug-resistant tuberculosis (DRTB) render it the most challenging form of the disease [2]. Even though global efforts have begun to decrease the overall incidence of T.B., there is a significant task ahead to reach elimination, particularly with the rising threat of drug resistance. As noted in the National Action Plan for Combating Multidrug-Resistant Tuberculosis (released by the White House, December 2015), the estimated global burden of 480,000 cases of multidrug-resistant tuberculosis (MDR-TB), only 10% are being cured each year [3]. In addition, Globally, only 39% and 32% of the estimated patients diagnosed with DR-TB are started on appropriate treatment, respectively. Ten high burden countries (H.B.C.s) in sub-Saharan Africa (S.S.A.) contributed 12% of the 484 000 estimated incident cases in 2018, mainly in Nigeria and South Africa. Nigeria and Mozambique were among ten countries contributing 75% of the global treatment enrollment gap [1]. Kenya is among the top 30 high burden countries for T.B., M.D.R. T.B., and TB-HIV W.H.O estimates that 1.3% of new T.B. cases and 4.4% of previously treated T.B. cases have MDR/RR T.B. According to the Kenya drug resistance survey of 2014, the prevalence of isoniazid monoresistance among new patients was 5.5% [4]. This study aimed to retrospectively review patients diagnosed with resistant tuberculosis in Kenya and analyze the treatment outcome and the associated factors to resistance patterns we have been enrolling for treatment. The multivariate regression method was applied to analyze the explanatory variable to quantitatively describe factors associated with the conversion patterns and then compared other research findings any associations with their models of care that they have been applying for the management of drug-resistant tuberculosis.

Methods

Study design

Retrospective cohort study.

Study site

Data were collected retrospectively from all health facilities accredited by the national tuberculosis and leprosy board for drug-resistant tuberculosis treatment.

Study population

Included all patients that had been tested positive of drug-resistant tuberculosis from the year 2014 to 2019.

Data source

Data was sourced from the Kenya national tuberculosis and leprosy board from their Electronic Medical Records (TIBU-System).

Data analysis

Data analysis was done through STATA software version 13 after abstraction and entering into excel. A multivariate data analysis method was applied to the abstracted data where chronologically, we did data simplification, sorted and grouped the data, investigation of independence of variables, prediction, and finally hypothesis testing.

Statistical methods

In the descriptive part, we majorly focused on the three aspects of the variables by looking at; the arithmetic mean, the spread or variance, and finally, the sample correlation coefficient (Pearson's product-moment correlation). It's with this then the assumption in our case is that we let $\chi_{11,}\ \chi_{12,}\ \ldots,\ \chi_{n1,}$ be n measurement on the first variable consequently the arithmetic average is *Equation 1* below,

$$\bar{x} = \frac{1}{n}\sum_{j=1}^{n} x_{j1} \quad (1)$$

n measurement represents a subset of which the entire set was observed; hence we computed the sample mean from the *n* measurement for each of *p* variables as; *Equation 2* below,

$$\bar{x}_k = \frac{1}{n}\sum_{j=1}^{n} x_{jk} \quad \text{where } k = 1,2,\ldots,p \quad (2)$$

The measure of spread was provided by the sample variance defined for *n* measurement on the first variable; *Equation 3* below,

$$S_1^2 = \frac{1}{n}\sum_{j=1}^{n}\left(x_{j1} - \bar{x}_1\right)^2 \quad (3)$$

Where $\bar{x}_1$ is the sample mean of the x_{j1}'S. In general, for the p variables, we have the variance as *Equation 4* below,

$$S_k^2 = \frac{1}{n}\sum_{j=1}^{n}\left(x_{jk} - \bar{x}_k\right)^2 \text{ where } k = 1,2,\ldots,p \quad (4)$$

A measure of linear association between measurement of two variables which we gave as the sample covariance and expressed as: given variable 1 and 2 in *Equation 5* below.

$$S_{12} = \frac{1}{n}\sum_{j=1}^{n}\left(x_{j1} - \bar{x}_1\right)^2\left(x_{j1} - \bar{x}_2\right)^2 \quad (5)$$

The sample covariance measured the association between different variants included in the study, i.e., i[th] and k[th] variables in *Equation 6* below;

$$S_{ik} = \frac{1}{n}\sum_{j=1}^{n}\left(x_{j1}-\bar{x}_1\right)^2\left(x_{jk}-\bar{x}_k\right) \quad \text{where } k = 1,2,....,p \quad (6)$$

Additionally, we considered the Pearson's product-moment correlation coefficient, in which the linear association between two variables does not depend on units of measurement for the i[th] and k[th] variable; which we defined with *Equation 7* below;

$$r_{ik} = \frac{s_{ik}}{\sqrt{S_{ii}}\sqrt{S_{kk}}} = \frac{\sum_{i=0}^{n}\left(x_{ji} - \bar{x}_i\right)\left(x_{jk} - \bar{x}_k\right)}{\sqrt{\sum_{j=1}^{n}\left(x_{ji} - \bar{x}_i\right)^2}\sqrt{\sum_{j=1}^{n}\left(x_{ji} - \bar{x}_i\right)^2}} \quad (7)$$

Where for $i = 1,2,....,p$ and $k = 1,2,....,p$

To note is that $r_{ik} = r_{ki}$ that's is for all i and k

Multivariate analysis

Multinomial logistic regression is often considered an attractive analysis because it doesn't assume normality, linearity, or homoscedasticity [5]. It is used to model nominal outcome variables, in which the log odds of the outcomes are modeled as a linear combination of the predictor variables. For this study, our interest was to determine factors associated with DR-TB products where we had three levels of outcome; 1) Treatment success, 2) Failing group, 3) Ongoing category. With a multinomial logistic regression, a model was fitted to the response variable categorized into three-level models; 1) Patient-related variables, (Model 1), 2) Resistance-related variables, (Model 2), 3) Institutional-related variables, (Model 3), which broadly formed our predictor variables. We predicted how the predictor variables influenced patients falling into different outcomes as the Treatment success group was classified as our base category. From this Model, we characterized the probability of a patient being in a specific outcome category by the predictor variable's influence on the outcome.

Once the Model was created, the predictor parameters were used to predict the probability of an event occurring compared to the reference category (treatment success). With this study, the interest was to know how the predictor contributed to the different types of treatment outcomes for DR-TB clients started on medication which we expressed as follows Equation 8.

$$p\left(\gamma = \frac{j}{X_1X_2},...,X_k\right) = P\left(\gamma = \frac{j}{k}\right); j = 1,2,..., J \quad (8)$$

In the multinomial case, response probabilities were represented in Equation 9 and Equation 10 as

$$P\left(\gamma = \frac{J}{X}\right) = \frac{\exp\left(\chi\beta_j\right)}{1+\sum_{h=1}^{j}\exp\left(\chi\beta_h\right)} = pj\left(X,\beta\right); j = 1,2,..., J \quad (9)$$

$$P\left(\gamma = \frac{0}{\chi}\right) = \frac{1}{1+\sum_{h=1}^{j}\exp\left(\chi,\beta_h\right)} = po\left(\chi,\beta\right) \quad (10)$$

We used maximum likelihood to estimate multinomial logit models in which the logarithm of the likelihood function that usually provides consistent and asymptotically standard estimators is expressed by Equation 11 as

$$l\left(\beta\right) = \sum_{i=1}^{n}\sum_{j=0}^{j}1\left[\gamma_1 = j\right]\log\left[p_j\left(\chi_i,\beta\right)\right] \quad (11)$$

Results

The analysis was based on a retrospective review of patients enrolled for drug-resistant tuberculosis treatment were in total, we had 33.5% female patients and 66.5% males. The enrollments of patients were from 2014 to 2019, which in 2018 had the highest number of registrations at 25.6% and in 2019 had the least amount at 7.4%. The sector where patients were being managed included public health facilities, the private sector, the prisons, and faith-based organizations. The public sector handled 83.2% of all DR-TB cases, which prisons had the least number at 1.27%. DR-TB cases were evenly distributed within all the 47 counties in Kenya, but Nairobi county had the most considerable treatment burden of 16.1%, and Wajir county had the least amount at 0.19%. In managing the T.B. cases, were from registered treatment centers and the caseload. We had 1095 health facilities following up the 2674 DR-TB cases for enrollment. The youngest patient enrolled was ten years, while the oldest was 99 years. The Resistance pattern type included Mon-Resistance, Rifampicin Resistance, Pre-XDR, Extremely Resistant (XDR), Multi-Drug Resistant (M.D.R.), and Poly Drug-Resistant TB (P.D.R.) from which the sampled patients, the M.D.R., Mono-resistant, and Rifampicin Resistant patterns accounted for 96.65% of all cases of the total resistance cases reported for the study period. XDR cases were only 0.3% of the actual cases reported. 98% of the cases enrolled were of Pulmonary type, and only 2% were Extra-pulmonary type. 58% of the patients enrolled were underweight, while the overweight and obese were 3.96%. With the age categories, patients aged between 20 years and 40 years accounted for the most considerable proportion of patients having DR-TB, who were 59% of the total enrolled patients. DR-TB's community model of care had the highest numbers at 69.2%, while the Isolation model of care had the least at 1.43%. For the registration groups, the category of newly registered patients was the highest proportion at 36.2%, while those transferred for treatment were the least at 2.92%.

Multivariate logistic analysis

For this analysis, we classified our variables into three categories made concerning (Table 1). Patient-related variables - age, weight, B.M.I., nutritional support, intensive phase regimen, continuation phase regimen, modification of both intensive and continuation phase, {*Model-1*} (Table 2)**.** Resistance related variables - registration group, the resistance pattern, LPA-Rif, LPA-H, DST-Rif, DST-H, DST-E,

Table 1: Summary of age weight height BMI.

Variable	Obs	Mean	Std. Dev.	Min	Max
WeightKgs-1	2645	49.94349	11.28567	19	107
HeightMtrs-1	2570	1.661024	0.1360411	0.6	3
BMI-1	2459	18.23869	3.61323	0.6	49.67
Age-reg-5	2637	36.22108	12.96063	10	99

This table shows how patients were enrolled in terms of weight where we have the least with 19 kgs and the highest at 107, B.M.I. least was six while the highest was 107, age the youngest was ten years old while the oldest was 99 years.

Table 2: Distribution patterns at enrollment.

	Proportion	Std. Err.	[95% Conf. Interval]
Sector-1			
-prop-1	0.0210486	0.0028087	0.0161917 0.0273219
Prisons	0.0130119	0.0022174	0.0093096 0.0181595
Private	0.1347111	0.0066803	0.1221411 0.148356
Public	0.8312285	0.0073286	0.8163667 0.8451157
Sex MF-1			
F	0.3421355	0.0092828	0.3241721 0.3605632
M	0.6578645	0.0092828	0.6394368 0.6758279
Type of TB-1			
EP	0.0187524	0.0026542	0.0141981 0.0247309
P	0.9812476	0.0026542	0.9752691 0.9858019
Registration Group 1			
FFT	0.2694221	0.0086809	0.252743 0.2867795
FRT	0.0776885	0.0052376	0.06802 0.0886005
LTFU	0.0841944	0.0054332	0.0741345 0.0954786
New	0.365863	0.0094246	0.3475874 0.3845331
O	0.0068886	0.0016184	0.004343 0.0109101
R	0.166858	0.0072954	0.1530387 0.1816576
TI	0.0290853	0.0032881	0.0232865 0.0362746
ResistancePattern-1			
MDR	0.3268274	0.0091777	0.3090921 0.3450721
-prop-17	0.2575584	0.0085562	0.2411405 0.2746895
PDR	0.0241102	0.0030013	0.0188754 0.0307514
-prop-19	0.0061232	0.0015264	0.0037534 0.0099745
RR	0.3823192	0.0095084	0.3638555 0.401129
XDR	0.0030616	0.001081	0.0015311 0.0061126
Model of Care-1			
CB	0.6923077	0.0090307	0.6743225 0.7097272
FB	0.293915	0.0089136	0.2767448 0.3116915
I	0.0137773	0.0022808	0.0099517 0.0190452

Table showing sector, gender, type of TB, registration group, resistance Pattern, and Model of care distribution for the patients enrolled.

Proportion Sector_1 Sex MF_1 Type of TB_1 Registration group_1 ResistancePattern-1 Model of Care_1

Proportion estimation; Number of obs = 2613; _prop_1: Sector_1 = Other Faith; _prop_17: Resistance Pattern_1 = Mono resistant TB; _prop_19: ResistancePattern_1 = Pre XDR

DST-Z, {*Model-2*}. (Table 3) Structurally related variables - County, health facility, Model of care and sector, {*Model 3*}. Our dependent variable in this Model was the treatment outcome which we divided into three levels of A). Treatment Success, B). Failed Treatment, C). Ongoing Medication.

Given the above predictor variables categorization, we have the following models:

Model one

We analyzed for *MODEL ONE expressed in Table 4***.** we evaluated the Model by inspecting the likelihood ratio, and the conclusion was that the Model containing the complete set of predictors represents a significant improvement in fit relative to the null Model $\left(LR\ \chi^2(16) = 212, p < 0.05\right)$ meaning at least one population slope is a non-zero, the Macfadden's, we would say that the full Model containing the predictor variables represents 1a 14.05% improvement in fit relative to the Null Model. In the *"Failure category,"* Nutrition Support, H.I.V. Status, and A.R.T. were the only significant predictors, having nutrition support with $\left(-0.271, se = 1.249, p = 0.005\right)$ which the interpretation was that or every one unit increase on nutritional support for the patient enrolled the log-odds of a client falling into the Failing category was predicted to decrease by 0.0262 *units*. The H.I.V. status predictor had $\left(b = 3.653, se = 1.249, p = 0.03\right)$ this was a positive curve of the predictor, meaning that a positive H.I.V. status was predicted to increase the log-odds of a client falling into the Failing Category by 3.653 units as compared to when their H.I.V. status was negative. The A.R.T. predictor variable was

Table 3: Distribution of resistance patterns of first-line T.B. drugs.

LPA-Rifampi	Cin	Freq
N/A	2,240	**********
Resistant	434	*********
Total	2,674	
LPA-Isoniaz		
Id	Freq.	
N/A	2,258	**********
Resistant	416	*********
Total	2,674	
R-DST	Freq.	
ND	15	
R	1,715	**********
S	426	**********
Total	2,156	
H-DST	Freq.	
ND	56	**
R	1,194	**********
S	374	**********
Total	1,624	
E-DST	Freq.	
ND	86	******
R	165	**********
S	814	**********
Total	1,065	
Z-DST	Freq.	
ND	118	*********
R	108	********
S	717	**********
Total	943	

tab1 LPA Rifampicin LPA Isoniazid RDST HDST EDST ZDST, plot

A table showing the distribution of resistance patterns of Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol. key words N.D.- not done, R - Resistant, S – Sensitive

Table 4: Model one multivariate logistic regression.

Treat_outcome_4	Coef.	Std. Err.	z	P > |z|	[95% Conf. Interval]	
Treatment - Success	(Base outcome)					
FailedSexMF-1	0.0001125	0.1782375	0.00	0.999	-0.3492265	0.3494515
M	-0.0516885	0.1471804	0.725	-0.35	-0.3401569	0.2367798
BMI-Cat3NutritionSupport-1Age_	-0.0270661	0.0096194	-2.81	0.005	-0.0459197	-0.0082124
registrn_2	0.0371438	0.1150748	0.32	0.747	-0.1883986	0.2626862
HIVStatus-1	3.652657	1.248597	2.93	0.003	1.205453	6.099861
Pos	-1.457199	0.6310172	-2.31	0.021	-2.69397	-0.2204283
ARTYN-1	0.0032203	0.0029832	1.08	0.280	-.0026266	0.0090672
Intens_phse_regimen_1cont-phse-	-0.0103776	0.0079737	-1.30	0.193	-.0260059	0.0052506
regimen-1 --cons	0.0467406	0.8357014	0.06	0.955	-1.591204	1.684685
Ongoing-Meds						
SexMF-1	0.2482052	0.2896057	0.86	0.391	-0.3194115	0.8158219
M	-0.0181541	0.2245291	-0.08	0.936	-0.458223	0.4219148
BMI-Cat3 NutritionSupport-1 Age-	0.0121478	0.0147266	0.82	0.409	-0.0167158	0.0410114
registrn-2	-0.1271593	0.1805295	-0.70	0.481	-0.4809906	0.2266719
HIVStatus-1	1.711165	2.626775	0.65	0.515	-3.43722	6.859551
Pos	-0.7891827	1.325283	-0.60	0.552	-3.38669	1.808325
ARTYN-1	-0.0261607	0.0030932	-8.46	0.000	-0.0322233	-0.0200981
Intens-phse-regimen-1 cont-phse-	0.0498746	0.0104255	4.78	0.000	0.0294409	0.0703082
regimen-1-cons	0.6121316	1.507744	0.41	0.685	-2.342992	3.567255

Table showing Multinomial logistic regression of drug-resistant tuberculosis treatment outcome as treatment success as the base outcome and ongoing treatment and fail on treatment as the comparative levels mlogit Treat_outcome_4 i.SexMF_1 BMI_Cat3 NutritionSupport_1Age_ registrn_2 i. HIVStatus_1 ARTYN_1 Intens_phse_regimen_1 cont_phse_regimen_ > 1

Iteration 0:log likelihood = -755.61234; Iteration 1: log likelihood = -695.87899;Iteration 2: log likelihood = -654.42391; Iteration 3: log likelihood = -649.4599; Iteration 4: log likelihood = -649.44322; Iteration 5: log likelihood = -649.44322. Multinomial logistic regression: Number of obs = 927; LR chi^2 (16) = 212.34; Prob > chi^2 = 0.0000; Log likelihood = -649.44322; Pseudo R2 = 0.1405

significant, and we had $(b = -1.457, se = 0.631, p = 0.21)$, this interpretation was that by starting a client who was H.I.V. positive on treatment, their log-odds of falling in Failing Category would decrease by 1.457 units as compared to if hey had not been started on A.R.T. medications. With the *ongoing treatment level*, we found the intensive phase regimen given and continuation phase regimen given to be only variables significant for this level, wherewith intensive phase regimen, $(b = -0.0263, se = 0.003, p < 0.001)$ with the type of intensive phase regimen given then a client was predicted to have a log-odds of 0.0263 units decrease for falling on the Ongoing Medication category, and with the continuation phase regimen predictor we had $(b = 0.0498, se = 0.0104, p < 0.001)$ interpretation was that for the continuation phase regimen type given would increase the log odds of one being in the Ongoing medication level by 0.0498 units *Model 1* (Table 4).

Model two

Model two, expressed in Table 5. An evaluation was done by a log-likelihood test where this Model contained the complete set of predictors representing a significant improvement in fit relative to the Null Model, $(LR\ \chi^2(20) = 92.46, p < 0.001)$ which indicated that at least one population slope was non-zero. With Macfadden's, we would say that the full Model containing the predictor variable represented a 5.54% improvement in fit relative to the Null Model. We run the predictor variables for the Model, with our base level being the treatment success. The Failure group and Ongoing group were levels of comparison wherein the failure group we had on the Gene-Expert result and LPA-Rif were the only significant variable among this level, which the Gene-expert had $(b = -0.844, se = 0.1093, p = 0.009)$ from this we would interpret as having Gene-expert results would decrease the log-odds of one falling into "Failing category" of treatment outcome with 0.2844 units with Line Probe Assay (L.P.A.) Rifampicin, we got $(b = 0.9054, se = 0.2694, p = 0.001)$ which, in essence, that patients who had a positive LPA-Rif had an increased log-odd of 0.9054 *units* of falling into "Failing category" compared who had negative LPA-Rif. From the category that had been ongoing on treatment, we had resistance Pattern, Gene-expert, LPA-Rif, Rifampicin-Drug Sensitivity test (RDST), Isoniazid-DST(HDST), Ethambutol DST(EDST), which were significant. With Resistance Pattern, we had $(b = 0.2518, se = 0.0653, p < 0.001)$ whereby into the interpretation that for the type of resistance pattern a patient had, it would increase the log-odds of one being on medication by 0.2518 *units*. The Gene-expert had $(b = -0.184, se = 0.0763, p = 0.013)$ The results were interpreted as decreasing the log-odds of one to an ongoing patient by 0.1894 *units* if the results had been availed, compared to if the gene-expert had not been done, LPA-Rif we had $(b = 0.5874, se = 0.2161, p = 0.001)$. By interpretation, this increased the log-odds of one falling into the ongoing category by 0.5297 *units* if the results were positive compared to when the results were not Positive. With RDST, we had $(b = 0.7091, se = 0.2122, p = 0.001)$

Table 5: Model two multivariate logistic regression.

Treat_outcome_4	Coef.	Std. Err.	z	P > |z|	[95% Conf. Interval]
Treatment - Success	(Base outcome)				
Failed TypeofTB-1	-1.825038	1.357333	-1.34	0.179	-4.485361 0.8352848
Registrationgroup-1	-0.0841873	0.0568274	-1.48	0.138	-0.195567 0.0271925
ResistancePattern-1	0.0930298	0.0853065	1.09	0.275	-0.0741678 0.2602275
GeneXpert-1	-0.2844209	0.1093212	-2.60	0.009	-0.4986865 -0.0701552
LPA-Rif-1	0.9053925	0.2693812	3.36	0.001	0.3774151 1.43337
LPA-H-1	-0.1876877	0.3089199	-0.61	0.543	-0.7931595 0.4177842
RDST-1	-0.1571005	0.3053129	-0.51	0.607	-0.7555028 0.4413017
HDST-1	-0.538345	0.316283	-1.70	0.089	-1.158248 0.0815582
EDST-1	0.3540237	0.3070321	1.15	0.249	-0.2477482 0.9557955
ZDST-	-0.2392338	0.2403558	-1.00	0.320	-0.7103225 0.2318549
-Cons	3.647367	2.85041	1.28	0.201	-1.939335 9.234068
Ongoing_Meds					
TypeofTB-1	-0.6064315	1.498924	-0.40	0.686	-3.544268 2.331405
Registrationgroup-1	-0.0125487	0.0414727	-0.30	0.762	-0.0938337 0.0687363
ResistancePattern-1	0.2517586	0.0652931	3.86	0.000	0.1237865 0.3797308
GeneXpert-1	-0.1894462	0.0762573	-2.48	0.013	-0.3389077 -0.0399847
LPA-Rif-1	0.5873974	0.216092	2.72	0.007	0.1638648 1.01093
LPA-H-1	0.3690152	0.2081382	1.77	0.076	-0.0389283 0.7769587
RDST-1	0.7091217	0.2122312	3.34	0.001	0.2931561 1.125087
HDST-1	-0.5297356	0.2211231	-2.40	0.017	-0.9631289 -0.0963423
EDST-1	0.1111455	0.2092462	0.53	0.595	-0.2989696 0.5212606
ZDST-	-0.3336719	0.1737019	-1.92	0.055	-0.6741214 0.0067777
-Cons	-0.1749003	3.064384	-0.06	0.954	-6.180983 5.831182

mlogit Treat_outcome_4 TypeofTB_1 Registrationgroup_1 ResistancePattern_1 GeneXpert_1 LPA_Rif_1 LPA_H_1 RDST_1 HDST_1 EDST_1 ZDST_1

Iteration 0:log likelihood = -834.14576; Iteration 1: log likelihood = -789.20785; Iteration 2: log likelihood = -787.94823; Iteration 3: log likelihood = -787.91722; Iteration 4: log likelihood = -787.91714; Iteration 5: log likelihood = -787.91714

Multinomial logistic regression Number of obs =828; LR $chi^2(20)$ =92.46; Prob > chi^2 = 0.0000; Log likelihood = -787.91714; Pseudo R_2 = 0.0554

. This interpretation translated to a positive RDST would increase the log-odds of a patient being an "ongoing case of medication" compared to if the RDST was negative. For the HDST, we had $(b = -0.5297, se = 0.2211, p = 0.017)$ which translated to a positive HDST test would reduce log-odds of one being on the 'ongoing medication "category by 0.5297 *units Model 2:* (Table 5).

Model three

Analysis was done for *MODEL THREE* and expressed in *Table 6*: For the model assessment, we did the likelihood ratio chi-square test comparing the Model's fit with the complete set of predictors with the Null Model, wherein our Model was significant. Based on the L.R. test, we can say that the Model containing the complete set of predictors represents a significant improvement in the fit relative to a Null Model $(LR\ \chi^2(10) = 57.46, p < 0.001)$ meaning at least one population slope is not zero. With Macfadden's $(psedo\ R^2)$. We can report that the full Model containing our predictor represents a 1.04% improvement in fit relative to the Null. With the "Failing category," we had the Quarter of the year, County, and Model of care is significant. The Quarter had $(b = 0.1169, se = 0.4514, p = 0.01)$ which translated to every unit increase in the Quarter of year the year log-odds of a patient falling into the "Failing category" increased by 0.1169 *units*. The County predictor variable had $(b = 0.0170, se = 0.0044, p < 0.01)$ which was interpreted as for every unit change in the county variable the log-odds of a patient falling on "*Failing Category*" were increased by 0.017 *units* and the Model of care had $(b = 0.2584, se = 0.1001, p = 0.01)$ which additionally translated for this Model that for every unit of change in the Model of care the log-odds of falling in this category of "Failing Treatment' increased by 0.2584 *units*. The ongoing treatment level had only County as the significant variable that $(b = 0.0206, se = 0.0038, p < 0.01)$ meaning for a unit change in the county level the client enrolled had a log-odds increasing by 0.0206 *units* in falling to 'ongoing treatment category ***Model 3:*** (Table 6).

Discussion

Multidrug-resistant tuberculosis (MDR-TB) requires long-term treatment, has a high fatality rate, and constitutes a global threat. Earlier detection of treatment failure is needed

Table 6: Multivariate logistic regression.

Treat_outcome_4	Coef.	Std. Err.	z	P > |z|	[95% Conf. Interval]
Treatment - Success	(Base outcome)				
Failed					
Quarter					
2	0.0550254	0.1410267	0.39	0.696	-0.2213819 0.3314327
3	0.2671141	0.1473716	1.81	0.070	-0.021729 0.5559572
4	0.3475711	0.1412895	2.46	0.014	0.0706488 0.6244934
County_1 HealthFacility_1	0.0141287	0.0044185	0.001	3.20	0.0054687 0.0227888--
	0.0000922	0.0001701	0.54	0.588	0.0002412 0.0004255
Sector_1					
Prisons	0.6115028	0.6218228	0.98	0.325	-0.6072474 1.830253
Private Public	0.0671998	0.432512	0.16	0.877	-0.7805082 0.9149079
	0.3733351	0.409629	0.91	0.362	-0.4295229 1.176193
ModelOfCare_1					
FB	0.0255268	0.1145843	0.22	0.824	-0.1990542 0.2501078
I	2.332626	0.5016934	4.65	0.000	1.349325 3.315927
-cons	-1.748054	0.4418323	-3.96	0.000	-2.61403 -0.8820788
Ongoing_Meds					
Quarter					
2	-0.1591966	0.1238194	-1.29	0.199	-0.4018781 0.0834848
3	0.3783635	0.1238157	3.06	0.002	0.1356891 0.6210379
4	-0.154734	0.1313156	-1.18	0.239	-0.412108 0.1026399
County_1 HealthFacility_1	0.0182387	0.0039221	4.65	0.000	0.0105515 0.0259258
	0.0000865	0.0001522	0.57	0.570	-0.0002117 0.0003848
Sector_1					
Prisons	0.2758945	0.5009495	0.55	0.582	-0.7059485 1.257737
Private Public	-0.8135085	0.3223696	-2.52	0.012	-1.445341 -0.1816757
	-0.2305065	0.2934007	-0.79	0.432	-0.8055612 0.3445483
Model of Care_1					
FB	-0.1277871	0.1037235	-1.23	0.218	-0.3310814 0.0755072
I	0.9465254	0.5563221	1.70	0.089	-0.143846 2.036897
-cons	-0.662439	0.3269804	-2.03	0.043	-1.303309 -0.0215692

mlogit Treat_outcome_4 i.Quarter County_1 HealthFacility_1 i.Sector_1 i.ModelOfCare_1

Iteration 0:log likelihood = -2753.7174 ; Iteration 1:log likelihood = -2693.7795; Iteration 2:log likelihood = -2691.7733; Iteration 3: log likelihood = -2691.6071; Iteration 4:log likelihood = -2691.6069; Iteration 5:log likelihood = -2691.6069

Multinomial logistic regression: Number of obs = 2648; LR $chi^2(20)$ = 124.22; Prob > chi^2 = 0.0000; Log likelihood = -2691.6069; Pseudo R_2 = 0.0226

to predict therapeutic efficacy [6]. For this study, we focused on drug-resistant tuberculosis treatment outcomes in Kenya and the associated factors that could have influenced the enrolled clients bearing in the devolved healthcare system and the centralization of tuberculosis management. We did our study from 2014 to 2019, serving as the enrollment period and a two-year follow-up period. Of the enrolled patients, males represented the most considerable number, with up to 65% of the total patients being males and females carrying only 35%, showing the magnitude of drug-resistant tuberculosis among the male patients.

From the county presentation, we had a uniform representation of all the counties having treatment centers for drug-resistant tuberculosis. We had 1095 health facilities, including the private sector, faith-based organizations, and the public sector. We can see that the government has tried to bring all sectors to manage the tuberculosis burden even though the public sector had 835 patients. They had DR-TB a significant step in the right direction in having inclusivity in the DTR-TB management. The distribution of the treatment center was more within the urban centers, with Nairobi County carrying the most significant number at 16% and Wajir County with the list at 0.17%. Interestingly, Garissa County has 5% of the total population, but the adjacent counties had insignificant numbers of less than 1%, and they are geographically correlated.

The registration groups of patients enrolled for treatment had the New client topped the list with 36 %, followed by Lost to Follow up client and then Failure to the first-line category. All these three cumulatively had 835 of the total registrations. With this, it meant we had three levels of community infection spread; from the new clients, meaning they had not been diagnosed and were unaware spreading to the community in which they live. Secondly, the clients who had gotten lost to follow up, meaning these are clients knowingly spreading the disease to the community. Still, our tracking system is wanting, given that we cannot track them.

With resistance patterns for enrolled patients, we registered six types of patter, including Mono-resistance, Rifampicin resistance, Pre-XDR, XDR, M.D.R., and Others. For patients enrolled, we had Mono-Resistance, M.D.R., and Rifampicin resistance cumulatively totaling 95% of all the registered cases, meaning for a positive Gene-expert that was recorded, we have a 0.95 probability that we were dealing with the three types of resistant tuberculosis.

Age on registration; we classified the patients below 20 years, between 20 to 40 years, 40 to 50 years, and those above 50 years. With these patients enrolled who had the biggest category of patients aged between 20 to 40 years of age, bearing in mind that this is the most reproductive age group and most mobile hence propagating the spread of drug-resistant tuberculosis among the community population. When they become sick, results are unproductiveness, meaning their dependant suffer financial constraints due to the disease; Households affected by T.B. incurred severe socio-economic consequences [7].

The country has come a long way in enhancing T.B. diagnosis through equitable distribution of diagnostic tools like expanded use of X-ray, availability of gene-expert machines, and provision of microscopy for diagnosis and follow-up for T.B. patients. Further, initiatives are still in place in bridging the gap of 40% missing T.B. cases reported by the T.B. prevalence survey of 2015-2016 [8]. With the treatment outcomes encountered in patients enrolled for DR-TB treatment, we classified them to treat successfully, Failed on treatment, and Ongoing on medication. For the "failing group category," enhancing Nutritional supplementation, availing of Gene-expert results, starting H.I.V. Positive clients on treatment were the major factors that helped a client not to be on the failing category of treatment outcome and for the elements that were contributing patients who got enrolled for the DR-TB medication to be on the failing class were; Positive H.I.V. status, LPA-Rif positive, enrollment in Quarter four of the year and being an isolation patient. In the Ongoing category of patients, we had factors that positively and negatively influenced patients to, or not to be on this group, availing Gene-Expert results, doing Isoniazid DST, and being on private sector follow up helped a client to have completed their medication. The factors that were negatively affecting clients to have successful treatment and be ongoing on medication were; the intensive regimen given, continuation phase regimen combination given, type of resistance pattern that a patient had on enrollment, positive LPA-Rif, and the County which a patient originated.

Conclusion

DR TB in Kenya is based on a systematic algorithm that identifies patients at high risk of developing DRTB compared to the general population who present with signs or symptoms of T.B. They include all previously treated T.B. patients, D.R. T.B. contacts, health care workers, patients who develop T.B. while on isoniazid preventive therapy (I.P.T.), refugees, prisoners, and smear positives at month two of treatment with first-line drugs [9]. From this, we can point out that in our case system, we have three prevalent resistant types contributing to the burden of DR-TB in Kenya; Mono-resistance, RR, and M.D.R. With the limited capacity to test and avail the results to various treatment centers in Kenya, we subconsciously lead patients to delay treatment and then spread to the community. With the finding of this study, we propose a holding regimen for all patients who get a positive Gene-expert result as the patient waits for a drug sensitivity test and as a result of the prevalent resistance patterns in circulation. If the DST results come from the contrary, then we can do the modification of the treatment. With this, we are sure there is a 0.95 probability that our patients are fully covered. The NTLP should continue keeping the profile of the cultured sputum DST to be able to monitor trends of resistance patterns for patients being put on DR-TB medications so that appropriate actions can be taken when necessary.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

Authors' contributions	MD	IO	AK	HK
Research concept and design	√	√	√	√
Collection and assembly of data	√	--	--	--
Data analysis and interpretation	√	--	--	--
Writing the article	√	--	--	--
Critical revision of the article	√	√	√	--
Final approval of the article	√	√	√	√
Statistical analysis	√	--	--	--

Acknowledgments

We acknowledge the Kenya National Tuberculosis and Leprosy Program for their assistance in the provision of data.

References

1. Onuka O, Ahukanna J, Okebaram C, et al. (2017) A Case study of multi drug-resistant tuberculosis (mdr-tb), hiv and diabetes mellitus (dm) comorbidity: Triple pathology; challenges and prospects. Adv Infect Dis 7: 70-79.
2. Daftary A, Mondal S, Zelnick J, et al. (2021) Dynamic needs and challenges of people with drug-resistant tuberculosis and HIV in South Africa: A qualitative study. Lancet Glob Health 9: e479-e488.
3. Guide AS, Clinicians for Drug-resistant tuberculosis.
4. Health MOF (2020) Treatment of drug resistant tuberculosis in kenya. Introduction of the injectable free regimens.
5. Kwak C, Clayton-Matthews A (2002) Multinomial logistic regression. Nurs Res 51: 404-410.
6. Lv L, Li T, Xu K, et al. (2018) Sputum bacteriology conversion and treatment outcome of patients with multidrug-resistant tuberculosis. Infect Drug Resist 11: 147-154.
7. Eunice M (2017) The first national tuberculosis patient cost survey in Kenya.
8. Kimani E, Muhula S, Kiptai T, et al. (2021) Factors influencing TB treatment interruption and treatment outcomes among patients in Kiambu County, 2016-2019. PLoS One 16: e0248820.
9. Magomere RS, Kosgei RJ, Kamene M, et al. (2017) Treatment outcomes for drug resistant tuberculosis among children below 15 years in Kenya, 2010-2016. East Afr Med J 94: S100-S109.

DOI: 10.36959/317/682