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MULTI-DRUG AND EXTENSIVELY-DRUG RESISTANT TUBERCULOSIS IN (M/XDR-TB) KANO STATE NIGERIA: MOLECULAR GENOTYPING APPROACH (LINE PROBE ASSAY)

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Abstract
This study of tuberculosis among patients was conducted in Kano State, Nigeria. Our objective is to determine the prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis (TB) using the Line Probe Assay, a molecular genotyping diagnostic method.
The line probe assay (LPA) was conducted following the manufacturer's protocol. This DNA strip-based test involves three main steps: DNA extraction, multiplex PCR amplification, and reverse hybridization. Each step was carried out in accordance with WHO guidelines. Among 401 TB patients (ages 18-88, mean 34.96±14.8 years), the 25-34 age group was most represented (35.4%), while only 3% were aged ≤14 years. Males were predominant (71.4% vs. 28.6% females).Most participants were married (58.9%). Hausa made up 98.8%, with small representation from other tribes like Idoma and Yoruba. A majority (94%) had some form of education. Most were self-employed (45.6%) or students (31.2%). Income levels varied, with 34% earning 18,000 - <35,000 Naira monthly. 10.2% of patients were found to have MDR-TB, with rifampicin mono-resistance at 6.5% and isoniazid mono-resistance at 1.5%. The highest prevalence of MDR-TB was seen among ages 25-34 (46.3%) and predominantly in males (80.5%).Two cases of XDR-TB were recorded (0.5%), both among females and largely from the 15-24 and 25-34 age groups. XDR-TB prevalence was also slightly higher among HIV-negative patients. The eight metropolitan LGAs accounted for 75.3% of MDR-TB cases, with Nassarawa and Fagge having the highest incidences. In terms of XDR-TB, only Tarauni LGA reported cases, while others had pre-XDR-TB cases. Individuals with no formal education exhibited higher resistance rates, particularly to MDR-TB. Among those resistant to fluoroquinolones, the most affected age groups were 25-34 and 35-44. No significant difference was observed in drug resistance across income levels. The findings indicate a high prevalence of MDR-TB, especially among younger adults, males, and those with limited education. The study underscores the need for targeted intervention in Kano State, especially in high-prevalence metropolitan LGAs, and highlights the critical need for better diagnostic and preventive measures, particularly for drug-resistant TB in high-risk demographics.

Keyword: Multi-drug, Tuberculosis Kano State, Nigeria

Introduction

Tuberculosis is one of the world's major causes of illness and death, mostly in low-income countries. Nigeria ranks 4th among the 22-high burden TB countries in the world and 2nd highest in Africa (Ijezi, 2017; Adepoju *et al.,* 2022) (Saad et al., 2023) (Sa'ad et al., 2024) (Abubakar et al., 2024). Tuberculosis is both preventable and curable as long as its causative agent *Mycobacterium tuberculosis (*TB) is susceptible to antibiotics (Adamu and Hafiz, 2015, Shahida *et al.*, 2024 and Ereso, 2024)
Multi drug-resistant Tuberculosis (MDR-TB) is caused by *Mycobacterium tuberculosis* that are resistant to least rifampicin and isoniazid (Lv et al., 2024). MDR-TB results from either primary infection with resistant bacteria or may develop in the cause of a patient's treatment (Rathored et al., 2024, WHO, 2010). Extensively drug-resistant TB (XDR-TB) is caused by *Mycobacterium tuberculosis* that are resistant at least rifampicin and isoniazid (which is the definition of MDR-TB) in addition to any fluoroqunolones, and at least one of the three injectable drugs used in anti-TB treatment; capreomycin, kanamycin and amikacin(Sanchini et al., 2024) (Migliori *et al.*, 2007). XDR-TB is caused mainly as a result of poor clinical and control practices in

congregate setting, while in high HIV prevalence settings XDR-TB was observed in patients never treated previously(Sanchini et al., 2024) (Migliori *et al.*, 2007).

The spread of drug resistant strains of Mycobacterium tuberculosis and the management of patients diagnosed with drug resistant disease is proving to be one of the most formidable obstacles faced by national tuberculosis control programmes (Dookie,*et al.,* 2022) (Karnan *et al.*, 2024) (WHO, 2010).

Multi-drug resistant TB (MDRTB) is significantly more difficult to treat than drug susceptible TB, in large part because the necessary second-line drugs are less effective, associated with more severe adverse effects, must be administered for a prolonged period of time, and are much more expensive, than conventional first-line anti-tuberculosis drugs (Sahra, 2024) (WHO/IUATLD, 2008). MDR-TB treatment requires prolonged therapy, frequent hospitalizations, and incurs high treatment costs, leading to a significant number of fatalities(Gu et al., 2024). The development of drug resistance is not only a tragedy for the patient but also poses a risk to others, as the patient can transmit drug-resistant organisms to those around them(Monday et al., 2024)

Multidrug-resistant and extensively drug-resistant TB are present worldwide, posing major challenges for public health and clinical management. Laboratory diagnosis is complex, and there is limited evidence to guide clinicians in effectively treating people with XDR-TB (Sanchini et al., 2024). In the past decade, there has been a significant resurgence in tuberculosis cases globally, creating an urgent need for faster diagnostic methods to prevent the spread of the disease (Fallahi et al., 2024). The alarming rise of MDR-TB has been documented worldwide, further exacerbated by the emergence of extensively drug-resistant TB (XDR-TB), which remains nearly untreatable in many regions (Chimfwembe & Mukuka, 2024). Deadly outbreaks of MDR-TB and XDR-TB associated with HIV infection have been reported in South Africa, often linked to transmission within healthcare facilities where infection control measures are insufficient(Hirpa et al., 2013). Since XDR-TB has only recently been defined, information about it remains scattered and incomplete(Shamsilev and Jumaev, 2024). A CDC study reported cases of XDR-TB across all continents, with unpublished data indicating that at least 17 countries have documented at least one case(Migliori et al., 2012). According to the World Health Organization, the proportion of new cases with multidrug-resistant tuberculosis (MDR-TB) was 3.7% in 2013, a rate that remained consistent through 2014. Also WHO estimated the incidence of tuberculosis (TB) in Nigeria at 322 cases per 100,000 people, with only 15% of the total TB burden being reported in 2015(World Health Organization, 2019). However, significantly higher levels of drug resistance and poor treatment outcomes remain a serious concern in certain parts of the world. In 2013, over 9 million people were estimated to have developed TB, with more than 56% of these cases occurring in the South-East Asia and Western Pacific Regions (WHO, 2014). An additional quarter of TB cases were found in the African region, which also recorded the highest rates of incidence and mortality relative to population size (WHO, 2014). The African region accounts for roughly four out of every five HIV-positive TB cases and TB-related deaths among people with HIV(Zhang et al., 2024). Within this region, nine countries—South Africa, Zimbabwe, DR Congo, Tanzania, Ethiopia, Kenya, Nigeria, Uganda, and Mozambique—are on the list of 22 high TB burden countries(Kassaw et al., 2024). As of 2011, South Africa had the highest TB burden in the region.(Sagonda et al., 2014).

To date, information on the drug-resistant TB disease burden in Nigeria has relied on indirect estimates from the WHO, based on available surveillance data. No nationally representative and robust surveys had been conducted to directly inform this assessment (Kassaw et al., 2024). Due to an unknown number of under-reported cases from the private sector, undiagnosed cases that do not reach health services, and various data quality issues—such as incomplete reporting across all states—routine surveillance data cannot accurately reflect the true disease burden. Without a reliable baseline, it is also challenging to monitor trends over time.(*National Drug-Resistant Tuberculosis Prevalence Survey Report Nigeria*, 2012). Our objective is to determine the prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis (TB) using the Line Probe Assay, a molecular genotyping diagnostic method.

Material and methods

The line probe assay (LPA) was conducted following the manufacturer's protocol. This DNA strip-based test involves three main steps: DNA extraction, multiplex PCR amplification, and reverse hybridization. Each step was carried out in accordance with WHO guidelines.

Study settings
This study was conducted at the North West Zonal TB Reference Laboratory (NWZTRL) in Aminu Kano Teaching Hospital (AKTH), Kano, Nigeria. AKTH serves as a referral laboratory for the North Western region of Nigeria, covering Kano, Jigawa, Katsina, Yobe, and Borno States, with a combined population of approximately 44.35 million people (Ezeamadu et al., 2023)**.** The laboratory has a moderately high workload for TB diagnostic testing, performing approximately 12,000 MTB Rif (GeneXpert), 6,000 cultures, and 1,200 first-line drug susceptibility tests (DSTs) annually.

Sputum Specimens
All handling of potentially infectious clinical specimens was conducted in a Class II safety cabinet within a BSL-2 laboratory. Sputum specimens were decontaminated using N-acetyl-L-cysteine-sodium hydroxide (Barnard et al., 2008)**.** Following centrifugation, the pellet was re-suspended in 1.0 ml of phosphate buffer (pH 6.8). A concentrated auramine smear was then prepared, examined under 100x magnification with a light microscope, and graded according to the guidelines of the International Union Against Tuberculosis and Lung Disease (IUATLD). (Rieder & IUATLD, 2007)**.** A 0.5-ml portion of the sediment was cultured on solid Lowenstein-Jensen medium. Positive cultures were confirmed as *Mycobacterium tuberculosis* complex through Ziehl-Neelsen staining and p-nitrobenzoic acid testing. (WHO, 1922)**.** Indirect drug susceptibility testing (DST) was conducted using the proportion method on Middlebrooks 7H11 agar slants, with 1.0 mg/ml rifampicin (RIF) and 0.2 mg/ml isoniazid (INH)(WHO, 1922)**.**

Rapid Drug Resistance Testing
The MTBDRplus test was carried out following the manufacturer's guidelines. (*GenoType ® MTBDRplus,* 2007). The test utilizes DNA strip technology and involves three main steps: DNA extraction, multiplex polymerase chain reaction (PCR) amplification, and reverse hybridization. For DNA extraction, a 500-ml sample of decontaminated sediment was processed in a one-hour procedure that included heating, sonication, and centrifugation. The amplification procedure, which included preparing the master mix and adding the DNA, also took 1 hour. Each step was conducted in separate, restricted-access rooms following a unidirectional workflow to prevent contamination. Hybridization was performed using the GT Blot 48 (Hain Lifescience), an automated hybridization machine. After hybridization and washing, the strips were removed, air-dried, and fixed onto paper. All tests were carried out independently of culture and drug susceptibility testing (DST) and completed before culture and DST results were available.

3.20 MTBDR*sl* line probe assays for detection of XDR Tuberculosis
MTBDR*sl* was performed indirectly on culture isolates according to the manufacturer's instructions (Hain Life science, Germany).The tests was blinded to the reference standard results. Manufacturer-recommended polymerase (HotStarTaq; Qiagen) was used for both LPAs. PCR on DNA from culture isolates was performed in the thermocycler using the following parameters: 95 °C for 15 min, 95 °C for 30 s, 58 °C for 2 min (10 cycles), 95°C for 25 s, 53 °C for 40 s, 70 °C for 40 s (20 cycles) and final extension at 70 °C for 8 min (the parameters used for detecting DNA from sputum using the LPAs used 50 cycles of elongation). A valid LPA result was defined by a *Mycobacterium tuberculosis* complex-specific control (TUB), conjugate controls (CC) and amplification control (AC) bands in conjunction with the target gene locus control.

Interpretation of Results: Each test strip includes 27 reaction zones (bands), comprising six control zones (for conjugate, amplification, M. tuberculosis complex, rpoB, katG, and inhA controls). There are eight rpoB wild-type (WT) and four mutant (MUT) probes, one katG wild-type and two mutant probes, and two inhA wild-type and four mutant probes. Results were interpreted following the manufacturer's instructions.

RESULTS

Demographical Distribution of the Study subjects

From 401 tuberculosis patients age 18 – 88 years enrolled, with mean± standard deviation (34.96±14.8). Majority of the study participants 35.4% belong to the age group 25-34 years followed by 20.2% and 18.7% that are aged 35-44, and 15-24 years, respectively. The least number of the study participants 3.0% are from those aged ≤14 years. The study participants are predominantly male (71.4%) than their counterpart female (28.6%). From entire participant 236 (58.9%) are married, and 165 (41.1%) single. Majority of the subject population 396 (98.8%) were *Hausa* by tribe, others includes; *Idoma* and *Yoruba*.

The educational status revealed that 376 (94%) of the surveyed population received one form of education or the other while 25 (6%) did not receive any form of formal education. Of all the surveyed population self-employed individuals had the highest frequency 183 (45.6%) followed by students 125 (31.2%). Those employed for wages are 56 (14.0%) while those who were unemployed and the retired had 23 (5.7%) and 14 (3.5%) respectively. Majority of the surveyed population 82 (34.3%) were menial job earners, followed by civil servants 56 (23.4%), traders, 52 (21.8%), farmers 30 (12.3%) and drivers 19 (7.9%). Eighty six (34.0%) of the study participants reported to earned 18,000 - <35,000 Naira monthly, 77 (30.4%) had N35, 000 – N70, 000, 43 (17.0) had N70, 000 – N120, 000, 29 (11.5%) had >N120, 000 while 18 (7.1%) had only <N18, 000 (Table 1a&b).

Table 1a Socio-demographic Characteristics

Variable	Frequency (n=401)	Percentage (%)
Age group		
≤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
*Other tribe	5	1.2
Educational attainment		
No formal education	25	6.2
Primary	31	7.7
Secondary	141	35.2
Tertiary	204	50.9

Key: *Other tribes: Idoma, Yoruba, Igbo, Single:

Table 1b Socio-demographic Characteristics

Variable	Frequency (n=401)	Percentage (%)
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		
<N18,000	18	7.1
N18,000 - <N35,000	86	34.0
N35,000 - <N70,000	77	30.4
N70,000 – N120,000	43	17.0
>N120,000	29	11.5

Prevalence of MDR-TB among TB patients in Kano state by MTB-DR plus (LPA first line)

Analysis for drug resistance using the LPA technique showed that, 41 (10.2%) of the study participants were found to be MDR-TB, 26 (6.5%) were rifampicin mono resistant while 6 (1.5%) were INH mono resistant as shown in table 2.

Prevalence of MDR-TB among TB patients in Kano state by LGA using the MTBDR plus (LPA First line)

Analysis for the distribution of MDR-TB by LGAs showed that the eight metropolitan LGAs accounted for (75.3%) of all the MDR-TB infections. Nassarawa had the highest prevalence 14 (34.1%) followed by Fagge with 6 (14.6%). Nine LGAs had the least prevalence of 1 (2.4%) each while 21 LGAs had no case recorded, as shown in table 3.

Prevalence of MDR-TB among TB patients in Kano by Demographic using the MTBDR plus (LPA First line)

Analysis for the distribution of MDR-TB by age groups using the LPA technique showed that, the highest prevalence was observed among age group (25-34)years, with 19 (46.3%), While the lowest prevalence was observed among the age group (45 -54) with 1 (2.4%). Age group >14years had no case recorded 0 (0.0%). Analysis for the distribution of MDR-TB by sex showed that, Males accounted for the highest prevalence of 33 (80.5%), while females had 8 (19.5%). Analysis for the distribution of MDR-TB by educational status showed that, the highest prevalence was observed among those with no any form of formal education 24 (58.5%) while the least was observed among those with secondary education with 1 (2.4%) as shown in table 4.

Prevalence of MDR-TB/HIV coinfection among TB patients in Kano state using the MTBDR plus (LPA first line).

MDR-TB/HIV coinfection was found to be 4 (9.8%) rifampicin and INH mono resistance recorded 0 (0.0%) respectively as shown in table 5.

4.12 Prevalence of XDR-TB among TB patients in Kano State by LGAs using the MTBDRsl (LPA second line)

Of all the surveyed population 2 (0.5%) were found to be XDR 6 (1.5%). The spread of XDR according to LGA was found to be in Nassarawa (1.4%) and Ungogo (1.4%) each, as shown in Table 4.11.

4.13 Prevalence of XDR-TB among TB patients in Kano state by Socio-Demographic using the MTBDRsl (LPA second line)

Prevalence of extensively drug-resistant tuberculosis (XDR-TB) was highest among individuals aged 15-24 and 25-34, each at 50%. Fluoroquinolone resistance was prominent in age groups 25-34 (50%), 35-44 (33.3%), and ≥65 (16.7%). Aminoglycoside resistance varied with 41.7%, 8.3%, 16.7%, and 0% among age groups 15-24, 25-34, 35-44, and 55-64 respectively, with low-level resistance only in the youngest group. XDR-TB was solely prevalent in females (1.8%), while fluoroquinolone and aminoglycoside resistance were higher in males (66.7% and 66.7% respectively). Those lacking formal education had a notable prevalence of XDR-TB (0.5%). Fluoroquinolone resistance spanned all education levels (1.5%, 3.0%, and 0.2%). Aminoglycoside resistance was prevalent among those with tertiary education and none, while amikacin low-level resistance was associated with tertiary education. The highest XDR-TB prevalence was among individuals with monthly incomes of N18,000-<N35,000 and N35,000-N70,000 (47.6% and 38.1% respectively), while the lowest was among those with >N120,000, <N18,000, and N70,000 (9.5%, 4.8%, and 0% respectively) as shown in table 7.

Table 2 Frequency of MDR-TB among TB patients in Kano state using the MTBDR plus (LPA First line)

LPA	MDR-TB (%)	RIF mono (%)	INH mono (%)
Positive	41 (10.2)	26 (6.5)	6 (1.5)
Negative	362 (89.8)	377 (93.5)	397 (98.5)
Total	**401**	**401**	**401**

Table 3. Prevalence of MDR-TB among TB patients in Kano state by LGAs using the MTBDR plus (LPA First line)

LGA of cases	MDR-TB (%)	RIF mono (%)	INH mono (%)
Ajingi	0 (0.0)	0 (0.0)	0 (0.0)
Albasu	1 (2.4)	1 (3.8)	0 (0.0)
Bagwai	0 (0.0)	0 (0.0)	0 (0.0)
Bebeji	0 (0.0)	1 (3.8)	0 (0.0)
Bunkure	2 (4.9)	0 (0.0)	0 (0.0)
Dala	2 (4.9)	0 (0.0)	0 (0.0)
Danbatta	1 (2.4)	1 (3.8)	0 (0.0)
Dawakin kudu	0 (0.0)	0 (0.0)	0 (0.0)
DawakinTofa	0 (0.0)	0 (0.0)	0 (0.0)
Fagge	6 (14.6)	1 (3.8)	0 (0.0)
Gabasawa	0 (0.0)	2 (7.7)	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 (3.8)	0 (0.0)
Gezawa	0 (0.0)	0 (0.0)	0 (0.0)
Gwale	3 (7.3)	1 (3.8)	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 (2.4)	5 (19.2)	0 (0.0)
Kumbotso	3 (7.3)	1 (3.8)	1 (16.7)
Kunchi	0 (0.0)	1 (3.8)	0 (0.0)
Kunya	1 (2.4)	0 (0.0)	0 (0.0)
Kura	1 (2.4)	0 (0.0)	0 (0.0)
Madobi	0 (0.0)	2 (7.7)	0 (0.0)
Minjibir	1 (2.4)	0 (0.0)	0 (0.0)
Nasarawa	14 (34.1)	5 (19.2)	2 (33.3)
Rano	2 (4.9)	0 (0.0)	0 (0.0)
RiminGado	0 (0.0)	0 (0.0)	1 (16.7)
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 (2.4)	1 (3.8)	2 (33.3)
Tofa	0 (0.0)	0 (0.0)	0 (0.0)
Tsanyawa	0 (0.0)	2 (7.7)	0 (0.0)
Tudun wada	0 (0.0)	0 (0.0)	0 (0.0)
Ungogo	1 (2.4)	0 (0.0)	0 (0.0)
Warawa	0 (0.0)	0 (0.0)	0 (0.0)
Wudil	1 (2.4)	1 (3.8)	0 (0.0)
Total	**41 (10.2)**	**26 (6.5)**	**6 (1.5)**

Table 4. Prevalence of MDR-TB among TB patients in Kano state by Socio-Demographic using the MTBDR plus (LPA First line)

Demographic Variables	**MDR-TB (%)**	**RIF mono (%)**	**INH mono (%)**
Age Group (Years)			
≤14	0 (0.0)	1 (3.8)	0 (0.0)
15 – 24	9 (22.0)	2 (7.7)	2 (33.3)
25 – 34	19 (46.3)	11 (42.3)	4 (66.7)
35 – 44	7 (17.1)	5 (19.2)	0 (0.0)
45 – 54	1 (2.4)	5 (19.2)	0 (0.0)
55 – 64	3 (7.3)	1 (3.8)	0 (0.0)
≥65	2 (4.9)	1 (3.8)	0 (0.0)
Total	**41 (10.2)**	**26 (6.5)**	**6 (1.5)**
Sex			
Males	33 (80.5)	20 (76.9)	4 (66.7)
Females	8 (19.5)	6 (23.1)	2 (33.3)
Total	**41 (10.2)**	**26 (6.5)**	**6 (1.5)**
Educational Status			
Primary	2 (4.9)	1 (3.8)	0 (0.0)
Secondary	1 (2.4)	5 (19.2)	1 (16.7)
Tertiary	14 (34.1)	8 (30.8)	3 (50.0)
No formal edu.	24 (58.5)	12 (46.2)	2 (33.3)
Total	**41 (10.2)**	**26 (6.5)**	**6 (1.5)**
Estimated Monthly Income			
<N18,000	1 (4.8)	2 (9.1)	0 (0.0)
N18,000 - <N35,000	10 (47.6)	8 (36.4)	3 (75.0)
N35,000 - <N70,000	8 (38.1)	7 (31.8)	1 (25.0)
N70,000 – N120,000	0 (0.0)	3 (13.6)	0 (0.0)
>N120,000	2 (9.5)	2 (9.1)	0 (0.0)
Total	**21 (8.3)**	**22 (8.7)**	**4 (1.6)**

Table 5 Prevalence of MDR-TB among TB patients in Kano state by HIV status using the MTBDR plus (LPA First line)

LPA First line	MDR-TB (%)	RIF mono (%)	INH mono (%)
Positive	4 (9.8)	0 (0.0)	0 (0.0)
Negative	37 (90.2)	26 (6.9)	6 (1.6)
Total	**41 (10.2)**	**26 (6.5)**	**6 (1.5)**

Table 6. Prevalence of XDR-TB among TB in Kano state by LGAs using the MTBDRsl (LPA second line)

LGAs	XDR-TB (%)	Flouroquinolones (%)	Aminoglycosides (%)	Amikacin low level (%)
Ajingi	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Albasu	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)
Bebeji	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bunkure	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dala	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)
Danbatta	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)
D/kudu	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
D/Tofa	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fagge	0 (0.0)	1 (16.7)	1 (8.3)	0 (0.0)
Gabasawa	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Garko	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
G/Malam	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gaya	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gezawa	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gwale	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)
Gwarzo	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)
Kabo	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Kibiya	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
KMC	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)
Kumbotso	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Kunchi	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Kunya	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Kura	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Madobi	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Minjibir	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nasarawa	1 (1.4)	1 (16.7)	3 (25.0)	0 (0.0)
Rano	0 (0.0)	1 (16.7)	0 (0.0)	1 (16.7)
Rimingado	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)
Rogo	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sumaila	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Takai	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tarauni	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)
Tofa	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tsanyawa	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
T/wada	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ungogo	1 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)
Warawa	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)
Wudil	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)
Total	**2 (0.5)**	**6 (1.5)**	**12 (3.0)**	**1 (0.2)**

Table 7. Prevalence of XDR-TB among TB in Kano state by Age group using the MTBDRsl (LPA second line)

Demographic	XDR-TB (%)	Flouroquinolones(%)	Aminoglycosides (%)	Amikacin low level(%)
Age Group (Years)				
≤14	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
15 – 24	1 (50.0)	0 (0.0)	2 (16.7)	1 (1.3)
25 – 34	1 (50.0)	3 (50.0)	5 (41.7)	0 (0.0)
35 – 44	0 (0.0)	2 (33.3)	1 (8.3)	0 (0.0)
45 – 54	0 (0.0)	0 (0.0)	2 (16.7)	0 (0.0)
55 – 64	0 (0.0)	0 (0.0)	2 (16.7)	0 (0.0)
≥65	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)
Total	**2 (0.5)**	**6 (1.5)**	**12 (3.0)**	**1 (0.2)**
Sex				
Males	0 (0.0)	4 (66.7)	8 (66.7)	1 (0.3)
Females	2 (1.8)	2 (33.3)	4 (33.3)	0 (0.0)
Total	**2 (0.5**	**6 (1.5)**	**12 (3.0)**	**1 (0.2)**
Educational Status				
Primary	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)
Secondary	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tertiary	0 (0.0)	2 (33.3)	6 (50.0)	1 (0.7)
No formal	2 (1.0)	3 (50.0)	6 (50.0)	0 (0.0)
Total	**2 (0.5)**	**6 (1.5)**	**12 (3.0)**	**1 (0.2)**
Estimated Monthly Income				
<N18,000	0 (0.0)	1 (25.0)	1 (10.0)	0 (0.0)
N18,000 - <N35,000	0 (0.0)	1 (25.0)	3 (30.0)	0 (0.0)
N35,000 - <N70,000	0 (0.0)	2 (50.0)	2 (20.0)	0 (0.0)
N70,000 – N120,000	0 (0.0)	0 (0.0)	2 (20.0)	0 (0.0)
>N120,000	0 (0.0)	0 (0.0)	2 (20.0)	0 (0.0)
Total	**0 (0.0)**	**4 (1.6)**	**10 (4.0)**	**0 (0.0)**

Age Group (Years)				
≤14	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
15 – 24	1 (50.0)	0 (0.0)	2 (16.7)	1 (1.3)
25 – 34	1 (50.0)	3 (50.0)	5 (41.7)	0 (0.0)
35 – 44	0 (0.0)	2 (33.3)	1 (8.3)	0 (0.0)
45 – 54	0 (0.0)	0 (0.0)	2 (16.7)	0 (0.0)
55 – 64	0 (0.0)	0 (0.0)	2 (16.7)	0 (0.0)
≥65	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)
Total	**2 (0.5)**	**6 (1.5)**	**12 (3.0)**	**1 (0.2)**
Sex				
Males	0 (0.0)	4 (66.7)	8 (66.7)	1 (0.3)
Females	2 (1.8)	2 (33.3)	4 (33.3)	0 (0.0)
Total	**2 (0.5**	**6 (1.5)**	**12 (3.0)**	**1 (0.2)**
Educational Status				
Primary	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)
Secondary	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tertiary	0 (0.0)	2 (33.3)	6 (50.0)	1 (0.7)
No formal	2 (1.0)	3 (50.0)	6 (50.0)	0 (0.0)
Total	**2 (0.5)**	**6 (1.5)**	**12 (3.0)**	**1 (0.2)**
Estimated Monthly Income				
<N18,000	0 (0.0)	1 (25.0)	1 (10.0)	0 (0.0)

N18,000 - <N35,000	0 (0.0)	1 (25.0)	3 (30.0)	0 (0.0)
N35,000 - <N70,000	0 (0.0)	2 (50.0)	2 (20.0)	0 (0.0)
N70,000 – N120,000	0 (0.0)	0 (0.0)	2 (20.0)	0 (0.0)
>N120,000	0 (0.0)	0 (0.0)	2 (20.0)	0 (0.0)
Total	**0 (0.0)**	**4 (1.6)**	**10 (4.0)**	**0 (0.0)**

Discussion of findings

Tuberculosis remains a global health priority due to the rising prevalence of drug-resistant strains, which pose a significant public health threat and undermine progress in the fight against the disease. The *Mycobacterium tuberculosis* complex, the causative agent of tuberculosis, continues to be one of the most important pathogens from both an epidemiological and clinical perspective(Kostyukova et al., 2023). *Mycobacterium tuberculosis* can develop resistance to any antibiotic, ranging from older drugs like streptomycin (now largely phased out) to newer ones like bedaquiline (Kostyukova et al., 2023). This adaptability underscores the risk of new drug-resistant strains emerging and spreading epidemically. The WHO strongly recommends drug susceptibility testing for all TB patients to improve treatment strategies and evaluate their effectiveness. However, resource limitations in many high-burden countries continue to pose significant challenges to implementing this approach widely(World Health Organization (WHO), 2017). In our study, drug susceptibility testing was conducted using the Hain Life Science Line Probe Assay (LPA) to detect multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB. We found that 10.2% of patients had MDR-TB, This prevalence of drug-resistant TB (DR-TB) observed in this study is lower than the rates reported by Onyedum et al., (2017) Nigeria, as well as the broader estimates from Iran, China, and Ethiopia. However, it is also lower than DR-TB rates reported in Burundi and Portugal(Suchindran et al., 2009; Zhang et al., 2024; Sanders et al., 2006). We also observed rifampicin mono-resistance at 6.5% and isoniazid mono-resistance at 1.5%. This finding that significant number of previously treated TB patients in Nigeria exhibit resistance to at least one first-line anti-TB drug is significant. Although this is lower than what Onyedum et al., (2017), Nigeria, Ethiopia (11.1 to 72.9%)(Weldegebreal & Mebrahtu, 2017) and was similar to the rate reported by a review in China (49.8%)(Duan et al., 2016), but lower than the rate reported from Iran (65.6%) (Nasiri et al., 2014), reported, it underscores a high prevalence of acquired drug resistance, likely due to incomplete treatment, improper medication use, or other factors that compromise treatment effectiveness (Etim et al., 2024). This trend poses a major challenge to TB control in Nigeria, as resistance to first-line drugs complicates treatment efforts, increases the risk of MDR-TB, and emphasizes the need for enhanced surveillance, treatment adherence programs, and potentially, the adoption of newer or more effective drug regimens.

The highest prevalence of MDR-TB in this study was observed among patients aged 25-34 (46.3%), a productive age group, and was more common in males (80.5%). This finding is consistent with data from Nigeria (Oladimeji et al., 2023), where most MDR-TB patients (61.4%) were also male. Similar trends have been reported in Pakistan(Siddiq et al., 2023) where TB positivity was higher among males (60.4%) compared to females (41.8%), and in China (Lv et al., 2024; Cheng et al., 2021), where the 21-30 age group, low family income, and occupational exposure were significant risk factors for MDR-TB, particularly among males. This disparity could be due to occupational exposure and the tendency for females to adhere more closely to therapy guidelines than males.

In contrast, findings from Tanzania indicate a higher proportion of female MDR-TB cases (61%) among those aged 15-34, compared to males (45%) in the same age range. Similarly, in India, female MDR-TB patients were reported to be twice as likely to fall in the 18-29 age group compared to male patients in the same age group (Oladimeji et al., 2023).

Two cases of XDR-TB (0.5%) were identified in this study, both among females in the 15-24 and 25-34 age groups. Although the proportion of XDR-TB is currently low, there is concern that it may be on the rise (Cheng, 2022; Wang et al., 2022). The resistance pattern of XDR-TB might be associated with very challenging outcomes such as delay to treatment initiation (Kimenye, 2020), low treatment success rate of around, a high mortality rate of about, and a significant treatment failure rate of (Sulaimon, 2020). XDR-TB was slightly more prevalent among HIV-negative patients than among those who were HIV-positive this is contrary to what was reported by Wang et al.,(2022) highlighted the growing global concern of HIV-TB co-

infection, noting a significant increase in HIV-associated XDR-TB cases from 1990 to 2019.This highlights an urgent need for rapid interventions, including advanced diagnostic measures and effective treatment strategies, to curb the spread of XDR strains in the population and to prevent the development of further resistance. A follow-up study is suggested to investigate specific predictors contributing to these outcomes in greater detail.

Conclusion and Recommendations

The study reveals a high prevalence of MDR-TB, particularly among young adults, males, and individuals with limited education in Kano State, with a concentration in high-prevalence metropolitan LGAs. This underscores an urgent need for targeted interventions, improved diagnostic and preventive measures, and enhanced treatment adherence programs, especially for high-risk groups. The increasing resistance to first-line drugs complicates TB control efforts, necessitating better surveillance, the potential use of newer drug regimens, and measures to curb XDR strains. A follow-up study is recommended to identify specific predictors driving these trends.

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