BMJ Open Treatment outcomes and associated factors among patients with multidrugresistant tuberculosis in Ashanti Region, Ghana: a retrospective, crosssectional study

Victoria Panford,¹ Emmanuel Kumah ^(a),² Collins Kokuro,³ Prince Owusu Adoma,² Michael Afari Baidoo,² Adam Fusheini,⁴ Samuel Egyakwa Ankomah,⁴ Samuel Kofi Agyei,⁵ Peter Agyei-Baffour⁶

ABSTRACT

To cite: Panford V, Kumah E, Kokuro C, *et al.* Treatment outcomes and associated factors among patients with multidrug-resistant tuberculosis in Ashanti Region, Ghana: a retrospective, crosssectional study. *BMJ Open* 2022;**12**:e062857. doi:10.1136/ bmjopen-2022-062857

Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi. org/10.1136/bmjopen-2022-062857).

Received 14 March 2022 Accepted 21 June 2022

Check for updates

© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to

Dr Emmanuel Kumah; ababiohemmanuel@gmail.com **Objective** Although several studies have assessed treatment outcomes of drug-susceptible tuberculosis (TB) in Ghana, very little has been done in the area of multidrug-resistant TB (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 being treated at the various TB centres in the region, was analysed between February and May 2021.

Participants The participants consisted of all registered patients with MDR-TB who were placed on treatment between 1 January 2015 and 31 December 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, standardised 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, 6 (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 OR (AOR)=1.27, 95% CI: 1.18 to 1.39, p=0.023), younger (AOR=0.53, 95% CI: 0.19 to 2.11, p=0.012), had a higher level of education (AOR=1.12, 95% CI: 0.65 to 1.90, p=0.034), had a baseline body mass index of 18.5 kg/m² or above (AOR=1.57, 95% CI: 1.23 to 2.47, p=0.011) and those who did not have a history of TB (AOR=0.47, 95% CI: 0.10 to 0.75, p=0.028) were more likely to have successful MDR-TB treatment outcomes.

Conclusions Favourable treatment outcomes for patients with MDR-TB can be achieved in a resource-limited

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study is among few to provide an important assessment of multidrug-resistant tuberculosis (MDR-TB) treatment outcome and its associated factors in Ghana.
- \Rightarrow 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 analysed 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 generalisability.

country. Although the recommended WHO target of \geq 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.

INTRODUCTION

Tuberculosis (TB) is 1 of the top 10 causes of morbidity and mortality worldwide, and the leading cause from a single infectious agent.¹ The 2020 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, 206030 MDR-TB cases were recorded in 2019, an increase of 10% from 186883 in 2018.² MDR-TB is diagnosed when a patient's sputum examination reveals resistance to at least isoniazid (INH) and rifampicin (RIF).⁴ Estimates from WHO indicate that over half a million new cases of RIF-resistant and 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 9 months and a maximum of 20 months.³ However, compared with drug-susceptible TB cases, treatment outcomes of MDR-TB cases are poorer. Globally, only 57% of patients with MDR-TB 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.²⁵⁶ 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 (MTB) 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 et al found that resistance to INH and RIF, the two most effective anti-TB drugs, was 3.2%.

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) programme, 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 programmes in improving the treatment success rate of patients with MDR-TB. 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, history of TB,¹⁹ smoking,¹⁶ alcohol consumption,²⁰ and comorbidities or underlining health conditions such as HIV²¹ and diabetes.²² However, other studies¹⁵ ²¹ ²³ have reported findings contrary to the above-mentioned factors. For instance, Elliott *et al* found no association between MDR-TB treatment outcome and positive smear at the start of treatment and HIV coinfection.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 patients with TB 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 km². The region has 43 districts and 132 subdistricts. There are 527 health facilities in the region. The Ghana Health Service 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 patients with MDR-TB being treated at the various DOT centres in the region. The study population consisted of all registered patients with MDR-TB who were placed on treatment between 1 January 2015 (when MDR-TB treatment started in the region) and 31 December 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 MTB and RIF resistance by direct sputum smear microscopy using Ziehl-Neelsen strain and Xpert MTB/RIF (Cepheid, California, USA). 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 for sputum culture and phenotypic drug susceptibility test for RIF, INH, streptomycin, ethambutol and pyrazinamide (PZA). All patients with positive diagnosis of MDR-TB are placed on a clinic-based model of treatment and care²⁵ at the various DOT centres in the Ashanti Region. This is a form of ambulatory care, where patients travel to the treatment centres 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 longer treatment regimens, patients considered in this study were treated with the standardised, longer treatment regimen consisting of an 8-month initial or intensive phase with a combination of capreomycin/kanamycin, levofloxacin, prothionamide, PZA, cycloserine and vitamin B denk/ pyridoxine; and a-12 month continuation phase with a combination of levofloxacin, PZA, prothionamide and vitamin B denk.

Study variables

The main outcome variable for the study was MDR-TB treatment outcome. This was standardised, 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, 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 2 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 comorbidities 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 were coded, entered and analysed using SPSS software V.20 (IBM Corporation). Categorical data were presented as frequencies and percentages, while continuous data were presented in the form of mean and SD. The main outcome variable, MDR-TB treatment outcome, was categorised 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 dichotomised as follows: age into <50 and \geq 50 years, BMI into <18.5 and \geq 18.5 kg/m², and body weight into <50 and \geq 50 kg.

Bivariate analysis was performed for all of the independent variables with the outcome variable. Using variables with p value of <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 OR with a 95% CI and p values of ≤ 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 \mathbb{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.

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 summarises 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).

Clinical characteristics

Table 2 summarises the clinical characteristics of the patients with MDR-TB included in the study. The majority (69%) of the patients had a baseline body weight \geq 50 kg. Also, more than half (59.1%) had a baseline BMI \geq 18.5 kg/m². About 16% had a history of comorbidities such as diabetes and hypertension, and 90% had no history of HIV coinfection. Regarding treatment regimen, 33.6% were new patients, whereas 66.4% had a history of TB treatment.

Table 1	Sociodemographic characteristics of the patients
with MD	R-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.			

Treatment outcomes

Of the 159 patients included in the analysis, 86 (54.1%) were declared cured, 28 (17.6%) completed their treatment successfully, 6 (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).

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

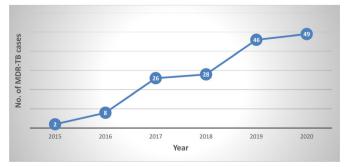


Figure 1 Trend in patients with MDR-TB placed on treatment from 2015 to 2020 in Ashanti Region, Ghana. MDR-TB, multidrug-resistant tuberculosis.

Table 2Clinical 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		
Comorbidity				
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.

(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 (adjusted OR (AOR)=1.27, 95% CI: 1.18 to 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 to 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 to 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/m² had higher odds (AOR=1.57, 95% CI: 0.13 to 2.17) of having a successful MDR-TB treatment outcome,

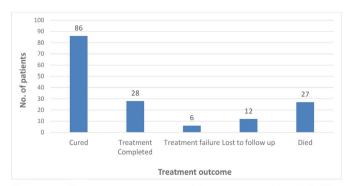


Figure 2 Treatment outcomes of the patients with MDR-TB (N=159). MDR-TB, multidrug-resistant tuberculosis.

 Table 3
 Bivariate analysis of factors associated with successful treatment outcome among patients treated for MDR-TB in

 Ashanti Region, 2015–2020
 Patients

		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
Comorbidity				
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; MDR-TB, multidrug-resistant tuberculosis.

compared with those having BMI <18.5 kg/m². Finally, compared with new patients, patients with a history of TB were less likely (AOR=0.47, 95% CI: 0.10 to 0.75) to have a successful MDR-TB treatment outcome.

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 unfavourable 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 18.5 kg/m^2 and above, and not having a history of TB were more likely to have successful MDR-TB treatment outcome. Marital status, baseline weight, HIV status and having comorbidity 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

Table 4	Independent predictors of successful treatment
outcome	among patients treated for MDR-TB in Ashanti
Region, 2	2015–2020 (N=159)

Variable	AOR	95% CI	P value
Gender			
Male	Reference		
Female	1.27	1.18 to 1.39	0.023
Age			
<50	Reference		
≥50	0.53	0.19 to 2.11	0.012
Education			
Below high school	Reference		
High school & above	1.12	0.65 to 1.90	0.034
Baseline weight (kg)			
<50	Reference		
≥50	1.22	0.94 to 2.84	0.068
Baseline BMI (kg/m ²)			
<18.5	Reference		
≥18.5	1.57	1.23 to 2.47	0.011
Comorbidity			
Yes	Reference		
No	2.42	2.33 to 2.51	0.212
HIV status			
Negative	Reference		
Positive	0.98	0.63 to 0.96	0.951
Treatment regimen			
New patient	Reference		
Retreatment	0.47	0.10 to 0.75	0.028
AOR, adjusted OR; BMI, be	ody mass inde	ex; MDR-TB, mu	ıltidrug-

resistant tuberculosis.

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 underestimation 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 generalisability. 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, patient population with MDR-TB in the country is not very large. For instance, Svlverken et al's recent nationwide survey found only 19 (3.2%) out of 927 patients with TB to be multidrug resistant.⁷ Thus, a sample of 159 is adequate to make a generalisation about the population with MDR-TB, 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 WHO⁴ 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 metaanalysis³¹ and 53.4% (44.55 cured and 8.9% treatment complete) found in a multicentric 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 women 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 to 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, comorbidities with complicated medication schedules, malnutrition and compromised immunity, older age patients respond poorly to anti-TB treatment.⁴¹

Individuals' level of education constitutes a unique dimension of social status and a key determining factor of health-seeking behaviour.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 to 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 18.5 kg/m^2 had decreased chances of a favourable 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

Comorbidity 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 coinfected 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 a history of TB were less likely (AOR=0.47, 95% CI: 0.10 to 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 patients' 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, policymakers and clinicians could influence the potentially modifiable ones to improve the management of MDR-TB cases in the region. For instance, nutritional counselling to increase energy intake and provision of nutritional supplements should be considered in patients having a baseline BMI below 18.5 kg/m²

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 to remind patients with TB 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 favourable 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 drugsusceptible 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.

Author affiliations

¹Department of Public Health, Kumasi South Hospital, Kumasi, Ghana ²Department of Health Administration and Education, Faculty of Science Education, University of Education, Winneba, Ghana

³Department of Medicine, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

⁴Department of Preventive and Social Medicine, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand

⁵Department of Physician Assistantship, Faculty of Health and Medical Sciences, Presbyterian University College of Ghana, Asante Akyem Campus, Ghana ⁶Department of Health Policy, Management and Economics, School of Public Health, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

Acknowledgements We are grateful to the Ashanti Regional Health Directorate for granting us permission to use data from the regional MDR-TB treatment register for this study.

Contributors All authors contributed to conceptualising the study. Literature search for background information was done by VP and EK. VP, EK, POA and MAB wrote the first draft of the paper. CK, AF, SEA, PA-B and SKA provided critical review of the manuscript. All the authors read and approved the final version of the paper. EK is the guarantor for this work.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval 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 were not linked to individual patients.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iD

Emmanuel Kumah http://orcid.org/0000-0002-3308-1703

REFERENCES

- 1 World Health Organization. Global Tuberculosis Report. Geneva; 2019.
- 2 World Health Organization. Global tuberculosis report. Geneva; 2020. https://apps.who.int/iris/bitstream/handle/10665/336069/ 9789240013131-eng.pdf
- 3 Mase SR, Chorba T. Treatment of drug-resistant tuberculosis. *Clin Chest Med* 2019;40:775–95.
- 4 World Health Organization. Multidrug and extensively drug-resistant TB: global report on surveillance and response. Geneva; 2017.
- 5 Brode SK, Varadi R, McNamee J, et al. Multidrug-resistant tuberculosis: treatment and outcomes of 93 patients. Can Respir J 2015;22:97–102.
- 6 Migliori GB, Tiberi S, Zumla A, et al. MDR/XDR-TB management of patients and contacts: challenges facing the new decade. The 2020 clinical update by the global tuberculosis network. Int J Infect Dis 2020;92S:S15–25.
- 7 Sylverken AA, Kwarteng A, Twumasi-Ankrah S, et al. The burden of drug resistance tuberculosis in Ghana; results of the first national survey. PLoS One 2021;16:e0252819.
- 8 Davies-Teye B, Vanotoo L, Dziedzom A, et al. Factors associated with multi-drug resistant tuberculosis incidence in Ghana: a 1:2 unmatched case control study, 2017. Value in Health 2017;20:A641–811.
- 9 Otchere ID, Asante-Poku A, Osei-Wusu S, et al. Detection and characterization of drug-resistant conferring genes in mycobacterium tuberculosis complex strains: a prospective study in two distant regions of Ghana. *Tuberculosis* 2016;99:147-154.
- Yeboah-Manu D, Asante-Poku A, Bodmer T, *et al.* Genotypic diversity and drug susceptibility patterns among M. tuberculosis complex isolates from south-western Ghana. *PLoS One* 2011;6:e21906.
- 11 Forson A, Kudzawu S, Kwara A. High frequency of first-line antituberculosis drug resistance among persons with chronic pulmonary tuberculosis at a teaching hospital chest clinic. *Ghana Med J* 2010;44.
- 12 Lawn SD, Frimpong EH, Al-Ghusein H, et al. Pulmonary tuberculosis in Kumasi, Ghana: presentation, drug resistance, molecular epidemiology and outcome of treatment. West Afr J Med 2001;20:92–7.
- 13 Ali MK, Karanja S, Karama M. Factors associated with tuberculosis treatment outcomes among tuberculosis patients attending tuberculosis treatment centres in 2016-2017 in Mogadishu, Somalia. *Pan Afr Med J* 2017;28:1–14.
- 14 Jain K, Desai M, Solanki R, et al. Treatment outcome of andardized regimen in patients with multidrug resistant tuberculosis. J Pharmacol Pharmacotherapeutics 2014;5:145–9.
- 15 Khan MA, Mehreen S, Basit A. "Predictors of poor outcomes among patients treated formultidrug- resistant tuberculosis at tertiary care hospital in Pakistan. *American-Eurasian J Toxicological Sci* 2015;7:162–72.
- 16 Kuchukhidze G, KumarAMV deCP, et al. Risk factors associated with loss to follow-up among multidrugresistant tuberculosis patients in Georgia. Public Health Action 2014;I:249–51.

- 17 Kwon YS, Kim YH, Suh GY, et al. Treatment outcomes for HIVuninfected patients with multidrug-resistant and extensively drugresistant tuberculosis. *Clin Infect Dis* 2008;47:496–502.
- 18 Elliott E, Draper HR, Baitsiwe P, et al. Factors affecting treatment outcomes in drug-resistant tuberculosis cases in the Northern Cape, South Africa. Public Health Action 2014;4:201–3.
- 19 Tang S, Tan S, Yao L, et al. Risk factors for poor treatment outcomes in patients with MDR-TB and XDR-TB in China: retrospective multicenter investigation. *PLoS One* 2013;8:1–8.
- 20 Tupasi TE, Garfin AMCG, Kurbatova EV, et al. Factors associated with loss to follow-up during treatment for multidrug-resistant tuberculosis, the Philippines, 2012-2014. Emerg Infect Dis 2016;22:491–502.
- 21 Elmi OS, Hasan H, Abdullah S, et al. Treatment outcomes of patients with multidrug-resistant tuberculosis (MDR- TB) compared with Non-MDR-TB infections in Peninsular Malaysia. MJMS 2016;23:17–25.
- 22 Periasamy A, Viswanatham KAP. Pulmonary & respiratory medicine predictors of outcome in drug resistant tuberculosis patients. *J Pulmonary Respiratory Med* 2007;7:1–4.
- 23 Zhang L, Meng Q, Chen S, et al. Treatment outcomes of multidrugresistant tuberculosis patients in Zhejiang, China, 2009–2013. Clinical Microbiology and Infection 2018;24:381–8.
- 24 Ghana Statistical Service. *Population and housing census*. 2019. Accra, 2021. https://census2021.statsghana.gov.gh/
- 25 World Health Organization. *Guidance for national tuberculosis programmes on the management of tuberculosis in children.* 2nd ed. Geneva, 2014.
- 26 Falzon D, Jaramillo E, Schünemann HJ, et al. Who guidelines for the programmatic management of drug-resistant tuberculosis: 2011 update. *Eur Respir J* 2011;38:516–28.
- 27 Bewick V, Cheek L, Ball J. Statistics review 13: receiver operating characteristic curves. *Crit Care* 2004;8:508–12.
- 28 Harris RJ. A primer of multivariate statistics. 2nd ed. New York: Academic Press, 1985.
- 29 Alene KA, Viney K, McBryde ES, et al. Treatment outcomes in patients with multidrug-resistant tuberculosis in north-west Ethiopia. *Trop Med Int Health* 2017;22:351–62.
- 30 Yu M-C, Chiang C-Y, Lee J-J, et al. Treatment outcomes of multidrug-resistant tuberculosis in Taiwan: tackling loss to follow-up. *Clin Infect Dis* 2018;67:202–10.
- 31 Eshetie S, Alebel A, Wagnew F, *et al.* Current treatment of multidrug resistant tuberculosis in Ethiopia: an aggregated and individual patients' data analysis for outcome and effectiveness of the current regimens. *BMC Infect Dis* 2018;18:486.
- 32 El Hamdouni M, Bourkadi JE, Benamor J, et al. Treatment outcomes of drug resistant tuberculosis patients in Morocco: multi-centric prospective study. BMC Infect Dis 2019;19:316.
- 33 Leveri TH, Lekule I, Mollel E, et al. Predictors of treatment outcomes among multidrug resistant tuberculosis patients in Tanzania. *Tuberc Res Treat* 2019;2019:1–10.
- 34 Khan I, Ahmad N, Khan S, et al. Evaluation of treatment outcomes and factors associated with unsuccessful outcomes in multidrug resistant tuberculosis patients in Baluchistan Province of Pakistan. J Infect Public Health 2019;12:809–15.
- 35 Javaid A, Ahmad N, Afridi AK, et al. Validity of time to sputum culture conversion to predict cure in patients with multidrug-resistant tuberculosis: a retrospective single-center study. Am J Trop Med Hyg 2018;98:1629–36.
- 36 Wahid A, Ahmad N, Ghafoor A, et al. Effectiveness of shorter treatment regimen in multidrug-resistant tuberculosis patients in Pakistan: a multicenter retrospective record review. Am J Trop Med Hyg 2021;104:1784–91.
- 37 Stosic M, Vukovic D, Babic D, et al. Risk factors for multidrugresistant tuberculosis among tuberculosis patients in Serbia: a casecontrol study. BMC Public Health 2018;18:1–8.
- 38 Murphy ME, Wills GH, Murthy S, et al. Gender differences in tuberculosis treatment outcomes: a post hoc analysis of the REMoxTB study. BMC Med 2018;16:1–11.
- 39 Javaid A, Shaheen Z, Shafqat M, et al. Risk factors for high death and loss-to-follow-up rates among patients with multidrug-resistant tuberculosis at a programmatic management unit. Am J Infect Control 2017;45:190.
- 40 Nagpal M, Chawla S, Devgun P, et al. Socio-demographic determinants of treatment outcome in multidrug resistant tuberculosis cases registered under programmatic management of drug resistant tuberculosis services in Amritsar, Punjab. Int J Community Med Public Health 2019;6:2688–93.
- 41 Ananthakrishnan R, Kumar K, Ganesh M, et al. The profile and treatment outcomes of the older (aged 60 years and above) tuberculosis patients in Tamilnadu, South India. PLoS One 2013;8:e67288.

- 42 Pampel FC, Krueger PM, Denney JT. Socioeconomic disparities in health behaviors. *Annu Rev Sociol* 2010;36:349–70.
- 43 Muture BN, Keraka MN, Kimuu PK, *et al.* Factors associated with default from treatment among tuberculosis patients in nairobi province, Kenya: a case control study. *BMC Public Health* 2011;11:696.
- 44 Mitnick C, Bayona J, Palacios E, *et al*. Community-based therapy for multidrug-resistant tuberculosis in Lima, Peru. *N Engl J Med* 2003;348:119–28.
- 45 Kim DH, Kim HJ, Park S-K, et al. Treatment outcomes and long-term survival in patients with extensively drug-resistant tuberculosis. Am J Respir Crit Care Med 2008;178:1075–82.
- 46 Ndwandwe ZSI, Mahomed S, Lutge E. Factors affecting nonadherence to tuberculosis treatment in uMgungundlovu health district in 2010. South Afr J Infect Dis 2015;29:56–9.
- 47 Oliveira O, Gaio R, Villar M, *et al.* Predictors of treatment outcome in multidrug-resistant tuberculosis in Portugal. *Eur Respir J* 2013;42:e9.