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Delay to Treatment Initiation among Rifampicin Resistant Tuberculosis Patients in Kenya

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Abstract

Drug-resistant tuberculosis surveillance attempts to detect and treat drug-resistant tuberculosis as early as possible in order to avoid transmission, illness, and mortality among people who are afflicted. In Kenya, the delay in starting RR TB treatment has not been established, and its relationship to treatment outcomes is unknown. To investigate the relationship between delayed RR TB therapy commencement and treatment results in Kenyan patients enrolled between January 2010 and June 2013. A retrospective cohort review of 208 randomly chosen RR TB patients treated between January 2010 and June 2013 was conducted. Delay was defined as the interval in days between sample collection and treatment beginning that was on the right side of the median. Logistic regression was used to determine the relationship between the delay in starting RR TB treatment and treatment outcomes, as well as the factors related with the delay. The male to female ratio in the 208 cases was 1.7:1. The youngest and oldest were 2 and 66 years old, respectively. The average age at registration was 34.48 years old [95% CI 32.7,36.3] and the average weight was 50kg [95% CI: 47.73,50.94]. 26.92% (56) were HIV +, and 95% (53) were on ART. 64% Culture and traditional DST were used to diagnose 65% of the patients, while GeneXpert was used to diagnose 35%. The average time to therapy (delay) was 99 days, with a range of 0 to 599 days. The treatment was 82% successful (59% cured, 23% completed). Unfavorable outcomes accounted for 18% of all outcomes. As indicated by X2 = (0.1858), p =0.666, which is more than 0.05, there was no significant difference between delayed and undelayed treatment outcomes. Male patients were 0.03048 times more likely to have an unfavorable outcome than female patients, and patients from the North Eastern region were 23.46 times more likely to have an unfavorable outcome than patients from the Central region. According to a single study, using culture and DST for RR TB diagnosis was substantially linked with delaying treatment beginning and starting treatment in the second quarter of the year (P of 0.000 and 0.005 respectively). Delay in starting treatment is not connected with treatment results in RR TB patients. When compared to culture and DST, GeneXpert considerably lowers time to therapy initiation. Early diagnostic and treatment efforts should be increased to prevent TB transmission and morbidity.

Keywords: *Delay to treatment, Rifampicin, Resistant, Tuberculosis, Patients*

1.0 Introduction

Surveillance of drug resistance tuberculosis is a pillar of Tuberculosis control program as a measure of its performance. It assists countries to make evidence based policies. Surveillance should be aimed at increasing early drug resistant TB detection and hence early treatment to prevent the transmission of a resistant strain in the community (WHO, 2013). Tuberculosis has remained a major public health concern globally with a high mortality rate especially in countries with high HIV burden. HIV is a known driver of the TB burden. Although new HIV infections are coming down (UNAIDS 2013), Sub Saharan Africa has the highest burden of HIV globally leading to higher burden of TB and difficulties in TB control. Kenya is amongthe highTB, HIV, and MDR TBburden countries with a MDR TB prevalence of 0.7% among new TB cases and 2.1% among previously treated TB cases (World Health Organization 2016).The Kenya MDR TB surveillance is carried out using GeneXpert, LPA, culture and DST. Over 85% of previously treated TB cases are tested annually for drug resistance tuberculosis and approximately, 7% of those who have culture results are diagnosed with MDR TB. Drug resistance TB surveillance has targeted the high-risk populations in Kenya. All risk groups should be tested for drug resistance by GeneXpert and then by culture and DST. The MDR TB surveillance has however been affected negatively by inadequate and low capacity laboratory network. There are mainly 3 culture and DST laboratories in Kenya but one of these caters only for the refugee population, leaving 2 laboratories for the other 44 million Kenyans. According to WHO, the ratio of culture laboratories to the population should be 1:10 million populations. The turnaround time for the culture and DST results is however very long. In 2012, Kenya adopted the use of GeneXpert and there are currently over 126 machines placed in various parts of the country. The burden of other resistance patterns other than RR TB such as monoresistant and poly drug resistance has been low in Kenya as shown in the diagram below.

The MDR TB treatment program, in Kenya, started in 2006 in the private sector and in 2008 in public sector. At the time, the recommendation was that MDR TB treatment should be carried out in isolation facilities. There was none in Kenya then. This led to delays in diagnosis and further delays in access to treatment for those on treatment as patients were put on long waiting lists while waiting for drugs. In an effort to achieve universal access to MDR TB management, Kenya adopted two models of care based on the patient preferences, severity of disease or side effects, convenience and access to quality of care. These included isolation model, facility based ambulatory and community based ambulatory care (DLTLD 2012). Since then, all patients found to have drug resistance are treated in the nearest facility or at home. This meant that, any treatment centre would become an MDR TB treatment site once a TB patient in the facility was found to have MDR TB. Kenya has treated over 1700 MDR TB cases since 2006 to date with good outcomes. Even with such good progress, there are challenges to access to care apart from the physical distance to treatment leading to some undefined delay. The MDR TB HIV co-infection rate in all treated patients is 25%,(DLTLD 2013). In 2011, the treatment success rate was 68% (NTLD-P 2015). This was lower than the 86% in 2009 and 81% in 2010. Despite all these efforts and success, the delay to RR TB treatment initiation in Kenya has been undefined and its association to treatment outcomes remain unknown. This research therefore sought to unravel this finding.

1.1 Statement of the problem

Rifampicin resistance is resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes any resistance to rifampicin, whether Monoresistance, multidrug resistance, Polydrug resistance or extensive drug resistance.(WHO 2013) Rifampicin is the most potent TB drug and loss of this drug in TB management reduces treatment option for the patients and the patients have to be treated for longer period with injectables and other less potent drugs. Surveillance of Rifampicin resistance with early treatment is important. Time to treatment from sample collection is part of the WHO indicators (delay to diagnosis and delay to treatment) since 2011. This indicator has not been measured. In addition, the relationship between this delay and treatment outcomes is unknown. In Kenya, a midterm review of the Tuberculosis program implementation of the 2011-2015 strategic plan identified that there exists a delay in treatment initiation among MDR and RR TB patients. The main cause of poor outcomes is also not known and delay could be a cause.

The Emergency WHO 2008 guidelines state that if drug resistant TB cases are not diagnosed on time, this leads to increase in morbidity, mortality, drug resistance amplification and transmission in the community. Diagnosis of drug resistant Tuberculosis has been a big challenge due to the long turnaround time of results, the high cost of diagnostic tools, diagnosis processes such as sample collection, special sample collection bottles, and the high cost of the level 3 bio safety laboratories. The Xpert MTB RIF (GeneXpert) is a DNA based tests that is used for the diagnosis of TB and Rifampicin resistance in a single test and has a turnaround time of 2 hours. However, it is not known if in practice this translates to a reduction in the duration to treatment initiation from the time the sample was collected. The conventional diagnostic methods have long turnaround time and those with a shorter one like the GeneXpert are not accessible to all. There is still no documented evidence of duration to treatment in MDR TB care and the association between duration to treatment and outcome of treatment is unknown in Kenya. To design better drug resistant control policies and interventions, there was need to measure the delay to treatment initiation and how this delay would affect treatment outcomes.

1.2 Objective

To determine association of delay in RR TB treatment initiation and treatment outcomes among patients enrolled on treatment between January 2010 and June 2013 in Kenya

2.0 Methodology

A retrospective cohort study was carried out on Rifampicin resistant TB patients initiated on treatment between January 2010 to June 2013 in which time to treatment and their outcomes were reviewed. The study was carried out in Kenya, a country in East Africa. The study population was the RR TB patients enrolled on treatment in Kenya between January 2010 and June 2013 in Kenya. RR TB in this study included a patient with any resistance to rifampicin, whether Monoresistance, multidrug resistance, Polydrug resistance or extensive drug resistance. All RR TB patients registered on the national drug resistant TB register who were enrolled on treatment during the period of study and met the selection criteria were extracted from the electronic system and exported into an excel file to form a sampling frame. 208 patients were randomly sampled.DRTB cases reported in years 2010, 2011, 2012 and 2013 were used in this study. Case based data collection by NTP is done using TIBU, the national electronic web based system. This case based data is stored in the national database. Individuals who present to the health facility with symptoms

of TB are either clinically or bacteriologically diagnosed. To check resistance, tests like GeneXpert, LPA and culture are performed. Thereafter, they are followed up for a period of up to 36 months. At the facility level, the clinicians who see patients are provided with DRTB facility registers (hard copy). The structure of NTP is that at the Sub County level, there are Sub County TB and Leprosy Coordinators (SCTLCs) who have been provided with tablets. The SCTLCs regularly visit treatment facilities within their Sub Counties transcribe patient details from the TB facility register to the TIBU system. The case based data is then transmitted directly to the National database via the mobile network. Data was abstracted using data abstraction tool from TIBU and Lab Management Information System (LMIS) into an Excel file. Data analysis was done using STATA.

3.0 Findings and Discussions

A total of 208 RR/MDR TB (Rifampicin Resistant/Multi drug resistant TB) patients who met the inclusion criteria were enrolled into the study. 92 % of the patients had MDR while 6.6% and 1.4% were RRTB and PRE-XDR TB respectively.65% of the patients were diagnosed based on culture and conventional DST while 35% has been subjected to GeneXpert. Sixty-three percent (63%) (n=130) of the participants were male, while 37% (n=78) were female with a male to female ratio of 1.7:1. The youngest was 2 years old and the oldest at 66 years. The average age on registration was 34.48 years of age [95% CI 32.7,36.3]: Their average weight was 50kgs [95% CI: 47.73,50.94] (table 1).

Table 1: Inclusion criteria

	N	Min	Max	Median	Mean	Std. Err	95% Confidence Interval	
							Lower	Upper
Age	208	2	66	33	34.48	13	32.7	36.3
Weight Kgs	185	15	95	50	49.33	.81	47.73	50.94
Height Metres	177	1	1.88	1.65	1.64	0.009	1.62	1.66
BMI	175	10.16	36.65	18.03	18.03	3.34	17.61	18.60
Date to Treatment	208	0	599	66	98.79	115.82	45.46	86.53

The males were more in all age groups with most of the participants aged between 15 and 54 which accounts for 88% of the total participants. The highest burden was noted within the productive age of 25 to 34 age group at 33%. Children who were defined as those less than 14 years, accounted for 4 percent and the elderly, over 66 years old accounting for 1% (figure 1).

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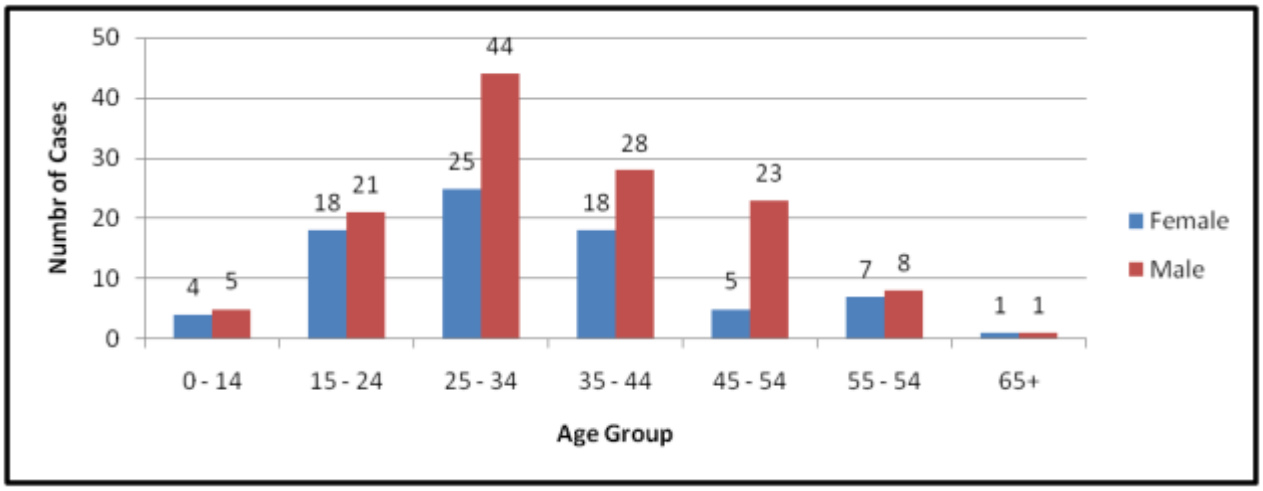

Figure 1: Number of cases and age group of individuals

The minimum weight was 15kgs while the maximum was 95kgs.The patients' average height was 1.64 meters with their BMI being 18.03. 21.15% and 28.37% were found to have severe and moderate malnutrition accounting for a total of 58% participants with a BMI of less than 18.5. Participants with normal and a BMI above 24 (upper normal) accounted for 3%. 73.08% (152) of the patients were HIV negative, while 26.92% (56) were HIV positive indicatinga TB/HIV coinfection rate of 26.92%.Of the HIV positive, 95% (53) of the patients were undergoing antiretroviral therapy, though 5% (3) were not.The treatment success rate was 82% of whom 59% were cured while 23% has completed treatment. The unfavourable outcomes, therefore accounted for 18% of the patient enrolled in the study.

Delay was defined as the time from the time sample was collected to the time patient was initiated on treatment. The median was used to determine delay with those on the right of the median being delay. The median time to treatment (delay) was 66 days, with a mean of 99 days to treatment and a range of 0 to 599 days. The 1st percentile was at 14.5 days and the 3rd one was at 131days. The time to treatment (delay) is skewed to the right, which means that the majority of the patients diagnosed were started on treatment early. However, it is important to note that there are still patients who take long to be initiated on treatment. For those that had delayed treatment, 83 (81.4%) of them had a favourable outcome while on the other hand 19(18.6%) of them had an unfavourable outcome. However, for those with no delay, 88 (79%) of them had a favourable outcome while 18(21%) had an unfavourable outcome. There was, however, no significant differences between delay or no delay as it relates to treatment outcomes as evidenced by X^2 = (0.1858), p =0.666 which is > 0.05 between delay to treatment and treatment outcome.

Delayin quartiles and treatment outcomes

Further analysis on the influence of delay on the outcomes was carried out by dividing the delay into quartiles. 19.2% of thosewithin the first quartile (delay less than 14.5 days), had a favourable outcome while 5.8% had an unfavourable outcome. Those in the 2nd quartile, (delay of between 14.5 and 66 days)21.2% had a favourable outcome and 3.8% had an unfavourable outcome. Moreover, in the 3rdquartile (delay of between 66 and 131 days), 22.2% had a favourable outcome while 2.9% had an unfavourable outcome. Finally, for patients in the 4th quartile (delay of over 131 days), 19.7% had a favourable outcome while 5.3% had an unfavourable outcome. Seventy five percent (75%) of the patients were initiated on treatment by the 75th percentile. The P value

is not less than 0.05 and hence there is no statistically significant difference in treatment outcome among those who start treatment early and those who start late.

Association of other variables and treatment outcome

Delay was not found to be associated with treatment outcome. Further analysis using logistic regression was carried out to look for variables that would be associated with unfavourable treatment outcome.

HIV status

From the results, 50.1% (125) of those that were HIV negative had a favourable outcome while 27 (19.98%) of them had an unfavourable outcome. The number of those that were HIV positive were lower. Only 22.1% (46) of those that were HIV positive had a favourable outcome while 4.8% (10) of them had an unfavourable outcome. There was no significant association between the outcome and HIV test as shown by $X^2 = (0.0002)$, $p< 0.05$.

Association between outcome and ART

Out of the 56 HIV positive patients, 53 patients (94.6%) were put on ART. Of these, 44 (83%) had a favourable outcome. For those that were not undergoing ART, 2 of them had a favourable outcome whereas 1 had an unfavourable outcome. The relationship between ART and outcome was not statistically significant $X^2 = (0.237)$, $p< 0.05$.

Factors associated with unfavourable outcomes among Rifampicin resistant TB cases

The table below illustrates the factors associated with unfavourable outcomes among Rifampicin resistant TB cases. The likelihood ratio chi-square of 46.29 with a p-value of 0.0085 tells us that our model as a whole fits significantly better than an empty model (that is, a model with no predictors).

Coefficients (log odds), their standard errors, the z-statistic, associated p-values, the 95% confidence interval of the coefficients and the odds of the coefficients (exp (B) would be observed. Both region and sex, indicator variables were statistically significant. The logistic regression coefficients gave the change in the log odds of the outcome for a one unit increase in the predictor variable (table 2).

i. From the results, the male patient was 0.0427 times more likely to have bad outcome when compared to a female patient.

ii. Patients from North Eastern region were 4.5 times more likely to have unfavourable outcomes than patients from the central region.

Age, HIV status, Food Support, Type of patient, time to treatment and BMI category were all found not to be statistically significant.

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Table 2: Factors associated with unfavourable outcomes among Rifampicin resistant TB cases

Variable	Categorical	B	Std. Dev.	Z	P>z	[95% CI]		EXP(B)
Type of patient	FFT	REF						
	FRT	0.2809	1.0085	0.2800	0.7810	0.1835	9.5598	1.3243
	LTFU	-1.4668	1.1205	-1.3100	0.1910	0.0257	2.0740	0.2307
	Missing	-1.0124	1.2056	-0.8400	0.4010	0.0342	3.8593	0.3633
	New	1.5518	1.1972	1.3000	0.1950	0.4517	49.3216	4.7202
	Relapse	-0.2123	0.6723	-0.3200	0.7520	0.2165	3.0201	0.8087
Time to treatment	No delay	REF						
	Delay	-0.0758	0.5354	-0.1400	0.8870	0.3246	2.6472	0.9270
Region	Central	REF						
	Coast	-0.5450	1.0189	-0.5300	0.5930	0.0787	4.2718	0.5798
	Eastern	-1.1603	0.9983	-1.1600	0.2450	0.0443	2.2175	0.3134
	Nairobi	1.2023	1.0847	1.1100	0.2680	0.3971	27.8915	3.3279
	North Eastern	3.1823	1.1948	2.6600	0.0080	2.3175	250.6524	24.1018
	Nyanza	-0.0998	1.2690	-0.0800	0.9370	0.0752	10.8863	0.9050
	Western	0.1657	1.3719	0.1200	0.9040	0.0802	17.3657	1.1802
Sex	Female	REF						
	Male	-1.1915	0.5590	-2.1300	0.0330	0.1016	0.9086	0.3038
Food Support	No	REF						
	Yes	-0.0764	0.5526	-0.1400	0.8900	0.3136	2.7366	0.9264
BMI		0.0274	0.0224	1.2200	0.2210	1.0000	1.0000	1.0277
Quarter	1	REF						
	2	1.1337	0.6633	1.7100	0.0870	0.5525	9.1418	3.1072
	3	0.8098	0.7159	1.1300	0.2580	0.4897	14.2353	2.2475
	4	0.9709	0.8596	1.1300	0.2590	.4896	14.2353	2.6403
Age		-0.0306	0.1045	-0.2900	0.7700	.7903	1.1904	0.9699
HIV	Negative	REF						
	Positive	-0.0002	0.5871	0.0000	1.0000	.31638	3.1595	0.9998
Age group	0 – 14	REF				0.0044	8.2852	1.0000
	15 – 24	-1.6507	1.9210	-0.8600	0.3900	0.0041	95.0716	0.1919
	25 – 34	-0.4654	2.5613	-0.1800	0.8560	0.0007	329.6970	0.6279
	35 – 44	-0.7284	3.3300	-0.2200	0.8270	0.0001	3022.1295	0.4827
	45 – 54	-0.6608	4.4259	-0.1500	0.8810	0.0000	66279.1071	0.5164
	55 – 54	-0.1442	5.7378	-0.0300	0.9800	1.0000	1.0000	0.8657
BMI Category	Moderate	REF						
	Normal	0.2593	1.2342	0.2100	0.8340	0.0010	3.4465	1.2960
	Obese	-2.8225	2.0714	-1.3600	0.1730	0.0046	56.7361	0.0595
	Overweight	-0.6687	2.4016	-0.2800	0.7810	0.4080	63.2669	0.5124
	Severe	1.6255	1.2867	1.2600	0.2060	1.0000	1.0000	5.0808
Type of Diagnosis	GeneXpert	REF						
	culture & DST	-0.1343	0.5994	-0.2200	0.8230	0.0200	303.4928	0.8744
Constant		0.9006	2.4565	0.3700	0.7140	1.0000	1.0000	2.4611

Likelihood Ratio (LR) = 54.96 and chi2 Prob> chi2 = 0.0036

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Further analysis of factors associated with delay to treatment initiation was also carried out. Both univariate and multiple logistic regression analysis showed that patients initiated on treatment in the second quarter of the year (April, May, June), were more likely to have treatment delay than those initiated on treatment in other quarters of the year with a P value of 0.005 and 0.016 respectively. There was also a strong significance between test used for diagnosis and delay to treatment initiation among the RR TB cases. Patients diagnosed with culture and DST had a higher risk of delay than those diagnosed using GeneXpert with a P value of 0.000 in both univariate and multiple logistic regression analysis (table 3).

Table 3: Factors associated with delay to treatment initiation of RR TB patient

Variable	Categorical	Univariate logistic regression analysis					Multiple logistic regression analysis				
		B	Z	P>z	[95% CI]		B	Z	P>z	[95% CI]	
Type of patient	FFT	REF									
	FRT	1.397	0.620	0.536	0.485	4.023	0.663	-0.380	0.702	0.081	5.452
	LTFU	0.857	-0.190	0.851	0.172	4.277	0.353	-0.680	0.499	0.017	7.218
	Missing	1.714	0.890	0.374	0.523	5.621	1.192	0.150	0.879	0.124	11.426
	New	1.048	0.090	0.928	0.383	2.865	0.429	-0.870	0.382	0.064	2.862
	Relapse	1.096	0.250	0.800	0.539	2.228	1.603	0.740	0.457	0.463	5.553
Region	Central						1.000				
	Coast	1.436	0.420	0.672	0.269	7.678	1.515	0.150	0.880	0.007	331.034
	Eastern	1.067	0.080	0.940	0.199	5.714	4.718	0.570	0.568	0.023	965.952
	Nairobi	3.200	1.410	0.158	0.637	16.066	5.581	0.640	0.523	0.028	1095.312
	North Eastern	1.059	0.070	0.943	0.218	5.140	2.598	0.360	0.722	0.013	502.117
	Nyanza	1.778	0.620	0.538	0.284	11.120	3.572	0.450	0.649	0.015	863.312
	Western	0.533	-0.550	0.579	0.058	4.912	6.318	0.630	0.527	0.021	1912.561
Sex	Female	REF									
	Male	1.398	1.170	0.242	0.797	2.452	2.278	1.530	0.127	0.791	6.557
BMI		1.002	0.640	0.523	0.996	1.008	1.002	0.110	0.914	0.963	1.042
Quarter	1	REF									
	2	2.863	2.790	0.005	1.368	5.992	6.505	2.400	0.016	1.413	29.942
	3	1.762	1.440	0.150	0.815	3.808	3.197	1.490	0.137	0.691	14.798
	4	1.664	1.170	0.241	0.710	3.902	3.269	1.310	0.189	0.558	19.147
Age		0.984	-1.440	0.149	0.964	1.006	0.924	-0.770	0.444	0.756	1.130
HIV	Neg	REF									
	Pos	1.538	1.350	0.178	0.822	2.877	2.948	1.830	0.068	0.925	9.392
Age group	0 – 14										
	15 - 24	1.719	0.730	0.468	0.398	7.431	5.804	1.040	0.298	0.212	159.037
	25 - 34	1.047	0.060	0.948	0.259	4.242	3.059	0.480	0.633	0.031	302.607
	35 - 44	2.344	1.150	0.249	0.551	9.972	14.707	0.840	0.398	0.029	7537.231
	45 - 54	0.417	-1.090	0.274	0.087	2.000	5.877	0.420	0.677	0.001	24397.870
	55 - 54	1.094	0.110	0.916	0.208	5.756	20.765	0.570	0.571	0.001	756896.100
	65+	1.250	0.140	0.887	0.058	26.869	40.831	0.570	0.570	0.000	14700000
BMI Category	Moderate	REF									
	Normal	0.730	-0.870	0.384	0.359	1.482	0.716	-0.290	0.768	0.078	6.600
	Obese	1.425	0.780	0.436	0.585	3.471	0.592	-0.270	0.784	0.014	25.247
	Overweight	0.450	-0.880	0.378	0.076	2.656	0.988	-0.010	0.995	0.018	53.633
	Severe	0.788	-0.600	0.550	0.360	1.723	1.514	0.340	0.732	0.141	16.265
Type of Diagnosis	GeneXpert	REF									
	culture & DST	0.005	-5.150	0.000	0.001	0.038	0.002	-4.990	0.000	0.000	0.025
Constant							6.665	0.530	0.596	0.006	7372.451

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4.0 Discussion

Drug resistant Tuberculosis is a public health threat with Kenya being among the high burden MDR TB countries globally. Following the new classification, Kenya is among the 14 high TB, MDR TB and HIV burden countries (STAG-TB, 2015). Tuberculosis is more common among male than female as it is also depicted in thisstudy. This is similar to many studies that have shown that TB is more common among males than females. In the annual reports from the national TB program, there were more males affected with TB than females (NTLD_P, 2016). This, however, varies with the prevalence of drug resistant TB in China in which a study showed that the females were more likely to have MDR TB than males (Qiao et al., 2013).The same study observes that the lower rate of MDR TB among women could be associated with poor access to health care for the women. However, among the HIV positive, showed that women progressed faster to developing TB than the males. The main cause of high burden of TB among men in Kenya could also mean that they have more access to care compared to women, or they are more exposed to TB based on their social behaviour as indicated by Long who noted that,health seeking behaviour of the different gender affects delay to diagnosis and access to treatment as was observed in Vietnam(Diwan et al., 1999).

According to Olivier, most countries, especially the developing countries have reported TB in males more than female. The study also noted that there may be more sex and genetic factors other than poor access to health care among females that would explain the high burden of TB among males than females (Neyrolles, 2009). According to the age-sex distribution, drug resistant TB is most common among the most productive age.This is common in most countries in which most cases are between the age of 15 years and 54. The body mass index in 60% of the patients was below normal. TB is a body wasting disease and hence the majority of the patients with TB would be expected to have a low BMI. The treatment success rate of MDR TB globally has remained low with the treatment success rate of patients enrolled on treatmentin 2013 having a treatment success rate of 52% (WHO, 2016). The main factors that lead to unfavourable treatment outcomes have been named as HIV co infection, low BMI, gender among others. In some studies, it has been observed that a low BMI less than 18.5would be associated with unfavourable outcomes, usually death (Tang, 13). In ourstudy, there was no association between the BMI and treatment outcome. However, this was BMI at the treatment initiation. Since, majority of the patients got patient nutrition support during this time, this could have reduced the mortality expected among these patients.

HIV AIDS is a driver of TB in Sub-Saharan Africa. The MDRTB HIV co infection rate was at 26.23% during this period, compared to 30% among the drug sensitive TB as per the annual report. In most high TB burden countries, MDR TB also has a high burden for HIV. Despite many studies show that HIV patients with MDR TB have are more likely to have poor outcomes, there was so no significance association between HIV positive patients with MDR TB and the HIV negative ones. This agrees with the Lesotho findings that showed that MDR TB patients treated with early Art initiation could achieve same outcomes as the HIV negative (Satti, 2012). Delay to diagnosis and eventual treatment initiation has been long in many countries. This was in most cases associated with the diagnostic method used, and the isolation mode of treatment which had many patients in waiting lists for treatment. Delay in this study was defined as the duration from the time sample was collected to the time patient was initiated on treatment. The median was used to determine delay with those on the right of the median being delay. The median time to treatment (delay) was 66 days, with a mean of 99 days to treatment and a range of 0 to 599 days.

The drug surveillance system in Kenya is based on the use of GeneXpert, Line probe assays and culture and DST withGeneXpert being the first test among drug resistant TBhigh risk groups. The country has 126 GeneXpert machines in 2015. GeneXpertwas adopted since it took 2 hours to do the test against culture which took 8 to 12 weeks translating to 56 to 84 days. However, as it was noted in the study, most patients took between zero (0) and 599 days to get results. 50% of the patients took between 0 and 66 days while the rest took over 66 days. In the study, only 36% of the patients were diagnosed using GeneXpert. This means that even with GeneXpert, there were patients who took longer than one week to get diagnosis and be initiated on treatment. The reasons for this delay could be associated with lab network systems and other regional factors.In general, the introduction of GeneXpert reduced the delay to treatment from a mean of 66 with most patients diagnosed using GeneXpert initiating treatment by at most 30 days. This meant that use of GeneXpert as a diagnostic method reduced the overall time to treatment initiation. An assessment on the impact of GeneXpert on time to treatment, a univariate analysis showed a significant evidence of an association between RR TB detection by Xpert and reduced time to treatment initiation (Stagg, 2016).

At that the period under review in the study, there were 11 GeneXpert in the country and one public culture and DST laboratory that also performed line probe assays.The country relied on bothe liquid and solid culure methods that take long to make a diagnosis and require specialized laboratories which is expensive for most countries (Tang, 2013). The use of GeneXpert for surveillance should be increased and barriers to its access addressed, as it has been shown to reduce delay to treatment.This is could be associated with its availability as a point of care test and the short turnaround time to diagnosis. Culture and DST takes an an average of 8 to 12 weeks to give results. In this study, the use of culture and DST as a diagnostic test contributed significantly to the delay in treatment initiation compared to the use of GeneXpert. It has been documented that delay to treatment leads to unfavourable treatment outcomes.According to Oliver, the long duration before initiation of MDR TB and XDR TB increased the risk of poor outcomes (Tang, 2013). The study here shows that there is no associated between delay to treatment and treatment outcomes. Efforts in early diagnosis and treatment should be escalated. This would ensure reduction indisease transmission. Patients who are initiated early on treatment are also more likely to have less post treatment complications than those who take long and treatment is initiated in advanced stages.

In addition, treatment outcomes in TB are usually defined based on absence of TB bacilli by laboratory methods such as microscopy or culture but not on the quality of patient life. Hence, if a patient meets the WHO definition of cure despite patient complications such as bronchiectasis and total lung destruction, the patient is given a favourable outcome. It would be advisable to carry out a further analysis on these patients after successful treatment completion to examine their quality of life. The treatment success rate of the study patients was 82% (favourable outcome) while 18% had unfavourable outcomes. The male gender was shown to be 0.3 ties more like to have poor outcomes compared to the female. Patents from the North-Eastern region were 23.46 times more likely than patients from the central region to have unfavourable outcomes. More than 30% of drug resistant TB patients in Kenya are found in North Eastern. These patients are mainly refugees of Somalia origin who travelled to Kenya to seek treatment after diagnosis with drug resistant TB in Somalia before Somalia got a treatment program. The burden of drug resistant TB in Somalia following the drug resistance survey done in 2011 showed that the prevalence of MDR TB was

5% among new patients and 40% among previously treated TB patients. This could explain the high burden of drug resistant TBin North Eastern.

5.0 Conclusion

Delay to treatment initiation among RR TB patients is not associated with treatment outcomes. GeneXpert significantly reduces time to treatment initiation. The use of GeneXpert for surveillance should be increased and barriers to its access addressed, as it has been shown to reduce delay to treatment. Efforts for early diagnosis and treatment should be enhanced to reduce TB transmission and morbidity

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