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Treatment Outcomes and Associated Factors among Multi Drug-Resistant Tuberculosis Patients in Ashanti Region, Ghana: A Retrospective Cross-Sectional Study

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Abstract

Objective: The aim of this study was to determine treatment outcomes and associated factors among patients treated for multidrug-resistant tuberculosis (MDR-TB) in the Ashanti Region, Ghana.

Design: A retrospective cross-sectional analysis

Setting: The study was conducted in the Ashanti Region, the second most populous region in Ghana. The Regional MDR-TB register, which contains information on all MDR-TB patients being treated at the various TB centers in the region, was analyzed between February and May, 2021.

Participants: The participants consisted of all of the registered MDR-TB patients who were placed on treatment between January 1 and December 31, 2020. Patients were included in the analysis if their treatment outcome had been assigned. Patients with no record of treatment outcome were excluded from the study.

Outcome measures: The main outcome variable for the study was MDR-TB treatment outcome, standardized as "cured", "treatment completed", "treatment failure", "died" and lost to follow-up".

Results: Out of 159 patients included in the analysis, 86 (54.1%) were declared cured, 28 (17.6%) completed their treatment successfully, six (3.8%) were declared treatment failure, 12 (7.5%) were lost to follow up, while 27 (17.0%) died. The overall treatment success rate was 71.7%. Factors associated with successful MDR-TB treatment outcome were gender, age, level of education, baseline BMI and treatment regimen.

Conclusions: The findings have demonstrated that favorable treatment outcomes for MDR-TB patients could be achieved in a resource-limited country. Although several studies have assessed treatment outcomes of drug-susceptible TB in Ghana, very little has been done in the aspect of MDR-TB. Further studies are, therefore, required in this area to bridge the dearth of information on MDR-TB treatment outcome and its associated factors in the country.

Keywords:

Tuberculosis, multi drug-resistant TB, treatment outcomes, Ashanti Region, Ghana

Strengths and limitations of this study

- This study is among the few to provide an important assessment of MDR-TB treatment outcome and its associated factors in Ghana
- The findings provide important baseline information for further broader studies in the country
- There may be under and/or overestimation of some of the findings as the secondary data used were not recorded systematically for research purposes.
- The nature of the secondary data analyzed limited the inclusion of other potential factors that could be associated with successful MDR-TB treatment outcome
- Due to the small sample drawn from a specific geographical location in Ghana, the findings might have limited generalizability

Background

Tuberculosis (TB) is one of the top 10 causes of morbidity and mortality worldwide, and the leading cause from a single infectious agent.[1] The 2020 World Health Organization (WHO) Global Tuberculosis Report indicates that in 2019, 10 million people were infected with TB globally, out of which 1.4 million resulted in deaths. Geographically, most cases occurred in the WHO regions of South-East Asia (44%), Africa (24%) and the Western Pacific (18%), with smaller shares in the Eastern Mediterranean (8%), the Americas (3%) and Europe (3%).[2]

Although the global incidence of TB is falling at about 2% per year,[1] the emergence of multidrug-resistant TB (MDR-TB) over the past few decades poses a public health crisis and a health security threat.[2,3] Globally, 206,030 MDR-TB cases were recorded in 2019, an increase of 10% from 186,883 in 2018.[2] MDR-TB is diagnosed when a patient's sputum examination reveals resistance to at least isoniazid (INH) and rifampicin (RMP).[4] Estimates from WHO indicate that over half a million new cases of rifampicin-resistant (RR) and multi-drug resistant (MDR) TB are recorded annually.[1] Four main factors are known to account for drug resistance: inappropriate use of anti-TB medications, incorrect prescription of drugs by care providers, poor quality drugs, and patient stopping treatment prematurely.[4]

MDR-TB is curable and treatment requires the administration of second-line anti-TB drugs for a minimum of nine months and a maximum of 20 months.[3] However, compared to drug-susceptible TB cases, treatment outcomes of MDR-TB cases are poorer. Globally, only 57% of MDR-TB patients were successfully treated in 2019.[2] The management of MDR-TB is complex as it puts a greater strain on countries and national health systems.[2,6] For example, culture-based methods can take weeks to months. They are also expensive and require sophisticated and well-established laboratory infrastructure, qualified and competent staff and strict quality and infection control systems.[6]

The global health aim of eliminating TB by 2035 will only be possible if drug-resistant strains of Mycobacterium Tuberculosis are effectively managed by countries.[6] Ghana is not ranked among the world's high-burden TB countries. Incidence of TB has fallen gradually from 214 cases per 100,000 people in 2001 to 143 cases per 100,000 people in 2020.[7] Nonetheless, studies have reported the emergence of MDR-TB in the country.[7-12] For instance, Davies-Teye et al. reported

a cumulative incidence of MDR-TB in the Greater Accra Region of 1.4/100,000 population, with a case fatality rate of 14%.[8] In a recent nationwide drug resistance survey to investigate the level and pattern of resistance to first-line TB drugs among newly and previously treated sputum smear-positive TB cases, Sylverken and colleagues found that resistance to isoniazid and rifampicin, the two most effective anti-TB drugs, was 3.2%.[7]

High-quality disease management is one of the key strategies in improving treatment outcomes of TB.[13] In Ghana, both susceptible TB and MDR-TB are managed under directly observed treatment short course (DOTS) program, which has demonstrated feasible and effective treatment in other resource-limited countries.[14] Gaining insight into treatment outcome of MDR-TB and its associated factors could assist national TB control programs in improving the treatment success rate of MDR-TB patients. Nonetheless, literature on factors influencing treatment outcomes of MDR-TB in Ghana is limited. Moreover, studies conducted in other countries have revealed a wide variation in predictors of MDR-TB treatment outcomes. Some of the factors that have been found to be associated with successful or unsuccessful MDR-TB treatment outcome include patient age,[15] gender,[16] pretreatment body mass index (BMI)[17] and body weight, drug adherence,[18] positive smear at the start of treatment, previous history of TB,[19] smoking,[16] alcohol consumption,[20] and comorbidities or underlining health conditions such as HIV[21] and diabetes.[22] However, other studies[15,21,23] have reported findings contrary to the above-mentioned factors. For instance, Elliott and colleagues found no association between MDR-TB treatment outcome and positive smear at the start of treatment and HIV co-infection.[18] Also, Khan et al. reported that MDR-TB treatment outcome was not significantly associated with gender, smoking and comorbidity status.[15]

Therefore, this study was conducted to determine treatment outcomes and associated factors among TB patients treated for MDR-TB in the Ashanti Region, Ghana. Understanding the factors that could determine successful treatment outcome would be useful in developing strategies and making informed decisions about MDR-TB management in the region. This would help promote efficient and effective MDR-TB treatment in the country.

Methods

Study setting

The Ashanti Region is the second most populous region in Ghana, with a population of 5,432,485.[24] It has a population density of 192.4 per sq. km. The region has 43 districts and 132 sub-districts. There are five hundred and twenty-seven health facilities in the region. The Ghana Health Service (GHS) operates about 33% of all health facilities in the region. Kumasi, the regional capital, has the highest number of health facilities (29%) with Ejura-Sekyedumase having the least (2%).[24]

Study design, population and sample

A retrospective cross-sectional analysis of the Ashanti Regional MDR-TB register was conducted between February and May, 2021. The Regional MDR-TB register is a standard register containing information on all MDR-TB patients being treated at the various DOT centers in the region. The study population consisted of all of the registered MDR-TB patients who were placed on treatment between January 1, 2015 (when MDR-TB treatment started in the region) and December 31, 2020. Patients were included in the analysis if their treatment outcome had been assigned. Patients with no record of treatment outcome were excluded from the study.

Study variables

The main outcome variable for the study was MDR-TB treatment outcome. This was standardized, as recommended by WHO, as "cured", "treatment completed", "treatment failure", "died" and "lost to follow-up".[25] According to the WHO guidelines for the management of drug resistance TB (DR-TB), a treatment outcome is classified cured when the treatment is completed with no evidence of failure and three or more consecutive sputum cultures taken at least 30 days apart are negative after the intensive phase. A patient is declared treatment completed when he/she completes his/her treatment with no evidence of failure, but there is no record indicating that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase. Treatment failure is when treatment is terminated due to poor clinical or radiological response or adverse drug reaction. Treatment outcome "died" is when a patient dies

for any reason during the course of treatment. Finally, a patient whose treatment is interrupted for two consecutive months is declared lost to follow-up.[25,26]

The explanatory variables included were: age, gender, educational level, marital status, treatment regimen (new vs. retreatment), baseline BMI, baseline weight, HIV status, and having co-morbidities other than HIV. These variables were selected based on previous studies (as indicated in the introductory section of the paper) and the availability of data.

Data collection

A designed data extraction tool, reflecting the various variables under study, was used to gather data from the Ashanti Regional MDR-TB register. Data extraction was done by two members of the research team, and assisted by four trained data collectors, comprising two public health nurses and two health information officers. Missing information in the register was completed with data from the patients' clinical records. All of the extracted information was audited and verified to check for completeness and quality.

Statistical analysis

Data collected was coded, entered and analyzed using Statistical Package for Social Sciences (SPSS) software version 20 (IBM© Corporation, Armonk, NY, USA). Categorical data was presented as frequencies and percentages, while continuous data was presented in the form of mean and standard deviation. The main outcome variable, MDR-TB treatment outcome, was categorized into successful (cured and completed) and unsuccessful (treatment failure, died and lost to follow-up) treatment outcomes, and scored as follows: successful treatment = 1, unsuccessful treatment = 0. The continuous variables were also dichotomized as follows: age into < 50 and ≥ 50 years, BMI into < 18.5 and ≥ 18.5 kg/m^2, and body weight into < 50 and ≥ 50 kg. Bivariate analysis was performed for all of the independent variables with the outcome variable. Using variables with p-value < 0.2, based on the bivariate analysis, a multiple logistic regression analysis was carried out to determine the independent predictors of successful MDR-TB treatment outcome. Variables with significant associations with successful MDR-TB

treatment outcome were identified based on the odds ratio (OR) with a 95% confidence interval (CS) and p-values ≤ 0.05.

Patient and public involvement

The nature of the study (retrospective cross-sectional analysis) did not permit the involvement of patients in the design of the research.

Ethical consideration

The study was approved by the Ethics Review Committee of the Ghana Health Service Research and Development Division, Accra (Protocol No. GHS-ERC-052/04/21). In addition, approval was obtained from the Ashanti Regional Health Directorate (ARHD) to use data from the Regional MDR-TB treatment register for the study. Data retrieved was not linked to any patient.

Results

In total, 159 MDR-TB patient records were reviewed. Table 1 summarizes the demographic characteristics of the study participants. The mean age of the patients was 43.69±14.86 years. The majority were male (111, 69.8%), between the age group of 40 and 49 years (46, 28.9%), having educational qualification below high school (121, 76.1%), and not married (8, 53.4%). There has been a steady increase in the number of patients placed on treatment in the region since 2015 (Figure 1).

Table 1: Socio-demographic characteristics of the MDR-TB patients (N=129)

Characteristics	Frequency	Percentage (%)
Gender:		
Male	111	69.8
Female	48	30.2
Age Group:		
< 20	5	3.1

20-29	28	17.6
30-39	26	16.4
40-49	46	28.9
50-59	26	16.4
≥ 60	28	17.6
Education:		
Below high school	121	76.1
High school and above	38	23.9
Marital Status:		
Married	74	46.6
Not married	85	53.4

*MDR TB=Multidrug resistant Tuberculosis

Figure 1: Trend in MDR-TB patients placed on treatment from 2015 to 2020 in Ashanti Region, Ghana

Clinical characteristics

Table 2 summarizes the clinical characteristics of the MDR-TB patients included in the study. The majority (69%) of the patients had a baseline body weight ≥ 50kg. Also, more than half (59.1%) had a baseline BMI ≥ 18.5 kg/m^2. About 16% had a history of comorbidities such as diabetes and hypertension, and 90% had no history of HIV co-infection. Regarding treatment regimen, 33.6% were new patients, whereas 66.4% had a previous history of TB treatment.

Table 2: Clinical characteristics and lifestyle behaviors of the MDR-TB Patients (N=129)

Variables	**Frequency**	**Percentage (%)**
Baseline weight (kg)		
< 50	49	31.0
≥ 50	110	69.0

Baseline BMI (kg/m^2)		
< 18.5	65	40.9
≥ 18.5	94	59.1
Co-morbidity		
Yes	26	16.3
No	133	83.7
HIV Status		
Negative	143	90.0
Positive	16	10.0
Treatment regimen		
New Patient	53	33.6
Retreatment	106	66.4

***BMI=Body Mass Index, MDR TB=Multidrug resistant Tuberculosis**

Treatment outcomes

Of the 159 patients included in the analysis, 86 (54.1%) were declared cured, 28 (17.6%) completed their treatment successfully, six (3.8%) were declared treatment failure, 12 (7.5%) were lost to follow up, while 27 (17.0%) died (Figure 2). The overall treatment success rate for the period under study (2015-2020) was 71.7%.

Figure 2: Treatment outcomes of the MDR-TB patients (N = 129)

Factors associated with MDR-TB treatment outcome

In the bivariate analysis, the covariates with p-values less than 0.2 level of significance for successful MDR-TB treatment outcome were gender, age, educational level, baseline BMI, baseline weight, comorbidity status, HIV status and treatment regimen (Table 3).

Table 2: Bivariate analysis of factors associated with successful treatment outcome* among *patients treated for MDR-TB in Ashanti Region, 2015-2020

	Overall Treatment Outcome

Characteristics	Frequency (N=159)	Successful N (%)	Unsuccessful N (%)	p-value
Gender				
Male	111	78 (70.3)	33 (29.7)	
Female	48	39 (81.1)	9 (18.9)	0.021
Age				
< 50	106	76 (71.7)	30 (28.3)	
≥50	53	35 (66.0)	18 (34.0)	0.001
Education				
Below high school	121	95 (78.6)	26 (21.4)	
High school & above	38	26 (68.4)	12 (31.6)	0.033
Marital Status				
Married	74	48 (65.0)	26 (35.0)	
Not Married	85	68 (80.0)	17 (20.0)	0.655
Baseline weight (kg)				
< 50	49	34 (69.4)	15 (30.6)	
≥50	110	75 (68.2)	35 (31.8)	0.032
Baseline BMI (kg/m^2)				
< 18.5	65	50 (76.9)	15 (23.1)	
≥ 18.5	94	63 (67.1)	31 (32.9)	0.043
Co-morbidity				
Yes	26	14 (53.8)	12 (46.2)	
No	133	100 (75.2)	33 (24.8)	0.108
HIV status				
Negative	143	104 (72.7)	39 (27.3)	
Positive	16	10 (62.5)	6 (37.5)	0.145
Treatment regimen				
New Patient	53	46 (86.8)	7 (13.2)	
Retreatment	106	67 (63.2)	39 (36.8)	0.023

***BMI= body mass index, HIV=human immunodeficiency virus, MDR-TB=multidrug resistant tuberculosis**

Results of the binary logistic regression analysis showed that the odds of having a successful MDR-TB treatment outcome were independently associated with gender, age, level of education, baseline BMI and treatment regimen (Table 4). Adjusting for the relationships of the other independent variables, we observed that the likelihood of having a successful MDR-TB treatment outcome among female patients was 1.3 times (AOR = 1.27, 95% CI: 1.18-1.39) higher compared with male patients. Also, patients who were 50 years and above were less likely

(AOR = 0.53, 95% CI: 0.19-2.11), compared with those below 50 years, to have a successful MDR-TB treatment outcome. Furthermore, patients whose educational level was high school or above were 1.1 times (AOR = 1.12, 95% CI: 0.65-1.90) more likely, compared with those below high school, to have a successful MDR-TB treatment outcome. Moreover, patients with baseline BMI ≥ 18.5 kg/m^2 had higher odds (AOR = 1.57, 95% CI: 0.13-2.17) of having a successful MDR-TB treatment outcome, compared with those having BMI <18.5 kg/m^2. Finally, compared with new patients, patients with previous history of TB were less likely (AOR=0.47, 95% CI: 0.10-0.75) to have a successful MDR-TB treatment outcome.

Table 4. Independent predictors of successful treatment outcome among patients treated for MDR-TB in Ashanti Region, 2015-2020 (N= 159)

Variable	AOR	95% CI	p-value
Gender			
Male	Ref.		
Female	1.27	1.18 – 1.39	0.023
Age			
< 50	Ref.		
≥ 50	0.53	0.19 – 2.11	0.012
Education			
Below high school	Ref.		
High school & above	1.12	0.65 – 1.90	0.034
Baseline weight (kg)			
< 50	Ref.		
≥50	1.22	0.94 – 2.84	0.068
Baseline BMI (kg/m^2)			
< 18.5	Ref.		
≥ 18.5	1.57	1.23 – 2.47	0.011
Comorbidity			
Yes	Ref.		
No	2.42	2.33 – 2.51	0.212
HIV status			
Negative	Ref.		
Positive	0.98	0.63 – 0.96	0.951
Treatment regimen			
New Patient	Ref.		
Retreatment	0.47	0.10 – 0.75	0.028

P ≤ 0.05, CI=confidence interval, AOR= adjusted odds ratio

Discussion

Summary of findings

Our study showed that more than two-thirds (N=114, 71.7%) of the patients had successful MDR-TB treatment outcome, while 28.3% had unfavorable treatment outcome. Cure rate was 54.1%, whereas mortality rate was 17.0%. A logistic regression model was fitted for eight variables, out of which five were independently associated with successful MDR-TB treatment outcome. Patients who were female, younger (less than 50 years), having higher level of education, having a baseline BMI of 18.5kg/$m^2$and above, and not having a previous history of TB were more likely to have successful MDR-TB treatment outcome. Marital status, baseline weight, HIV status, and having co-morbidity other than HIV had no significant association with MDR-TB treatment outcome.

Strengths and limitations

To the best of our knowledge, the present study, if not the first, is among the few to provide an important assessment of MDR-TB treatment outcome and its associated factors in Ghana. The findings provide baseline information for further broader studies in the country. Nonetheless, the study is not without limitations. First, being a retrospective analysis, findings were based on secondary data obtained from patients' medical records and registers. Since these records are not intended for research, they are not recorded systematically. This may have led to under and/or overestimation of some of our findings. Second, the nature of the secondary data we used permitted us to review only records available in the regional MDR-TB register and the patients' medical records. This did not allow us to include in the analysis other potential factors, such as smoking history, alcohol use, income level and place of residence that could be associated with successful MDR-TB treatment outcome. Third, and most importantly, due to the small sample size drawn from a specific geographical location in Ghana, the study findings might have limited generalizability. That notwithstanding, the sample size used satisfies the general rule of thumb for the number of participants required to examine associations.[27] The rule has been that for regression equations using six or more predictors, a minimum of 10 participants per predictor is required.[27] Going by this, and with nine predictors used in the study, a minimum of 90

participants would have been sufficient to examine the associations. Also, compared with normal TB cases, MDR-TB patient population in the country is not very large. For instance, Svlverken and colleagues' recent nationwide survey found only 19 (3.2%) out of 927 TB patients to be multidrug-resistant.[7] Thus, a sample of 159 is adequate to make a generalization about the MDR-TB population, particularly in the study area. Furthermore, except for patients whose treatment outcomes had not been confirmed at the time of the study, all of the registered MDR-TB patients in the region for the study period (2015-2020) were included in the analysis. This approach implied the sample was more likely to be representative of the population.

Comparison with existing literature

The overall treatment success rate achieved in this study is lower than the 75–90% target recommended by WHO[4] and values reported from Northwest-Ethiopia (80%)[28] and Taiwan (82.8%),[29] but higher compared with similar other studies, including 59% reported in a meta-analysis[30] and 53.4% (44.55 cured & 8.9% treatment complete) found in a multi-centric observational cohort analysis.[31] Also, the 54.1% cure rate found in this study is lower compared with 62.7% reported in Tanzania.[32] These observed differences could, however, be a result of differences in sample size, study setting and study period.

Consistent with the global epidemiology of male predominance in TB cases,[33] the majority of the patients in the current study were male (69.8%). However, compared with their male counterparts, more females had a higher treatment success rate (81.1%). The plausible reason for this observation could be attributed to women being more likely than men to adhere to treatment regimens, thus resulting in better health outcomes.[34]

We observed that as the age of the patients increased, the likelihood of having successful MDR-TB treatment outcome decreased (AOR = 0.53, 95% CI: 0.19-2.11). This observation concurs with the literature that older age is a risk factor for unsuccessful MDR-TB treatment outcome.[35,36] Generally, owing to factors such as physical deterioration, co-morbidities with complicated medication schedules, malnutrition and compromised immunity, older age patients respond poorly to anti-TB treatment.[37]

Individual's level of education constitutes a unique dimension of social status and a key determining factor of health-seeking behavior.[38] Higher educational levels are noted to be

associated with desirable treatment outcomes of TB.[39] This assertion has been confirmed in the present study where we observed that the likelihood of having a successful MDR-TB treatment outcome was higher (AOR = 1.12, 95% CI: 0.65-1.90) among patients with higher levels of education. Higher educational attainment creates desirable health outcomes because it reduces ignorance and increases knowledge, regarding medication management and consequences.[39]

Earlier studies have revealed that MDR-TB treatment failure and death are associated with low BMI.[19,32,40] Our study generally supports this finding as we found that patients who started MDR-TB treatment at a BMI below 18.5kg/m^2 had decreased chances of a favorable outcome. Although baseline body weight was not significantly associated with MDR-TB treatment outcome in this study, it was close to significance (p = 0.068). Underweight has been shown to be an independent predictor of poor outcome for patients treated for MDR-TB.[41]

Co-morbidity and HIV status were not significantly associated with MDR-TB treatment outcome in this study. Nonetheless, it is acknowledged that conditions such as diabetes, hypertension and HIV positive status place patients at greater risk of poor treatment outcome.[42] For instance, Ndwandwe et al. reported that patients co-infected with HIV were twice as likely to interrupt TB treatment and, thus, had poor outcomes.[42]

The current study demonstrated that most of the newly diagnosed patients had higher successful treatment rates (86%) and that patients with previous history of TB were less likely (AOR=0.47, 95% CI: 0.10-0.75) to have successful MDR-TB treatment outcome. This finding is consistent with the literature that re-treated patients are at higher risks of poor outcomes than newly diagnosed patients.[23,43]

Implications for policy and practice

The successful treatment outcome reported in this study demonstrates the success and promising performance of MDR-TB control which has been achieved through increasing awareness of TB over time and stability of service provision by treatment facilities. In addition, the result is an indication of the effectiveness of the various strategies that have been adopted to promote MDR-TB treatment in the region. These include: regular visits of patients by health professionals, assigning treatment supports from patient's family to assist with directly observed therapy, and

supporting patients with food and money. There is therefore the need to sustain and improve these strategies to promote more efficient and effective MDR-TB treatment in the region and the country as a whole to catapult the global target of ending the TB epidemic by 2030 through high-quality disease management.

The rate of successful treatment outcome of MDR-TB in the region could be improved further by paying attention to the risk factors of poor outcomes identified in this study. While some of the factors are not modifiable, especially in the short-term, policy makers and clinicians could influence the potentially modifiable ones to improve the management of MDR-TB cases in the region. For instance, nutritional counseling to increase energy intake and provision of nutritional supplements should be considered in patients having a baseline BMI below 18.5kg/m^2 and those with low body weight. Also, to prevent situations of treated people being diagnosed again with TB, there is the need to intensify health education, as well as addressing issues of relapse, treatment failure and loss to follow-ups during first-line treatment. The use of mobile health (mHealth) to remind TB patients about their treatment and to ensure follow-up could also help in reducing the number of patient stopping treatment prematurely. In the long-term, formal education should be encouraged to improve the educational levels of the citizenry so they could read well to appreciate the risk factors associated with MDR-TB.

Conclusions

MDR-TB continues to pose a great threat to the elimination of TB due to the increasing incidence and mortality rate recorded each year worldwide. The main objective of this study was to determine treatment outcomes of MDR-TB and associated factors among TB patients in the Ashanti Region, Ghana. The findings have demonstrated that favorable treatment outcomes for MDR-TB patients could be achieved in a resource-limited country. Although the recommended WHO target was not met, the current result (71.7% treatment success rate) is still commendable considering all the challenges associated with TB treatment in Ghana. The study has provided useful information that could inform policy decisions on strategies to improve MDR-TB management in the Ashanti Region and the country as a whole. Although several studies have assessed treatment outcomes of drug-susceptible TB in Ghana, very little has been done in the

aspect of MDR-TB. We, therefore, recommend further studies in this area to bridge the dearth of information on MDR-TB treatment outcome and its associated factors in the country.

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Contributors
All authors contributed to conceptualizing the study. Literature such for background information was done by VP and EK. VP, EK, POA and MAB wrote the first draft of the paper. CK, AF, SEA, PAB and SKA provided critical review of the manuscript. All the authors read and approved the final version of the paper.

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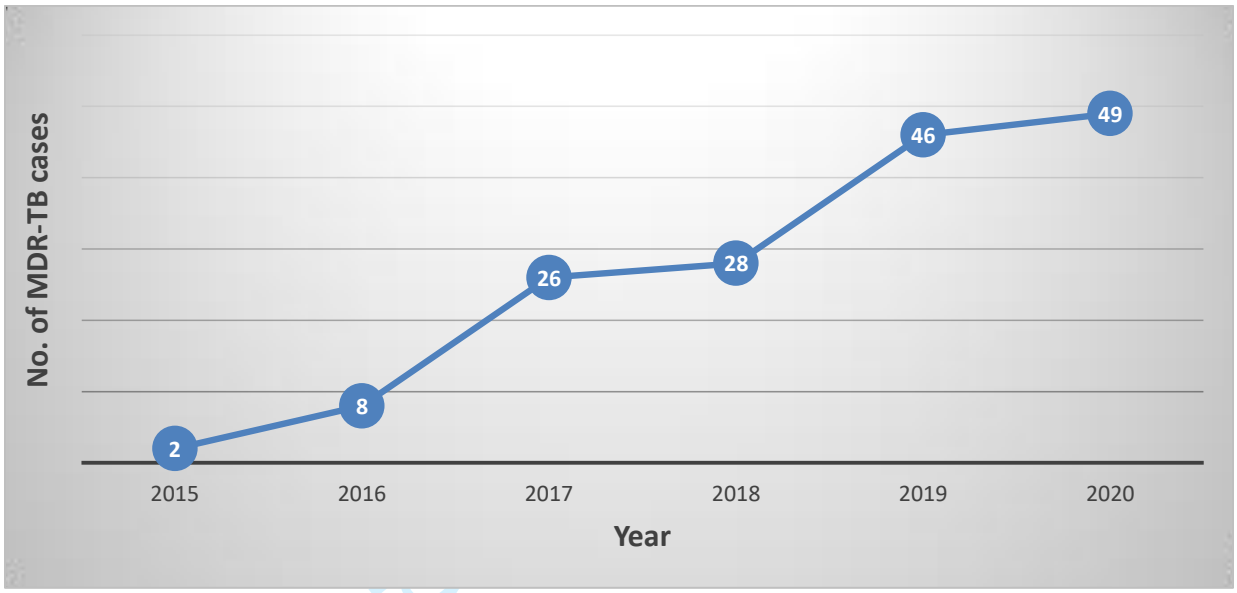

Figure 1: Trend in MDR-TB patients placed on treatment from 2015 to 2020 in Ashanti Region, Ghana

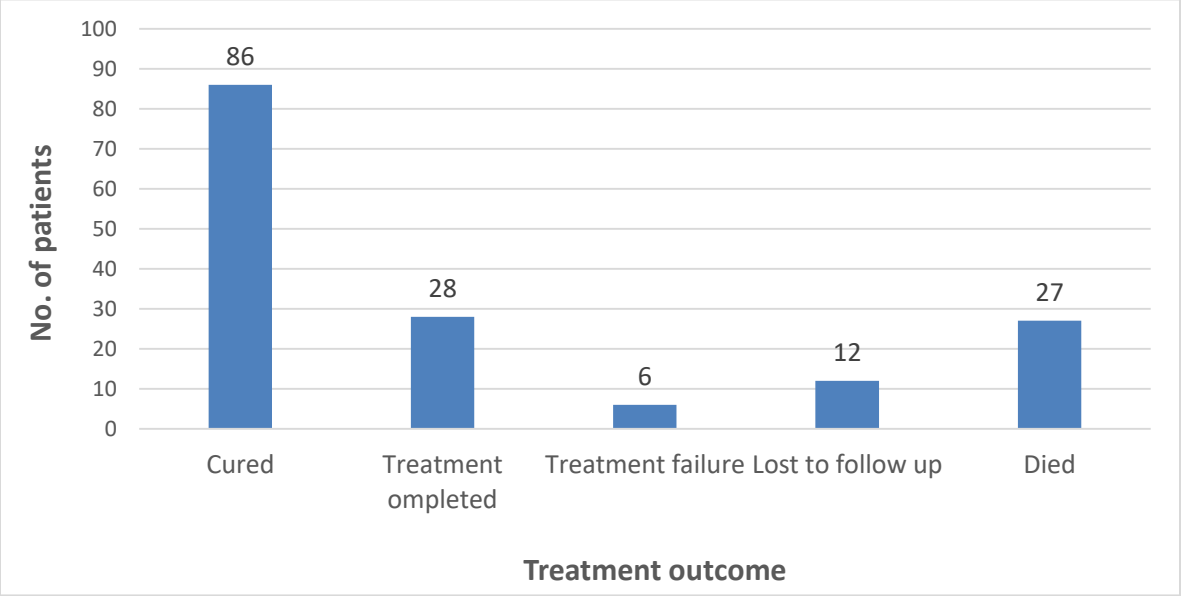

Figure 2: Treatment outcomes of the MDR-TB patients (N = 129)

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Treatment outcomes and associated factors among patients with multidrug-resistant tuberculosis in Ashanti Region, Ghana: a retrospective, cross-sectional study

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Treatment outcomes and associated factors among patients with multidrug-resistant tuberculosis in Ashanti Region, Ghana: a retrospective, cross-sectional study

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Abstract

Objective: Although several studies have assessed treatment outcomes of drug-susceptible TB in Ghana, very little has been done in the area of multidrug-resistant tuberculosis (MDR-TB). The aim of this study was to determine treatment outcomes and associated factors among patients treated for MDR-TB in the Ashanti Region, Ghana.

Design: A retrospective, cross-sectional analysis.

Setting: The study was conducted in the Ashanti Region, the second most populous region in Ghana. The Regional MDR-TB register, which contains information on all patients with MDR-TB patients being treated at the various TB centers in the region, was analyzed between February and May, 2021.

Participants: The participants consisted of all registered patients with MDR-TB who were placed on treatment between January 1, 2015, and December 31, 2020. Patients were included in the analysis if their treatment outcome had been assigned. Patients with no record of treatment outcome were excluded from the study.

Outcome measures: The main outcome variable for the study was MDR-TB treatment outcome, standardized as "cured", "treatment completed", "treatment failure", "died" and lost to follow-up". A logistic regression model was fitted for factors associated with the outcome measure.

Results: Out of 159 patients included in the analysis, 86 (54.1%) were declared cured, 28 (17.6%) completed their treatment successfully, six (3.8%) were declared treatment failure, 12 (7.5%) were lost to follow up, and 27 (17.0%) died. The overall treatment success rate was 71.7%. Patients who were female (adjusted odds ratio [AOR] 1.27, 95% CI 1.18–1.39, p-value 0.023), younger (AOR 0.53, 95% CI = 0.19–2.11, p-value 0.012), had a higher level of education (AOR 1.12, 95% CI 0.65–1.90, p-value 0.034), had a baseline BMI of 18.5kg/m^2or above (AOR 1.57, 95% CI 1.23–2.47, p-value 0.011), and those who did not have a previous history of TB (AOR 0.47, 95% CI 0.10–0.75, p-value 0.028) were more likely to have successful MDR-TB treatment outcomes.

Conclusions: Favorable treatment outcomes for patients with MDR-TB can be achieved in a resource-limited country. Although the recommended WHO target of ≥75% was not met, the current result (71.7% treatment success rate) is still commendable considering all the challenges associated with TB treatment in Ghana.

Keywords: Tuberculosis, multi drug-resistant TB, treatment outcomes, Ashanti Region, Ghana

Strengths and limitations of this study

- This study is among few to provide an important assessment of MDR-TB treatment outcome and its associated factors in Ghana.
- The findings provide important baseline information for further broader studies in the country.
- There may be underestimation and/or overestimation of some of the findings as the secondary data used were not recorded systematically for research purposes.
- The nature of the secondary data analyzed limited the inclusion of other potential factors that could be associated with successful MDR-TB treatment outcome.
- Due to the small sample drawn from a specific geographical location in Ghana, the findings might have limited generalizability.

Introduction

Tuberculosis (TB) is one of the top 10 causes of morbidity and mortality worldwide, and the leading cause from a single infectious agent [1]. The 2020 World Health Organization (WHO) Global Tuberculosis Report indicates that in 2019, 10 million people were infected with TB globally, out of which 1.4 million resulted in deaths. Geographically, most cases occurred in the WHO regions of South-East Asia (44%), Africa (24%) and the Western Pacific (18%), with smaller shares in the Eastern Mediterranean (8%), the Americas (3%) and Europe (3%) [2].

Although the global incidence of TB is falling at about 2% per year [1], the emergence of multidrug-resistant TB (MDR-TB) over the past few decades poses a public health crisis and a health security threat [2,3]. Globally, 206,030 MDR-TB cases were recorded in 2019, an increase of 10% from 186,883 in 2018 [2]. MDR-TB is diagnosed when a patient's sputum examination reveals resistance to at least isoniazid (INH) and rifampicin (RMP) [4]. Estimates from WHO indicate that over half a million new cases of rifampicin-resistant (RR) and multi-drug resistant (MDR) TB are recorded annually [1]. Four main factors are known to account for drug resistance: inappropriate use of anti-TB medications, incorrect prescription of drugs by care providers, poor quality drugs, and patient stopping treatment prematurely [4].

MDR-TB is curable and treatment requires the administration of second-line anti-TB drugs for a minimum of nine months and a maximum of 20 months [3]. However, compared to drug-susceptible TB cases, treatment outcomes of MDR-TB cases are poorer. Globally, only 57% of MDR-TB patients were successfully treated in 2019 [2]. The management of MDR-TB is complex as it puts a greater strain on countries and national health systems [2,5,6]. For example, culture-based methods can take weeks to months. They are also expensive and require sophisticated and well-established laboratory infrastructure, qualified and competent staff and strict quality and infection control systems [6].

The global health aim of eliminating TB by 2035 will only be possible if drug-resistant strains of Mycobacterium Tuberculosis are effectively managed by countries [6]. Ghana is not ranked among the world's high-burden TB countries. Incidence of TB has fallen gradually from 214 cases per 100,000 people in 2001 to 143 cases per 100,000 people in 2020 [7]. Nonetheless, studies have reported the emergence of MDR-TB in the country [7-12]. For instance, Davies-Teye et al.

reported a cumulative incidence of MDR-TB in the Greater Accra Region of 1.4/100,000 population, with a case fatality rate of 14% [8]. In a recent nationwide drug resistance survey to investigate the level and pattern of resistance to first-line TB drugs among newly and previously treated sputum smear-positive TB cases, Sylverken and colleagues found that resistance to isoniazid and rifampicin, the two most effective anti-TB drugs, was 3.2% [7].

High-quality disease management is one of the key strategies in improving treatment outcomes of TB [13]. In Ghana, both susceptible TB and MDR-TB are managed under directly observed treatment short course (DOTS) program, which has demonstrated feasible and effective treatment in other resource-limited countries [14]. Gaining insight into treatment outcome of MDR-TB and its associated factors could assist national TB control programs in improving the treatment success rate of MDR-TB patients. Nonetheless, literature on factors influencing treatment outcomes of MDR-TB in Ghana is limited. Moreover, studies conducted in other countries have revealed a wide variation in predictors of MDR-TB treatment outcomes. Some of the factors that have been found to be associated with successful or unsuccessful MDR-TB treatment outcome include patient age [15], gender [16], pretreatment body mass index (BMI) [17] and body weight, drug adherence [18], positive smear at the start of treatment, previous history of TB [19], smoking [16], alcohol consumption [20], and comorbidities or underlining health conditions such as HIV [21] and diabetes [22]. However, other studies [15,21,23] have reported findings contrary to the above-mentioned factors. For instance, Elliott and colleagues found no association between MDR-TB treatment outcome and positive smear at the start of treatment and HIV co-infection [18]. Also, Khan et al. reported that MDR-TB treatment outcome was not significantly associated with gender, smoking and comorbidity status [15].

Therefore, this study was conducted to determine treatment outcomes and associated factors among TB patients treated for MDR-TB in the Ashanti Region, Ghana. Understanding the factors that could determine successful treatment outcome would be useful in developing strategies and making informed decisions about MDR-TB management in the region. This would help promote efficient and effective MDR-TB treatment in the country.

Methods

Study setting

The Ashanti Region is the second most populous region in Ghana, with a population of 5,432,485 [24]. It has a population density of 192.4 per sq. km. The region has 43 districts and 132 sub-districts. There are five hundred and twenty-seven health facilities in the region. The Ghana Health Service (GHS) operates about 33% of all health facilities in the region. Kumasi, the regional capital, has the highest number of health facilities (29%) with Ejura-Sekyedumase having the least (2%) [24].

Study design, population and sample

A retrospective, cross-sectional analysis of the Ashanti Regional MDR-TB register was conducted between February and May, 2021. The Regional MDR-TB register is a standard register containing information on all MDR-TB patients being treated at the various DOT centers in the region. The study population consisted of all registered patients with MDR-TB who were placed on treatment between January 1, 2015 (when MDR-TB treatment started in the region) and December 31, 2020. Patients were included in the analysis if their treatment outcome had been assigned. Patients with no record of treatment outcome were excluded from the study.

Drug susceptibility testing and treatment protocol

Drug resistant TB suspects are initially evaluated for both Mycobacterium tuberculosis (MTB) and rifampicin (RIF) resistance by direct sputum smear microscopy using Ziehl-Neelsen strain and Xpert MTB/RIF (Cepheid, CA, US). Sputum samples of patients with positive results are sent to the National TB reference laboratory located at the Kumasi Center for Collaborative Research in Tropical Medicine (KCCR) for sputum culture and phenotypic drug susceptibility test (DST) for RIF, ionized (INH), streptomycin (STR), ethambutol (EMB), and pyrazinamide (PZA).

All patients with positive diagnosis of MDR-TB are placed on a clinic-based model of treatment and care [25] at the various DOT centers in the Ashanti Region. This is a form of ambulatory care, where patients travel to the treatment centers daily for directly observed therapy. Although the current treatment of patients with MDR-TB in the region is based on both the shorter and the loner treatment regimens, patients considered in this study were treated with the standardized, longer treatment regimen consisting of an 8-month initial or intensive phase with a combination of capreomycin/kanamycin, levofloxacin, prothionamide, pyrazinamide, cycloserine, and vitamin B

denk/pyridoxine; and a-12 month continuation phase with a combination of levofloxacin, pyrazinamide, prothionamide, and vitamin B denk.

Study variables

The main outcome variable for the study was MDR-TB treatment outcome. This was standardized, as recommended by WHO, as "cured", "treatment completed", "treatment failure", "died" and "lost to follow-up". [25] According to the WHO guidelines for the management of drug resistance TB (DR-TB), a treatment outcome is classified cured when the treatment is completed with no evidence of failure and three or more consecutive sputum cultures taken at least 30 days apart are negative after the intensive phase. A patient is declared treatment completed when he/she completes his/her treatment with no evidence of failure, but there is no record indicating that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase. Treatment failure is when treatment is terminated due to poor clinical or radiological response or adverse drug reaction. Treatment outcome "died" is when a patient dies for any reason during the course of treatment. Finally, a patient whose treatment is interrupted for two consecutive months is declared lost to follow-up [25,26].

The explanatory variables included were: age, gender, educational level, marital status, treatment regimen (new vs. retreatment), baseline BMI, baseline weight, HIV status, cavitation on baseline chest X-ray, and having co-morbidities other than HIV. These variables were selected based on previous studies (as indicated in the introductory section of the paper) and the availability of data.

Data collection

A designed data extraction tool, reflecting the various variables under study, was used to gather data from the Ashanti Regional MDR-TB register. Data extraction was done by two members of the research team, and assisted by four trained data collectors, comprising two public health nurses and two health information officers. Missing information in the register was completed with data from the patients' clinical records. All of the extracted information was audited and verified to check for completeness and quality.

Statistical analysis

Data collected was coded, entered and analyzed using Statistical Package for Social Sciences (SPSS) software version 20 (IBM© Corporation, Armonk, NY, USA). Categorical data was presented as frequencies and percentages, while continuous data was presented in the form of mean and standard deviation. The main outcome variable, MDR-TB treatment outcome, was categorized into successful (cured and completed) and unsuccessful (treatment failure, died and lost to follow-up) treatment outcomes, and scored as follows: successful treatment = 1, unsuccessful treatment = 0. The continuous variables were also dichotomized as follows: age into < 50 and ≥ 50 years, BMI into < 18.5 and ≥ 18.5 kg/m^2, and body weight into < 50 and ≥ 50 kg.

Bivariate analysis was performed for all of the independent variables with the outcome variable. Using variables with p-value < 0.2, based on the bivariate analysis, a multiple logistic regression analysis was carried out to determine the independent predictors of successful MDR-TB treatment outcome. Variables with significant associations with successful MDR-TB treatment outcome were identified based on the odds ratio (OR) with a 95% confidence interval (CS) and p-values ≤ 0.05. We evaluated the predictive accuracy of the model using Receiver Operating Characteristic (ROC) curve analysis. The area under the ROC curve was 0.93, indicating the model classified much of the data correctly [27]. Also, by computing the deviance R^2, we observed that the model explained 89.17% of the total deviance in the outcome variable. This indicates further that the model provides a good fit to the data.

Ethical considerations

The study was approved by the Ethics Review Committee of the Ghana Health Service Research and Development Division, Accra (Protocol No. GHS-ERC-052/04/21). In addition, approval was obtained from the Ashanti Regional Health Directorate (ARHD) to use data from the Regional MDR-TB treatment register for the study. Data retrieved was not linked to individual patients.

Patient and public involvement

There was no patient or public involvement in the study.

Results

In total, records of 159 patients with MDR-TB were reviewed. Table 1 summarizes the demographic characteristics of the study participants. The mean age of the patients was 43.69±14.86 years. The majority were male (111, 69.8%), between the age group of 40 and 49 years (46, 28.9%), having educational qualification below high school (121, 76.1%), and not married (8, 53.4%). There has been a steady increase in the number of patients placed on treatment in the region since 2015 (Figure 1).

Table 1. Socio-demographic characteristics of the patients with MDR-TB (N=129)

Characteristics	Frequency	Percentage (%)
Gender:		
Male	111	69.8
Female	48	30.2
Age Group:		
< 20	5	3.1
20-29	28	17.6
30-39	26	16.4
40-49	46	28.9
50-59	26	16.4
≥ 60	28	17.6
Education:		
Below high school	121	76.1
High school and above	38	23.9
Marital Status:		
Married	74	46.6
Not married	85	53.4

MDR TB=Multidrug resistant tuberculosis.

Clinical characteristics

Table 2 summarizes the clinical characteristics of the patients with MDR-TB included in the study. The majority (69%) of the patients had a baseline body weight ≥ 50kg. Also, more than half

(59.1%) had a baseline BMI ≥ 18.5 kg/m^2. About 16% had a history of comorbidities such as diabetes and hypertension, and 90% had no history of HIV co-infection. Regarding treatment regimen, 33.6% were new patients, whereas 66.4% had a previous history of TB treatment.

Table 2. Clinical characteristics of the patients with MDR-TB (N=159)

Variables	Frequency	Percentage (%)
Baseline weight (kg)		
< 50	49	31.0
≥ 50	110	69.0
Baseline BMI (kg/m^2)		
< 18.5	65	40.9
≥ 18.5	94	59.1
Co-morbidity		
Yes	26	16.3
No	133	83.7
HIV Status		
Negative	143	90.0
Positive	16	10.0
Treatment regimen		
New Patient	53	33.6
Retreatment	106	66.4
Cavitation on baseline chest X-ray		
Yes	110	69.2
No	49	30.8

BMI=Body Mass Index, MDR TB=Multidrug resistant tuberculosis.

Treatment outcomes

Of the 159 patients included in the analysis, 86 (54.1%) were declared cured, 28 (17.6%) completed their treatment successfully, six (3.8%) were declared treatment failure, 12 (7.5%) were lost to follow up, while 27 (17.0%) died (Figure 2). The overall treatment success rate for the period under study (2015-2020) was 71.7%.

Factors associated with MDR-TB treatment outcome

In the bivariate analysis, the covariates with p-values less than 0.2 level of significance for successful MDR-TB treatment outcome were gender, age, educational level, baseline BMI, baseline weight, comorbidity status, HIV status and treatment regimen (Table 3).

Table 2. Bivariate analysis of factors associated with successful treatment outcome among patients treated for MDR-TB in Ashanti Region, 2015-2020

Characteristics	Frequency (N=159)	Overall Treatment Outcome		p-value
		Successful N (%)	Unsuccessful N (%)	
Gender				
Male	111	78 (70.3)	33 (29.7)	
Female	48	39 (81.1)	9 (18.9)	0.021
Age				
< 50	106	76 (71.7)	30 (28.3)	
≥50	53	35 (66.0)	18 (34.0)	0.001
Education				
Below high school	121	95 (78.6)	26 (21.4)	
High school & above	38	26 (68.4)	12 (31.6)	0.033
Marital Status				
Married	74	48 (65.0)	26 (35.0)	

Not Married	85	68 (80.0)	17 (20.0)	0.655
Baseline weight (kg)				
< 50	49	34 (69.4)	15 (30.6)	
≥50	110	75 (68.2)	35 (31.8)	0.032
Baseline BMI (kg/ m^2)				
< 18.5	65	50 (76.9)	15 (23.1)	
≥ 18.5	94	63 (67.1)	31 (32.9)	0.043
Co-morbidity				
Yes	26	14 (53.8)	12 (46.2)	
No	133	100 (75.2)	33 (24.8)	0.108
HIV status				
Negative	143	104 (72.7)	39 (27.3)	
Positive	16	10 (62.5)	6 (37.5)	0.145
Cavitation on baseline chest X-ray				
Yes	110	77 (70.0)	33 (30.0)	
No	49	39 (79.6)	10 (20.4)	0.483
Treatment regimen				
New Patient	53	46 (86.8)	7 (13.2)	
Retreatment	106	67 (63.2)	39 (36.8)	0.023

BMI= body mass index, HIV=human immunodeficiency virus, MDR-TB=multidrug resistant tuberculosis.

Results of the binary logistic regression analysis showed that the odds of having a successful MDR-TB treatment outcome were independently associated with gender, age, level of education, baseline BMI and treatment regimen (Table 4). Adjusting for the relationships of the other independent variables, we observed that the likelihood of having a successful MDR-TB treatment outcome among female patients was 1.3 times (AOR = 1.27, 95% CI: 1.18-1.39) higher compared with male patients. Also, patients who were 50 years and above were less likely (AOR = 0.53, 95% CI: 0.19-2.11), compared with those below 50 years, to have a successful MDR-TB treatment outcome. Furthermore, patients whose educational level was high school or above were 1.1 times

(AOR = 1.12, 95% CI: 0.65-1.90) more likely, compared with those below high school, to have a successful MDR-TB treatment outcome. Moreover, patients with baseline BMI ≥ 18.5 kg/m^2 had higher odds (AOR = 1.57, 95% CI: 0.13-2.17) of having a successful MDR-TB treatment outcome, compared with those having BMI <18.5 kg/m^2. Finally, compared with new patients, patients with previous history of TB were less likely (AOR=0.47, 95% CI: 0.10-0.75) to have a successful MDR-TB treatment outcome.

Table 4. Independent predictors of successful treatment outcome among patients treated for MDR-TB in Ashanti Region, 2015-2020 (N=159)

Variable	AOR	95% CI	p-value
Gender			
Male	Ref.		
Female	1.27	1.18 – 1.39	0.023
Age			
< 50	Ref.		
≥ 50	0.53	0.19 – 2.11	0.012
Education			
Below high school	Ref.		
High school & above	1.12	0.65 – 1.90	0.034
Baseline weight (kg)			
< 50	Ref.		
≥50	1.22	0.94 – 2.84	0.068
Baseline BMI (kg/m^2)			
< 18.5	Ref.		
≥ 18.5	1.57	1.23 – 2.47	0.011
Comorbidity			
Yes	Ref.		
No	2.42	2.33 – 2.51	0.212
HIV status			
Negative	Ref.		
Positive	0.98	0.63 – 0.96	0.951
Treatment regimen			
New Patient	Ref.		
Retreatment	0.47	0.10 – 0.75	0.028

CI=confidence interval, AOR=adjusted odds ratio.

Discussion

Summary of findings

Our study showed that more than two-thirds (N=114, 71.7%) of the patients had successful MDR-TB treatment outcome, while 28.3% had unfavorable treatment outcome. Cure rate was 54.1%, whereas mortality rate was 17.0%. A logistic regression model was fitted for eight variables, out of which five were independently associated with successful MDR-TB treatment outcome. Patients who were female, younger (less than 50 years), having higher level of education, having a baseline BMI of 18.5kg/$m^2$and above, and not having a previous history of TB were more likely to have successful MDR-TB treatment outcome. Marital status, baseline weight, HIV status, and having co-morbidity other than HIV had no significant association with MDR-TB treatment outcome.

Strengths and limitations

To the best of our knowledge, the present study, if not the first, is among the few to provide an important assessment of MDR-TB treatment outcome and its associated factors in Ghana. The findings provide baseline information for further broader studies in the country. Nonetheless, the study is not without limitations. First, being a retrospective analysis, findings were based on secondary data obtained from patients' medical records and registers. Since these records are not intended for research, they are not recorded systematically. This may have led to under and/or overestimation of some of our findings. Second, the nature of the secondary data we used permitted us to review only records available in the regional MDR-TB register and the patients' medical records. This did not allow us to include in the analysis other potential factors, such as smoking history, alcohol use, drug resistance status, time to culture conversion, income level and place of residence that could be associated with successful MDR-TB treatment outcome. Third, and most importantly, due to the small sample size drawn from a specific geographical location in Ghana, the study findings might have limited generalizability. That notwithstanding, the sample size used satisfies the general rule of thumb for the number of participants required to examine associations [28]. The rule has been that for regression equations using six or more predictors, a minimum of 10 participants per predictor is required.[28] Going by this, and with 10 predictors used in the study, a minimum of 100 participants would have been sufficient to examine the associations. Also, compared with normal TB cases, MDR-TB patient population in the country is not very large. For instance, Svlverken and colleagues' recent nationwide survey found only 19 (3.2%) out of 927 TB

patients to be multidrug-resistant [7]. Thus, a sample of 159 is adequate to make a generalization about the MDR-TB population, particularly in the study area. Furthermore, except for patients whose treatment outcomes had not been confirmed at the time of the study, all of the registered patients with MDR-TB in the region for the study period (2015-2020) were included in the analysis. This approach implied the sample was more likely to be representative of the population.

Comparison with existing literature

The overall treatment success rate achieved in this study is lower than the 75–90% target recommended by WHO [4] and values reported from Northwest-Ethiopia (80%) [29] and Taiwan (82.8%) [30], but higher compared with similar other studies, including 59% reported in a meta-analysis [31] and 53.4% (44.55 cured & 8.9% treatment complete) found in a multi-centric observational cohort analysis [32]. Also, the 54.1% cure rate found in this study is lower compared with 62.7% reported in Tanzania [33], and 69.4%, [34] 76.9% [35] and 83.7% [36] all reported in Pakistan. These observed differences could, however, be a result of differences in sample size, study setting and study period.

Consistent with the global epidemiology of male predominance in TB cases [37], the majority of the patients in the current study were male (69.8%). However, compared with their male counterparts, more females had a higher treatment success rate (81.1%). The plausible reason for this observation could be attributed to women being more likely than men to adhere to treatment regimens, thus resulting in better health outcomes [38].

We observed that as the age of the patients increased, the likelihood of having successful MDR-TB treatment outcome decreased (AOR = 0.53, 95% CI: 0.19-2.11). This observation concurs with the literature that older age is a risk factor for unsuccessful MDR-TB treatment outcome [39,40]. Generally, owing to factors such as physical deterioration, co-morbidities with complicated medication schedules, malnutrition and compromised immunity, older age patients respond poorly to anti-TB treatment [41].

Individual's level of education constitutes a unique dimension of social status and a key determining factor of health-seeking behavior [42]. Higher educational levels are noted to be associated with desirable treatment outcomes of TB [43]. This assertion has been confirmed in the present study where we observed that the likelihood of having a successful MDR-TB treatment

outcome was higher (AOR = 1.12, 95% CI: 0.65-1.90) among patients with higher levels of education. Higher educational attainment creates desirable health outcomes because it reduces ignorance and increases knowledge, regarding medication management and consequences [43].

Earlier studies have revealed that MDR-TB treatment failure and death are associated with low BMI [19,33,44]. Our study generally supports this finding as we found that patients who started MDR-TB treatment at a BMI below 18.5kg/m^2 had decreased chances of a favorable outcome. Although baseline body weight was not significantly associated with MDR-TB treatment outcome in this study, it was close to significance (p = 0.068). Underweight has been shown to be an independent predictor of poor outcome for patients treated for MDR-TB [45].

Co-morbidity and HIV status were not significantly associated with MDR-TB treatment outcome in this study. Nonetheless, it is acknowledged that conditions such as diabetes, hypertension and HIV positive status place patients at greater risk of poor treatment outcome [46]. For instance, Ndwandwe et al. reported that patients co-infected with HIV were twice as likely to interrupt TB treatment and, thus, had poor outcomes [46].

The current study demonstrated that most of the newly diagnosed patients had higher successful treatment rates (86%) and that patients with previous history of TB were less likely (AOR=0.47, 95% CI: 0.10-0.75) to have successful MDR-TB treatment outcome. This finding is consistent with the literature that re-treated patients are at higher risks of poor outcomes than newly diagnosed patients [23,47].

Implications for policy and practice

The successful treatment outcome reported in this study demonstrates the success and promising performance of MDR-TB control which has been achieved through increasing awareness of TB over time and stability of service provision by treatment facilities. In addition, the result is an indication of the effectiveness of the various strategies that have been adopted to promote MDR-TB treatment in the region. These include: regular visits of patients by health professionals, assigning treatment supports from patient's family to assist with directly observed therapy, and supporting patients with food and money. There is therefore the need to sustain and improve these strategies to promote more efficient and effective MDR-TB treatment in the region and the country

as a whole to catapult the global target of ending the TB epidemic by 2030 through high-quality disease management.

The rate of successful treatment outcome of MDR-TB in the region could be improved further by paying attention to the risk factors of poor outcomes identified in this study. While some of the factors are not modifiable, especially in the short-term, policy makers and clinicians could influence the potentially modifiable ones to improve the management of MDR-TB cases in the region. For instance, nutritional counseling to increase energy intake and provision of nutritional supplements should be considered in patients having a baseline BMI below 18.5kg/m^2 and those with low body weight. Also, to prevent situations of treated people being diagnosed again with TB, there is the need to intensify health education, as well as addressing issues of relapse, treatment failure and loss to follow-ups during first-line treatment. The use of mobile health (mHealth) to remind TB patients about their treatment and to ensure follow-up could also help in reducing the number of patients stopping treatment prematurely. In the long-term, formal education should be encouraged to improve the educational levels of the citizenry so they could read well to appreciate the risk factors associated with MDR-TB.

Conclusions

MDR-TB continues to pose a great threat to the elimination of TB due to the increasing incidence and mortality rate recorded each year worldwide. The main objective of this study was to determine treatment outcomes of MDR-TB and associated factors among patients with TB in the Ashanti Region, Ghana. The findings have demonstrated that favorable treatment outcomes for patients with MDR-TB could be achieved in a resource-limited country. Although the recommended WHO target was not met, the current result (71.7% treatment success rate) is still commendable considering all the challenges associated with TB treatment in Ghana. The study has provided useful information that could inform policy decisions on strategies to improve MDR-TB management in the Ashanti Region and the country as a whole. Although several studies have assessed treatment outcomes of drug-susceptible TB in Ghana, very little has been done in the aspect of MDR-TB. We, therefore, recommend further studies in this area to bridge the dearth of information on MDR-TB treatment outcome and its associated factors in the country.

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Contributors

All authors contributed to conceptualizing the study. Literature such for background information was done by VP and EK. VP, EK, POA and MAB wrote the first draft of the paper. CK, AF, SEA, PAB and SKA provided critical review of the manuscript. All the authors read and approved the final version of the paper.

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Competing interests

None declared.

Data availability statement

No additional data are available.

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FIGURE TITLES

Figure 1. Trend in patients with MDR-TB placed on treatment from 2015 to 2020 in Ashanti Region, Ghana

Figure 2. Treatment outcomes of the patients with MDR-TB (N=159)

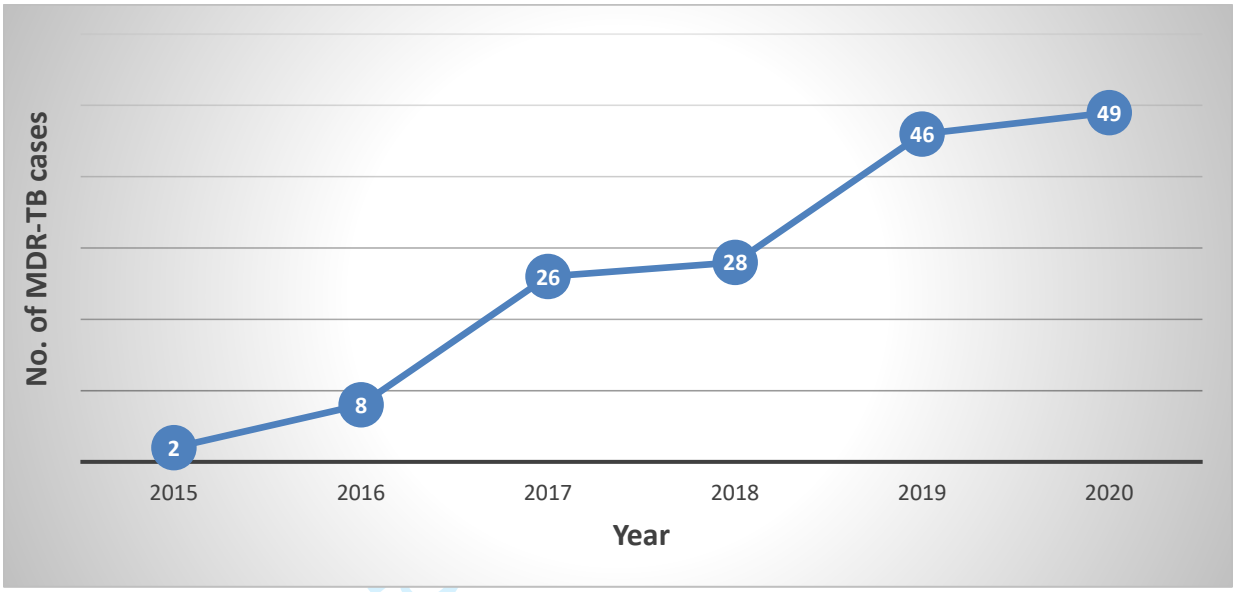

Figure 1: Trend in patients with MDR-TB placed on treatment from 2015 to 2020 in Ashanti Region, Ghana

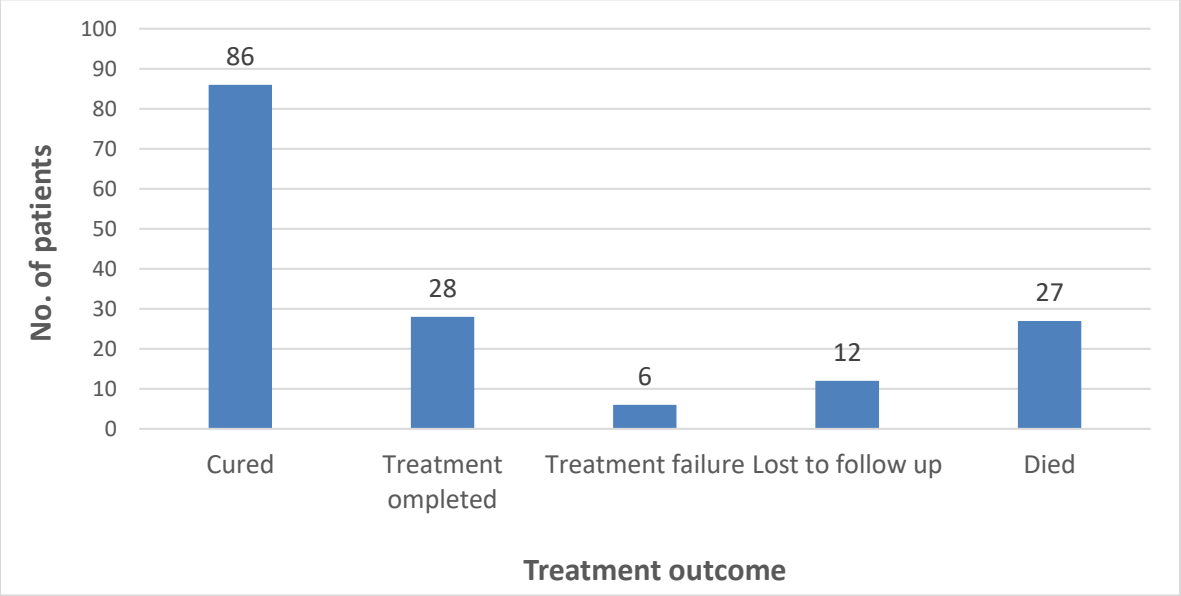

Figure 2: Treatment outcomes of the patients with MDR-TB (N = 159)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4	
Objectives	3	State specific objectives, including any prespecified hypotheses	4	
Methods				
Study design	4	Present key elements of study design early in the paper	5	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6	
Bias	9	Describe any efforts to address potential sources of bias	7	
Study size	10	Explain how the study size was arrived at	5	

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	6
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-13
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.