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Research Article

Assessment of Fluoroquinolone and Aminoglycoside Resistance Using Line Probe Assay in Multidrug-Resistant Tuberculosis Patients

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ABSTRACT

Background: Multidrug-resistant tuberculosis (MDR-TB) is a severe public health issue, especially if resistance to fluoroquinolones (FQs) and aminoglycosides (AGs) limits therapeutic choices.

Objective: To assess the prevalence of FQ and AG resistance and the corresponding resistance mutations among MDR-TB patients by line probe assay (LPA).

Methods: This descriptive cross-sectional study was done in the TB diagnostic laboratory of a tertiary care hospital in Pakistan during six months from February to July 2026. Patients with confirmed MDR-TB were consecutively sampled, and 100 patients were enrolled. Specimens were tested using the GenoType MTBDRsl VER 2.0 LPA (Hain Lifescience, Nehren, Germany), which is able to detect mutations in gyrA and gyrB (FQ resistance) and in rrs and the eis promoter (AG resistance). Descriptive analysis and 95% Wilson confidence intervals for proportions were used to analyse data. No phenotypic drug susceptibility testing was done.

Results: FQ resistance was detected in 38% of patients (95% CI 29.1–47.8) and AG resistance in 24% (95% CI 16.7–33.2). 47% had at least one drug class resistance, and 15% had both drug classes resistance. Mutations in gyrA were responsible for 81.6% (31/38) of FQ-resistant cases, and mutations in rrs for 75.0% (18/24) of AG-resistant cases. The 38 patients who were found to be resistant to FQ were classified as pre-extensively drug-resistant TB (pre-XDR-TB) according to the WHO definitions; susceptibility to bedaquiline and linezolid was not tested and could not be used to classify as extensively drug-resistant TB (XDR-TB).

Conclusion: MDR-TB cases had second-line drug resistance rates. LPA can quickly identify resistance-associated mutations and assist in providing timely, individual treatment decisions, preferably with phenotypic confirmation.

Keywords: Multidrug-Resistant Tuberculosis, Fluoroquinolone Resistance, Aminoglycoside Resistance, Line Probe Assay, Drug Resistance, Mycobacterium Tuberculosis.

INTRODUCTION

Multidrug-resistant tuberculosis (MDR-TB), which is resistance to at least rifampicin and isoniazid, continues to be a major challenge to TB control. Resistance to the fluoroquinolones (FQs) and also to the second-line injectable aminoglycosides (AGs) further reduce treatment options and increase the likelihood of the development of pre-extensively drug-resistant TB (pre-XDR-TB) and extensively drug-resistant TB (XDR-TB). Prompt detection of resistance is critical to ensure that the right treatment is used at the right time. However, molecular techniques, such as line probe assays (LPAs), have been gaining in popularity and are now used alongside slower phenotypic

drug susceptibility testing (DST) as they can not only identify the M. tuberculosis complex but also specific mutations associated with resistance to certain drugs within a short time (1). LPAs have also been found to be predictive of resistance patterns and to aid in earlier clinical decisions in patients suspected to have TB (2).

The GenoType MTBDRsl assay is designed to detect mutations associated with FQ and AG resistance, providing a fast molecular option for slower second-line DST. Comparative testing of GenoType MTBDRsl version 2 has demonstrated that it is a valuable tool for detecting resistance to these drugs and to inform treatment (3). Likewise, the Xpert MTB/XDR assay is able to detect resistance to FQs and AGs along with other major anti-TB drugs (4). LPAs have been used in tertiary care centers to guide second-line therapy and to provide information for the clinician to adjust therapy prior to the arrival of conventional susceptibility results (5). The importance of rapid molecular testing for FQ and AG resistance in pulmonary TB has also been demonstrated by recent data from Bangladesh (6).

There is variation in assay performance and resistance patterns between populations and settings. The AID LPA has been assessed in Romanian patients with suspected TB for the simultaneous detection of M. tuberculosis and drug resistance (7), and GenoType MTBDRsl has been applied for the fast detection of FQ and AG resistance mutations in patients with MDR-TB (8). This is clinically useful because second-line resistance impacts the drug composition and effectiveness of personalized treatment. In the INNOVA4TB cohort, LPA-based testing was used to guide treatment for patients with rifampicin-resistant TB (9), and epidemiological studies have shown significant FQ and AG resistance rates among MDR-TB cases with different genetic determinants (10). Molecular and phenotypic techniques vary in the speed of analysis, the gene(s) targeted, the technical requirements, and the interpretation (11).

Furthermore, correct identification of FQ resistance is crucial for the classification and treatment of advanced drug-resistant tuberculosis; comparative studies of Xpert MTB/XDR and FluoroType XDR in MDR-TB isolates have demonstrated this (12). Genotypic studies have indicated that resistance to FQs and other second-line drugs is a driver of pre-XDR-TB and XDR-TB and highlight the importance of timely recognition of resistance to avoid continued ineffective treatment (13). MDR-TB can be treated with carefully designed all-oral regimens, which further underscores the need for accurate resistance data to select an individualized regimen (14).

The genotypic results should be used in conjunction with traditional DST, as resistance may be different in terms of mechanism and expression. Comparisons of the two methods in high-burden settings highlight the complementary nature of their use for the detection of MDR-TB and the monitoring of MDR-TB progression to XDR-TB (15), and clinical isolates from high-burden settings have identified FQ and second-line injectable resistance in rifampicin- and isoniazid-resistant M. tuberculosis (16). The clinical outcome is also affected by the extent and type of resistance, including to isoniazid (17), highlighting the need for accurate DST. In Pakistan, an evaluation of MTBDRsl in pre-XDR and XDR isolates from Punjab has been reported (18); further data on the frequency of FQ and AG resistance among patients with confirmed MDR-TB would help to guide local treatment decisions.

Objective: To estimate the prevalence of FQ and AG resistance and the resistance mutations in patients with MDR-TB using an LPA.

MATERIALS AND METHODS

Study Design and Setting: Descriptive cross-sectional study.

Study Duration: The study period was six months (February 2026 to July 2026).

Ethical Approval: The institutional ethical review committee approved the study.

Sample Size: The minimum sample size was determined using the formula for estimating a single proportion: $n = Z^2p(1 - p)/d^2$ with a 95% confidence level ($Z = 1.96$), an expected prevalence of FQ resistance among people with MDR-TB of 30% (p), and an absolute precision (d) of 9%, resulting in $n \approx 100$. Therefore, 100 patients were enrolled. The 95% CI for the observed FQ resistance estimate for this sample is about ±9 percentage points.

Sampling Technique: Consecutive (non-probability) sampling was used. Patients were enrolled based on availability until the desired

sample size was obtained. The unit of analysis was the patient; if more than one specimen was received from the same patient, only the first specimen that met the criteria was analysed. The numbers of patients screened, excluded, and included are reported in the Results.

Inclusion Criteria: Patients of all ages and sexes who had a specimen of adequate quality and quantity for molecular testing and had confirmed MDR-TB were included.

Exclusion Criteria: Patients with no confirmed MDR-TB (including isoniazid-monoresistant TB and rifampicin-monoresistant TB), specimens lacking sufficient material for molecular testing, specimens lacking proper identification or labelling, repeat specimens from the same patient, and specimens with invalid or uninterpretable LPA results were all excluded.

Confirmation of MDR-TB: MDR-TB was considered as resistance to at least rifampicin and isoniazid (19). Routine diagnostic testing with the GenoType MTBDRplus LPA was performed prior to enrolment to confirm MDR-TB status in patients, based on mutations associated with rifampicin and isoniazid resistance.

Specimen Collection and Processing: Each patient's sputum specimen was collected in a sterile leak-proof container and sent to the laboratory immediately. Decontamination and concentration of specimens was performed with the N-acetyl-L-cysteine–sodium hydroxide (NALC–NaOH) method and centrifuged, and DNA was extracted from the decontaminated and concentrated sediment using the GenoLyse kit (Hain Lifescience) according to the manufacturer's instructions. The LPA was conducted on the isolated DNA.

Line Probe Assay: The resistance to FQs and AGs was determined using the GenoType MTBDRsl VER 2.0 (Hain Lifescience GmbH, a Bruker company, Nehren, Germany). The target regions were amplified according to the manufacturer's instructions (20), and the amplicons were denatured and hybridized with a nitrocellulose strip coated with wild-type (WT) and mutation (MUT) probes. The washed samples were subjected to stringent washing, followed by the addition of a streptavidin–alkaline phosphatase conjugate and substrate, and then the bands were read against the manufacturer's evaluation template.

Genetic Targets and Mutations Tested: There are 27 probes in the strip, including 20 probes for the M. tuberculosis complex and locus controls, and a conjugate. Three WT probes are designed to detect gyrA codons 85-97, and one is designed to detect gyrB codons 536-541; six probes detect substitutions in gyrA (A90V, S91P, D94A, D94N/D94Y, D94G, D94H) and two probes detect substitutions in gyrB (N538D, E540V). Two WT probes are designed to detect rrs A1401G and G1484T, and three probes are designed to detect the eis promoter region (positions −37, −14 to −10, and −2) (Table 1). Mutations that occur outside of these regions are not discovered. Resistance was assumed if a MUT probe hybridized or a WT probe failed to hybridize, based on the manufacturer's interpretation criteria. The substitutions rrs A1401G and G1484T are correlated with cross-resistance to kanamycin, amikacin, and capreomycin, while the eis C−14T promoter substitution only provides low-level kanamycin resistance.

Table 1. Genetic targets and mutations detected by the GenoType MTBDRsl VER 2.0 line probe assay

Drug class	Gene (region covered)	WT probes	Mutations detected by MUT probes	Resistance inferred
FQ	gyrA (codons 85–97)	WT1–WT3	A90V; S91P; D94A; D94N/D94Y; D94G; D94H	FQ class
FQ	gyrB (codons 536–541)	WT (1 probe)	N538D; E540V	FQ class
AG	rrs (nucleotides 1401–1402 and 1484)	WT1 (1401–1402); WT2 (1484)	A1401G; G1484T	KAN, AMK, CAP
AG	eis promoter (positions −37, −14 to −10, −2)	WT1–WT3	C−14T	Low-level KAN

Note. According to the manufacturer (20). WT = wild-type; MUT = mutation; FQ = fluoroquinolone; AG = aminoglycoside; KAN = kanamycin; AMK = amikacin; CAP = capreomycin.

Classification of Resistance and Mutation Categories: FQ resistance was considered to be any mutation or loss of a WT band in gyrA or gyrB, while AG resistance was defined as any mutation or loss of a WT band in rrs and/or the eis promoter. Patients were classified into four mutually exclusive categories (FQ resistance only, AG resistance only, resistance to both classes, and no resistance detected). The overlapping marginal totals (any FQ resistance, any AG resistance, resistance to either class) are reported separately. Each resistant specimen was assigned to the gene where the resistance was found (gyrA or gyrB for FQs; rrs or eis for AGs) for the analysis of mutations. Confirm how specimens that had more than one mutation in the same class were treated. The 38 FQ-resistant patients and 24 AG-resistant patients were either patients with no concurrent mutations or patients with concurrent mutations assigned to only one gene (gyrA or rrs) in the present data. According to the 2021 WHO definitions, pre-XDR-TB is defined as MDR-TB that has developed resistance to one or more FQs, and XDR-TB is defined as pre-XDR-TB that has developed resistance to bedaquiline or linezolid (19).

Phenotypic DST: Phenotypic DST was not conducted in parallel with the LPA as the study was designed to identify molecular resistance patterns for rapid diagnostic testing. The resistance described in this report is genotypic (mutation-based), and agreement with phenotypic susceptibility was not possible. Bedaquiline and linezolid susceptibility were also not tested.

Quality Control: Each strip contained the manufacturer's conjugate, amplification controls, locus controls, and only strips with all the control bands were accepted.

Data Collection and Statistical Analysis: Data were collected on a structured data sheet, which included demographic and clinical information. Data were analysed using [statistical software and version]. Categorical variables are summarized as frequencies and percentages, and continuous variables are summarized as mean ± standard deviation or median (interquartile range) depending on their distribution. The 95% CIs for proportions were calculated by the Wilson score method. Mutations are reported as a percentage of the number of resistant specimens in each drug class. The discordant categories (FQ-only and AG-only) were tested for the imbalance using the same McNemar test. A two-sided p-value < 0.05 was considered statistically significant. All the LPA results were interpretable, and there were no missing data.

RESULTS

Participant Flow: From February to July 2026, [N] presumptive MDR-TB patients were screened, of whom [n] were confirmed MDR-TB. Of these, [n] were excluded (due to insufficient specimens, [n] due to inadequate identification or labelling, [n] repeat specimens from the same patient, and [n] due to invalid or uninterpretable LPA results), leaving 100 patients for analysis (add a flow diagram if the journal requires one).

Demographic and Clinical Characteristics: The mean age of the patients was [___ ± ___] years, and [n (%)] were male. [N (%)] were previously treated for TB, and [n (%)] had a positive sputum smear. The characteristics of the study population are summarized in Table 2, which includes other relevant characteristics such as comorbidities and prior exposure to FQs or injectable drugs.

Table 2. Demographic and clinical characteristics of the patients with MDR-TB (N = 100)

Characteristic	Category	n (%) or mean ± SD
Age (years)	Mean ± SD	[___]
Age group	[categories]	[n (%)]
Sex	Male / Female	[n (%)]
Residence	Urban / Rural	[n (%)]
TB treatment history	New / Previously treated	[n (%)]
Sputum smear grade	Negative / Scanty / 1+ / 2+ / 3+	[n (%)]
Diabetes mellitus	Yes / No	[n (%)]

HIV status	Positive / Negative	[n (%)]
Previous FQ or injectable drug exposure	Yes / No	[n (%)]

Note. SD = standard deviation. Replace the highlighted fields with the study data and delete any rows that were not collected.

Overall Resistance: 100% of the LPA results were interpretable. FQ resistance was detected in 38 patients (38.0%; 95% CI 29.1–47.8) and AG resistance in 24 patients (24.0%; 95% CI 16.7–33.2). Forty-seven (47.0%) patients had resistance to at least one of the two classes, 15 (15.0%) were resistant to both classes, and 53 (53.0%) were not resistant to either class (Table 3). FQ resistance was 14 percentage points more common than AG resistance.

Table 3. Distribution of FQ and AG resistance among patients with MDR-TB (N = 100)

Resistance pattern	n	% of total (N = 100)	95% CI (Wilson)	% of resistant (n = 47)
Mutually exclusive categories				
FQ resistance only	23	23.0	15.8 to 32.2	48.9
AG resistance only	9	9.0	4.8 to 16.2	19.1
Resistance to both classes	15	15.0	9.3 to 23.3	31.9
No resistance detected	53	53.0	43.3 to 62.5	n/a
Total	**100**	**100.0**	**n/a**	**100.0**
Overlapping (marginal) totals				
Any FQ resistance	38	38.0	29.1 to 47.8	n/a
Any AG resistance	24	24.0	16.7 to 33.2	n/a
Resistance to either class	**47**	**47.0**	**37.5 to 56.7**	**n/a**

Note. CI = Wilson 95% confidence interval; FQ = fluoroquinolone; AG = aminoglycoside; n/a = not applicable. Percentages of the resistant subgroup are calculated on the 47 patients with resistance to either class. The four mutually exclusive categories sum to 100; the overlapping marginal totals are not additive.

FQ resistance alone (23.0%), AG resistance alone (9.0%), and resistance to both classes (15.0%) were the most common patterns. Of the 47 patients who were resistant, 48.9% were resistant to FQs only, 19.1% to AGs only, and 31.9% to both classes. In 15/38 (39.5%) FQ-resistant patients and 15/24 (62.5%) AG-resistant patients, dual resistance to FQs and AGs was observed, with the majority of AG-resistant patients also being FQ-resistant. FQ-only resistance was significantly more common than AG-only resistance among patients with resistance to only one class (23 vs 9; exact McNemar p = 0.020; Figure 1).

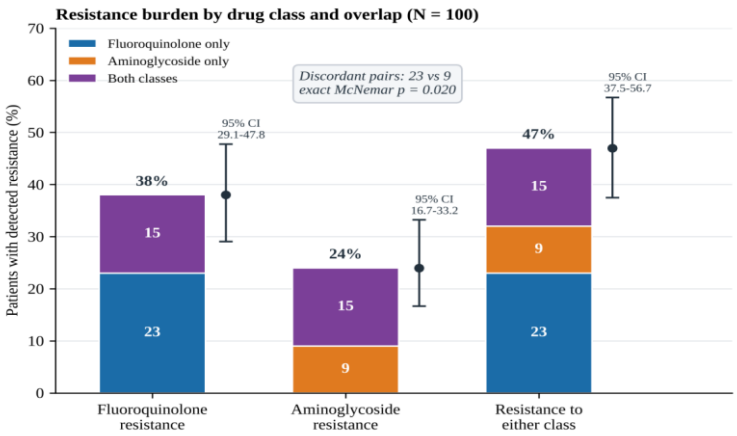


Figure 1. Resistance burden by drug class. Stacked bars show the single-class and dual-resistance components; markers with whiskers show the 95% Wilson CI of the total. The exact McNemar test compares the discordant FQ-only and AG-only groups.

Mutation Distribution: Thirty-one of 38 patients with FQ resistance had gyrA mutations (81.6%), and 7 had gyrB mutations (18.4%). Of 24 patients resistant to AGs, 18 (75.0%) had mutations in rrs, and 6 (25.0%) had mutations in the eis promoter (Table 4). Under one gene, each resistant specimen is counted once (confirm; see Methods). [Insert the distribution of the specific mutations (A90V, S91P, D94A, D94N/D94Y, D94G, D94H, N538D, E540V, A1401G, G1484T, C−14T), including patients with loss of a WT band without a MUT band, if available.]

Table 4. Distribution of detected resistance-associated mutations by drug class

Drug class (resistant n)	Resistance-associated target	n	% among resistant	95% CI (Wilson)
FQ (n = 38)	gyrA mutation	31	81.6	66.6 to 90.8
	gyrB mutation	7	18.4	9.2 to 33.4
AG (n = 24)	rrs mutation	18	75.0	55.1 to 88.0
	eis promoter mutation	6	25.0	12.0 to 44.9

Note. Percentages use the number of resistant specimens in each drug class as the denominator. Each resistant specimen is assigned to one gene only. FQ = fluoroquinolone; AG = aminoglycoside; CI = Wilson 95% confidence interval.

Overall, 47% of patients were resistant to at least one of the classes (23 FQ only, 9 AG only, 15 both), while 53% were susceptible to both classes (Figure 2). There was a significant overlap between FQ resistance and AG resistance, as only 9 of 24 AG-resistant patients (37.5%) were not FQ-resistant.

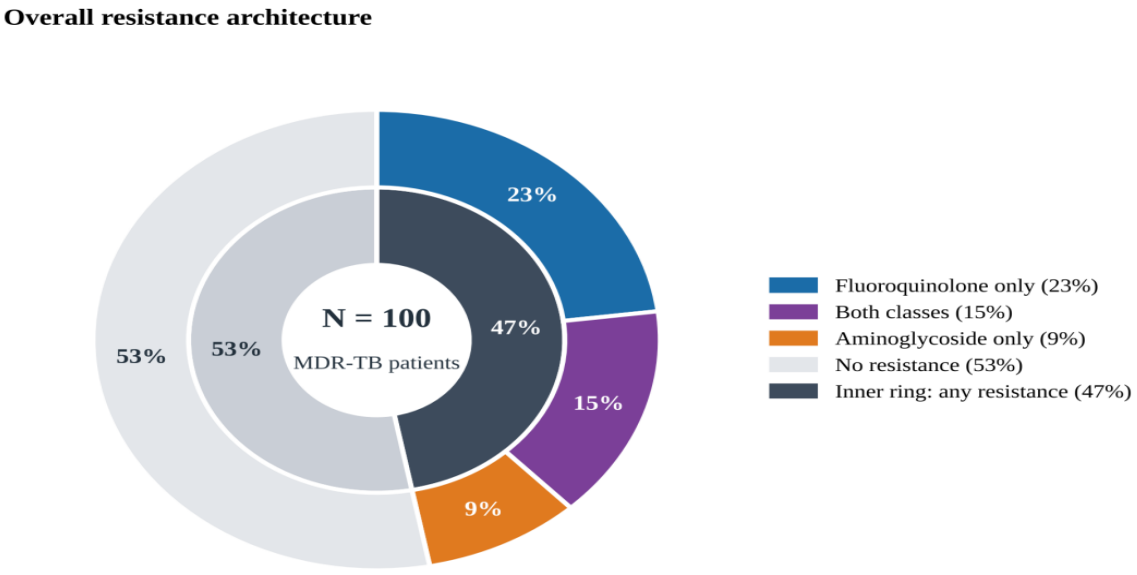


Figure 2. Nested donut chart of the overall resistance architecture among 100 patients with MDR-TB. The inner ring separates patients with any resistance (47%) from those without (53%); the outer ring splits the resistant group by pattern.

The molecular results are summarized in Figure 3. The 95% CIs for gyrA (66.6–90.8%) and rrs (55.1–88.0%) were entirely above 50%, and for gyrB (9.2–33.4%) and the eis promoter mutations (12.0–44.9%) were entirely below 50%, which confirmed the predominance of gyrA and rrs mutations. The large range of gyrB is due to the low number of mutations in this group, and the subgroup estimates should be taken with caution.

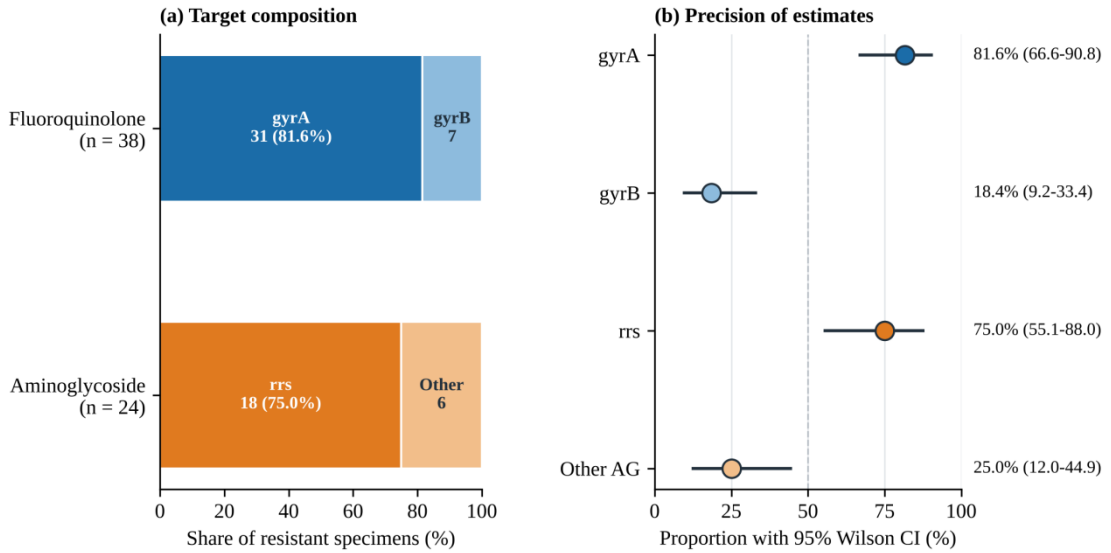


Figure 3. Resistance-associated mutations by genetic target. (a) Composition of detected targets within FQ-resistant (n = 38) and AG-resistant (n = 24) specimens. (b) Proportion of each target with 95% Wilson CIs; the dashed line marks 50%.

Pre-XDR-TB and XDR-TB Classification: Pre-XDR-TB was seen in 38 patients (38.0%) who were FQ resistant, according to the 2021 WHO definitions (19). The 9 patients (9.0%) who had AG resistance only did not meet this definition. However, XDR-TB was not determined due to the lack of testing for bedaquiline and linezolid susceptibility.

DISCUSSION

In this cross-sectional study of 100 patients with confirmed MDR-TB, LPA identified 38% (95% CI 29.1–47.8) as FQ resistant and 24% (95% CI 16.7–33.2) as AG resistant. Forty-seven percent of patients were resistant to at least one class, and 15% were resistant to both classes of antibiotics, with FQ-only resistance more common than AG-only resistance (23% vs 9%). These results are in line with existing data showing that LPAs can quickly detect resistance and mutations associated with it, and can aid in the diagnosis and treatment of MDR-TB (1,2). The high prevalence of FQ resistance highlights the importance of early molecular assessment of second-line resistance, as FQs are important drugs for drug-resistant TB.

Comparison with previous studies

The FQ resistance rate of 38% is similar to the 34.5% (39 of 113) FQ resistance among MDR-TB isolates in an Indian study (21), but is considerably higher than the 17.8% (33 of 185) of MDR-TB isolates with FQ resistance mutations in Brazil (16) and the 7.4% (6 of 81) FQ resistance proportion among MDR-TB patients in Ghana, where no XDR-TB was detected (13). In Punjab, Pakistan, 73.6% (39/53) of pre-selected isolates were positive for FQ resistance by the MTBDRsl assay, which is reflective of a higher proportion of FQ resistance in a pre-selected group and cannot be directly compared to the unselected consecutive patients in this study. The 24% AG resistance rate was also higher than the resistance mediated by rrs reported from Brazil, where only 2 out of 623 RIF- or INH-resistant isolates were confirmed to be rrs (0.3%) (16) (denominators differ). The variation in prevalence rates of FQ and AG resistance among these studies is likely due to differences in the study population (previously treated or not, referral or community setting), the version of the assay used, and the type of sample collected, as well as local prescribing practices for FQs and injectable drugs.

Mutation spectrum

In the present study, the mutations in the QRDR of the gyrA gene caused 81.6% of the cases of FQ resistance, while the mutations in the gyrB gene caused 18.4% of cases, which further substantiates the importance of QRDR mutations in determining FQ resistance. The presence of gyrB mutations requires the use of version 2.0 of the assay, which contains gyrB probes (20) not contained in version 1.0. The most frequently reported gyrA mutations reported elsewhere were D94G (18) in Punjab, D94G (21) in India, and D94A (13) in Ghana. In the AG-resistant group, rrs mutations were the most common (75.0%), as reported in

Ghana, where C1402T was the most common AG-associated mutation (13). The other 25.0% had eis promoter mutations, which usually result in low-level kanamycin resistance, and not in resistance to amikacin or capreomycin. The 24% AG resistance should therefore be interpreted as resistance to at least one AG and not necessarily to amikacin. This is important for choosing treatment and is useful for confirming the phenotype of AG resistance.

Pre-XDR-TB and XDR-TB definitions

WHO has classified pre-XDR-TB as MDR/rifampicin-resistant TB with additional resistance to any FQ and XDR-TB as pre-XDR-TB with additional resistance to at least one of bedaquiline or linezolid (19). According to these definitions, 38 patients (38.0%) were classified as having FQ resistance, and 9 patients (9.0%) as having AG resistance alone, but the latter did not meet the definition of pre-XDR-TB. However, due to the lack of testing for bedaquiline and linezolid, XDR-TB could not be assessed. All 15 patients (15.0%) who were resistant to both classes would have been considered XDR-TB according to the old definition (FQ plus second-line injectable) and would be confirmed phenotypically for AG resistance. Earlier studies using that definition report XDR-TB frequencies that cannot be directly compared with the current definition (13). All-oral regimens (14) are also affected by FQ resistance.

Genotypic and phenotypic testing

Genotypic and phenotypic methods are not mutually exclusive, but complementary (15). Molecular assays provide rapid data on specific resistance-associated mutations, while phenotypic DST provides information on the actual drug susceptibility. The MTBDRsl VER 2.0 is highly sensitive to FQ resistance and less sensitive to AG resistance; for example, a 76% sensitivity has been reported for kanamycin and 47% sensitivity for capreomycin (3). Since phenotypic DST was not performed here, the agreement of the LPA with phenotypic results could not be calculated, and the frequency of AG resistance may be underestimated because mutations outside the regions assayed would not be detected (3,15). Furthermore, there may be differences between the FQ and AG resistance (such as low-level resistance or heteroresistance). Molecular data should therefore be used in conjunction with clinical and other laboratory data.

Clinical and programmatic implications

Rapid LPA results can inform treatment decisions: in INNOVA4TB, LPA was used to inform treatment decisions in rifampicin-resistant TB (9); in NExT, an all-oral treatment for 6 months is effective in treating MDR-TB, increasing the importance of accurate knowledge of FQ susceptibility (14). The high rate of resistance in both single-class and dual-class cases here justifies the provision of resistance information early in the regimen, before it is finalized, and tracking resistance patterns in MDR-TB populations (10,16). This study was limited to FQ and AG resistance, but other resistance patterns also influence outcomes; a national cohort showed that outcomes varied with the degree of isoniazid resistance (17).

LIMITATIONS

There are a number of limitations in this study. First, it was carried out in one tertiary care laboratory with consecutive sampling, as there is a risk of referral bias and the results may not be representative of the broader MDR-TB population. Secondly, the sample size (N = 100) results in relatively broad confidence intervals, especially for the less common mutation categories (gyrB, eis). Third, resistance was only genotypically determined; no phenotypic DST or DNA sequencing was performed to confirm the LPA results and mutations outside the region covered by the assay, as well as heteroresistance, may have been missed. Fourth, susceptibility testing was not performed for bedaquiline or linezolid, preventing the diagnosis of XDR-TB based on the current definitions. Finally, clinical characteristics, treatment history, and treatment outcomes were not analysed in relation to resistance – confirm and adjust. Lastly, the design of the cross-sectional study does not permit the evaluation of the development of resistance over time. Multicentre studies in the future should incorporate LPA with phenotypic DST and sequencing and should also incorporate treatment outcomes.

CONCLUSION

In this study, resistance to FQs and AGs was common among patients with MDR-TB. FQ resistance (38%) was more common than AG resistance (24%), and 15% were resistant to both classes. FQ resistance was mainly associated with gyrA mutations, and AG resistance with rrs mutations. According to the

current WHO definition, 38% of patients had genotypic pre-XDR-TB. Rapid identification of resistance-associated mutations by LPA can help provide timely individualised treatment, but results should be complemented by phenotypic DST where available, and further multicentre studies to include testing for bedaquiline and linezolid are required.

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