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Clinical, Bacteriological Characteristics, and Outcomes of Primary versus Secondary MDR/RR-TB Patients in Togo: A Retrospective Cohort Study

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Abstract

Background and **Objective**: Anti-tuberculosis drug resistance is a worldwide health concern with a higher burden in resource-limited countries and vulnerable individuals. This study aimed to compare epidemiology, biological characteristics, and treatment outcomes of primary and secondary MDR/RR-TB patients in the Republic of Togo. **Materials** and **Methods**: A retrospective cohort study was conducted from January 2016 to December 2021 at the DR-TB unit at the Department of Pulmonology of Sylvanus Olympio Teaching Hospital in Togo. Data were collected from the medical records of TB patients hospitalized for rifampicin resistance based on the Xpert/MTB/RIF® results. A structured questionnaire was used to collect clinical, sociodemographic, biological, radiological, and patients' outcomes data after the 9-month treatment regimen with the injectable TB drugs. Univariate and multivariate logistic regression analyses were performed to identify secondary MDR/RR associated factors. **Results**: A total of 89 patients, including 43 primary and 46 secondary MDR/RR-TB patient records, were enrolled in the final analysis. The sex ratio (male/female) was 1.3, and the mean age was 36.02 years. The secondary/acquired drug-resistant group was more likely to have dyspnea (aOR: 3.88, 95% CI: 1.01 - 14.38), nodules and infiltrates on chest-X-ray, respectively (aOR:3.62, 95% CI: 1.23 - 10.67) and (aOR: 4.66,

95% CI: 1.51 - 14.38). In addition, they were more likely to have a delay in MDR treatment initiation (aOR: 3.04, 95% CI: 1.08 - 8.58). Resistant to any first-line drugs was most found in the secondary drug-resistant group, while pre-XDR and XDR-TB were found in both groups. **Conclusion**: The secondary drug-resistant patients have the highest proportion of resistance patterns, including pre-XDR. Moreover, they are significantly associated with more lung lesions on chest X-ray. These results suggest a lack of treatment adherence and/or a high transmission rate of drug-resistant strains within the community. Hence, the importance of a non-pharmacological approach to improve adherence, contact tracking, and the improvement of laboratory capacities.

Keywords

Drug-Resistant TB, Primary, Secondary, Togo

1. Introduction

Tuberculosis (TB) remains a public health threat worldwide despite the progress made in the diagnosis and treatment over time [1]. According to the WHO report, in 2022, 1.6 million people died of TB among the 10.6 million individuals diagnosed [2]. The HIV pandemic and drug-resistant TB are some of the causes of TB burden persistence, especially in resource-limited countries. Growing resistance rate and patterns, limited access to health care facilities are some factors related to TB mortality and morbidity [1]-[3].

Globally, in 2022 among 410.000 individuals who were expected to develop rifampicin-resistant TB, 43% received treatment after diagnosis. The prevalence of DR TB was 3.3% of new cases and 17% in previously treated patients notified [2]. More than 90% of DR-TB-affected people have poor conditions and live in resource-limited countries. These vulnerabilities are increased by limited access to health care facilities and a weak health system. Moreover, disruption in medication supplies, lack of funding, and the emergence of other infectious diseases favor TBR spreading [4] [5]. In 2016, TBR incidence in the African region was 93/1000 hbts, with an incidence that varies across countries and years. The incidence of TB steadily declined while TBR notification was increasing, despite difficulties in analyzing isolates accurately for resistance identification. Like many African countries, TB is endemic in Togo with 0.11/1000 hbts incidental cases of MDR/RR-TB [4].

The detection rate of DR-TB cases is increasing from 3 cases in 2010 to 18 cases in 2021 and 33 in 2022 [6]. The WHO reports an estimation of 0.6 RR/MR-TB among new TB cases and 3% among previously treated TB patients. Meanwhile, a national cohort study of former TB patients has found at least 24% MDR-TB after laboratory tests [5]. This increasing notification of RR-TB is

mainly due to the progressive implementation of the Xpert-MTB/Rif test at TB diagnosis and treatment centers in the country [7]. Despite this implementation, the national TB program is struggling with low performance, mainly due to health service delivery dysfunctions and a low TB suspicion rate by physicians [6]. To address TB-R, all TB patients with Rifampicin resistance based on Xpert-MTB/Rif are admitted to a single referral center in the capital district of Lomé.

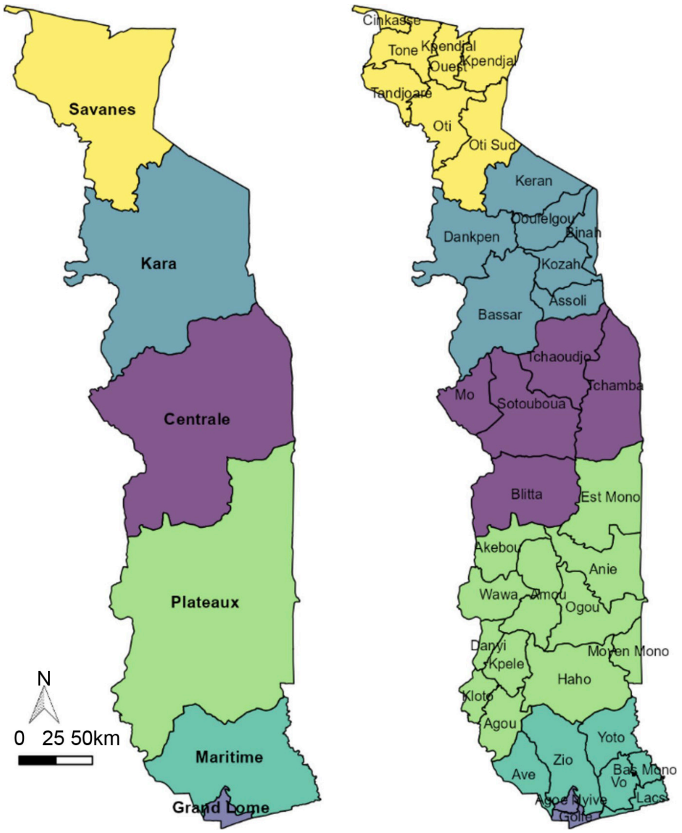
The diagnosis of MDR/RR-TB in resource-limited settings is based on the use of Xpert/MTB-Rif, which detects at least rifampicin resistance cases among patients with various TB treatment histories [1] [8] [9]. The detection of Rifampicin resistance by Xpert/MTB/Rif implies a high probability of associated resistance to isoniazid, defined as Multidrug-resistant TB (MDR-TB). Resistant to both Isoniazid and Rifampicin (MDR-TB) and or rifampicin resistance TB (RR-TB), is the most common type targeted by TB programs in resource-limited settings through Xpert test [1] [2]. However, an Xpert result with Rifampicin resistance could hide extensively drug-resistant TB (XDR-TB) or pre-XDR-TB. Pre-XDR-TB is defined as RR-TB plus resistance to any fluoroquinolone used for MDR treatment, and XDR-TB is pre-XDR-TB plus at least one of either bedaquiline or linezolid. Thus, XDR-TB could also become a growing concern if MDR-TB detection and treatment are not properly implemented. TB-resistant strains can be developed by TB patients when compliance is poor, and further strains are transmitted to a naïve contact person. The treatment of drug-resistant tuberculosis requires the use of medications that are more toxic and less effective than first-line treatment [2] [10]. The treatment history of TB patients having resistance to rifampicin is important to understand strain circulation in the community and build better, more effective measures.

Our study aimed to compare clinical, biological characteristics, and outcomes of TB patients with primary/transmitted vs secondary/acquired drug resistance treated with a 9-month second-line TB regimen that includes injectable drugs at the TB referral hospital in Togo.

2. Methods

2.1. Study Type, Setting, and Duration

We conducted a retrospective cohort study from January 2016 to December 2021 at the Department of Pulmonology at Sylvanus Olympio Teaching Hospital (CHUSO) in Togo. Togo is a West African country split into 5 administrative regions (**Figure 1**). The majority of the population (62%) lives in rural areas, while 44% live in the peri-urban coastal region, which includes the capital town Lomé. The referral center for drug-resistant TB patients' treatment and management is located in Grand-Lomé within the pulmonology department of CHUSO. According to the national TB program, all patients diagnosed with TBR should be hospitalized at least for the intensive phase of the treatment regimen and culture conversion.



Source: Map is Togo and the health sanitary regions.

Figure 1. Togo capital district with sanitary region.

2.2. Study Population

All patients diagnosed with DR-TB and hospitalized during our study period were included, and their medical records were used to collect data. Patients diagnosed with at least a Rifampicin Resistance after Xpert/MTB Rif, treated with the 9-month MDR-TB/RR-TB regimen that encompassed an injectable drug, were selected for the study. The regimen was 4 months of intensive phase with amikacin, moxifloxacin, prothionamide, clofazimine, pyrazinamide, isoniazid, ethambutol (Am-Mfx-Pto-Cfz-Z-H-E) following by a 5-months continuation phase with moxifloxacin, clofazimine, ethambutol and pyrazinamide (Mfx-Cfz-E-Z). Drug dosage administration protocol followed the national TB program guidelines for TBR management [PNLT Togo].

Patients treated for XDR-TB, with oral drug regimen only, and those with missing Xpert results or outcome data were excluded.

2.3. Data Collection

The sampling was exhaustive, including all the MDR TB patients who fulfilled our inclusion criteria and registered during the study period. Their medical records served as support to collect demographic data such as age, gender, marital status, clinical data (symptoms, history of prior TB treatment, and BMI), baseline Blood

Cell Count (CBC) results, and chest X-ray radiological characteristics were also collected. Bacteriological results with monthly sputum smear microscopy and culture, patients' sputum conversion assessed at month 4 and month 9 of treatment, and if available, drug susceptibility test (DST) for first-line drug DST and/or second-line drug Line Probe Assay (LPA) for drug resistance patterns. Patients' treatment outcomes were defined as:

- Cured: A patient was declared cured when 9-month treatment was completed without signs of failure and at least 3 consecutive culture-negative results with ≥ 30 days intervals.
- Treatment completed: a patient is classified as treatment completed when he/she has completed 9-months of taking drugs without signs of failure but does not fulfill the criteria for cured (lack of bacteriological results proof, less than 3 negative cultures).
- Treatment failure: an MDR-TB patient is classified as failed if the culture was positive at M6.
- Lost to follow-up: a patient who interrupted the treatment for two consecutive months or more.
- Death: MDR-TB patient was classified as dead if the death occurred during treatment, regardless of the cause of death.

2.4. Data Validation and Analysis

A structured questionnaire was developed and tested for the study. Data were entered and checked on the Koboocolect system, then extracted and de-identified on an Excel sheet before analysis. Data were analyzed using SPSS 23.0.

For analysis, patients were categorized into two groups based on their history of TB treatment. Group 1 (G1) or primary/transmitted resistance for patients naïve to any first-line anti-tuberculosis drugs (new cases). Group 2 (G2) or secondary/acquired resistance for patients with a history of first-line TB treatment with the previous outcome of cured, defaulted, failed, and relapse (retreatment cases). We have also classified outcomes into two categories: good outcomes, including cured and treatment completed, and poor outcomes for treatment failure, loss to follow-up, and death.

Fisher's exact test was used to compare proportions between the two groups. Descriptive analyses were done to determine proportions; the univariate association test was performed to assess relationships. Multivariate analysis was performed to identify the independent associated factors. Adjusted Odds Ratios (aORs) were calculated when the p-value was less than 0.05. We included variables that had a relationship with secondary Drug-Resistant TB with a p-value less than 0.05. Differences were considered statistically significant if at a 95% confidence interval (CI) the p-value < 0.05.

2.5. Ethical Considerations

The use of retrospective data for this study was approved by the scientific com-

mittee and the head of the department of pulmonology of the CHUSO. Data were extracted from the TBR patient's records or the registry and were coded before analysis to respect anonymity and confidentiality. No patients were physically seen, and no additional data were collected from them.

3. Results

3.1. Patients' Characteristics

During four years, 96 Drug-resistant TB patients were initiated on MDR-TB treatment of whom 7 were excluded due to incomplete information, and data from 89 patients were included in the study's final analysis.

Males were predominant in the study population with a sex ratio of 1.3. Informal working activities constituted 49.4% of the subjects. The mean age was 36.02 years (±14.21 years), ranging from 5 months to 75 years. Of these patients, 41.6% were from Grand Lomé and 27% were from the maritime region, which are both considered urban and peri-urban areas, respectively. Among the cohort participants, 31.5% patients were HIV-co-infected, and 2 of them were ART-naïve. Among the study participants, 11.2% were smokers among them 2 were current smokers. Close contact with a patient diagnosed with tuberculosis (TB) was found in 22.5%. Based on clinical records, 51.7% had received first-line TB treatment; among them 20.2% had first-line treatment failure and 5.6% had second-line treatment failure. Furthermore, 20.2% of patients relapsed after the first treatment, and 3.4% of patients relapsed after the second treatment. The mean duration between the diagnosis of drug resistance (RR) and treatment initiation was 41.7 ± 7.1 days, with a median of 22 days. The overall mean BMI of patients was 17.64 ± 3.74 kg/m^2 (Table 1).

Table 1. Comparison of sociodemographic, clinical, and paraclinical features of patients in each group.

Characteristics		G1: Primary n = 43	G2: Secondary n = 46	p value
Sex	Female	24 (55.8)	15 (32.6)	0.0338*
	Male	19 (44.2)	31 (67.4)	
Age (years)	≤33	25 (58.1)	20 (43.5)	0.2052
	≥34	18 (41.9)	26 (56.5)	
HIV test	Negative	24 (55.8)	37 (80.4)	0.0215*
	Positive	19 (44.2)	9 (19.6)	
Smoking status	No	40 (93.0)	39 (84.8)	0.3175
	Yes	3 (7.0)	7 (15.2)	
Close Contact of TB patient	No	32 (74.4)	37 (80.4)	0.6131
	Yes	11 (25.6)	9 (19.6)	
Delay before starting Second-line treatment (days)	≤22	26 (60.5)	16 (34.8)	0.0198*
	≥23	17 (39.5)	30 (65.2)	

Continued

Dyspnea	No	38 (88.4)	31 (67.4)	0.0226*
	Yes	5 (11.6)	15 (32.6)	
Chest pain	No	32 (74.4)	37 (80.4)	0.6131
	Yes	11 (25.6)	9 (19.6)	
Hemoptysis	No	42 (97.7)	43 (93.5)	0.6172
	Yes	1 (2.3)	3 (06.5)	
Fever	No	11 (25.6)	16 (34.8)	0.3669
	Yes	32 (74.4)	30 (65.2)	
BMI (Kg/m^2)	<18	25 (58.1)	24 (52.2)	0.6709
	≥18	18 (41.9)	22 (47.8)	
Cavity	No	20 (46.5)	9 (19.6)	0.0121*
	Yes	23 (53.5)	37 (80.4)	
Nodules	No	21 (48.8)	11 (23.9)	0.0165*
	Yes	22 (51.2)	35 (76.1)	
Infiltrates	No	21 (48.8)	9 (19.6%)	0.0065*
	Yes	22 (51.2)	37 (80.4)	
Anemia	No	13 (30.2)	14 (30.4)	1.0000
	Yes	30 (69.8)	32 (69.6)	
Treatment outcome	Good	31 (72.1)	42 (91.3)	0.0263*
	Poor	12 (27.9)	4 (08.7)	

3.2. Univariate Analysis Results

In univariate analysis, the following factors: male gender (OR: 2.61, 95% CI: 1.1 - 6.2); delay before second line treatment initiation (OR: 2.86, 95% CI: 1.21 - 6.78); dyspnea (OR: 3.67, 95% CI: 1.20 - 11.24), HIV positive (OR: 0.31; 95% CI 0.11 - 0.79) were associated with the secondary resistance group. Poor treatment outcome was less likely to be associated with secondary resistance group (OR: 0.24; 95% CI: 0.07 - 0.83).

Considering the chest X-ray results, the following factors were found to be associated with secondary resistance group: cavities (OR: 3.75, 95% CI: 1.39 - 9.18); Nodules (OR: 3.03, 95% CI: 1.23 - 7.49), infiltrates (OR: 3.92, 95% CI: 1.52 - 10.07) (Table 2).

Table 2. Associated factors secondary drug-resistant.

Characteristics		G1: Primary n = 43	G2: Secondary n = 46	OR (95% CI)	p value	aOR (95% CI)	p value
Sex	Female	24 (55.8)	15 (32.6)	1	0.0338*	1	0.083
	Male	19 (44.2)	31 (67.4)	2.61 (1.1 - 6.2)		2.68 (0.89 - 8.15)	
HIV test	Negative	24 (55.8)	37 (80.4)	1	0.0215*	1	0.801
	Positive	19 (44.2)	9 (19.6)	0.31 (0.11 - 0.79)		0.85 (0.25 - 2.93)	

Continued

Delay before Second-line TTT (days)	≤22	26 (60.5)	16 (34.8)	1	0.0198*	1	0.036*
	≥23	17 (39.5)	30 (65.2)	2.86 (1.21 - 6.78)		3.04 (1.08 - 8.58)	
Dyspnea	No	38 (88.4)	31 (67.4)	1	0.0226*	1	0.048*
	Yes	5 (11.6)	15 (32.6)	3.67 (1.20 - 11.24)		3.88 (1.01 - 14.89)	
Cavity	No	20 (46.5)	9 (19.6)	1	0.0121*	1	0.051
	Yes	23 (53.5)	37 (80.4)	3.75 (1.39 - 9.18)		3.21 (0.99 - 10.40)	
Nodules	No	21 (48.8)	11 (23.9)	1	0.0165*	1	0.020*
	Yes	22 (51.2)	35 (76.1)	3.03 (1.23 - 7.49)		3.62 (1.23 - 10.67)	
Infiltrates	No	21 (48.8)	9 (19.6%)	1	0.0065*	1	0.007*
	Yes	22 (51.2)	37 (80.4)	3.92 (1.52 - 10.07)		4.66 (1.51 - 14.38)	
Treatment outcome	Good	31 (72.1)	42 (91.3)	1	0.0263*	1	0.636
	Poor	12 (27.9)	4 (08.7)	0.24 (0.07 - 0.83)		0.71 (0.17 - 2.98)	

*Statistically significant

A multivariate logistic regression was performed to assess independent factors associated with Secondary Drug resistant TB. Four independent factors were identified namely, dyspnea, lung nodules and Infiltrates at imaging and long second-line treatment delay. However, lung cavity represented 3-times higher in secondary drug-resistant TB but was not statistically significant.

3.3. Multivariate Analysis Results

The multivariate analysis test revealed that the following factors: Delay before Second-line TTT (days) (aOR: 3.04, 95% CI: 1.08 - 8.58); dyspnea (aOR: 3.88; 95% CI: 1.01 - 14.89) were found to be significantly associated with secondary resistance group as well as 2 types abnormalities on chest X-ray Nodules (aOR: 3.62, 95% CI: 1.23 - 10.67) and Infiltrates (aOR: 4.66; 95% CI: 1.51 - 14.38) (Table 2).

3.4. Resistance Patterns

Among the 89 MDR/RR-TB cases, 59 had DST results, and 29 benefited from LPA. Based on the DST results, 54 RR-TB patients were confirmed MDR-TB. Except for the resistance to Streptomycin (S) and pyrazinamide (Z), MDR-TB and resistance to any first-line TB drug were common in the secondary resistance group. Four (4) cases of polyresistance were found in the primary resistance group. MDR-TB was found among 91.5% of whom having DST, which is 60.6% of our study sample. Based on LPA results, there were 5 pre-XDR-TB and 2 XDR-TB, with one in each resistance group (Table 3).

Table 3. Resistance to TB first-line drugs among culture-positive patients, and second-line drugs based on LPA.

	Drug resistance	Total N = 59	G1: Primary n (%)	G2: Secondary n (%)
	Any Resistance to one drug			
DST (n = 59)	R	58	20 (34.5%)	38 (65.5%)
	H	55	18 (32.7%)	37 (67.3%)

Continued

	Z	19	10 (52.6%)	9 (47.4%)
	E	15	6 (40.0%)	9 (60.0%)
	S	18	5 (27.8%)	13 (72.2%)
	Resistance to 2 drugs			
	R + H	15	4 (6.7%)	11 (18.6%)
	RZ	1	1 (1.7%)	0 (0%)
	HE	1	1 (1.7)	0 (0%)
	Resistance to 3 drugs			
	RHZ	7	3 (5%)	4 (6.7%)
	RHE	5	1 (1.7%)	4 (6.7%)
	RHS	7	3 (5%)	4 (6.7)
	RZE	2	2(3.4%)	0
	Resistance to 4 drugs			
	RHZE	3	2 (3.4%)	1 (1.7%)
	RHZS	6	2(3.4%)	4 (6.7%)
	RHES	3	0	3 (5%)
	At least R and H	54	17 (29%)	37 (62.5%)
LPA (n = 26)	R	26	15 (57.7%)	11 (42.3%)
	H	19	9 (47.4%)	10 (52.6%)
	Fluoroquinolone (FLQ)	06	3 (50.0%)	3 (50.0%)
	Aminoside	2	1 (50.0%)	1 (50.0%)
	MDR	19	9 (34.6%)	10 (38.4%)
	Pre XDR (RHFLQ)	5	2 (7.7%)	3(11.5%)
	XDR	2	1 (3.8%)	1(3.8%)

R = Rifampicin; H = Isoniazid; E = Ethambutol; S = Streptomycin

3.5. Evolution and Treatment Outcome

At baseline, 94.4% had positive sputum microscopy, while 5.6% had negative esults. Smear microscopy and culture conversion rates at month 4 were 76.6% and 92.2% of the 77 patients tested respectively. At month 9, smear microscopy and culture conversion rate were 98.6% and 98.6% of 73 patients tested, respectively.

The overall death rate during the follow-up was 15.7% of patients, among them 78.5% occurred before the month 4 visit, including one XDR-TB. Patients declared cured and treatment completed were 80.9%, and 1.12%, respectively. Lost to follow-up and treatment failures were recorded in 1.1% case each. The treatment failure case was one of the two patients who were diagnosed with XDR-TB. Globally, the case-fatality rate of resistant TB was 16.8% in our study.

4. Discussion

4.1. Clinical Characteristics

This study used a quantitative approach to show differences between patients with primary and secondary drug resistance. We compared their epidemiological, clinical features, and outcomes under the 9-month second-line treatment regimen with an injectable drug. Despite a small study population, our data suggested that secondary resistance was associated with dyspnea, more radiological lung lesions, and longer duration before MRD treatment initiation.

The clinical characteristics of our population have a similar pattern to the general TB population; thus, MDR/RR-TB seems to affect male and younger people. Studies across African regions found that most patients with RR-TB are aged under 40 years [11]-[13], suggesting that drug-resistant TB may affect patients' capacity to work as well as a country's economy. Tanimura *et al.*, and Menzies *et al.* have found a high financial cost for TB patients living with the disease in low- and middle-income countries. Loss of work capacity and income, due to temporary disabilities and TB complication-related treatment costs, are some of the financial issues encountered by them [14] [15]. Patients living in the urban area accounted for more than half of our population. Dickson *et al.* in South Africa and Mbuh *et al.* in Cameroon found the same findings in their studies [16] [17]. In Africa, people assume that the quality of health care is better in town, thus they often move there when sick [17]. However, younger age, male gender, and inappropriate behaviors may impede this health quality access opportunity [11] [17]. Moreover, Longo *et a*l. have found an association between urban/periurban setting and a risk of developing MDR/RR-TB in the Republic of Central Africa [12].

More than half of our population had a history of first-line TB treatment intake. Similarly, Fara *et al.* in the Central African Republic found a resistance rate of up to 46.6% among those previously treated. In their study, a TB relapse was associated with a 3 times higher risk of developing TBR [18]. Even with TB incidence varying from one country to another, results show that poor previous treatment outcomes and lack of adherence remain the main triggers of TB drug resistance [9] [12] [18] [19].

In our study, no association was found between having a former close contact with a TB patient and the resistance group. This contrasts with findings of studies held in Ethiopia and Namibia, where close contact with a TB case was strongly associated with TB drug resistance [18] [19]. This fact is highlighted in Chinese studies that have unveiled a community transmission of DR strains and exogenous reinfection among former TB patients [20] [21]. Hence, the importance of TB contact tracking. The low number of close-contact cases in our study could be due to patients being unaware of TB cases in their surroundings or difficulty recalling.

Univariate analysis has found an association between HIV-positive status, being male gender, having dyspnea, lung scars at X-Ray (cavity, nodule, and infiltrate), delay in DR treatment initiation, and treatment outcome with secondary resistance group. However, after multivariate analysis, factors remaining associ-

ated were dyspnea, having nodules or infiltrates at X-Ray, and delay in DR treatment initiation.

Wang *et al.* found that pulmonary lesions among MDR-TB patients tend to be extended and bilateral [22]. The finding in the chest Tomography scan was a tree-in-bud sign, patchy or lobular areas of consolidation, cavitation, and bronchiectasis [22] [23]. In our study, the secondary resistant group patients were more likely to present nodules and infiltrates on chest X-rays. Oladimeji and al in Nigeria found that MRD TB patients with previous treatment are 6.9 times more likely to have abnormalities in chest X-ray. Lesions found in their studies were mostly cavitation, fibrosis, and infiltrates [24]. Even if the type of lesions were different, multiple radiological patterns were observed among resistant TB patients previously treated [22]-[24]. Each pattern may have different therapeutic implications. Nodules and infiltrates express more disease current activity, while cavities are associated with slow sputum conversion, increased risk of transmission, and developing additional drug resistance [22]. The more extensive the cavities, the worse the outcome of patient during second-line treatment. [1] [20] [22]. Therefore, initial radiological evaluation may help to screen patients who need additional treatment supplies and follow-up investigation. Our data also shows that dyspnea was associated with the secondary resistant group, which can be in line with the extension of lung damage on chest X-ray.

4.2. Resistance Patterns

Our study also revealed the importance of drug susceptibility testing to avoid misdiagnosis of resistance patterns that can lead to ineffective treatments and worse outcomes [1] [8].

The drug susceptibility test was performed on 59 positive cultures of our patients. Resistance to any first-line drugs and resistance patterns were most frequent in the secondary resistance group. Anyway, finding any resistance patterns in the primary resistance group may be due to the circulation of resistant strains within the community. This may reflect the efficacy of the TB programs on DOTS implementation [1] [2]. Resistance to both rifampicine (R) and isoniazid (H) were found among 60% of those having DST and classified as the secondary resistance group. In addition, one patient had rifampicin resistance associated with other drugs different from isoniazid. Our results are close to those from an Ethiopian study, where people with a history of TB treatment had 8 times the risk of developing resistance to any first-line drugs and were at least 7 times more likely to have MDR-TB [25] [26]. R and H are the most powerful anti-TB drugs, mutations are the main noticeable way of resistance occurrence. Some mutation regions associated with resistance to R and H are responsible for greater transmission and cross-resistance to ethionamide, respectively [27].

Patients with MDR TB, compared to those with monoresistance to INH or RIF, are more likely to develop resistance to another drug during the treatment. This new resistance often occurs within the first 6 months of treatment and could be a

source of ultra-resistance [28] [29]. Follow-up DSTs can exhibit MDR TB, pre-XDR, and XDR during treatment. In this study, participants were admitted to the hospital during the first 4 months for DOT and amikacin injections. The long waiting time to obtain the DST result could delay the use of the appropriate drugs in case of resistance. These situations could increase the risk of new resistance development and transmission of resistant strains in the community.

It appears necessary to perform DST at treatment initiation and follow-up to track additional drug resistance, as some of our study participants were carrying pre-XDR and XDR strains.

4.3. Outcome

Overall, the treatment success rate was 82,03%, which is higher than the MDR/RR-TB global treatment success rate in 2023 and lower than 86% of Mbuh *et al.* in Cameroon [2] [17]. Both Togo and Cameroon have implemented TBMR management, which encompasses hospitalization and directly observed treatment during the intensive phase of treatment, along with comorbidities screening [7] [17]. The higher success rate in Cameroon can be explained by the inclusion of a narrow population from one region rather than the whole country. In South Africa (SA), Ndjeka *et al.* had a success rate of 60% which could be explained by a higher number of HIV-infected patients in their study [30]. Globally, our results are better than those in West and Central Africa, with a success rate ranging from 69 to 81% [13]. Reasons for poor outcomes of R-TB treatment are linked to HIV infection disease stage, occurrence of side effects, lack of adherence, unemployment, and high duration between Drug-resistant confirmation and treatment initiation [1] [13] [30] [31].

In our study, we had a death rate of 16.8%, which is slightly below the global trend [2]. Surprisingly, a poor outcome was associated with primary resistance in univariate analysis. Even if the association dropped after multivariate analysis, our results are contrary to what was observed in other studies [31] [32]. Our results are close to those of Ockenga *et al.*, who found that the primary resistance group tends to be under 40 years old, have bilateral and cavitary diseases on lung imaging, and are associated with poor outcomes [33]. Thus, the poor outcome of the primary resistance group observed in our study could be explained by the younger age, HIV positivity rate, and the influence of female gender. Our results show that being HIV positive seems to be protective for the secondary group participant at univariate analysis. Despite the loss of that protection, we assume that being already in the TB management system for a longer time was an opportunity for better care. Knowing that the Togo TB program is associated with HIV one for coinfection management in health care facilities [7] [9]. The secondary resistance group had had much time to benefit from both care compared to their counterpart from the primary resistance group. The latter included more females, and some have also shown that socio-cultural barriers, stigma, lack of financial autonomy, or inequity often impede women's access to care compared to men [32]. Studies

found that bilateral lung damage and cavities are associated with poor outcomes and death [22] [31] [33]. In our study, cavities were not associated with the secondary group that had better outcomes. The radiological abnormalities and clinical signs associated with a negative impact could have been counterbalanced by the low proportion of HIV, the higher BIM, male gender, and age of the secondary group participants.

5. Conclusions

Our study shows that secondary MDR/RR-TB patients are generally those with a history of first-line TB treatment failure or relapse. Furthermore, they were more likely to have dyspnea, X-ray lesions, and a delay before treatment initiation. Moreover, pre-XDR and XDR cases were unveiled during treatment follow-up. Hence, the need for community DOT implementation of a first-line treatment course, reinforcement of DOTS, and strengthening laboratory capacity.

Our study has some limitations due to the retrospective data collection, which favors missing data. In addition, lung lesions were assessed by chest X-ray instead of a CT scan, which better characterized them. In addition, not all isolates were tested for first-line and second-line anti-TB drugs due to contaminated sputum culture or lack of laboratory capacity, which may affect our results.

Conflicts of Interest

There are no conflicts of interest.

References

[1] The WHO (2022) WHO Consolidated Guidelines on Tuberculosis. Module 4: Treatment-Drug-Resistant Tuberculosis Treatment, Update. World Health Organization. https://www.who.int/publications/i/item/9789240063129

[2] The WHO (2023) Global Tuberculosis Report 2023. World Health Organization.

[3] Litvinjenko, S., Magwood, O., Wu, S. and Wei, X. (2023) Burden of Tuberculosis among Vulnerable Populations Worldwide: An Overview of Systematic Reviews. *The Lancet Infectious Diseases*, **23**, 1395-1407. https://doi.org/10.1016/s1473-3099(23)00372-9

[4] Adebisi, Y.A., Agumage, I., Sylvanus, T.D., Nawaila, I.J., Ekwere, W.A., Nasiru, M., *et al.* (2019) Burden of Tuberculosis and Challenges Facing Its Eradication in West Africa. *International Journal of Infection*, **6**, e92250. https://doi.org/10.5812/iji.92250

[5] Otchere, I.D., Asante-Poku, A., Akpadja, K.F., Diallo, A.B., Sanou, A., Asare, P., *et al.* (2024) Opinion Review of Drug-Resistant Tuberculosis in West Africa: Tackling the Challenges for Effective Control. *Frontiers in Public Health*, **12**, Article ID: 137470. https://doi.org/10.3389/fpubh.2024.1374703

[6] Afanvi, K.A., Dogo, M.F., Aziagbé, K.A., Adjoh, K.S. and Ekouévi, K.K.D. (2023) Quality Mindset: The Missing Ingredient in Tuberculosis Care and Control in Togo. *European Journal of Theoretical and Applied Sciences*, **1**, 36-41. https://doi.org/10.59324/ejtas.2023.1(4).04

[7] PNLT-Togo (2022) Guide national de prise en charge de la TB MR/RR. Ministere de la sante, PNLT, Première édition, 1-77.

[8] Guillet-Caruba, C., Martinez, V. and Doucet-Populaire, F. (2014) Les nouveaux outils de diagnostic microbiologique de la tuberculose maladie. *La Revue de Médecine Interne*, **35**, 794-800. https://doi.org/10.1016/j.revmed.2014.05.001

[9] Villalva-Serra, K., Barreto-Duarte, B., Miguez-Pinto, J.P., Queiroz, A.T.L., Rodrigues, M.M., Rebeiro, P.F., *et al.* (2024) Impact of Xpert MTB/RIF Implementation in Tuberculosis Case Detection and Control in Brazil: A Nationwide Intervention Time-Series Analysis (2011-2022). *The Lancet Regional Health-Americas*, **36**, Article ID: 100804. https://doi.org/10.1016/j.lana.2024.100804

[10] Alexander, P.E. and De, P. (2007) The Emergence of Extensively Drug-Resistant Tuberculosis (TB): TB/HIV Coinfection, Multidrug-Resistant TB and the Resulting Public Health Threat from Extensively Drug-Resistant TB, Globally and in Canada. *Canadian Journal of Infectious Diseases and Medical Microbiology*, **18**, 289-291. https://doi.org/10.1155/2007/986794

[11] Faye, L., Hosu, M. and Apalata, T. (2024) Drug-Resistant Tuberculosis in Rural Eastern Cape, South Africa: A Study of Patients' Characteristics in Selected Healthcare Facilities. *International Journal of Environmental Research and Public Health*, **21**, Article No. 1594. https://doi.org/10.3390/ijerph21121594

[12] de Dieu Longo, J., Woromogo, S.H., Tekpa, G., Diemer, H.S., Gando, H., Djidéré, F.A., *et al.* (2023) Risk Factors for Multidrug-Resistant Tuberculosis in the Central African Republic: A Case-Control Study. *Journal of Infection and Public Health*, **16**, 1341-1345. https://doi.org/10.1016/j.jiph.2023.06.007

[13] Toft, A.L., Dahl, V.N., Sifna, A., Ige, O.M., Schwoebel, V., Souleymane, M.B., *et al.* (2022) Treatment Outcomes for Multidrug- and Rifampicin-Resistant Tuberculosis in Central and West Africa: A Systematic Review and Meta-Analysis. *International Journal of Infectious Diseases*, **124**, S107-S116. https://doi.org/10.1016/j.ijid.2022.08.015

[14] Tanimura, T., Jaramillo, E., Weil, D., Raviglione, M. and Lönnroth, K. (2014) Financial Burden for Tuberculosis Patients in Low- and Middle-Income Countries: A Systematic Review. *European Respiratory Journal*, **43**, 1763-1775. https://doi.org/10.1183/09031936.00193413

[15] Menzies, N.A., Allwood, B.W., Dean, A.S., Dodd, P.J., Houben, R.M.G.J., James, L.P., *et al.* (2023) Global Burden of Disease Due to Rifampicin-Resistant Tuberculosis: A Mathematical Modeling Analysis. *Nature Communications*, **14**, Article No. 6182. https://doi.org/10.1038/s41467-023-41937-9

[16] Dickson, L., Le Roux, S.R., Mitrani, L., Hill, J., Jassat, W., Cox, H., *et al.* (2023) Organisation of Care for People Receiving Drug-Resistant Tuberculosis Treatment in South Africa: A Mixed Methods Study. *BMJ Open*, **13**, e067121. https://doi.org/10.1136/bmjopen-2022-067121

[17] Mbuh, T.P., Mendjime, P., Goupeyou-Wandji, I., Donkeng-Donfack, V.F., Kahou, J., Endale Mangamba, L., *et al.* (2024) Trends of Drug-Resistant Tuberculosis and Risk Factors to Poor Treatment-Outcome: A Database Analysis in Littoral Region-Cameroon, 2013-2022. *BMC Public Health*, **24**, Article No. 3195. https://doi.org/10.1186/s12889-024-20585-8

[18] Farra, A., Danebera, L.V., Ngaya, G., Yambiyo, B.M., Manirakiza, A. and Mossoro-Kpinde, C.D. (2023) The Contribution of the Xpert® MTB/RIF Assay to the Surveillance of Drug-Resistant Tuberculosis in the Central African Republic. *Journal of Tuberculosis Research*, **11**, 23-32. https://doi.org/10.4236/jtr.2023.111003

[19] Biru, D. and Woldesemayat, E.M. (2020) Determinants of Drug-Resistant Tubercu-

losis in Southern Ethiopia: A Case-Control Study. *Infection and Drug Resistance*, **13**, 1823-1829. https://doi.org/10.2147/idr.s256536

[20] Yang, C., Luo, T., Shen, X., Wu, J., Gan, M., Xu, P., *et al.* (2017) Transmission of Multidrug-Resistant Mycobacterium Tuberculosis in Shanghai, China: A Retrospective Observational Study Using Whole-Genome Sequencing and Epidemiological Investigation. *The Lancet Infectious Diseases*, **17**, 275-284. https://doi.org/10.1016/s1473-3099(16)30418-2

[21] Li, X., Zhang, Y., Shen, X., Shen, G., Gui, X., Sun, B., *et al.* (2007) Transmission of Drug-Resistant Tuberculosis among Treated Patients in Shanghai, China. *The Journal of Infectious Diseases*, **195**, 864-869. https://doi.org/10.1086/511985

[22] Wáng, Y.X.J., Chung, M.J., Skrahin, A., Rosenthal, A., Gabrielian, A. and Tartakovsky, M. (2018) Radiological Signs Associated with Pulmonary Multi-Drug Resistant Tuberculosis: An Analysis of Published Evidences. *Quantitative Imaging in Medicine and Surgery*, **8**, 161-173. https://doi.org/10.21037/qims.2018.03.06

[23] Nofal, I.M.M., AbdelHalim, H.A., Almaraghy, A.A., Awad, A.M. and Farrag, M.A. (2024) Characteristics and Treatment Outcomes of Patients with Multi-Drug-Resistant Tuberculosis at Abbassia Chest Hospital. *The Egyptian Journal of Bronchology*, **18**, 1-11. https://doi.org/10.1186/s43168-024-00348-0

[24] Oladimeji, O., Adeniji-Sofoluwe, A.T., Othman, Y., Adepoju, V.A., Oladimeji, K.E., Atiba, B.P., *et al.* (2022) Chest X-Ray Features in Drug-Resistant Tuberculosis Patients in Nigeria; a Retrospective Record Review. *Medicines*, **9**, Article No. 46. https://doi.org/10.3390/medicines9090046

[25] Hamusse, S.D., Teshome, D., Hussen, M.S., Demissie, M. and Lindtjørn, B. (2016) Primary and Secondary Anti-Tuberculosis Drug Resistance in Hitossa District of Arsi Zone, Oromia Regional State, Central Ethiopia. *BMC Public Health*, **16**, Article No. 593. https://doi.org/10.1186/s12889-016-3210-y

[26] Eshetie, S., Gizachew, M., Dagnew, M., Kumera, G., Woldie, H., Ambaw, F., *et al.* (2017) Multidrug Resistant Tuberculosis in Ethiopian Settings and Its Association with Previous History of Anti-Tuberculosis Treatment: A Systematic Review and Meta-Analysis. *BMC Infectious Diseases*, **17**, Article No. 219. https://doi.org/10.1186/s12879-017-2323-y

[27] Palomino, J. and Martin, A. (2014) Drug Resistance Mechanisms in Mycobacterium Tuberculosis. *Antibiotics*, **3**, 317-340. https://doi.org/10.3390/antibiotics3030317

[28] Loutet, M.G., Davidson, J.A., Brown, T., Dedicoat, M., Thomas, H.L. and Lalor, M.K. (2018) Acquired Resistance to Antituberculosis Drugs in England, Wales, and Northern Ireland, 2000-2015. *Emerging Infectious Diseases*, **24**, 524-533. https://doi.org/10.3201/eid2403.171362

[29] O'Toole, R.F. (2022) Antibiotic Resistance Acquisition versus Primary Transmission in the Presentation of Extensively Drug-Resistant Tuberculosis. *The International Journal of Mycobacteriology*, **11**, 343-348. https://doi.org/10.4103/ijmy.ijmy_187_22

[30] Ndjeka, N., Campbell, J.R., Meintjes, G., Maartens, G., Schaaf, H.S., Hughes, J., *et al.* (2022) Treatment Outcomes 24 Months after Initiating Short, All-Oral Bedaquiline-Containing or Injectable-Containing Rifampicin-Resistant Tuberculosis Treatment Regimens in South Africa: A Retrospective Cohort Study. *The Lancet Infectious Diseases*, **22**, 1042-1051. https://doi.org/10.1016/s1473-3099(21)00811-2

[31] Bhering, M. and Kritski, A. (2020) Primary and Acquired Multidrug-Resistant Tuberculosis: Predictive Factors for Unfavorable Treatment Outcomes in Rio De Janeiro, 2000-2016. *Revista Panamericana de Salud Pública*, **44**, e178. https://doi.org/10.26633/rpsp.2020.178

[32] The Global Fund (2020) Technical Brief Tuberculosis, Gender and Human Rights.

[33] Ockenga, J., Fuhse, K., Chatterjee, S., Malykh, R., Rippin, H., Pirlich, M., *et al.* (2023) Tuberculosis and Malnutrition: The European Perspective. *Clinical Nutrition*, **42**, 486-492. https://doi.org/10.1016/j.clnu.2023.01.016