Uptake of Drug Susceptibility Testing and Factors Associated among TB Patients in Bungoma County, 2018-2022

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Abstract

BACKGROUND

Drug Susceptibility Tests play an important role in developing strategies to identify and treat patients at high risk of Drug-Resistant Tuberculosis. Kenya is among countries with a high burden for Tuberculosis, and Multidrug-resistant/Rifampicin Resistant Tuberculosis. Early diagnosis and detection of drug-resistant Mycobacterium tuberculosis is a priority to identify patients not responding to treatment and avoid transmission of resistant strain. This study aimed to determine the uptake of the Drug Susceptibility Test and associated factors among tuberculosis patients in Bungoma County from 2018 to 2022

METHODOLOGY

Descriptive analysis was done, and patients' characteristics were summarized in tables. Logistic regression was used to calculate the odds ratio at a 95% confidence interval (CI) and to check the association between drug susceptibility uptake and varied patient characteristics. *P* value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 3204(42%), accessed a DST. Patients 25-44 years of age were 3262(37%). Females were more likely to have a DST with OR 1.03 (p<0.0123; 95% (1.04, 1.35). A patient being HIV negative was more likely to access a DST with OR 1.1 (p<0.0001; 95% (1.63, 2.15).

CONCLUSION

Access to a DST test among TB patients was sub-optimal. Most patients were found in the age group 25-44 years. Being a female, you were more likely to access a DST, and HIV-positive patients were unlikely to receive a DST test.

***Keywords**: Drug Susceptibility, Tuberculosis, Uptake, Factors, Drug-Resistant*

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Introduction

In 2021, approximately 10.6 million individuals acquired tuberculosis (TB), representing a 4.5% increase from 2020 (1). World Health Organization (WHO) end TB strategy:2025 target of treating Multi-Drug Resistant/Rifampicin Resistant tuberculosis (MDR/RR-TB) (all ages) only achieved 43% in 2018-2022(2). In Africa, drug-resistant tuberculosis mirrors the global trend of being markedly underreported(3). Kenya is among the 30 high-burden TB states(4). In the country, a total of 90769 TB cases and 760 drug-resistant TB (DR-TB) were notified in 2022(5).

National TB Control Program encounters challenges related to drug-resistant strains of Mycobacterium tuberculosis (MTB) transmission and the treatment of patients afflicted with this form of drug-resistant disease. These hurdles are aggravated by insufficient diagnostic tools and limited laboratory capacity(6). A study in western Kenya in 2021 showed that Mycobacterium drug resistance was prevalent in all the 10 counties surveyed based on the drug susceptibility tests**(7).**

In Bungoma County, among the notified 8393 TB patients between 2012 and 2016, there was a treatment success rate of 96% among the patients whose smears converted at two months. However, for those who delayed conversion, the treatment success rate was 77% with 5% among patients developing drug-resistant TB(8).

Drug Susceptibility Test (DST) plays an important role in identifying and treating patients with high risk of drug-resistant TB(9)**.** To address the challenge of DR-TB, it's crucial to secure access to top-tier drug susceptibility testing. This is necessary to tailor individualized treatment plans for every TB patient, especially in resource-scarce settings with a high disease burden (10). Early diagnosis and treatment, improving treatment outcomes, and expanding diagnostic capacity for mycobacterial culture and DST are crucial to limiting disease burden and the spread of drug-resistant TB strains(11). The available DST methods in Kenya include Gene Xpert, Culture (Solid Lowenstein Jensen), True Nat, and Line Probe Assay (LPA).

In Bungoma County, the available DST method is Gene Xpert available in 4 out of 10 sub-counties. The 6 sub-counties without gene Xpert do sample referral networking. Access to alternative DST methods requires sample referral from health facilities to the National TB Reference Laboratory Nairobi or Kenya Medical Research Institute (KEMRI) Kisumu.

This study describes the DST uptake and associated factors among TB patients in Bungoma County for 2018-2022. A DST access in this study refers to either a gene Xpert or a culture test. This information will be vital in strengthening and improving access of TB patients to a DST as an entry tool to determining drug susceptibility and subsequent resistance against the available tuberculosis drugs.

Methodology

Study design

This was a retrospective cohort study of drug-susceptible tuberculosis (DS-TB) patients notified in the period 2018-2022 in Bungoma County.

Definitions of key terms

Susceptibility tests. They determine a microbe's vulnerability to antimicrobial drugs by exposing a standardized concentration of organism to specific concentrations of antimicrobial drugs. Susceptibility testing can be done for bacteria, fungi, and viruses.

Study setting and population

We performed this study in Bungoma County which borders the Republic of Uganda to the West, Teso and Busia districts to the Southwest, Mumias to the South, and Trans-Nzoia, Lugari, and Kakamega to the North East. The population of Bungoma is estimated at 1,670,570 of which females constitute 52% while 48% are male (12). Bungoma is divided into ten administrative units called sub-counties.

This study included all patients who were on the drug-susceptible tuberculosis (DS-TB) register of Bungoma County in the period of 2018-2022. Clinical, demographic, and microbiological data were obtained for all patients notified in the same period. This included patients from public, private, prisons, and faith-based sectors.

Sample size and assumptions

We sampled all patients notified in the DS-TB register from all the health facilities of Bungoma County for the period 2018-2022.

Data collection

The TIBU electronic system was the secondary data source for this study. Therefore,

data collection entailed abstracting records of all TB patients in Bungoma County who were diagnosed with active TB and later were eligible for a DST as defined by WHO criteria.

The data collection sheet had provisions to record all relevant data for the study, namely: gender, age, Sector type, whether DST was done or not done, final treatment outcomes, co-morbidities, nutritional status, type of diagnosis, and sub-county of registration.

Data analysis

Descriptive statistics of frequency, proportion, mean and standard deviation were used to summarize patients' cohort characteristics. Logistic regression was used to calculate the odds ratio and 95% confidence interval (CI) to check the association between variables. *P* value ≤ 0.05 with 95% CI was considered an indicator of a statistically significant association.

Table 1:
Demographics, and Characteristics of the Study Participants

Variable (n=7629)	Variable Category	Frequency	Proportion (%)
Age group	0-14	861	11%
	15-24	1217	16%
	25-34	1593	21%
	35-44	1669	22%
	45-54	1053	14%
	55-64	644	8%
	65+	592	8%
Sex	Female	2950	39%
	Male	4679	61%
Sector	FBO	648	8%
	Prisons	36	<1%
	Private	373	5%
	Public	6572	86%
Nutrition Status	Severely Malnourished	1072	14%
	Moderately Malnourished	2007	26%
	Normal	2959	39%
	Overweight	320	4%
	Obese	399	5%
	Not Evaluated	872	11%
Type of TB	Extra Pulmonary TB(EPTB)	906	12%
	Pulmonary TB	6723	88%
HIV Status	Declined	24	<1%
	HIV Exposed Infant	2	<1%
	Not Done	267	3%
	Negative	5484	72%
	Positive	1852	24%
Treatment Outcome	Cured	3333	44%
	Died	760	10%
	Failure	34	<1%
	Loss to Follow-up	478	6%
	Moved to Category IV	34	<1%
	Not Completed	45	1%
	Treatment completed	2932	38%
	Transferred out	13	<1%
Type of Diagnosis	Bacteriologically Confirmed	4715	62%
	Clinically Diagnosed	2914	38%
DST	No	4425	58%
	Yes	3204	42%

Ethical considerations

Ethical approval was sought from the Amref Health Africa Ethics and Scientific Review Committee approval number ESRC P1471/2023. The confidentiality of patients was secured throughout the study period.

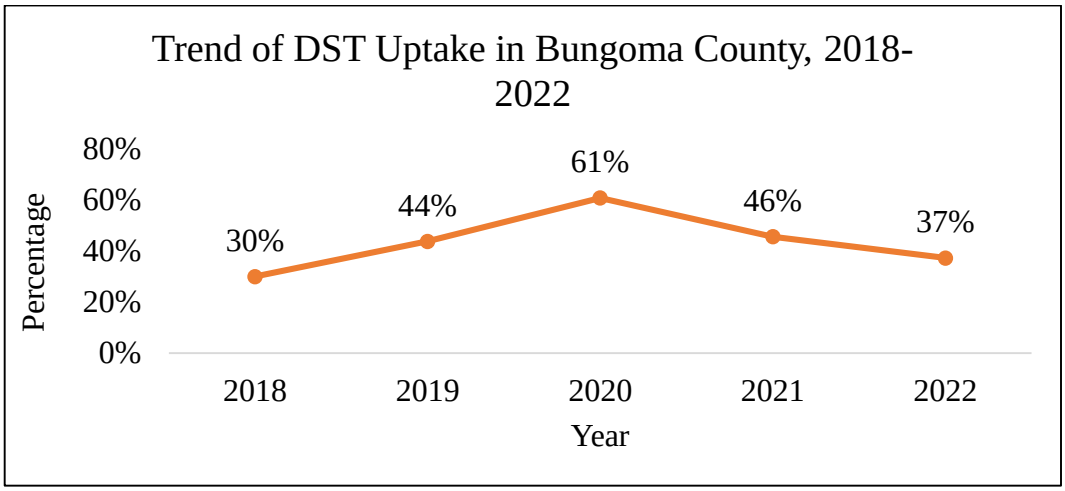

Figure 1:
Trends of DST Uptake among Patients notified in 2018-2022, Bungoma County

Table 2:
Demographics and Clinical characteristics of drug-susceptible TB patients of Bungoma County 2018-2022

Variable	Variable Category	Coefficient (β)	Standard Error	Odds Ratio (Exp(β))	95% CI for Exp(β)	p-value
	Public	-	-	-	-	-
Sector	Private	0.04591	0.14421	1.046	(0.79, 1.39)	0.7502
	Prisons	-0.86034	0.35813	0.8	(0.21, 0.85)	0.0163
	FBO	-0.08743	0.10576	0.97	(0.75, 1.13)	0.4084
Age-group	15-24	-0.08179	0.14963	0.99	(0.69, 1.24)	0.5846
	25-34	-0.3343	0.14	0.94	(0.54, 0.94)	0.0170
	35-44	-0.45182	0.13757	0.91	(0.49, 0.83)	0.0010
	45-54	-0.38594	0.14486	0.93	(0.51, 0.90)	0.0077
	55-64	-0.42328	0.15679	0.93	(0.48, 0.89)	0.0069
	65+	-0.8279	0.15301	0.89	(0.32, 0.59)	<0.0001
Sex	Female	0.16715	0.0668	1.03	(1.04, 1.35)	0.0123
Nutrition status	SM	-0.45227	0.09022	0.93	(0.53, 0.76)	<0.0001
	MM	-0.0894	0.07892	0.98	(0.78, 1.07)	0.2573
	Overweight	0.32242	0.18596	1.04	(0.96, 1.99)	0.0829
	Obese	0.31133	0.19269	1.08	(0.94, 1.99)	0.1062
	NE	-0.4639	0.09729	0.93	(0.52, 0.76)	<0.0001
Type of TB	EP	-0.19877	0.10467	0.98	(0.67, 1.01)	0.05756
Type of Patient	PT	1.80483	1.02908	1.14	(0.81, 45.7)	0.0795
	F	-0.41309	0.48615	0.92	(0.26, 1.72)	0.3955
	R	0.24264	0.14409	1.02	(0.96, 1.69)	0.0922
	TLF	-0.54819	0.15887	0.9	(0.42, 0.79)	0.0006
	THU	-0.76473	1.2567	0.86	(0.04, 5.46)	0.5428
HIV Status	Neg	0.62803	0.07085	1.1	(1.63, 2.15)	<0.0001
	FBO	1.35146	0.7475	1.17	(0.89, 16.7)	0.0706
	HEI	-1.47061	1.43693	0.77	(0.01, 3.84)	0.3061
	FBO	-0.67597	0.14243	0.88	(0.39, 0.67)	<0.0001
Diagnosis Type	CD	-0.02348	0.09462	0.99	(0.81, 1.18)	0.80403
DST Uptake	No	0.08205	0.08245	1.01	(0.92, 1.28)	0.31966

Results

Patients' demographic, clinical and microbiological characteristics

A total of 7629 records were reviewed. Most patients were aged 25-44 years, 1593(21%) and 1669(22%) respectively. A total of 4679(61%) were male gender. About 7336 (96%) had HIV results and 1852(24%) were HIV positive. Regarding DST uptake, only 3204 (42%) had access to a DST test.

Trends of DST Uptake

The county registered a peak DST uptake of 740 (61%) in 2020. Declining trends were noted in subsequent years at 620 (46%) in 2021 and 592 (37%) in 2022.

Patients' characteristics and the likelihood of a DST test

Tuberculosis patients who were lost follow-up and later returned to treatment, had a 10% lower likelihood of accessing DST compared to those who were never lost to follow. Since the entire confidence interval (CI), was below 1, it supports the finding that treatment after loss to follow-up patients were less likely to access DST and that the true effect size was precise and not likely to be due to random chance.

Female TB patients were more likely to access DST compared to males. Since the p-value was less than the significance level of 0.005, it suggests that this finding was significant. The CI greater than 1 reinforces this finding.

HIV-negative TB patients were more likely to undergo DST compared to HIV-positive TB patients. The p-value less than the significance level indicates evidence against the null hypothesis, and the CI suggests that this finding was not due to random chance.

An OR of 0.93 suggests a lower likelihood of severely malnourished TB patients accessing DST. A p-value less than the significance level suggests that this finding was statistically significant, and since the CI was less than 1, it reinforces the conclusion that severely malnourished TB patients were less likely to access DST.

Discussion

This study aimed to describe the DST uptake and associated factors among TB patients notified from 2018 to 2022 in Bungoma County. Generally, our study identified a low uptake of DST in Bungoma County falling short of the WHO requirements(13). This indicates a significant gap in the DST uptake, a diagnostic process necessary for effective TB management. Accessing a DST underscores the importance of identifying drug resistance early to guide appropriate treatment strategies and prevent further transmission of resistant strains(14). Some previous research has similarly highlighted challenges in meeting WHO DST targets in various settings. A study by the World Health Organization reported that many low-resource settings struggle with the implementation of comprehensive TB diagnostic services(15). In Bangladesh, a study found barriers such as limited laboratory capacity and inadequate healthcare infrastructure significantly impact DST uptake(16). Our findings align with these studies, emphasizing the need for targeted interventions to improve DST access in Bungoma County.

Several factors could contribute to the low uptake of DST in Bungoma County. Firstly, the region may face limitations in laboratory infrastructure and human resources, both of which are essential for conducting DST (16). Secondly, a lack of awareness and education about the importance of DST among both patients and healthcare workers may also contribute to the low testing rates. This aligns with findings from a study that reported a similar lack of awareness and education about DST among healthcare providers and patients contributing to low testing rates(17). Thirdly, the cost and time required to travel to these facilities for regular treatment and follow-up appointments could substantially deter patients from seeking DST(18). A further study showed that TB patients in many settings face a range of indirect costs that can significantly impact

their treatment adherence and outcomes (19). Furthermore, the stigma associated with TB, coupled with the fear of a diagnosis of drug-resistant TB, may discourage patients from undergoing DST(20).

Low DST uptake can lead to inadequate treatment of TB patients and increase the risk of drug-resistant TB strains. Public health initiatives should focus on strengthening the healthcare infrastructure, reducing financial barriers, and combating TB-related stigma within Bungoma County's healthcare system and community. Sufficient resources should be allocated to improve the laboratory capacity and train more healthcare workers. Additionally, public health campaigns could be conducted to raise awareness about the importance of DST among patients and healthcare providers.

This study also showed that most patients were from age group 25-44. This finding reflects the common age group of TB case notification, significant for socioeconomic, biological, and public health implications in Kenya (2). This age range typically includes individuals who are still establishing their careers and may face financial instability leading to the majority living in poor conditions, overcrowding, and limited access to healthcare, which could elevate the risk of contracting TB(21). A study highlighted that healthcare workers in this age group had a significantly higher incidence of TB compared to the general population(22). This finding is contrary to a study which indicated that individuals in this age group are often employed, potentially leading to better living conditions and reduced exposure to TB compared to younger individuals who may be in school or older individuals who might be in congregate living setups (23). The increased likelihood of TB infection among individuals aged 25-44 in Bungoma County underscores the need for comprehensive public health strategies that address the socio-economic, biological, and behavioral factors contributing to this trend.

Furthermore, our study found that female TB patients were more likely to access a DST compared to male TB patients. This suggests a gender disparity in the utilization of DST among TB patients. Previous research has shown mixed results regarding gender differences in TB diagnosis and treatment. A study found that women often have better healthcare-seeking behaviour compared to men (21). However, other studies, have highlighted that women may face barriers in accessing healthcare services due to socio-cultural factors(24). Our finding aligns with the notion that women may be more proactive in seeking healthcare services, including DST. Several factors could explain why female TB patients are more likely to access DST. First, women may be more likely to seek healthcare due to societal roles and responsibilities related to family health (25). Secondly, a study found that women were generally more compliant with medical advice compared to men (26). In Kenya, some of the TB gender-related barriers included self-stigmatization and fear that they may have HIV when diagnosed with TB(27), which could be a possible reason for poor health-seeking behaviour among males. Understanding the gender disparities in accessing DST can help in designing targeted interventions to ensure equitable healthcare. Public health programs should aim to improve DST access for all TB patients while addressing the specific barriers faced by male patients. Policymakers should consider integrating gender-sensitive approaches in TB control programs to enhance overall diagnostic coverage. This could include educational campaigns that emphasize the importance of DST for both men and women and training healthcare providers to recognize and address gender-specific barriers to DST access.

Another finding of our study was that HIV-negative TB patients were more likely to undergo a DST compared to HIV-positive TB patients. This finding indicates that HIV-positive TB patients face substantial barriers to accessing DST. The presence of co-morbidities in HIV-positive patients might lead to a focus

on managing the primary HIV infection, sometimes at the expense of thorough TB diagnostics (28). Furthermore, the typical presentation of TB in HIV-positive patients might result in diagnostic delays and underutilization of DST (29). Studies have shown that HIV-positive TB patients without access to a DST had higher rates of treatment failure and mortality (30). Another study has shown that there was a significant association between the lack of DST and the emergence of multidrug-resistant TB (MDR-TB) among HIV-positive patients (21). However, another study has shown that TB/HIV co-infection is associated with higher mortality rates, necessitating more aggressive diagnostic and treatment approaches (31) and that the prevalence of drug-resistant TB in HIV-positive populations leads to a higher clinical suspicion and increased use of DST (32).

HIV-positive patients might face additional barriers to accessing healthcare, such as stigma and discrimination, which can reduce their likelihood of undergoing comprehensive TB diagnostic procedures, including DST. Our finding underscores the need for targeted interventions, reducing barriers to DST, and ensuring that all TB patients receive timely and comprehensive diagnostic testing regardless of their HIV status to optimize treatment outcomes and manage drug resistance effectively.

Our study also found that severely malnourished TB patients were less likely to access DST compared to their non-malnourished counterparts. This highlights a critical gap in the care of TB patients with severe malnutrition. This could be due to the effects of co-morbidity of malnutrition and TB and is consistent with a study finding that malnourished-TB, patients had poorer treatment outcomes and higher mortality rates (33). However, there is limited research specifically addressing the relationship between malnutrition and access to DST. Our findings contribute to this gap by highlighting the reduced likelihood of DST access among severely malnourished TB patients. However, our finding was not in agreement with a study which indicated that malnourished TB patients were more likely to receive comprehensive clinical evaluations due to their vulnerable health status (34).

Several factors could contribute to the reduced likelihood of DST access for severely malnourished TB patients. First, malnutrition can lead to a weakened immune system and general physical debility, making it more challenging for patients to travel to healthcare facilities for testing. As noted in a study, malnourished patients often face greater barriers to accessing healthcare services (35). Secondly, healthcare providers may prioritize immediate nutritional and clinical stabilization over diagnostic testing for these patients (36). According to a study, poverty directly affects TB transmission, progression, and outcomes by limiting access to healthcare services and nutritious food(23). The financial burden associated with TB treatment, including direct costs can be overwhelming for impoverished patients.

Ensuring that severely malnourished TB patients have access to DST is crucial for effective TB management and control. Public health programs should prioritize nutritional support alongside TB diagnosis and treatment. Policymakers should consider implementing integrated care models that address both the nutritional and diagnostic needs of TB patients. This could include the provision of nutritional supplements and transportation support to ensure that malnourished patients can access necessary diagnostic services.

Our study found that TB patients who returned to treatment after being lost to follow-up were less likely to access DST compared to those who were never lost to follow-up. These findings align with a study in China, which showed that patients lost to follow-up had a lower likelihood of undergoing DST compared to those who completed their treatment as planned (37). The TB patients who are lost to follow-up were at risk of developing drug-resistant strains of TB, thus needing to do DR TB surveillance (14). Furthermore, studies have

shown that many lost to follow-up patients often face significant barriers when they return to care, including fragmented health services and a lack of continuity in treatment (37). The absence of timely DST can complicate the management of TB, particularly if the patient has developed drug resistance during the period of being lost to follow-up (37). Ensuring that all TB patients, including those who return after being lost to follow-up, have access to DST is crucial for effective TB management and control. Drug resistance can develop and spread if DST is not performed, leading to more difficult and costly treatment regimens. Policymakers should focus on strengthening patient follow-up systems and addressing barriers to DST access. Interventions could include patient tracking systems, financial support for patients, and training programs for healthcare providers on the importance of DST for all TB patients.

Study limitations

The study was a retrospective cohort study which did not allow data collection on some social factors, such as socio-cultural barriers and patient behaviors that may have influenced DST access.

Conclusion

From the findings, the study concludes that the uptake of DST surveillance among the TB population in the Bungoma County was below the recommended levels. This implies that the population was at risk of contracting drug-resistant TB strains emerging from delayed diagnoses and commencement of treatment schedules. Age, gender, and HIV status are significant factors in DST uptake performance; thus, it is important to consider them as major variables when assessing the risk factors for MDR-TB surveillance. This could enhance efforts to combat drug-resistant TB effectively in the county

Recommendations

There is a need to improve DST testing uptake for better diagnoses and management of TB spread in the county. To achieve this, the county should upscale drug susceptibility testing in all age groups, genders, and all TB clients irrespective of HIV status. Furthermore, the county could utilize community outreach programs, workshops, and informational sessions to address misconceptions, reduce stigma, and promote DST testing uptake. The county should prioritize expanding access to drug sensitivity testing by procuring relevant DST testing equipment and strengthening sample referral networks.

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Availability of data statement

The data that support the findings of this study are available in a national case-based surveillance system (TIBU) that stores details on individual patient episodes of TB reported to the national TB program.

Conflict of Interest

The authors have no conflicts of interest to declare, and there is no financial interest to report.

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Author contributions

- Callistus Muliro Barasa: Principal investigator.
- Aiban Rono, Adano Godana and Joan Thiga: Initial draft of manuscript and integration of contributions from all co-authors into final version.
- Jane Ong'ango and Andrew Sifuna: manuscript review for accuracy, clarity,

and suggestion of revisions to improve the paper's quality.

- Everlyne Kimani, Drusilla Nyaboke, Titus Kiptai, Stella Mamuti and Eunice Omesa: Protocol development and writing,
- Gabriel Muyemba and Asman Musa, consolidation of literature review.
- Joyce Kiarie and Richard Kiplimo: Statistical analysis and interpretation of data, providing insights into the results.

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