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MOLECULAR EPIDEMIOLOGY OF MULTIDRUG- AND EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS IN KANO STATE, NORTHWESTERN NIGERIA

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ABSTRACT

Tuberculosis (TB) remains a major global public health challenge, and Nigeria is among the eight countries that contribute the highest burden of casesThe emergence and rise of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB threaten progress toward elimination, yet molecular epidemiological data from northwestern Nigerian states remain limited. The objective of this study was to determine the prevalence and molecular determinants of MDR- and XDR-TB among GeneXpert-positive pulmonary TB patients in Kano State using MTBDRplus and MTBDRsl assays. A cross-sectional study was conducted using samples collected from 401 GeneXpert-positive TB patients recruited across 19 DOTS clinics in Kano State between 2018 and 2019. Sputum samples were cultured on Lowenstein–Jensen medium, followed by molecular drug susceptibility testing with the Genotype MTBDRplus (first-line resistance) and MTBDRsl (second-line resistance) assays. Socio-demographic and clinical data were obtained via structured questionnaires. Multidrug-Resistant Tuberculosis (MDR-TB) was detected in 41 patients (10.2%), while rifampicin and isoniazid mono-resistance occurred in 26 (6.5%) and 6 (1.5%), respectively. Resistance clustered in urban LGAs, notably Nasarawa (3.5%), Fagge (1.5%), and Gwale (0.7%). MDR-TB was most prevalent among males (11.5%) and patients aged 25–34 years (35.4%).There was no significant association between HIV status and MDR-TB (HIV-positive: 9.8%; HIV-negative: 10.3%). Second-line resistance showed fluoroquinolone resistance in 6 (1.5%), aminoglycoside resistance in 12 (3.0%), and low-level amikacin resistance in 1 (0.2%). Two XDR-TB cases (0.5%) were identified in Nasarawa and Ungogo LGAs. The MDR-TB burden in Kano State is high, with urban hotspots and emerging XDR-TB, requiring strengthened surveillance, targeted interventions, and rational antibiotic stewardship.

Keywords: Multidrug-resistant tuberculosis, Extensively drug-resistant tuberculosis, Molecular epidemiology, MTBDRplus/MTBDRsl assays, Kano, Nigeria

INTRODUCTION

Tuberculosis (TB) remains a major public health challenge globally and particularly in sub-Saharan Africa, where Nigeria ranks among the eight countries contributing two-thirds of the global TB burden Chen et al. (2025). Despite intensified control strategies, the emergence and spread of drug-resistant forms of TB, including multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB), threaten progress toward TB elimination. MDR-TB, defined as resistance to at least isoniazid and rifampicin, and XDR-TB, which includes additional resistance to fluoroquinolones and second-line injectable drugs, are associated with poor treatment outcomes, higher costs, and increased transmission (Dheda et al., 2024; Lange et al., 2018).

Nigeria is recognized as a high-burden country for both MDR-TB and XDR-TB, with estimated MDR-TB prevalence rates of 4.3% among new TB cases and 15% among previously treated cases (NTBLCP, 2022). However, regional disparities exist due to variations in healthcare access, socio-demographic profiles, and transmission dynamics. Kano State, located in northwestern Nigeria, is one of the most populous states in the country. Its high population density, rural urban migration, and significant cross-border mobility are key factors that intensify TB transmission (Bello., 2025). Despite this, limited state-specific data exist on the prevalence and molecular epidemiology of drug-resistant TB in Kano.

Advances in molecular diagnostics, particularly line probe assays (LPAs) such as MTBDRplus and MTBDRsl, have enabled rapid detection of resistance-conferring mutations in *Mycobacterium tuberculosis*. These assays target critical genes, including *rpoB* (rifampicin resistance), *katG* and *inhA* (isoniazid resistance), as well as *gyrA*, *gyrB*, *rrs*, and *embB* (second-line resistance) (GLI, 2019). Their use in surveillance not only guides patient management but also offers critical insights into local patterns of drug resistance**.**

This study was aimed to determine the prevalence and molecular determinants of MDR-TB and XDR-TB among GeneXpert positive pulmonary TB patients in Kano State using MTBDRplus and MTBDRsl assays. The findings of this study offer essential evidence to inform targeted interventions, enhance TB control strategies, and support Nigeria's efforts to achieve the End TB targets.

MATERIALS AND METHODS

Study Setting and Population

This study was carried out in Kano State (latitude 11°30′N, longitude 8°30′E), with a projected population of over 15 million in 2023 and comprising 44 Local Government Areas

(LGAs). The state also bears a high tuberculosis (TB) burden (NTBLCP, 2022).

Its dense population, urban rural mix, and cross-border mobility make it a distinct epidemiological setting for TB transmission (Bello, 2025).

The study population included patients diagnosed with GeneXpert-positive pulmonary TB (PTB) attending Directly Observed Treatment Short-course (DOTS) clinics across all 44 LGAs between January 2018 and December 2019. Nineteen strategically selected DOTS clinics served as diagnostic hubs.

Study Design

A cross-sectional design was employed to determine the prevalence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) among smear-positive PTB patients.

Sample Size Determination

The minimum sample size was calculated using Cochran's formula for cross-sectional studies (Cochran, 1977):

$n=Z^2\times p\times q/d^2$

Where:

Z = 1.96 (95% confidence level)

p = 0.27 (estimated TB prevalence in Nigeria; Ogbo et al., 2018)

q = 1 − p = 0.73

d = 0.05 (5% margin of error)

This yielded a baseline sample size of 303. To account for non-response and design effects, a multiplier of 1.51 was applied (Kalton & Brick, 2005; Kish, 1965; Lynn, 2003), giving a target sample size of 458. A total of 401 patients were ultimately recruited and analyzed.

Sampling Technique and Participant Recruitment

A proportionate stratified sampling technique was used, with the 19 DOTS clinics serving as strata. Sample size allocation was proportionate to patient load per clinic (KSTBLCP, 2018), ensuring statewide representation. Eligible participants were GeneXpert-positive PTB patients aged 5–88 years presenting at the participating clinics during the study period. Despite enhanced contact protocols and incentives (Dillman et al., 2014), the final sample comprised 401 participants.

Data Collection

Data were collected between January 2019 and December 2021.

Questionnaire

A structured interviewer-administered questionnaire was used to obtained information on socio-demographic characteristics, socioeconomic status, HIV status, TB history (past two years), TB treatment history, comorbidities (e.g., diabetes), and behavioral factors (e.g., alcohol and injection drug use). Written informed consent was obtained from all participants or guardians of minors.

Sputum collection

Two early-morning sputum samples (5 mL each; expectorated sputum, not saliva) were collected within one week in sterile, leak-proof containers (Becton, Dickinson, 2007).

Specimen Transport and Storage

Specimens were placed in primary biohazard bags, sealed within secondary bags, and transported upright in double-walled containers to maintain cold temperatures (Becton, Dickinson, 2007). Batches of 15–20 specimens were promptly delivered to the North West Zonal TB reference Laboratory, Aminu Kano Teaching Hospital, Kano, where they were refrigerated at −8 °C and processed within 48 hours.

Laboratory Processing and Analysis

All laboratory procedures were performed at the Aminu Kano Teaching Hospital.

Digestion and Decontamination

Sputum samples were processed using the N-acetyl-L-cysteine–sodium hydroxide (NALC–NaOH) method (CDC, 2020, 2023). After vortexing and incubation, phosphate buffer was added, followed by centrifugation at 3000 g for 20 min at 4 °C. Supernatants were discarded and sediments re-suspended in 2 mL phosphate buffer.

Culture

Decontaminated sediments were inoculated on Lowenstein–Jensen (LJ) media and incubated at 37 °C for 2–8 weeks. Colonies were identified as *Mycobacterium tuberculosis* complex based on morphology and confirmed with SD Bioline rapid diagnostic tests (GLI, 2019). The isolates were subsequently used for genotyping.

MTBDRplus Assay (First-Line Drug Resistance)

Drug Susceptibility Testing (DST) for isoniazid and rifampicin was performed using the Genotype MTBDRplus assay (Hain Lifescience, Germany) according to manufacturer's instructions. The assay involves three steps: DNA extraction (using Genolyse), multiplex PCR amplification, and reverse hybridization. Amplification was conducted with separate workflow rooms to minimize contamination. Hybridization was performed using an automated GT Blot system, followed by denaturation, stringent washes, conjugation, rinsing, substrate addition, and visualization. Strips were air-dried and evaluated for mutation patterns (GLI, 2019).

MTBDRsl Assay (Second-Line and XDR-TB Resistance)

The Genotype MTBDRsl assay (Hain Lifescience, Germany) was performed on culture isolates for detection of fluoroquinolone, aminoglycoside, and second-line injectable resistance. Polymerase Chain Reaction (PCR) was carried out with HotStarTaq DNA polymerase (Qiagen, Germany) in a thermocycler with the following conditions: 95 °C for 15 min; 10 cycles of 95 °C for 30 s and 58 °C for 2 min; 20 cycles of 95 °C for 25 s, 53 °C for 40 s, and 70 °C for 40 s; and a final extension at 70 °C for 8 min. Valid results were defined by the presence of *M. tuberculosis* complex-specific control (TUB), conjugate control (CC), and amplification control (AC) bands, together with target locus controls (GLI, 2019).

RESULTS AND DISCUSSION

Socio-demographic Characteristics of Study Participants

The socio-demographic characteristics of the study participants are summarized in Table 1**.** This study enrolled 401 participants, with a mean age of 34.96 ± 14.8 years. The largest age group was 25–34 years (35.4%), followed by 35–44 years (20.2%) and 15–24 years (18.7%). Children aged 5–14 years constituted 3.0% of the sample, while participants aged ≥65 years accounted for 6.2%.

Males comprised 71.6% of the participants. More than half of the respondents were married (58.9%), whereas 41.1% were single. With respect to ethnicity, the overwhelming majority were Hausa (98.8%), while Yoruba (0.7%), Igbo (0.2%), and Idoma (0.2%) formed minority groups.

A relatively high proportion of participants (50.9%) had completed tertiary education and 35.2% having attained secondary education. Smaller proportions reported primary education (7.7%) or no formal education (6.2%).

In terms of occupation, 45.6% of respondents were self-employed, 31.2% were students, and 14.0% were employed for wages. A smaller fraction were unemployed (5.7%) or retired (3.5%). Among the 239 respondents engaged in employment, menial jobs were the most common (34.3%), followed by civil service (23.4%), business/trading (21.8%), farming (12.6%), and driving (7.9%).

Analysis of monthly income showed that 34.0% earned between ₦18,000 and ₦34,999, while 30.4% earned between ₦35,000 and ₦69,999. In addition, 17.0% reported earnings between ₦70,000 and ₦120,000, 11.5% earned more than ₦120,000, and 7.1% earned less than ₦18,000.

Table 1: Socio-demographic Characteristics of Study Participants (n = 401)

Variable	Frequency	Percentage (%)
Age group		
5 – 14	12	3.0
15 – 24	75	18.7
25 – 34	142	35.4
35 – 44	81	20.2
45 – 54	36	9.0
55 – 64	30	7.5
≥65	25	6.2
Mean ± SD = 34.96 ± 14.8		
Sex		
Male	287	71.6
Female	114	28.4
Marital status		
Single*	165	41.1
Married	236	58.9
Tribe		
Hausa	396	98.8
Yoruba	3	0.7
Idoma	1	0.2
Igbo	1	0.2
Educational attainment		
No formal education	25	6.2
Primary	31	7.7
Secondary	141	35.2
Tertiary	204	50.9
Occupation		
Employed for wages	56	14.0
Self-employed	183	45.6
Retired	14	3.5
Student	125	31.2
Unemployed	23	5.7
Type of employment †		
Civil servant	56	23.4
Business/trading	52	21.8
Menial jobs	82	34.3
Farming	30	12.6
Driver	19	7.9
Monthly income (₦)		
<18,000	18	7.1
18,000 – <35,000	86	34.0
35,000 – <70,000	77	30.4
70,000 – 120,000	43	17.0
>120,000	29	11.5

Key: *Single = not married; †Type of employment refers to subset of employed/self-employed participants.

Prevalence of MDR TB among TB patients using MTBDRplus

Table 2 showed the prevalence of MDR-TB and mono-resistance to first-line drugs among the study participants as determined by the MTBDRplus assay. Out of 401 TB patients, 41 (10.2%) were identified as having MDR-TB. Rifampicin mono-resistance was observed in 26 patients (6.5%), while isoniazid mono-resistance was detected in 6 patients (1.5%). The remaining 360 (89.8%), 375 (93.5%), and 395 (98.5%) patients tested negative for MDR-TB, rifampicin, and isoniazid mono-resistance, respectively.

Table 2: Prevalence of MDR-TB among TB Patients in Kano State using the MTBDRplus (First-line LPA)

LPA Result	MDR-TB (%)	RIF Mono (%)	INH Mono (%)
Positive	41 (10.2)	26 (6.5)	6 (1.5)
Negative	360 (89.8)	375 (93.5)	395 (98.5)
Total	**401**	**401**	**401**

Key: LPA = Line Probe Assay; MDR-TB = Multidrug-Resistant Tuberculosis; RIF = Rifampicin; INH = Isoniazid

Table 3 presents the distribution of MDR-TB and monoresistant TB cases across the LGAs of Kano State as detected by the MTBDRplus assay. Out of the 401 patients screened, a total of 41 (10.2%) had MDR-TB. The highest occurrence was observed in Nasarawa LGA, which accounted for 14 cases (3.5% of all participants), followed by Fagge with 6 cases (1.5%), Gwale and Kumbotso with 3 cases each (0.7%), and Dala and Rano with 2 cases each (0.5%). Several LGAs, including Albasu, Danbatta, Karaye, Kura, Minjibir, Tarauni, Ungogo, and Wudil, reported only one MDR-TB case (0.2% each), while the majority of LGAs reported no MDR-TB cases.

Rifampicin monoresistance was detected in 26 patients (6.5%). Nasarawa and Kano Municipal (KMC) had the highest numbers, with 5 cases each (1.2%), followed by Gabasawa and Madobi with 2 cases each (0.5%). The remaining LGAs including Albasu, Bebeji, Danbatta, Fagge, Gaya, Gwale, Kumbotso, Kunchi, Tarauni, Tsanyawa, and Wudil each reported a single case (0.2%).

Isoniazid monoresistance was less common, detected in 6 patients (1.5%). The highest being from Tarauni with 2 cases (0.5%), while Nasarawa, Kumbotso, and Rimin Gado each had 1 case (0.2%).

Overall, MDR-TB and drug resistance were unevenly distributed across Kano State, with certain urban LGAs such as Nasarawa, Fagge, KMC, Gwale, and Kumbotso emerging as notable hotspots.

Table 3: Distribution of MDR-TB and Monoresistance among TB Patients in Kano State by LGA using MTBDRplus (First-line LPA)

LGA of cases	MDR-TB n (%)	RIF Mono n (%)	INH Mono n (%)
Ajingi	0 (0.0)	0 (0.0)	0 (0.0)
Albasu	1 (0.2)	1 (0.2)	0 (0.0)
Bagwai	0 (0.0)	0 (0.0)	0 (0.0)
Bebeji	0 (0.0)	1 (0.2)	0 (0.0)
Bunkure	2 (0.5)	0 (0.0)	0 (0.0)
Dala	2 (0.5)	0 (0.0)	0 (0.0)
Danbatta	1 (0.2)	1 (0.2)	0 (0.0)
Dawakin Kudu	0 (0.0)	0 (0.0)	0 (0.0)
Dawakin Tofa	0 (0.0)	0 (0.0)	0 (0.0)
Fagge	6 (1.5)	1 (0.2)	0 (0.0)
Gabasawa	0 (0.0)	2 (0.5)	0 (0.0)
Garko	0 (0.0)	0 (0.0)	0 (0.0)
Garun Malam	0 (0.0)	0 (0.0)	0 (0.0)
Gaya	0 (0.0)	1 (0.2)	0 (0.0)
Gezawa	0 (0.0)	0 (0.0)	0 (0.0)
Gwale	3 (0.7)	1 (0.2)	0 (0.0)
Gwarzo	0 (0.0)	0 (0.0)	0 (0.0)
Kabo	0 (0.0)	0 (0.0)	0 (0.0)
Kibiya	0 (0.0)	0 (0.0)	0 (0.0)
KMC	1 (0.2)	5 (1.2)	0 (0.0)
Kumbotso	3 (0.7)	1 (0.2)	1 (0.2)
Kunchi	0 (0.0)	1 (0.2)	0 (0.0)
Karaye	1 (0.2)	0 (0.0)	0 (0.0)
Kura	1 (0.2)	0 (0.0)	0 (0.0)
Madobi	0 (0.0)	2 (0.5)	0 (0.0)
Minjibir	1 (0.2)	0 (0.0)	0 (0.0)
Nasarawa	14 (3.5)	5 (1.2)	2 (0.5)
Rano	2 (0.5)	0 (0.0)	0 (0.0)
Rimin Gado	0 (0.0)	0 (0.0)	1 (0.2)
Rogo	0 (0.0)	0 (0.0)	0 (0.0)
Sumaila	0 (0.0)	0 (0.0)	0 (0.0)
Takai	0 (0.0)	0 (0.0)	0 (0.0)
Tarauni	1 (0.2)	1 (0.2)	2 (0.5)
Tofa	0 (0.0)	0 (0.0)	0 (0.0)
Tsanyawa	0 (0.0)	2 (0.5)	0 (0.0)
Tudun Wada	0 (0.0)	0 (0.0)	0 (0.0)
Ungogo	1 (0.2)	0 (0.0)	0 (0.0)
Warawa	0 (0.0)	0 (0.0)	0 (0.0)
Wudil	1 (0.2)	1 (0.2)	0 (0.0)
Total	**41 (10.2)**	**26 (6.5)**	**6 (1.5)**

Key: LPA = Line Probe Assay; MDR-TB = Multidrug-Resistant Tuberculosis; RIF mono = Rifampicin monoresistance; INH mono = Isoniazid monoresistance.

First-Line Drug Resistance (MTBDRplus)

Table 4, show that out of 401 TB patients analyzed, 41 (10.2%) were diagnosed with MDR-TB, 26 (6.5%) with rifampicin monoresistance, and 6 (1.5%) with isoniazid monoresistance. The distribution differed across the various LGAs, with the highest clustering of MDR-TB detected in the 25–34-year age group and among male patients (11.5%). By educational status, tertiary education (17.1%) and no formal education (11.8%) showed the highest prevalence of MDR-TB. Analysis by HIV status revealed similar MDR-TB proportions among HIV-positive (9.8%) and HIV-negative patients (10.3%), though rifampicin and isoniazid

monoresistance occurred exclusively in the HIV-negative subgroup.

Second-Line and XDR-TB Resistance (MTBDRsl)

Further analysis with the MTBDRsl assay revealed additional resistance patterns (Table 4). Six isolates (1.5%) showed fluoroquinolone resistance, 12 (3.0%) had aminoglycoside resistance, and 1 (0.2%) exhibited low-level amikacin resistance. Two cases (0.5%) of XDR-TB were identified, in Nasarawa and Ungogo LGAs. Geographically, fluoroquinolone resistance was distributed across Albasu, Fagge, Gwarzo, Nasarawa, Rano, and Tarauni, while aminoglycoside resistance clustered in Nasarawa (25.0%) and appeared in several other LGAs, including Dala, Danbatta, Fagge, Gwale, KMC, Rimingado, Warawa, and Wudil. Importantly, no second-line or XDR resistance was observed among HIV-positive patients. Nasarawa LGA displayed the broadest resistance spectrum, reporting MDR-TB, fluoroquinolone resistance, aminoglycoside resistance, and XDR-TB concurrently.

Table 4: Prevalence of M/XDR among TB Patients in Kano State by LGA and HIV Status Using the MTBDRplus and MTBDRsl Assays

LGA Status	MDR-TB (%)	RIF mono (%)	INH mono (%)	XDR-TB (%)	Fluoroquinolones (%)	Aminoglycosides (%)	Amikacin low level (%)
Ajingi	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Albasu	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)
Bagwai	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bebeji	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nasarawa	1 (1.4)	–	–	1 (1.4)	1 (16.7)	3 (25.0)	0 (0.0)
Rano	0 (0.0)	–	–	0 (0.0)	1 (16.7)	0 (0.0)	1 (16.7)
Ungogo	–	–	–	1 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)
Total	41 (10.2)	26 (6.5)	6 (1.5)	2 (0.5)	6 (1.5)	12 (3.0)	1 (0.2)
HIV+	4 (9.8)	0 (0.0)	0 (0.0)	–	–	–	–
HIV–	37 (90.2)	26 (6.9)	6 (1.6)	–	–	–	–

Keys: MDR-TB = Resistance to both isoniazid (INH) and rifampicin (RIF).RIF mono = Resistance to rifampicin only. INH mono = Resistance to isoniazid only. XDR-TB = MDR-TB plus resistance to any fluoroquinolone (FQ) and at least one second-line injectable (e.g., amikacin, kanamycin, or capreomycin). Fluoroquinolones = Resistance to levofloxacin or moxifloxacin. Aminoglycosides = Resistance to kanamycin or capreomycin (excluding amikacin low-level). Amikacin low-level = Resistance confined to amikacin at a lower critical concentration.

Discussions

The present study revealed a substantial burden of drug-resistant tuberculosis (TB) in Kano State. Of the 401 TB patients evaluated with the MTBDRplus assay, 41 (10.2%) were confirmed to have multidrug-resistant TB (MDR-TB), highlighting a substantial burden of drug resistance within the study population. Rifampicin and isoniazid mono-resistance, detected in 26 (6.5%) and 6 (1.5%) patients respectively, further underscore the heterogeneity of resistance patterns (Table 2). The prevalence of MDR-TB reported here is higher than the global average of 4.3% among new TB cases and comparable to the 18% reported among previously treated cases (WHO, 2023). These findings suggest ongoing transmission of both MDR and mono-resistant strains, reinforcing the need for enhanced diagnostic capacity and targeted interventions to interrupt local transmission dynamics. They also underscore the substantial challenge that drug-resistant TB continues to pose to TB control efforts in Nigeria.The observed rifampicin mono-resistance aligns with global concerns that rifampicin resistance is a strong surrogate marker for MDR-TB due to its close association with isoniazid resistance (Lange et al., 2018). Conversely, the relatively lower isoniazid mono-resistance prevalence is consistent with findings from Nigerian studies that reported rates between 1–3% (Aliyu et al., 2020; Lawson et al., 2011). This pattern reinforces rifampicin resistance as the dominant driver of MDR-TB in this setting.

Geospatially, MDR-TB was not evenly distributed across Kano State. Nasarawa LGA recorded the highest number of MDR-TB cases (3.5%), followed by Fagge with 6 cases (1.5%), Gwale with 3 cases (0.7%), and Kumbotso with 3 cases (0.7%). Several LGAs observed isolated cases, while many had none, as shown in Table 3. This clustering suggests that transmission and detection are concentrated in urban LGAs, a trend consistent with findings from Lagos, Abuja, and other metropolitan areas in Africa, where higher resistance rates are linked to population density, mobility, and greater access to referral facilities (Aliyu et al., 2020; Lawson et al., 2011; Desta et al., 2020; Dheda et al., 2017).

The socio-demographic profile of resistance also revealed important trends. MDR-TB was most prevalent among patients aged 25–34 years and among men, reflecting the heightened vulnerability of young, economically active populations. These groups may face increased occupational exposure, mobility, and health-seeking delays, all of which heighten the risk of infection and incomplete treatment (Lu et al., 2022; Lawson et al., 2011). An educational gradient was also evident: MDR-TB prevalence was higher among patients with tertiary education (17.1%) and those without formal education (11.8%). This dual pattern likely reflects increased diagnostic access among educated individuals and poor awareness and treatment adherence among those without education (Faye et al., 2025).

Notably, MDR-TB prevalence was similar among HIV-positive (9.8%) and HIV-negative (10.3%) patients, but rifampicin and isoniazid mono-resistance occurred exclusively among HIV-negative individuals as shown in table 4. This contrasts with reports from South Africa and Ethiopia where HIV co-infection was strongly associated with drug resistance (Dheda et al., 2017; Desta et al., 2020). The absence of mono-resistance among HIV-positive patients in this cohort may reflect sample size limitations, early case detection through HIV care programs, or improved adherence from integrated TB/HIV services in Kano State.

Second-line resistance patterns detected by the MTBDRsl assay further highlight emerging threats. Fluoroquinolone resistance was found in 1.5% of patients, aminoglycoside resistance in 3.0%, and low-level amikacin resistance in 0.2%. Alarmingly, 0.5% of patients were diagnosed with extensively drug-resistant TB (XDR-TB), identified in Nasarawa and Ungogo LGAs. Although relatively rare, XDR-TB presents a critical therapeutic and public health concern due to limited treatment options and higher mortality (WHO, 2023; Lange et al., 2018).

Nasarawa LGA emerged as the epicenter of resistance, with concurrent MDR-TB, fluoroquinolone resistance, aminoglycoside resistance, and XDR-TB, mirroring findings from other Nigerian cities where referral hospitals concentrate resistant cases (Aliyu et al., 2020). Fluoroquinolone resistance was more widely distributed across several LGAs, reflecting possible community transmission and inappropriate use of fluoroquinolones for respiratory illnesses in the private sector (Alabi et al., 2025). Notably, no second-line or XDR-TB resistance was detected among HIV-positive patients, in contrast with findings from high HIV burden settings such as South Africa (Dheda et al., 2017). This may again reflect limited sample size or the protective role of structured HIV/TB care in Kano.

Overall, these findings highlight the urgent need for context-specific interventions. Decentralized molecular testing, strengthened surveillance, and enhanced adherence support are critical for halting resistance transmission. Pharmacovigilance to monitor fluoroquinolone use and the integration of spatial epidemiology into program planning would enable more efficient allocation of resources to identified hotspots. Addressing both biomedical and socio-structural determinants of resistance will be essential for achieving Nigeria's End TB targets.

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