



Epidemiology of first-and second-line anti-tuberculosis drug resistance in new pulmonary tuberculosis cases in Addis Ababa metropolitan area, Ethiopia

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Introduction

- Globally, TB is the leading cause of infectious disease morbidity and mortality with many diagnostic uncertainties.
- Access to affordable and rapid diagnostics remained a major challenge for many developing countries which bear the greatest burden of TB.
- However, conventional wisdom wrongly holds that the microbiological detection of *Mycobacterium tuberculosis* complex in clinical specimens via culture and phenotypic drug susceptibility testing allows people to be correctly diagnosed and ensures that an effective treatment regimen is selected.

Objectives

- To describe the phenotypic DST and characteristics of isolates against FLDs and SLDS.
- To analyze the diagnostic accuracies of rapid molecular assay Vs. reference standard methods in the detection of RRTB and MDRTB.

Materials and Methods

- A cross-sectional study was conducted between October 2019 and June 2021 on clinically suspected and bacteriologically confirmed pulmonary tuberculosis cases.
- GeneXpert MTB/RIF assay was used to detect *M. tuberculosis* complex and resistant to rifampicin.
- Mycobacterial culture and drug susceptibility testing were performed against 15 anti-tuberculosis drugs using the BD BACTEC™ MGIT™ 960 automated liquid culture system.
- Sociodemographic and clinical characteristics were captured using a structured tool.

Statistical analysis

- Data were entered in Microsoft Excel 2021, checked for inconsistency, cleaned promptly, and exported to IBM SPSS Statistics for Windows, Version 26.0. Armonk, N.Y: IBM Corp, the USA for analysis.
- Descriptive analysis, sensitivity, Specificity, PPV, NPV and Kappa value were performed.
- All statistical significance was determined at a 95% confidence level.

Results

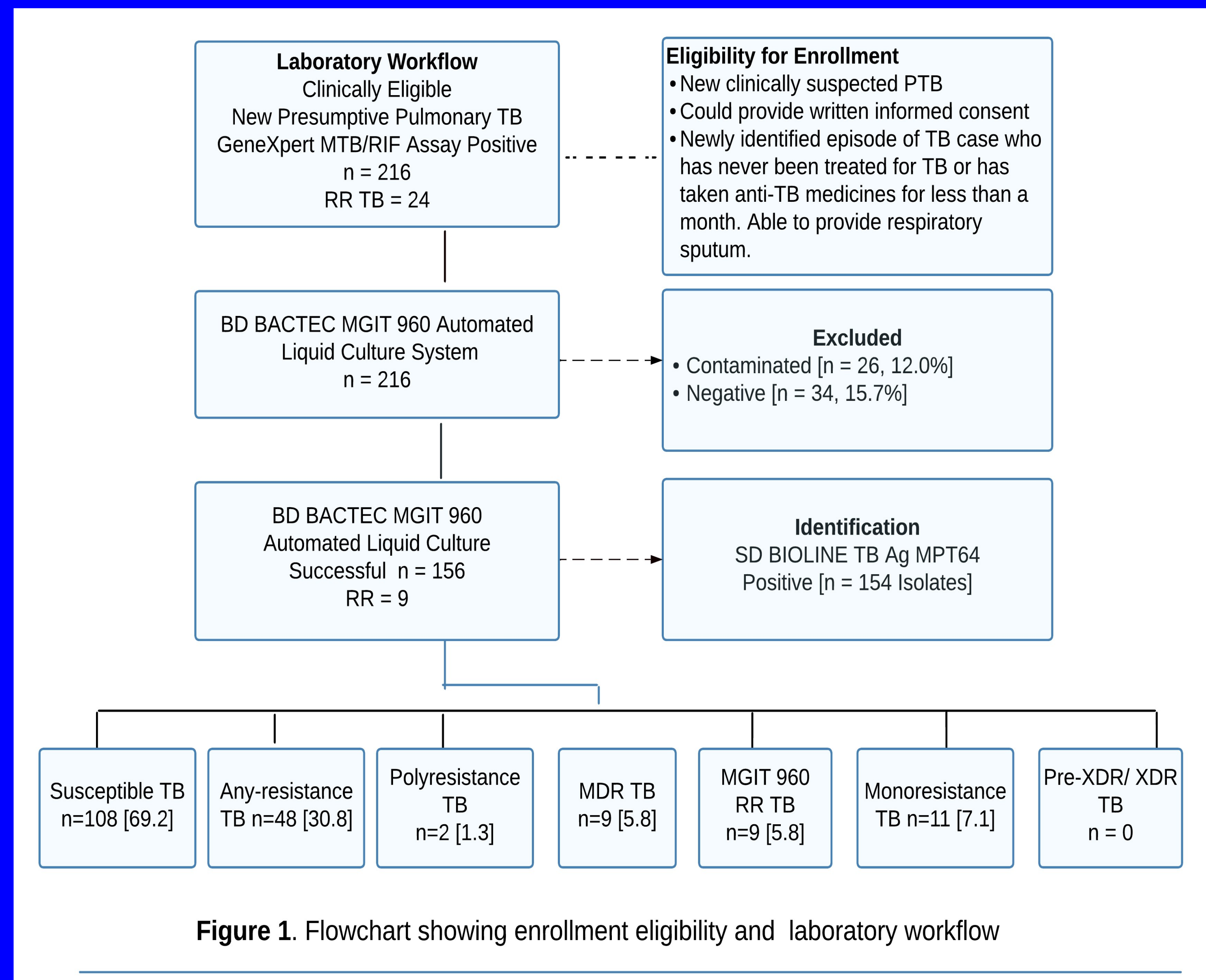


Table 1: . Phenotypic drug susceptibility of first- and second-line anti-TB drugs

Drug Profile and Regimen Category	Frequency Distribution		Type of Drug Resistance TB
	Susceptible n [%]	Resistant n [%]	
First Line Drug Profile			
All isolates with Resistance Profile	134 [85.9]	22[14.1]	Any resistant TB
STM	142 [91.0]	14[9.0]	
INH	138 [88.5]	18[11.5]	
RIF	147 [94.2]	9[5.8]	
EMB	149 [95.5]	7[4.5]	
STM+INH	155 [99.4]	1 [0.6]	Poly-resistant TB
STM+INH+EMB	155 [99.4]	1 [0.6]	
Total		2[1.3]	
INH	148 [94.9]	8 [5.1]	Mono-resistant TB
STM	153 [98.1]	3 [1.9]	
Total		11[7.1]	
INH+RIF	155 [99.4]	1 [0.6]	MDR-TB
INH+RIF+STM	154 [98.7]	2 [1.3]	
INH+RIF+STM+EMB	150 [96.2]	6 [3.8]	
Total		9[5.8]	
Second-Line Drug Profile			
MDR+AMK	22 [100]	0	Pre-XDR-TB
MDR+CAP	22 [100]	0	
MDR+KAN	22 [100]	0	
MDR+LFX	22 [100]	0	
MDR+MFX	22 [100]	0	
MDR+OFX	22 [100]	0	
MDR+BDQ	22 [100]	0	
MDR+CZF	22 [100]	0	
MDR+DLM	22 [100]	0	
MDR+LZD	22 [100]	0	
MDR+ETO	4[18.2]	18 [81.8]	
MDR+LFX+MFX+OFX	21 [100]	0	XDR-TB
MDR+LFX+MFX+BDQ+LZD	21 [100]	0	

STM: Streptomycin; INH: Isoniazid; RIF: Rifampicin; EMB: Ethambutol; MDR: Multidrug-resistant; AMK: Amikacin; CAP: Capreomycin; KAN: Kanamycin; LFX: Levofloxacin; MFX: Moxifloxacin; OFX: Ofloxacin; BDQ: Bedaquiline; CFZ: Clofazimine; DLM: Delamanid; LZD: Linezolid; ETO: Ethionamide; TB: Tuberculosis; MDR-TB: Multidrug-resistant tuberculosis; XDR: Extensively drug-resistant tuberculosis.

Table 2. Comparison of RR-TB detection rate between GeneXpert MTB/RIF Assay and BACTEC TM MGITM 960 automated liquid culture system

Measurement	Performance Rate [%]	95% CI
Sensitivity	100	[66.4 – 100]
Specificity	94.6	[89.6 – 97.6]
PPV	52.9	[36.5 – 68.8]
NPV	100	.
Accuracy	94.9	[90.2 – 97.8]
Kappa Value	0.667	.

Conclusions

- The rate of MDR-TB among new pulmonary TB cases remained high at fivefold the national and nearly twofold the global estimated rate.
- The rate of monoresistance against anti-TB drugs was also high.
- The absence of resistance against recommended second-line anti-TB drugs was quite encouraging.
- However, the high rate of resistance against Ethionamide would mean that its inclusion in the regimen may not have therapeutic benefit in this geographic area.
- The use of GeneXpert MTB/RIF assay alone for the detection of *M. tuberculosis* might introduce 15.7% false positivity and 47.1% false rifampicin resistance leading patients erroneously assigned in the MDR-TB category and placing on an unnecessary second-line anti-TB-treatment regimen.
- Initial drug susceptibility testing is critical from both patient and program perspectives before initiation of treatment with second-line antituberculosis drugs.

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