

Evaluation of the BACTEC MGIT 960 SL DST Kit and the GenoType MTBDRsl Test for Detecting Extensively Drug-resistant Tuberculosis Cases

YİD-TB Olgularının Tespitinde BACTEC MGIT 960 SL DST Kitinin ve GenoType MTBDRsl Testinin Değerlendirilmesi

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ABSTRACT

Objective: The present study aimed to evaluate the performances of the BACTEC MGIT 960 SL DST kit and the GenoType MTBDRsl test for detecting second-line antituberculosis drug resistance in Multidrug-resistant TB (MDR-TB) cases.

Materials and Methods: Forty-six MDR-TB strains were studied. Second-line antituberculosis drug resistances were detected using the BACTEC MGIT 960 SL DST kit and the GenoType MTBDRsl test. The Middlebrook 7H10 agar proportion method was used as the reference test.

Results: The sensitivity and specificity values for the BACTEC MGIT 960 SL DST kit were both 100% for amikacin, kanamycin, capreomycin (4 µg/mL), and ofloxacin; 100% and 95.3%, respectively, for capreomycin (10 µg/mL); and 85.7% and 100%, respectively, for moxifloxacin (0.5 µg/mL). The sensitivity and specificity values for the GenoType MTBDRsl test to detect fluoroquinolone and aminoglycoside/cyclic peptide resistance were 88.9% and 100%, respectively, for ofloxacin and 85.7% and 94.9%, respectively, for moxifloxacin (0.5 µg/mL). The accuracy of the GenoType MTBDRsl assay for kanamycin, capreomycin, ofloxacin, and moxifloxacin was lower than that of the BACTEC MGIT 960 SL DST.

Conclusion: The BACTEC MGIT 960 SL DST kit and the GenoType MTBDRsl were successful in detecting second-line antituberculosis drug resistance. Preliminary results of the GenoType MTBDRsl are very valuable for early treatment decisions, but we still recommend additional BACTEC MGIT 960 SL DST kit usage in the routine evaluation of drug-resistant tuberculosis.

Keywords: *Mycobacterium tuberculosis*, agar proportion method, MDR-TB, second-line drug susceptibility

Öz

Amaç: Bu çalışmanın amacı, çok ilaca dirençli tüberküloz (ÇİD-TB) vakalarında, BACTEC MGIT 960 SL DST kitinin ve GenoType MTBDRsl testinin, ikincil antitüberküloz ilaçlara karşı duyarlılığı saptamasındaki performansının değerlendirilmesidir.

Gereç ve Yöntem: 46 tane ÇİD-TB şüpheli çalışıldı. BACTEC MGIT 960 SL DST kiti ve GenoType MTBDRsl testi ile ikincil antitüberküloz ilaçlara karşı direnç durumu tespit edilmiştir. Middlebrook 7H10 agar proporsiyon metodu referans yöntem olarak kullanılmıştır.

Bulgular: BACTEC MGIT 960 SL DST kitinin duyarlılık ve özgüllüğü; amikasin, kanamisin, kapreomisin (4 µg/mL) ve ofloksasin için her ikisi de %100; kapreomisin (10 µg/mL) için sırasıyla %100 ve %95,3; moksifloksasin (0,5 µg/mL) için sırasıyla %85,7 ve %100 olarak bulunmuştur. GenoType MTBDRsl testinin florokinolon ve aminoglikozid/siklik peptid dirençli tespitinde duyarlılık ve özgüllüğü; ofloksasin için sırasıyla %88,9 ve %100; moksifloksasin (0,5 µg/mL) için sırasıyla %85,7 ve %94,9 olarak bulunmuştur. GenoType MTBDRsl yönteminin kanamisin, kapreomisin, ofloksasin ve moksifloksasin için doğruluğu, BACTEC MGIT 960 SL DST kitine göre daha düşük saptanmıştır.

Sonuç: BACTEC MGIT 960 SL DST kiti ve GenoType MTBDRsl testi ikincil antitüberküloz ilaçlara karşı dirençli saptanmasında başarılı bulunmuştur. GenoType MTBDRsl testi ile elde edilen ön bilgiler, erken dönemde tedavi kararlarının alınmasında değerlidir, ancak ilaçlara dirençli tüberküloz olgularının rutin değerlendirilmesinde ek olarak BACTEC MGIT 960 SL DST kitinin kullanılmasını tavsiye etmekteyiz.

Anahtar Kelimeler: *Mycobacterium tuberculosis*, agar proporsiyon yöntemi, ÇİD-TB, ikincil antitüberküloz ilaç duyarlılığı

Introduction

Tuberculosis (TB) remains one of the most fatal infectious diseases worldwide [1]. The emergence of drug-resistant strains of *Mycobacterium tuberculosis* has put status of TB to threatening levels. Multidrug-resistant TB (MDR-TB) is caused by *M. tuberculosis* complex (MTBC) strains that are resistant to at least two first-line antituberculosis (anti-TB) drugs, isoniazid (INH) and

rifampicin (RIF) [2, 3]. The Global Extensively Drug-Resistant Tuberculosis (XDR-TB) Task Force of the World Health Organization (WHO) stated in 2006 that XDR-TB is a form of MDR-TB defined as resistant to at least any of the fluoroquinolones and at least one of the injectable anti-TB drugs (kanamycin, capreomycin, and amikacin) [4].

The agar proportion method on Middlebrook 7H10 agar is accepted as a gold standard for drug susceptibility tests (DST), although it is laborious and can hardly be standardized in routine laboratory applications. Thus, liquid culture methods are widely used and facilitate more rapid and reliable results. However, the major disadvantage of both of these methods is the long incubation time. Recently, molecular methods providing more accurate and rapid results have been developed and used in many routine TB laboratories in many countries [5].

The present study aimed to evaluate the performances of the BACTEC MGIT 960 SL DST kit (Becton Dickinson, USA) and the GenoType MTBDRs/ (Hain Lifescience, Germany) method compared with that of agar proportion as the reference method for detecting resistance to second-line anti-TB drugs in MDR-TB cases.

Materials and Methods

In this study, 46 MTBC strains previously evaluated for first-line anti-TB DST and detected as MDR (resistant to at least INH and RIF) at the National Tuberculosis Reference Laboratory of National Public Health Institution were used. These strains were further evaluated using the proportion method on Middlebrook 7H10 agar, the BACTEC MGIT 960 SL DST kit (Becton Dickinson, USA), and the GenoType MTBDRs/ (Hain Lifescience, Germany) method to test susceptibilities to second-line anti-TB drugs [amikacin (AMI), kanamycin (KAN), cap-

reomycin (CAP), ofloxacin (OFL), and moxifloxacin (MOXI)] and to determine whether they are XDR-TB, or not. Single concentrations of AMI, KAN, and OFL were tested. The Clinical and Laboratory Standards Institute (CLSI) and WHO recommend different concentrations for CAP and MOXI in susceptibility testing, both concentrations suggested for each anti-TB drug were included in the study (10 µg/mL vs 4 µg/mL of CAP concentrations were tested in the agar proportion method and 0.5 µg/mL vs 2 µg/mL of MOXI concentrations were tested in both the agar proportion method and the BACTEC MGIT 960 SL DST kit) [6, 7].

All authors do not declare any “conflict of interest” for publication of this study. All authors have participated in the design, execution, and analysis of the paper and have approved the final version of the manuscript for publication. This study was approved by Ethics Committee of our Institute.

Agar proportion method: Commercially dehydrated forms of second-line anti-TB drugs were dissolved according to the manufacturer’s recommendations and antimicrobial susceptibility guides for mycobacteria [6, 7]. The amount of each drug was calculated using the formula “Mass (mg)=Volume (mL)×Concentration (µg/mL)/Potency (µg/mg)” according to the critical concentrations in Table 1. Potency levels were obtained from the manufacturer’s certificates of analysis. Drug-containing and control plates (without drug addition) were prepared. All strains were subcultured on Löwenstein–Jensen medium before DST. *M. tuberculosis* H37Rv strain indicating pan-susceptibility was used for quality control of DST. All strains were inoculated onto 5% sheep blood agar to ensure purity prior to testing.

Following inoculation on Middlebrook 7H10 medium, the plates were inserted into polyethylene

bags and were incubated for 21 days in 5% CO₂ atmosphere at 37°C. After incubation, growth on control plates was compared with that on drug-containing plates to detect susceptibility. DST results were evaluated as resistant or susceptible.

BACTEC MGIT 960 SL DST kit: Commercially dehydrated forms of second-line anti-TB drugs for BACTEC MGIT 960 SL DST were dissolved and adjusted to critical concentrations (Table 1) according to guidelines (Personal Communication; Siddiqi, SH., Guidelines for Second-line Drug Susceptibility Testing in MGIT Based on Published Studies: Critical Concentrations and Procedures). The agar proportion method and BACTEC MGIT 960 SL DST were performed simultaneously to compare testing times. Strains determined to be positive by the BACTEC MGIT 960 system after 4 days were used in this study.

GenoType MTBDRs/ v1.0: The GenoType MTBDRs/ line probe assay was performed according to the manufacturer’s instructions (Hain Lifescience GmbH, Nehren, Germany). The method depends on PCR-based amplification and a reverse blotting assay to detect resistance to second-line anti-TB drugs (fluoroquinolones and aminoglycosides/cyclic peptides) and ethambutol by evaluating particular wild-type and mutant genes [8].

Statistical analysis

Statistical Package for Social Sciences software version 15.0 (SPSS Inc.; Chicago, IL, USA) was used to analyze data. In performance evaluations of the BACTEC MGIT 960 SL DST kit and the GenoType MTBDRs/ method, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy rates were analyzed. The McNemar test was used for comparing results, and the Kappa test was used for evaluating accuracy.

Table 1. Performance analysis of the BACTEC MGIT 960 SL DST kit and the GenoType MTBDRs/ test

Second Line Antituberculosis Drug	Agar Proportion Method			GenoType MTBDRs/								BACTEC MGIT 960 SL DST								
	C (µg/mL)	n (R/Total)	%	Sensitivity (%)	Specificity (%)	PPV	NPV	Accuracy (%)	McNemar (>%5)	Kappa (<%5)	C (µg/mL)	n	Sensitivity (%)	Specificity (%)	PPV	NPV	Accuracy (%)	McNemar (>%5)	Kappa (<%5)	
AMI	4	6/46	13	6/6	100	100	100	100	100	1.0	<0.001	1	6/6	100	100	100	100	100	1.0	<0.001
KAN	5	7/46	15.2	6/7	85.7	100	100	97.5	97.8	1.0	<0.001	2.5	7/7	100	100	100	100	100	1.0	<0.001
CAP	4	5/46	10.9	5/5	100	97.5	83.4	100	97.8	1.0	<0.001	2.5	5/5	100	100	100	100	100	1.0	<0.001
	10	3/46	6.5						93.5	0.25	<0.001	3/3	100	95.3	60	100	95.6	0.5	<0.001	
OFL	2	9/46	19.6	8/9	88.9	100	100	97.4	97.8	1.0	<0.001	2	9/9	100	100	100	100	100	1.0	<0.001
MOXI	0.5	7/46	15.2	6/7	85.7	94.9	75	97.4	93.5	1.0	<0.001	0.5	6/7	85.7	100	100	97.5	97.8	1.0	<0.001
	2	N	N	NA	83	NA	100			NA		2	N	NA	100	NA	100		NA	

C: concentration; AMI: amikacin; KAN: kanamycin; CAP: capreomycin; OFL: ofloxacin; MOXI: moxifloxacin; N:none; NA: not applicable; PPV: positive predictive value; NPV: negative predictive value

Table 2. Results of drug-resistance in 46 strains

Number of Strains ^b (n=46)	Drug Susceptibility Methods														GenoType MTBDRsI		
	Agar Proportion Method							BACTEC MGIT 960 SL DST							Q ^c	AG/CP ^d	
	AMI (4 µg/mL)	KAN (5 µg/mL)	CAP (4 µg/mL)	CAP (10 µg/mL)	OFL (2 µg/mL)	MOXI (0.5 µg/mL)	MOXI (2 µg/mL)	AMI (1 µg/mL)	KAN (2.5 µg/mL)	CAP (2.5 µg/mL)	OFL (2 µg/mL)	MOXI (0.5 µg/mL)	MOXI (2 µg/mL)				
32 Strains	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S
3 strains	S	S	S	S	R	R	S	S	S	S	R	R	S	R	S		
2 Strains	S	S	S	S	R	S	S	S	S	S	R	S	S	R	S		
2 Strains	R	R	R	S	S	S	S	R	R	R	S	S	S	S	R		
2 Strains	R	R	R	R	S	S	S	R	R	R	S	S	S	S	R		
1 Strain	S	S	S	S	R	R	S	S	S	S	R	S	S	R	S		
1 Strain	R	R	S	S	R	R	S	R	R	S	R	R	S	R	R		
1 Strain	S	R	S	S	S	S	S	S	R	S	S	S	S	S	S		
1 Strain	S	S	S	S	R	R	S	S	S	S	R	R	S	S	S		
1 Strain	R	R	R	R	R	R	S	R	R	R	R	R	S	R	R		

^aS: Susceptible, R: Resistant; ^bStrains with the same results were written in the same line; ^cQuinolones; ^dAminoglikozid & Cyclic peptides
AMI: Amikacin; KAN: Kanamycin; CAP: Capreomycin; OFL: Ofloxacin; MOXI: Moxifloxacin

Results

In our study, susceptibilities to second-line anti-TB drugs of 46 MDR-TB strains were evaluated using the agar proportion method, BACTEC MGIT 960 SL DST kit, and GenoType MTBDRsI method. The numbers and rates of resistance to AMI, KAN, CAP (4 µg/mL), CAP (10 µg/mL), OFL, MOXI (0.5 µg/mL), and MOXI (2 µg/mL) as well as drug susceptibility results and performance analyses of the BACTEC MGIT 960 SL DST kit and GenoType MTBDRsI test are shown in Table 1, and drug susceptibility profiles are presented in Table 2. No strain was resistant to MOX (2 µg/mL). Two strains (4.3%) were detected as XDR-TB strains.

For agar proportion method, the testing period for each strain was 12 (±2) days, for BACTEC MGIT 960 SL DST test it was 8 (±1) days, and it was approximately 4 h for the GenoType MTBDRsI method.

The McNemar test revealed no statistically significant difference ($p > 0.05$), whereas accuracy analysis using the Kappa test revealed statistically significant results.

Discussion

According to a WHO report in 2015, 9.7% of MDR-TB patients also had XDR-TB and 105 countries worldwide reported at least one XDR-TB case [9]. Rapid and accurate detection of resistance to second-line anti-TB drugs is crucial to protect public health by preventing transmission and treating drug-resistant TB cases effectively. Therefore, our study aimed to evaluate the performances of the BACTEC MGIT 960 SL DST kit and GenoType MTBDRsI

method in comparison with that of the agar proportion method as the reference method for detecting resistance to second-line anti-TB drugs in MDR-TB cases.

BACTEC MGIT 960 SL DST kit: In our study, two XDR-TB strains were detected accurately by the BACTEC MGIT 960 SL DST kit (100%). Mean testing time was 7 days and 23 h, and regarding to result rapidity, no superiority for BACTEC MGIT 960 SL DST was observed over the GenoType MTBDRsI method.

Amikacin: Six strains were identified as resistant to AMI by the agar proportion method. The sensitivity, specificity, PPV, and NPV rates of the BACTEC MGIT 960 SL DST kit were all 100%. Van Ingen et al. [10] studied 28 MDR/XDR-TB strains using Middlebrook 7H10 agar dilution and BACTEC MGIT 960 methods, and their results were consistent with our results. In addition, Morcillo et al. [11] studied with 144 MDR/XDR-TB strains and found identical results (100%) for all parameters.

Some other researchers reported different results. Lopez-Roa et al. [12] studied 26 MDR-TB strains using the BACTEC MGIT 960 SL DST and reported sensitivity and specificity rates for AMI as 50% and 72.7%, respectively, which were lower than those in our study. We believe that this discordance might have been due to the different in the number of isolates studied or improper preparations of antibiotic solutions. Furthermore, we used new, commercially available, dehydrated forms of antibiotics in ready-to-use falcon tubes, which do not require any preparations.

Kanamycin: In total, seven strains were identified as resistant to KAN. The sensitivity, specificity, PPV, and NPV rates of the BACTEC MGIT 960 SL DST kit were all 100%. Zhao et al. [13] studied 321 isolates (sensitivity 100% and specificity 98.6%) and Kim et al. [14] studied 193 clinical isolates (sensitivity 100%, specificity 95%) using the BACTEC MGIT 960 SL DST, and their results were consistent with our results. However, Said et al. [15] evaluated 343 isolates using the BACTEC MGIT 960 method and reported sensitivity of 27%, which was considerably lower than that in our study. We believe that this discordance occurred because Said et al. [15] used a KAN concentration higher (5 µg/mL) than the concentration recommended by CLSI and WHO (2.5 µg/mL) [7, 8]. This higher concentration might have caused false susceptibility due to inability to detect at MIC levels of 2.5-5 µg/mL.

Capreomycin: CAP concentrations for the agar proportion method in the CLSI (10 µg/mL) and WHO (4 µg/mL) documents are different [6, 7]. In our study, we evaluated both CLSI and WHO concentrations in the reference method and compared results with those data obtained using the BACTEC MGIT 960 method to determine which concentration was more appropriate.

The sensitivity, specificity, PPV, and NPV rates of the BACTEC MGIT 960 SL DST kit were all 100% compared to those of the agar proportion method employed using 4-µg/mL CAP; five strains were identified as resistant to CAP. The results reported by Morcillo et al. [11], Van Ingen et al. [10], Kim et al. [14] and Zhao et al. [13] were consistent with those of our study.

The sensitivity, specificity, PPV, and NPV rates of the BACTEC MGIT 960 SL DST kit compared with those of the agar proportion method employed using 10- $\mu\text{g}/\text{mL}$ CAP were 100%, 95.3%, 60%, 100%, respectively; three strains were identified as resistant to CAP. This concentration caused a decrease in the number of resistant strains (from five resistant strains to three strains), resulting in a wrong assessment as the other two resistant strains detected using the BACTEC MGIT 960 SL DST kit were interpreted as "false resistant." Thus, the PPV rate was considerably lower in our study than in many other studies [10, 13]. Consequently, we believe that a CAP concentration of 4 $\mu\text{g}/\text{mL}$ WHO is more appropriate to use in the Middlebrook 7H10 agar proportion method [8].

Ofloxacin: Nine strains were identified as resistant to OFL. The sensitivity, specificity, PPV, and NPV rates of the BACTEC MGIT 960 SL DST kit were all 100%. The results reported by Zhao et al. [13] and Morcillo et al. [11] were consistent with our results. On the other hand, Said et al. [15] reported PPV of 18%, which is considerably lower than that in our study (100%). We believe that this low PPV was because of the OFL concentration used in the BACTEC MGIT 960 method (1 $\mu\text{g}/\text{mL}$), which may have caused "false resistant" results (OFL concentration in our study: 2 $\mu\text{g}/\text{mL}$).

Lopez-Roa et al. [12] reported sensitivity of 50%, which is inconsistent with our results, although OFL concentrations were identical to those in our study. In addition, Lopez-Roa et al. [12] reported lower sensitivity for AMI (72.7%) than that other studies and our study (100%). We believe that this discordance was due to the low number of isolates they studied ($n=26$) or the different concentrations of the antibiotic solutions prepared in their study [10, 11].

Moxifloxacin: World Health Organization recommends two different MOXI concentrations (0.5 and 2 $\mu\text{g}/\text{mL}$) for both the agar proportion method and the BACTEC MGIT 960 method, both of which were studied by us [7].

Seven strains were identified as resistant to MOXI (0.5 $\mu\text{g}/\text{mL}$). One strain was found to be resistant to MOXI using the reference method (0.5 $\mu\text{g}/\text{mL}$) and the GenoType MTBDRs/ method but was found to be susceptible to MOXI (0.5 $\mu\text{g}/\text{mL}$) using the BACTEC MGIT 960 SL DST kit (false susceptible).

The sensitivity, specificity, PPV, and NPV rates of the BACTEC MGIT 960 SL DST kit for 0.5- $\mu\text{g}/\text{mL}$ MOXI were 85.7%, 100%, 100%, and 97.5%

respectively. For this MOXI concentration, Kim et al. [14] and Van Ingen et al. [10] reported results similar to those in our study.

In our study, because no strain was resistant to 2- $\mu\text{g}/\text{mL}$ MOXI, only specificity (100%) and NPV (100%) rates could be calculated. Compared to Van Ingen et al.'s [10] report of 71%, our specificity rate (100%) was higher. Because there was no strain resistant to 2- $\mu\text{g}/\text{mL}$ MOXI, for proper clinical evaluation of MOXI in the treatment of MDR-TB, we strongly recommend evaluating both 0.5- $\mu\text{g}/\text{mL}$ and 2- $\mu\text{g}/\text{mL}$ concentrations simultaneously in DSTs.

GenoType MTBDRs/: Two XDR strains were correctly detected by the GenoType MTBDRs/ method (100%). This method was the most advantageous among the methods we tested in terms of providing rapid results (in approximately 4 h).

Fluoroquinolones (OFL, MOXI): The sensitivity, specificity, PPV, and NPV rates were 88.9%, 100%, 100%, and 97.4%, respectively, for OFL and 85.7%, 94.9%, 75%, and 97.4%, respectively, for MOXI (0.5 $\mu\text{g}/\text{mL}$). For 2- $\mu\text{g}/\text{mL}$ MOXI, no strain was found to be resistant, and we could only obtain specificity (83%) and NPV (100%) rates.

Our results were consistent with those of Ignatyeva et al. [16]. However, the sensitivity rate for OFL in our study was higher than those reported by Tukvadze et al. [17] and Jin et al. [18]. Our results were consistent with those of the meta-analysis study of Theron et al. [19] in which performance of the GenoType MTBDRs/ method was evaluated by analyzing 21 studies. Our study results for MOXI, except for the sensitivity rate, were consistent with those reported by Ferro et al. [20] and Fan et al. [21]. Our sensitivity rate for MOXI was lower. We believe that geographic variability of resistance profiles or the relatively lower number of isolates we studied may have caused these differences. Notably, the older version of the GenoType MTBDRs/ method (v1.0) did not contain probes of *gyrB*, which may have caused such variation in rates. In recent studies, a new version of the GenoType MTBDRs/ method (v2.0) containing probes of *gyrB* in addition to *gyrA* has shown high concordance with sequencing, but the clinical relevance is controversial [22].

Aminoglycosides/Cyclic peptides (AG/CPs) (AMI, KAN, CAP): In our study, seven strains were identified as resistant to AG/CPs. One strain was susceptible with the agar proportion method and the BACTEC MGIT 960 SL DST kit, but resistant with the GenoType MTBDRs/

method (false resistant). We think that this discordance may depend on mutations not causing resistance or phenotypically unshown resistance profiles with low MIC levels. However, we were not able to define the exact genetic region causing false resistance in the GenoType MTBDRs/ method due to lack of sequence analysis. On the other hand, one strain was identified as false susceptible by the GenoType MTBDRs/ method. We think that this resistance occurred because of genetic regions that are not included on the test strip.

In our study, sensitivity, specificity, PPV and NPV rates of the GenoType MTBDRs/ method for AMI were all 100%; for KAN 85.7%, 100%, 100%, 97.5% and for CAP 100%, 97.5%, 83.4%, 100%, respectively. In addition to higher sensitivity rate for KAN, our results were similar to those of Ignatyeva et al. [16] and Huang et al. [22] and to those Theron et al. [19] highlighted in their review article. Resistance to KAN can occur with *eis* promoter gene regions other than *rrs* regions, which are commonly responsible for resistance to AG/CPs. The new version of the GenoType MTBDRs/ method (v2.0) contains probes of *eis* promoter regions on its strips and so it can detect resistance originating from these regions [22]. Our sensitivity rates may rise if we use this new version. Therefore, low sensitivity for KAN may have depended on resistant TB strains containing different genetic regions [23, 24].

Due to the low sensitivity of the second-line line probe assay (the GenoType MTBDRs/ method), conventional DST methods have gained main attention to rule out resistance [25]. Although recent studies have reported that by adding the new probes, the sensitivity rates have increased and the method can detect phenotypically-undetectable low and moderate resistance, the clinical impact is debatable due to lack of published *in vivo* research data [22]. We have studied the older version (v1.0) of the GenoType MTBDRs/ method, which is a limitation, however the results of both methods were found quite successful. Of note, first performing the GenoType MTBDRs/ and then confirming all the negative results with the BACTEC MGIT 960 SL DST is very costly, especially for low-income and TB-pandemic geographic locations. On the other hand, early detection and starting treatment of drug-resistant TB cases are crucial and the GenoType MTBDRs/ method is valuable for its ability to detect directly from the patient sample.

In conclusion, XDR-TB strains (100%) and resistance to AG/CPs and fluoroquinolones were successfully detected by the BACTEC MGIT 960 SL DST kit and the GenoType MTBDRs/ method.

We think that by avoiding improper preparations of drug concentrations by removing manual procedures, the BACTEC MGIT 960 SL DST kit will provide standardization to second-line anti-TB drug susceptibility results. On the other hand, the sensitivity of the GenoType MTBDRsl method in detecting KAN and fluoroquinolone resistance may be increased using the new version (v2.0). A CAP concentration of 4 µg/mL WHO seems to be more appropriate for the Middlebrook 7H10 agar proportion method. All strains detected resistant to fluoroquinolones were found to be susceptible to MOXI with a concentration of 2 µg/mL. Therefore, for MDR-TB strains that were identified as resistant to 0.5-µg/mL MOXI, we strongly recommend retesting with 2-µg/mL MOXI and reconsidering to count in MOXI for the treatment regime.

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