Original Article

Patterns of Drug Resistance Tuberculosis and Predictors of Treatment Outcomes: A Retrospective Study Among Patients in Selected Health Facilities in Benue State

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ABSTRACT

Drug-resistant tuberculosis (DR-TB) remains a major public health challenge globally and in Nigeria, undermining tuberculosis (TB) control efforts. Benue State has recorded increasing cases of multidrug-resistant TB (MDR-TB) and rifampicin-resistant TB (RR-TB), with implications for treatment outcomes. The aim of this study was to determine the pattern of drug resistance and predictors of treatment outcomes among DR-TB patients managed in selected treatment centers in Benue State. This study was a retrospective review of 310 DR-TB patient records registered between January 2019 and December 2022 which was conducted across three treatment centers in Benue State. Data were extracted on sociodemographic characteristics, resistance patterns, HIV status, patient category, and treatment outcomes. Diagnosis was based on GeneXpert MTB/RIF, sputum culture, and line probe assay (LPA). Data were analyzed using SPSS version 23. Chi-square tests and logistic regression were performed at a 95% confidence interval, with $p \leq 0.05$ considered statistically significant. Results showed that majority of patients were aged >15 years (98.7%), male (71.9%), rural residents (63.9%), and farmers (43.2%). MDR-TB constituted 71.2% of resistance patterns, followed by RR-TB (19.7%), pre-XDR-TB (4.9%), and mono-resistance (4.2%). Treatment success was achieved in 87.1% of patients. Formal education (AOR=5.2; 95% CI: 1.5–18.1), new patient category (AOR=15.6; 95% CI: 6.5–37.5), and HIV-negative status were significant predictors of successful outcomes. In conclusion, MDR-TB is the predominant resistance pattern in Benue State, with relatively high treatment success rates. Educational status, HIV co-infection, and previous TB treatment significantly influence outcomes. Strengthening early diagnosis, adherence support, and TB–HIV collaborative care is essential.

Keywords: Benue State, Drug-resistant tuberculosis, Nigeria, Predictors, Resistance patterns, Treatment outcomes

INTRODUCTION

Tuberculosis (TB) remains a significant global health issue, with drug resistance complicating efforts to control the disease.[1] Drug resistance in TB typically emerges due to inadequate or incomplete treatment regimens, misuse of antibiotics, or poor healthcare infrastructure.[2]The national Multi-Drug Resistance /Rifampicin Resistance (MDR/RR) TB burden is estimated to be 21,000 annually, however, case notification is suboptimal, with only 2,384 cases diagnosed, representing an abysmally low 11% case notification rate.[3] The latest statistics from the National Tuberculosis and Leprosy Control Program (NTBLCP) estimate that about 10% of all TB cases in Nigeria are drug-resistant.[4] Specifically, the prevalence of MDR-TB in Nigeria has been

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estimated at around 2.5% among new TB cases and 13% among previously treated cases, with Benue State reflecting similar trends in its local health facilities. As at 2021, TB-related mortality in Nigeria was estimated at approximately 125,000 , with a significant proportion attributed to complications arising from DR-TB.[5]

Resistance can be classified into two broad categories: primary resistance (in individuals who have never received TB treatment) and acquired resistance (in those who have received treatment).[6] The most concerning forms of drug-resistant TB are multi-drug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB). MDR-TB refers to resistance to at least two first-line drugs, isoniazid and rifampin, which are the cornerstone of standard TB treatment.[7] Pre-XDR TB and XDR-TB involves resistance to MDR-TB drugs plus additional resistance to any fluoroquinolone and at least one second-line injectable drug (amikacin, kanamycin, or capreomycin). These forms of resistance make TB treatment longer, more expensive, and less effective.[8] Resistance occurs through specific genetic mutations in the TB bacterium *Mycobacterium tuberculosis*. For example, mutations in the *katG* gene lead to resistance to isoniazid, while mutations in the *rpoB* gene confer resistance to rifampin.[9] Resistance to second-line drugs, such as fluoroquinolones, results from mutations in the *gyrA* gene, and resistance to injectable drugs often involves mutations in the *rrs* or *relA* genes.[9] Early detection of drug-resistant TB is crucial for effective treatment.[1,9] Standard methods, such as culture-based testing, are slow, taking several weeks. However, newer molecular techniques like GeneXpert MTB/RIF provide faster diagnosis, identifying both TB and rifampin resistance within hours.[10]

Despite this progress, access to these diagnostic tools remains limited in resource-poor settings. Treatment of MDR-TB and XDR-TB requires a combination of second-line drugs, which are less effective and more toxic than first-line treatments.[11] The long duration of therapy, often extending up to two years, leads to poor patient adherence, further complicating the treatment regimen. The BPaL regimen for drug-resistant tuberculosis (DR-TB) consists of bedaquiline (B), pretomanid (Pa), and linezolid (L).[12] This combination has shown effectiveness against multidrug-resistant (MDR-TB) and extensively drug-resistant (XDR-TB) strains, offering a shorter and potentially less toxic treatment alternative compared to traditional second-line drug regimens.[13]

Several factors influence the treatment outcomes of DR-TB patients in Benue State. These predictors include patient-related factors, healthcare system-related factors, and social determinants.[14] Understanding these predictors is crucial for improving the effectiveness of DR-TB treatment strategies and reducing the prevalence of resistant strains.[14] One of the most significant predictors of DR-TB treatment outcomes is patient adherence to the prescribed treatment regimen.[15] Non-adherence, which is common in TB management, leads to incomplete drug courses and increases the risk of drug resistance.[16] Various barriers to adherence exist, including the side effects of TB drugs, lack of knowledge about the disease, and financial constraints.[17] Poor adherence results in the survival of drug-resistant bacteria, which ultimately results in the development of MDR-TB.[18] Ensuring that patients fully complete their treatment is essential to preventing further drug resistance.[17] Factors that improve adherence include patient education, community health worker support, and the availability of medications at local healthcare facilities.[19] Outreach programs aimed at educating the public about the importance of completing the full course of treatment can significantly reduce the incidence of DR-TB. Furthermore, strengthening adherence support programs, such as directly observed therapy (DOT), where healthcare workers or trained community members supervise the patient's drug intake, has been shown to improve treatment outcomes.[20] Timely diagnosis and early initiation of the correct treatment are essential to successful TB management. Delays in diagnosing drug-resistant TB significantly contribute to treatment failures and poor outcomes.[21] Access to molecular diagnostic tests like GeneXpert, which can detect MDR-TB rapidly, remains limited as a result, patients often remain on incorrect or ineffective regimens for extended periods before

receiving the appropriate treatment.[22] Late diagnosis not only affects individual outcomes but also increases the risk of transmission to others.[23]

The availability of diagnostic facilities, the quality of laboratory services, and the healthcare professionals' ability to interpret diagnostic results are all factors that influence the time to diagnosis and the initiation of proper treatment.[24] The cost of transportation to healthcare centers, the inability to afford essential diagnostic tests, and the expense of drugs necessary for treating MDR-TB can all contribute to treatment interruption.[25] In addition to financial constraints, the educational level of patients impacts their understanding of the importance of adhering to TB treatment.[26] Low levels of education may result in inadequate knowledge of the disease and its treatment protocols.[27] The nutritional status of TB patients is a crucial determinant of treatment success. Malnutrition weakens the immune system, making it harder for the body to fight off infections and respond to TB treatment.[28] Co-infection with HIV is another significant factor that complicates TB treatment. HIV-positive patients are more vulnerable to TB due to their weakened immune systems, which can lead to delayed diagnosis and inadequate immune responses to treatment.[29] Providing integrated care for TB and HIV patients, which includes antiretroviral therapy (ART) alongside TB treatment, is crucial for improving outcomes in co-infected individuals.[30] Early HIV testing and regular screening for TB in HIV patients can help detect and treat both diseases more effectively. [31]

This study examines the patterns of drug-resistant tuberculosis and identifies predictors of treatment outcomes among patients managed in selected health facilities. By generating facility-based evidence, the study aims to inform programmatic decision-making, improve patient management, and contribute to strengthening TB control strategies in high-burden settings.

MATERIALS AND METHODS

Study Area

Benue State lies within the lower river Benue trough in the north-central region of Nigeria. Its geographic coordinates are longitude 7° 47' and 10° 0' East Latitude 6° 25' and 8° 8' north. The State shares boundaries with five other States namely: Nasarawa (to the north), Taraba (to the east), Cross-River (to the south), Enugu (to the south-west), and Kogi (to the west). The State has a total population of 4,219,244 (2006 census) and a projected figure of 6,109,9798 persons in 2023 using an annual growth rate of 3%, with a landmass of 32,518 square kilometers.[32] The State has 1408 health facilities, including 862 publicly owned primary health facilities and 427, privately-owned primary health facilities, 24 public, and 93 private secondary facilities, and three government tertiary health care facilities.[33] There are three DRTB Treatment Centres offering continuum of care for DRTB patients across the three senatorial zones, A, B, and C and these facilities are selected for this study.

Study Design

This was a retrospective study of Drug Resistance Tuberculosis patients registered and commenced on treatment between January 2019 and December 2022. All patients were followed up until the end of treatment to ascertain treatment outcomes.

Study population

The study population consisted of Drug Resistance Tuberculosis patients who received treatment in three treatment centers in Zone A, B and C in Benue State.

Inclusion criteria

Drug Resistance Tuberculosis patients who were registered and received treatment in three treatment centers in Benue State.

Exclusion criteria

Drug Resistance Tuberculosis patients who were transferred in from other states to any of our treatment centers in the three senatorial zones in Benue State.

Data collection and analysis

In order to increase the power of this study, the case records of 310 patients who met the inclusion and exclusion criteria were retrospectively reviewed from the electronic register of Drug Resistance Tuberculosis Patients who were diagnosed and treated in the three treatment centers between January 2019 and December 2022 in the three

senatorial zones of the state. The patients in this study were diagnosed using Xpert MTB/RIF, Sputum culture and LPA assay to determine the pattern of resistance and guide treatment decision. Data analysis was carried out using SPSS version 23 analysis software. Quantitative variable such as age were described using mean and frequency. Chi-square and Fischer's exact tests were used to compare variables. At 95% confidence interval, a p-value of ≤ 0.05 was considered significant statistically.

Ethical Consideration

Ethical clearance was sought from the BSUTH ethical committee before the commencement of the study. Permission was obtained from the Research and Statistics Department, Benue State Ministry of Health.

RESULTS

A total of 310 records of DR-TB patients were extracted from the registers. Information on sociodemographic characteristics, pattern of drug resistance and the outcome of treatment were all extracted for analysis and presentation. The study had no ethical issues and those of attrition. Analysis was done and results were presented in tables and charts as seen below Majority 306(98.7%) of the respondents were more than fifteen years old while. Males constituted the majority (71.94%) in this study. Almost all 298(96.13%) the respondents were Christians and more than half 202(63.16%) were of Tiv ethnicity. Majority 198(63.81%) were rural dwellers and more than one-third were farmers. (Table 1)

MDR constituted 221(71.2%) of drug resistance followed by Rifampicin resistance with 61(19.7%). Monoresistance and Pre-XDR TB were 13(4.2%) and15(4.9%) respectively Multidrug resistance Tuberculosis constituted the majority of cases of Pulmonary Tuberculosis in 2019, however there was a sharp decline in case reporting rate in 2020 with a sharp rise again in 2021 and 2022 respectively. Rifampicin resistance was next and rise in 2020 but declined in 2021 with another quick rise in 2022. Monoresistance was low in 2019 and remained at the same level in 2020 and 2021 and rose again in 2022. Pre-XDR TB in 2019 remained at the same level with monoresistance but increased in 2020 and dropped again in 2021 and finally rose again in 2022. (Figure: 2)

The Bar Chart shows that; successful treatment constituted 270(87.1%) of the tretment outcomes while unsuccessful treatment outcomes constituted 40(12.9%) (Figure: 3).

Majority of the respondents with successful treatment outcomes were more than 15 years 268(86.5%) in age, and were mostly 194(62.6%) males who lived in urban communities 175(56.5%) and had formal education 255(82.2%). Most of the respondents were new patients 190(61.3%) and were mostly HIV negative 260(83.9%) (Table: 2)

Patients who had Formal education were 5.2 times more likely to have successful treatment outcome compared to those who had no Formal education. New patients were 15.6 times more likely to have successful treatment outcome compared to those who had relapse. Those who were HIV positive were 2 times less as likely to have successful treatment outcome as those who were of HIV negative status (Table : 3)

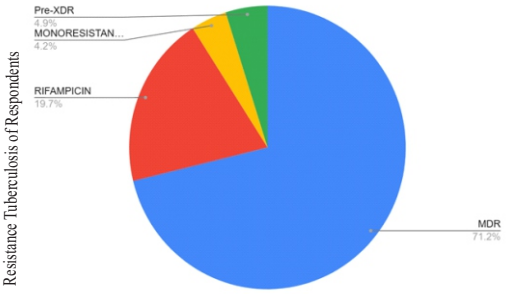

Fig. 1: A Pie Chart showing the Pattern of Drug Resistance Tuberculosis of Respondents

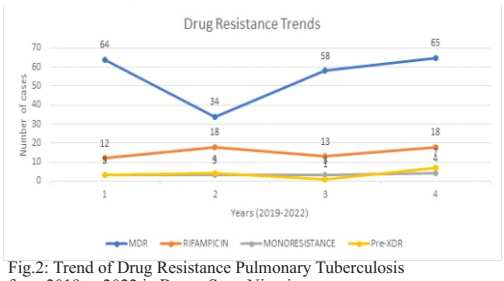

Fig.2: Trend of Drug Resistance Pulmonary Tuberculosis from 2019 to 2022 in Benue State Nigeria

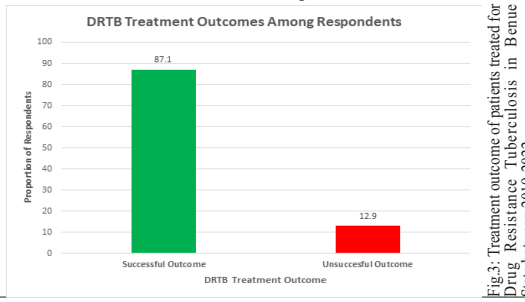

Fig.3: Treatment outcome of patients treated for Drug Resistance Tuberculosis in Benue State between 2019-2022.

Table 1: Socio-demographic Characteristics of Respondents

Variable	Frequency N(310)	Percent
Age(years)		
>15	306	98.71
<15	4	1.29
Sex		
Male	223	71.94
Female	87	28.06
Educational Status		
Formal education	288	92.90
No formal Education	22	7.10
Religion		
Christians	298	96.13
Non -Christians	12	3.87
Ethnicity		
Tiv	202	65.16
Idoma/Igede	94	30.32
Others	14	4.52
Location		
Rural	198	63.87
Urban	112	36.13
Occupation		
Farming	134	43.23
Trading	121	39.03
Artisan	54	17.42
Civil servant	1	0.32

*Fischers Exact Test

Table 2: Factors affecting the treatment outcome of drug resistance tuberculosis in Benue State, Nigeria

Variable	Successful n=270(%)	Unsuccessful n=40(%)	X^2	p-value
Age(Years)				
>15	268(86.5)	38(12.3)		
<15	2(0.6)	2(0,6)		**0.076.***
Sex				
Male	194(62.6)	29(9.4)		
Female	76(24.5)	11(3.5)	0.563	0.453
Location				
Urban	175(56.5)	23(7.4)		
Rural	95(30.6)	17(5.5)	0.003	0.403
Education				
Formal Education	255(82.2)_	33(10.6)		
No formal education	15(4.8)	7(2.4)	8.5271	0.0034
Patient Category				
New	190(61.3)	10(3.2)		
Relapse	80(25.8)	30(9.7)	36.350	< 0.001
HIV Status				
Positive	10(3.2)	26(8.4)		
Negative	260(83.9)	14(4.5)	69.520	0.001

Table 3: Predictors of treatment outcome of drug resistance tuberculosis in Benue State, Nigeria

Variable	Odds Ratio	Confidence Interval	P-value
Education			
No formal Education	1		
Formal education	5.2	1.5 - 18.1	0.034
Patient Category			
New	1		
Relapse	15.6	6.5 - 37.5	0.001
HIV Status			
Negative	1		
Positive	0.02	0.005 - 0.08	0.01

DISCUSSION

Majority of the respondents were young persons above fifteen years of age. This finding is in consonance with a study in Zaria in which majority of the respondents were above 30 years of age. The age in this study is that which the immunity conferred by BCG vaccine begins to wane in the body of young persons. During this time, any health problem that lowers the immunity makes the individual susceptible to such infections.[34] This study also shows that males constituted the majority (71.94%) of the respondents. This finding is similar to studies in Nigeria, where majority (66.9%) of the respondents were males. Males are more adventurous and do jobs that may affect their health and sometimes lower their immunity making them more prone to Tuberculosis.[35] Almost all (96.13%) the respondents were Christians and more than half (63.16%) were (63.81%) were rural dwellers and more than one-third were farmers. This is also in consonance with a study in Zaria, North Western Nigeria were 70% of the respondents lived in rural communities outside Kaduna.[36]

[36]In this study the MDR constituted the majority (74.2%) of the resistance followed by Rifampicin while monoresistance and Pre-XDR Tuberculosis were the same. This finding is similar with that s in Cameroon and Nigeria in which 3.4% RR-TB, 94.6% MDR-TB, 1.3% pre-XDR-TB, and 0.7% XDR-TB were found while in Nigeria, the cases of MDR was 58.6% among the respondents.[3737,38] This finding is different from studies carried out in Kenya and Ethiopia in which MDR constituted less than half of the cases studied Mbuh et al., 2024.[39] This difference could be as a result of regional resistance pattern as Nigeria and Cameroon share the same borders perhaps movement across borders may introduce similar resistance strains between the two countries. Also, the genetic susceptibility, environmental and social factors may be similar between individuals in these countries. Ethiopia and Kenya are countries in Eastern Africa and may share such variables too. Genetic mutation patterns of the bacilli and other researches may be needed to uncover some of these similarities.

In this study, findings showed that the successful treatment outcome constituted 87.1% while unsuccessful treatment outcome constituted 12.9%. This finding is similar to studies carried out in Cameroon, Oyo State, and another study in South western Nigeria in which the treatment success rate was 87.2%, 85.3% and 70,0% respectively.[38,40,41] This finding is however different from studies carried out in Southern Ethiopia, and Ebonyi State in which the treatment success rate was low (50% and 40.3% respectively).[42,43] Education, Category of Patients and being HIV-Negative were significant predictors of successful outcome. This finding is in consonance with two studies carried out in North Western Nigeria in which being educated and employed were four times associated with successful treatment as well as being HIV Negative was associated with successful treatment outcome.[44,45] A study carried out in Osun, South Western Nigeria showed that, good adherence and normal haemoglobin were significant

predictors of treatment success among respondents.[46] Treatment success rate depends on adherence to medications, existing comorbidities and the virulence of the strains of the bacilli in question. The introduction of the BPaL regimen may likely be the reason for the high success rates in the African subregion. Even in regions where the treatment success rate looks low, they are within th[46]e limits that when the reasons behind the problems are identified, the gaps can easily be closed.

CONCLUSION

This study revealed that, Drug Resistance Tuberculosis is common among young persons who are mostly farmers residing in rural communities in the State. MDR TB is the most prevalent pattern of Tuberculosis in Benue State, however, Rifampicin resistance is also of important proportion. Even though the proportion of Pre-XDR TB is low, it of immense public health significance. Finally, Education, Category of Patients and co-morbidity with HIV were significant predictors of successful outcome.

Recommendations

The State TBLCP should include molecular diagnosis e.g. LPA and Sputum culture in addition to the routine Genexpert/MTB/Riff Assay to properly identify the TB resistance pattern at the beginning as well as work in synergy with the HIV program and community leaders to strengthen adherence to both HIV and anti-Tuberculosis medications and community support to improve viral load suppression of among HIV/TB Coinfected patients and prevent relapse of treatment of Tuberculosis.

Limitations

Reliance on routinely recorded data, and inaccuracies in patient records could have affected some outcomes.

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Conflict of Interests

I declare that I have no competing interest as a reviewer.

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