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ORIGINAL ARTICLE

Observational Study

Profile and determinants of unsuccessful tuberculosis outcome in rural Nigeria: Implications for tuberculosis control

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Abstract

AIM: To determine the treatment outcomes and predictors for unsuccessful tuberculosis (TB) outcomes in rural Nigeria.

METHODS: Adult rural TB patients treated during 2011 and 2012 in two healthcare facilities (one urban public and one rural private) were identified from the TB treatment registers and retrospectively reviewed. Tuberculosis treatment outcomes were assessed according to World Health Organisation guidelines. Determinants of unsuccessful treatment outcomes were identified using a multivariable logistic regression analysis.

RESULTS: Between January 2011 to December 2012, 1180 rural TB patients started treatment, of whom 494 (41.9%) were female. The treatment success rate was 893 (75.7%), while the rates of death, loss-to-follow-up, and treatment failure were 129 (10.9%), 100 (8.5%), and 18 (1.5%) respectively. In the final multivariable logistic regression model, the odds of unsuccessful treatment outcome were higher among patients who received care at the urban public facility (aOR = 2.9, 95%CI: 1.9-4.4), smear-negative (1.3,



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CONCLUSION: Treatment success among rural TB patient in Nigeria is low. High risk groups should be targeted for closer monitoring, socio-economic support, and expansion of TB/HIV activities.

Key words: Tuberculosis; Treatment outcome; Rural; Health services; Nigeria

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Core tip: Of 1180 tuberculosis (TB) patients enrolled, overall treatment success rate was 893 (75.7%). Also, death, default, and treatment failure rates were 10.9%, 8.5%, and 1.5%, respectively. Treatment success rate were significantly higher among all human immunodeficiency virus (HIV)-negative TB cases (79.3% *vs* 60.9%; *P* < 0.001). The difference was due to higher death rates among HIV-infected TB patients. Predictors of unsuccessful outcomes were; public facility-care, smear-negative or extrapulmonary TB, HIV co-infection, and receiving the 8-mo regimen.

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INTRODUCTION

Despite recent progress in tuberculosis (TB) control, the disease is still a leading cause of mortality globally and a major public health challenge in low- and middleincome countries^[1]. Adverse outcomes of TB tend to be high in poor populations^[2]. As poverty is both a cause and outcome of TB, it is closely associated with the socioeconomic status of a population - and it remains a major driver of the disease-poverty trap seen in underserved populations^[2]. Rural residence can be a marker for poverty and, thus vulnerability to $TB^{[3]}$. Previous studies demonstrate that rural TB patients often do not recognise TB symptoms^[4]. This have resulted in prolonged delays in seeking care for TB^[4,5], and may lead to increased risk of continuing community TB transmission and important burden of undiagnosed active TB in the community^[6]. Moreover, when these rural patients eventually present to health services, they arrive with more advanced TB disease^[7]. Furthermore, a qualitative study suggests that rural TB are less likely to complete TB treatment due to being unaware of the duration of TB treatment, stopping treatment once

symptoms subsided, and lack of family support^[8]. Thus, addressing poverty in TB control should include not only the needs of those facing economic impoverishment but also all relatively vulnerable, disadvantaged, marginalized sections of the population like TB patients residing in rural areas^[2,3,5].

Although the expansion of TB treatment services and coverage through the directly observed treatment short course (DOTS) strategy have resulted in considerable progress in TB control in high TB burden countries^[9], there is limited information on outcomes of TB treatment in underserved populations in those settings. Assessing the outcomes of TB treatment is essential for the evaluation of the effectiveness of the DOTS services^[1,10]. Furthermore, identifying the specific determinants for unsuccessful outcomes is important to design interventions that would improve treatment systems^[9,11]. As addressing the needs of TB among the poor and vulnerable populations is one of the key components of the StopTB strategy^[12], information on the treatment outcomes and the determinants of adverse outcomes in rural TB patients is crucial. To date, only few studies have evaluated the outcomes of TB among rural TB patients^[10,13-17], and far less have documented independent risk factors for poor treatment outcomes among them in high-burden settings^[15,16].

More than 70% of Nigerians live in the rural area where up to 80% of the population lives below poverty line, and public healthcare services are hardly available in this setting in Nigeria^[18,19]. Also, a high proportion of rural TB patients in Nigeria face substantial patient and health systems delays before reaching an appropriate health care provider^[5]. Poor care in the TB care-seeking pathway increases the costs that already impoverished individuals and families encounter and commonly results in TB patients being unable to work for long periods while at the same time incurring catastrophic costs^[19,20]. Thus, there is a need to assess the performance of the tuberculosis control programme in rural Nigeria in order inform health policy solutions crucial for improving programme performance. The aim of this study was to investigate the treatment outcomes of TB and the determinants of adverse outcomes in rural Nigeria.

MATERIALS AND METHODS

Study design

This was a retrospective observational study using routine programme data. The study was part of large operational research project to evaluate the profile and treatment outcomes of subpopulations of TB patients as well as identify possible determinants of unsuccessful outcomes in these patients in order to highlight areas for priority intervention for the TB control programme in Ebonyi State^[21-23]. The present study population consisted of all adult (\geq 15 years) TB patients treated between 1 January 2011 and 31 December 2012 who were recorded in the TB treatment registers as resident



in a rural area.

Study area

The study was carried out in Ebonyi state Southeastern Nigeria. Ebonyi state has a population of over 2.5 million people, 75% of them resides in the rural area^[18]; and 74% live below the poverty line^[24]. TB notification rate for new cases was 77/100000 in 2009^[25]. Due to health system gaps, there is limited availability of public facilities in rural settings in the state^[19,20]. Thus, several mission (private) hospitals give primary and secondary care services in those settings. Two hospitals - one rural secondary-care (faith-based/mission) private and the one only tertiary-care (urban/public) hospital in the state were selected as the study sites due to their geographic spread and high TB notification rate. Both hospitals accounts for about 50% of annual TB notification in Ebonyi State^[25]; and receives referrals from nearby states in Southern Nigeria.

Diagnosis of TB

Any person with a cough lasting for two or more weeks with or without weight loss, night sweats, fever, and shortness of breath were evaluated for TB. Three sputum specimens were submitted for light microscopy using Ziehl-Neelsen staining methods. The presence of acid-fast bacilli (AFB) in one or more sputum samples in a patient qualifies as a case of smear-positive pulmonary TB (SPTB)^[26]. Patients with smear-negative sputum are given broad spectrum antibiotics and further evaluated using clinical assessments, radiographs, and repeat sputum examinations for AFB before the diagnosis of smear-negative TB (SNTB) is made. Extrapulmonary TB (EPTB) is diagnosed on the basis of clinical/laboratory evidence and a decision by an experienced medical officer^[26]. TB/human immunodeficiency virus (HIV) collaborative activities exist in all the study facilities; therefore, all TB patients are counselled and tested for HIV, and vice versa^[26].

Tuberculosis treatment

The treatment was based on the community DOTS strategy - where intake of the anti-TB medications is being observed daily by a DOTS-supporter or a community health worker residing in the same community as the patient. The intensive phase of treatment lasted for two months for new patients and three months for retreatment patients. Before 2012, all new pulmonary tuberculosis patients were treated using an eight-month anti-tuberculosis regimen consisting of two months of intensive phase treatment with rifampicin (R) and isoniazid (H), pyrazinamide (Z) and ethambutol (E); and six months of isoniazid and ethambutol, i.e., 2RHZE/ 6EH^[26,27]. However, from January 2012, the regimen was changed to a six-month regimen containing 6 mo of rifampicin (2RHZE/4RH) in line with the recent World Health Organization (WHO) guidelines^[27]. All retreatment cases received a 3-mo intensive phase with the addition of streptomycin to RHZE in the first two months; and a continuation phase of 5RHE^[26,27]. During the intensive phase of treatment, medications were collected twice a month; afterwards, medications were collected monthly. Fixed-dose combinations of anti-TB drugs were used^[26].

Definitions of TB treatment outcomes

We used the standard WHO definitions of TB treatment outcomes^[1,26,27]. Briefly these include: Cured (a patient who was initially smear-positive and who was smearnegative in the last month of treatment and on at least one previous occasion), completed treatment (a patient who completed treatment, but who did not meet the criteria for cure or failure - this definition applies to smear-positive and smear-negative patients and to patients with EPTB), death (a patient who died from any cause during the course of treatment), treatment failure (a patient who was initially smear-positive and who remained smear positive at month 5 of treatment or later during treatment), lost to follow-up (a patient whose treatment was interrupted for 2 consecutive months or longer), and transferred-out (a patient who transferred to another reporting unit and for whom treatment outcome is unknown). A successfully treated individual is a patient who was cured or who completed treatment.

Data collection and variables

Variables retrieved from the TB treatment registers were related to the study objectives. Patients' age, gender, facility (public vs private), type of TB, treatment category, treatment regimen (six-month vs eight-month) and HIV-status were the main explanatory variables. In addition to standard outcome definitions, we classified the final treatment outcome as a dichotomous variable, *i.e.*, successful (cured or treatment completed) vs unsuccessful (death, loss to follow-up, failure or transferred-out) outcomes.

Sample size

The sample size was calculated using Win Episcope 2.0. With a sample size of at least 246 patients, we were able to detect an 80% prevalence of successful outcomes^[28], at 95% confidence level and an absolute sampling error of 0.05.

Statistical analysis

The data were double-entered, checked, and analyzed using Epi Info 3.4.1 (CDC, Atlanta, GA United States). Treatment outcomes were expressed as proportions (%). OR and their 95%CIs were estimated using multivariable logistic regression analysis, with treatment outcome (successful *vs* unsuccessful) as the outcome variable. The likelihood ratio test was used to assess the association between explanatory variables and outcome variable. A stratified analysis was conducted to determine the occurrence of interaction and confounding between the main outcome variable and exposure



Table 1	Demogra	phic and clinical	profile of	rural	tubercul	osi
patients,	Nigeria,	2011-2012				

Variables	<i>n</i> (%)
Age (yr)	
$\leqslant 40$	728 (61.7)
> 40	452 (38.3)
Gender	
Female	494 (41.9)
Male	686 (58.1)
Facility	
Private	1035 (87.7)
Public	145 (12.3)
Treatment category	
New	1099 (93.1)
Retreatment	81 (6.9)
Type of TB	
Pulmonary TB	1134 (96.1)
Extrapulmonary TB	46 (3.9)
HIV status	
HIV - positive	233 (19.7)
HIV - negative	947 (80.3)
Treatment regimen ($n = 1099$)	
Regimen 1	579 (52.7)
Regimen 2	520 (47.3)

Regimen 1: 8-mo regimen; Regimen 2: 6-mo regimen. TB: Tuberculosis; HIV: Human immunodeficiency virus.

variables. A multivariable logistic regression model was then constructed using the full model fits. P < 0.05 was considered statistically significant.

The statistical methods of this study were reviewed by Femi Gbenga from Femo Stat Consult, Abakaliki, Ebonyi State, Nigeria.

RESULTS

Socio-demographic characteristics

A total of 1180 rural TB patients were treated during the study period; of whom 494 (41.9%) were female. Majority of the patients 1099 (93.1%) had newly diagnosed TB while 81 (6.9%) were retreatment cases. The mean \pm SD age of all patients was 39.3 \pm 15.1 years. Also, 708 (60%) of them had smear-positive pulmonary TB, 426 (36.1%) had smear-negative pulmonary TB and 46 (3.9%) had extrapulmonary TB. Furthermore, 1035 (87.7%) of all the patients were treated at the private faith-based (rural) health facility; 233 (19.7%) were HIV-positive, and 520 (47.3) were treated using the shorter six-month regimen. Table 1 shows the demographic and clinical characteristics of all patients included in the study.

Treatment outcomes

Treatment outcomes by type and category of TB are shown in Table 2. Among all TB cases seen during the study period, the treatment success rate was 893 (75.7%), while the rates of death, loss-to-follow-up, and treatment failure were 129 (10.9%), 100 (8.5%), and 18 (1.5%), respectively (Table 2). For SPTB cases (n = 708), the overall treatment success rate was 572

(80.8%); while unsuccessful outcomes were due to lossto-follow-up 66 (9.3%), deaths 46 (6.5%), treatment failure 18 (2.5%), and transfer-out 6 (0.8%). For SNTB cases (n = 426), treatment success rate was 303 (71.7%); and unsuccessful outcomes were due to death 75 (17.6%), loss-to-follow-up 22 (5.2%), and transferout 26 (6.1%). Among EPTB cases (n = 46), treatment success rate was 18 (39.1%); with loss-to-follow-up 12 (26.1%) accounting for most of the unsuccessful outcomes (Table 2). Also, treatment success rate was 832 (75.7%) among new cases compared with 61 (75.3%) among retreatment cases; P = 0.9 (Table 2).

Furthermore, comparing HIV-negative vs HIVinfected TB patients (Table 2), treatment success rates were significantly higher among all HIV-negative TB cases compared to all HIV co-infected cases (79.3% vs 60.9%, P <0.001). The difference was accounted for mainly by higher death rates among HIV-infected TB patients (23.2% vs 7.9%, P < 0.001). Also, in pulmonary TB and new TB cases, treatment success rates were higher in HIV-negative compared to HIV coinfected cases (81% vs 61.8%, P < 0.001) and (79.4% vs 60.8%, P < 0.001), respectively. And, in both cases, this was mainly due to a significantly higher death rate among HIV-infected TB patients (P < 0.001; Table 2). In EPTB or re-treatment TB cases, there were no significant differences in treatment success rates according to HIV status (P > 0.05; Table 2).

Of the 708 SPTB patients, 665 (93.9%) had a sputum AFB microscopy done at the end of the second month of treatment. From these 665 patients, 144 (21.7%) had persistent smear positive smears; while 521 (78.3%) had a negative smear conversion after the first two months of treatment. Also, 607/665 (91.3%) of the patients who had a smear test after intensive treatment had sputum AFB result at the end of the fifth month of treatment with 17 (2.8%) still being smear positive.

Determinants of unsuccessful outcomes

Univariate and multivariable logistic regression analysis was performed to determine socio-demographic and clinical risk factors for unsuccessful outcomes (Table 3). The independent predictors for unsuccessful outcomes were: Type of facility, type of TB, HIV status and treatment regimen. The risk of unsuccessful outcomes was 2.9 (1.9-4.4) times higher among TB patients who received care in the urban public facility compared to those treated at the rural private hospital. Compared to smear-positive TB patients, smear-negative and extrapulmonary TB patients were 1.3 (1.0-1.8) and 2.7 (1.3-5.6) times more likely to have unsuccessful outcomes respectively. HIV-positive TB patients had 2.1 (1.5-3.0) times greater risk of unsuccessful outcomes compared to HIV-negative patients. Unsuccessful treatment outcomes was 1.3 (1.1-1.8) times more frequent in patients who received the longer (eight-month) regimen than among those treated with the shorter (sixmonth) regimen (Table 3).



Ebonyi, Nigeria, 20)11-2012			
Treatment outcome	Both HIV- and HIV+ <i>n</i> (%)	HIV-negative <i>n</i> (%)	HIV-positive n (%)	χ^2 (P value)
All TB cases				34.2 (< 0.001)
Successful	893 (75.7)	751 (79.3)	142 (60.9)	· · · ·
Unsuccessful	287 (24.3)	196 (20.7)	91 (39.1)	
Failure	18 (1.5)	13 (1.4)	5 (2.1)	1.84 (0.18)
Death	129 (10.9)	75 (7.9)	54 (23.2)	49.0 (< 0.001)
Default	100 (8.5)	79 (8.3)	21 (9.0)	1.70 (0.19)
Transfer-out	40 (3.4)	29 (3.1)	11 (4.7)	3.76 (0.05)
Total	1180	947	233	
Pulmonary TB				37.7 (< 0.001)
Successful	875 (77.2)	736 (81.0)	139 (61.8)	· · · ·
Unsuccessful	259 (22.8)	173 (19.0)	86 (38.2)	
Failure	18 (1.6)	13 (1.4)	5 (2.2)	1.84 (0.18)
Death	121 (10.7)	69 (7.6)	52 (23.1)	50.3 (< 0.001)
Default	88 (7.8)	69 (7.6)	19 (8.4)	1.9 (0.17)
Transfer-out	32 (2.8)	22 (2.4)	10 (4.4)	5.3 (0.02)
Total	1134	909	225	
Extrapulmonary TB				$0.01 (0.47)^1$
Successful	18 (39.1)	15 (39.5)	3 (37.5)	
Unsuccessful	28 (60.9)	23 (60.5)	5 (62.5)	
Failure	0	0 (0)	0 (0)	-
Death	8 (17.4)	6 (15.8)	2 (25.0)	$0.25(0.5)^{1}$
Default	12 (26.1)	10 (26.3)	2 (25.0)	$0.0(0.68)^{1}$
Transfer-out	8 (17.4)	7 (18.4)	1 (12.5)	$0.07 (0.64)^1$
Total	46	38	8	
New cases				32.5 (< 0.001)
Successful	832 (75.7)	700 (79.4)	132 (60.8)	
Unsuccessful	267 (24.3)	132 (20.6)	85 (39.2)	
Failure	15 (1.4)	11 (1.2)	4 (1.4)	1.28 (0.26)
Death	118 (10.7)	67 (7.6)	51 (23.5)	49.7 (< 0.001)
Default	97 (8.8)	76 (8.6)	21 (9.7)	2.1 (0.15)
Transfer-out	37 (3.4)	28 (3.2)	9 (4.1)	1.86 (0.17)
Total	1099	882	217	
Retreatment cases				$1.8(0.10)^{1}$
Successful	61 (75.3)	51 (78.5)	10 (62.5)	
Unsuccessful	20 (24.7)	14 (21.5)	6 (37.5)	
Failure	3 (3.7)	2 (3.1)	1 (6.3)	$0.58(0.44)^{1}$
Death	11 (13.6)	8 (12.3)	3 (18.8)	$0.75(0.31)^{1}$
Default	3 (3.7)	3 (4.6)	0 (0)	$0.58 (0.59)^1$
Transfer-out	3 (3.7)	1 (1.5)	2 (12.5)	$4.74(0.08)^1$
Total	81	65	16	

¹Fisher's exact *P*-value was reported; TB: Tuberculosis; HIV: Human immunodeficiency virus; HIV+: HIV-positive; HIV-: HIV-negative.

DISCUSSION

In order to improve TB control in an underserved population, we assessed the treatment outcomes of adult TB patients living in rural Ebonyi State, Nigeria. The study showed that treatment success rate was below recommended target and the current national levels; and was associated with the type of facility where treatment was given, type of TB, HIV status and treatment regimen received. The treatment success rate observed among rural TB patients was lower than the national TB programme and WHO target of 85%^[1]. By 2011, both Nigeria and Ebonyi State had reached the WHO target treatment success rate of 85% among all TB patients^[1,28]. Our finding of a success rate of 75.7% in rural patients and even lower rates in the various subgroups of TB patients studied suggests that figures reported nationally and locally

are likely to mask lower treatment success levels in underserved rural populations. It also suggests that achieving the treatment success target for rural TB patients is a major challenge that needs to be tackled. Our finding agrees with other studies that evaluated outcomes of TB treatment in rural settings where treatment success rates for Angola (66.3%)^[13], China (74.5%)^[14] and Ghana (60.7%)^[29] were all found to be below recommended target. However, other studies showed that in rural Ethiopia, Haiti, and Hunan, China TB treatment success rates were over $85\%^{[10,16,29]}$. Our finding suggests the need to improve education, monitoring of cases and quality of TB management in rural settings of Nigeria.

In this study we have shown that receiving treatment at the public facility was a predictor of unsuccessful outcomes among rural TB patients. This may be due to difficulty in accessing care at the urban



 Table 3 Multivariable logistic regression analysis of factors associated unsuccessful treatment outcomes among rural tuberculosis patients, Nigeria, 2011-2012

Variables	n = 1180 n (%)	Unsuccessful outcomes n (%)	Crude OR (95%CI)	Adjusted OR (95%CI)	Adjusted <i>P</i> -value
Total	1180	287 (24.3)			
Age (yr)					
≤ 40	728	168 (23.1)	1		
> 40	452	119 (26.3)	1.2 (0.9-1.6)	1.3 (1.0-1.8)	0.08
Gender					
Female	494	115 (23.3)	1		
Male	696	172 (25.1)	1.1 (0.8-1.5)	1.2 (0.9-1.6)	0.25
Facility					
Private	1035	210 (20.3)	1		
Public	145	77 (53.1)	4.5 (3.1-6.4)	2.9 (1.9-4.4)	< 0.001
Type of TB					
PTB smear positive	708	136 (19.2)	1		
PTB smear negative	426	123 (28.9)	1.5 (1.1-1.9)	1.3 (1.0-1.8)	0.09
Extrapulmonary	46	28 (60.9)	5.3 (2.9-9.7)	2.7 (1.3-5.6)	0.009
Treatment category					
New	1099	267 (24.3)	1		
Retreatment	81	20 (24.7)	1.0 (0.6-1.7)	1.1 (0.6-1.9)	0.75
Regimen (<i>n</i> = 1099)					
Regimen 1	579	157 (27.1)	1.4 (1.1-1.8)	1.3 (1.1-1.8)	0.04
Regimen 2	520	110 (21.2)			
HIV status					
Negative	947	196 (20.7)	1		
Positive	233	91 (31.7)	2.5 (1.8-3.3)	2.1 (1.5-3.0)	< 0.001

Regimen 1: 8-mo regimen; Regimen 2: 6-mo regimen. TB: Tuberculosis; HIV: Human immunodeficiency virus.

public facility due to distance from the patients home. Previous studies have used place of residence and distance from treatment centre as a proxy measures of access to care^[17,30]. None of these, however, may be an appropriate indicator. Access to health services and treatment outcome is associated with a complex interplay of patient and health-provider-related factors including patient health belief model, knowledge, significant others, language, costs, and availability of local public services^[5,17,19,30]. An important step, however, in improving access to care is to further expand TB and other healthcare services closer to the homes of rural patients.

Consistent with previous studies in Nigeria, Ethiopia, and elsewhere^[1,31,32], SNTB and EPTB were predictors of unsuccessful outcomes. This may be because these patients have a higher frequency of HIV co-infection, and the depressed immune status results in their inability to develop an adequate immune response to control the disease^[1,31]. Also, lack of cavitary lesions in their lungs makes them prone to misdiagnosis, delayed diagnosis, and higher co-morbidities often resulting in poor outcome^[1,31,32]. Also, as previously documented^[31,32], HIV co-infection was also a predictor of unsuccessful outcome. The reasons why HIV-infected TB patients had poorer outcomes have been speculated to be because of immunosuppression making them less able to develop adequate immune response even during treatment^[31]. Furthermore, it has also been suggested that TB/HIV patients have higher rates of unsuccessful outcomes due to higher catastrophic costs of seeking care separately for HIV and TB^[2,19,20], however, this needs to be confirmed in further studies. Compared to HIV-negative TB patients, higher death rates in HIV-infected TB patients was responsible for higher rates of unsuccessful outcomes among them in this study. There is therefore a need for a detailed assessment of factors responsible for death among TB/HIV patients. The WHO recommends the promotion of TB/HIV collaborative activities through: Improving mechanisms of collaboration between TB and HIV programmes, continuous surveillance of HIV among TB/HIV co-infected patients^[33]. Thus, scaling-up TB/HIV collaborative activities in rural settings could improve treatment outcomes.

In this study, we have shown that receiving the eight-month regimen was a predictor of unsuccessful outcomes. The new WHO guidelines recommended that this regimen be phased out^[27]. Our study supports this policy in rural TB patients in a high-burden setting. Also, unlike the findings of other studies age, gender, and treatment category were not determinants of TB treatment outcomes in this study^[13,15-17,31]. The reasons for these differences are not clear.

The strengths of this study are twofold: The data used were obtained under programme conditions and therefore are likely to reflect operational reality; and through several reporting and record training sessions by the TB programme there were no missing data on outcomes and we therefore believe the data were robust. However, the study had some limitations. The variables used for the analysis were derived from routine surveillance data; additional important variables such as employment status, co-morbidities like diabetes mellitus, income levels, and adverse effects of medications could have improved our study but these information are not routinely recorded in TB registers. Also, although data on HIV status were recorded in the registers for each patient, details of CD4⁺ T cell count, antiretroviral therapy use and cotrimoxazole preventive therapy use were not adequately documented in the registers. These could have affected treatment outcomes. A prospective study with these additional details documented will improve upon these limitations.

In conclusion, treatment success rate among TB patients in rural Nigeria was 75.7%, and receiving care at an urban public facility, smear-negative or extrapulmonary TB, HIV co-infection, and receiving the eight-month regimen were predictors for unsuccessful outcomes. These findings have implications that could modify the National TB Control Programme policy. We recommend that: (1) urgent measures should be adopted to reduce default and deaths among TB patients especially TB/HIV patients; (2) there is need to further expand quality TB education, services and TB/HIV collaborative activities in rural Nigeria; and (3) targeted interventions to reduce unsuccessful outcomes for patients in the high-risk groups should be implemented.

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COMMENTS

Background

Rural residence is marker of poverty. Thus, addressing poverty in tuberculosis (TB) control should include the needs of vulnerable, disadvantaged, marginalized sections of the population like TB patients residing in rural areas. The authors investigated the treatment outcomes of TB and the determinants of adverse outcomes in rural Nigeria.

Research frontiers

Only few studies have investigated the outcomes and its determinants of TB treatment in rural high burden settings. Knowledge of this information is needed for developing health systems and policy solutions for persons with TB residing in rural areas in resource-limited settings.

Innovations and breakthroughs

In this study, the authors found that treatment success rate among rural TB patients was very poor - which was mainly due to death or default during treatment. These poor outcomes were highest among persons who received care at the urban facility, those who had smear-negative TB, extrapulmonary TB, human immunodeficiency virus (HIV) co-infection, and patients who received the (8-mo) anti-TB regimen.

Applications

This observational study suggests that there is need to improve treatment success rate of TB in Nigeria. This may require targeting individuals who came for care at the urban facility, those who were HIV co-infected, and patients who received the longer (8-mo) anti-TB regimen for intervention.

Peer-review

This manuscript investigated outcomes of TB treatment and analyzed factors for unsuccessful TB outcomes in rural Nigeria. The manuscript is basically well written. Although this study has some limitations as authors stated in Discussion section, the findings are useful to improve TB treatment outcomes in area similar to rural Nigeria.

REFERENCES

- World Health Organization. Global Tuberculosis Control: WHO Report 2013. Geneva, Switzerland: World Health Organisation, 2013
- 2 Ukwaja KN, Modebe O, Igwenyi C, Alobu I. The economic burden of tuberculosis care for patients and households in Africa: a systematic review. *Int J Tuberc Lung Dis* 2012; 16: 733-739 [PMID: 22410546 DOI: 10.5588/ijtld.11.0193]
- 3 Cambanis A, Yassin MA, Ramsay A, Bertel Squire S, Arbide I, Cuevas LE. Rural poverty and delayed presentation to tuberculosis services in Ethiopia. *Trop Med Int Health* 2005; 10: 330-335 [PMID: 15807796 DOI: 10.1111/j.1365-3156.2005.01393.x]
- 4 **Verhagen LM**, Kapinga R, van Rosmalen-Nooijens KA. Factors underlying diagnostic delay in tuberculosis patients in a rural area in Tanzania: a qualitative approach. *Infection* 2010; **38**: 433-446 [PMID: 20878458 DOI: 10.1007/s15010-010-0051-y]
- 5 Ukwaja KN, Alobu I, Nweke CO, Onyenwe EC. Healthcareseeking behavior, treatment delays and its determinants among pulmonary tuberculosis patients in rural Nigeria: a cross-sectional study. *BMC Health Serv Res* 2013; 13: 25 [PMID: 23327613 DOI: 10.1186/1472-6963-13-25]
- 6 Pronyk PM, Joshi B, Hargreaves JR, Madonsela T, Collinson MA, Mokoena O, Tollman SM, Hausler HR. Active case finding: understanding the burden of tuberculosis in rural South Africa. *Int J Tuberc Lung Dis* 2001; 5: 611-618 [PMID: 11467367]
- 7 Guderian LJ, Miller WC, Seña AC, Stout JE. Increased prevalence of advanced tuberculosis in rural low tuberculosis caseload counties in North Carolina. *Int J Tuberc Lung Dis* 2011; 15: 1455-1460, i [PMID: 22008756 DOI: 10.5588/ijtld.11.0103]
- 8 Ayisi JG, van't Hoog AH, Agaya JA, Mchembere W, Nyamthimba PO, Muhenje O, Marston BJ. Care seeking and attitudes towards treatment compliance by newly enrolled tuberculosis patients in the district treatment programme in rural western Kenya: a qualitative study. *BMC Public Health* 2011; **11**: 515 [PMID: 21714895 DOI: 10.1186/1471-2458-11-515]
- 9 Obermeyer Z, Abbott-Klafter J, Murray CJ. Has the DOTS strategy improved case finding or treatment success? An empirical assessment. *PLoS One* 2008; 3: e1721 [PMID: 18320042 DOI: 10.1371/journal.pone.0001721]
- 10 Endris M, Moges F, Belyhun Y, Woldehana E, Esmael A, Unakal C. Treatment outcome of tuberculosis patients at enfraz health center, northwest ethiopia: a five-year retrospective study. *Tuberc Res Treat* 2014; 2014: 726193 [PMID: 24891948 DOI: 10.1155/2014/726193]
- 11 Veen J, Raviglione M, Rieder HL, Migliori GB, Graf P, Grzemska M, Zalesky R. Standardized tuberculosis treatment outcome monitoring in Europe. Recommendations of a Working Group of the World Health Organization (WHO) and the European Region of the International Union Against Tuberculosis and Lung Disease (IUATLD) for uniform reporting by cohort analysis of treatment outcome in tuberculosis patients. *Eur Respir J* 1998; **12**: 505-510 [PMID: 9727811 DOI: 10.1183/09031936.98.12020505]
- 12 World Health Organization. The Stop TB Strategy: building on enhancing DOTS to meet the TB related Millennium Development Goals. Geneva: World Health Organization, 2006
- 13 López T, Moreno M, Salvador F, Zacarías A, Carvalho Rd, Tomás E, Estevao G, Eugenio AN, Burgos J, Sulleiro E, Molina I, Falcó V. Tuberculosis diagnosed in a rural setting in Angola. Accuracy of follow-up sputum smears to predict outcome. *Pathog Glob Health* 2013; **107**: 5-10 [PMID: 23432857 DOI: 10.1179/2047773212Y.00 00000066]



- 14 Xu L, Gai R, Wang X, Liu Z, Cheng J, Zhou C, Liu J, Zhang H, Li H, Tang W. Socio-economic factors affecting the success of tuberculosis treatment in six counties of Shandong Province, China. *Int J Tuberc Lung Dis* 2010; 14: 440-446 [PMID: 20202302]
- 15 Ai X, Men K, Guo L, Zhang T, Zhao Y, Sun X, Zhang H, He G, van der Werf MJ, van den Hof S. Factors associated with low cure rate of tuberculosis in remote poor areas of Shaanxi Province, China: a case control study. *BMC Public Health* 2010; 10: 112 [PMID: 20205941 DOI: 10.1186/1471-2458-10-112]
- 16 Ollé-Goig JE, Alvarez J. Treatment of tuberculosis in a rural area of Haiti: directly observed and non-observed regimens. The experience of H pital Albert Schweitzer. *Int J Tuberc Lung Dis* 2001; 5: 137-141 [PMID: 11258507]
- 17 Abubakar I, Crofts JP, Gelb D, Story A, Andrews N, Watson JM. Investigating urban-rural disparities in tuberculosis treatment outcome in England and Wales. *Epidemiol Infect* 2008; 136: 122-127 [PMID: 17359565 DOI: 10.1017/S0950268807008333]
- 18 National Population Commission. The 2006 Population and Housing Census of the Federal Republic of Nigeria. Priority Tables (Volume I). Abuja, Nigeria: The National Population Commission, 2009
- 19 Ukwaja KN, Alobu I, Abimbola S, Hopewell PC. Household catastrophic payments for tuberculosis care in Nigeria: incidence, determinants, and policy implications for universal health coverage. *Infect Dis Poverty* 2013; 2: 21 [PMID: 24044368 DOI: 10.1186/2049-9957-2-21]
- 20 Ukwaja KN, Alobu I, Lgwenyi C, Hopewell PC. The high cost of free tuberculosis services: patient and household costs associated with tuberculosis care in Ebonyi State, Nigeria. *PLoS One* 2013; 8: e73134 [PMID: 24015293 DOI: 10.1371/journal.pone.0073134]
- 21 Ukwaja KN, Oshi DC, Oshi SN, Alobu I. Profile and treatment outcome of smear-positive TB patients who failed to smear convert after 2 months of treatment in Nigeria. *Trans R Soc Trop Med Hyg* 2014; 108: 431-438 [PMID: 24846911 DOI: 10.1093/trstmh/ tru070]
- 22 Oshi DC, Oshi SN, Alobu I, Ukwaja KN. Profile, Outcomes, and Determinants of Unsuccessful Tuberculosis Treatment Outcomes among HIV-Infected Tuberculosis Patients in a Nigerian State. *Tuberc Res Treat* 2014; 2014: 202983 [PMID: 25478222 DOI:

10.1155/2014/202983]

- 23 Oshi DC, Oshi SN, Alobu I, Ukwaja KN. Profile and treatment outcomes of tuberculosis in the elderly in southeastern Nigeria, 2011-2012. *PLoS One* 2014; 9: e111910 [PMID: 25369001 DOI: 10.1371/journal.pone.0111910]
- 24 **National Bureau of Statistics**. The Nigeria Poverty Profile: 2010 Report. Abuja: Nigeria, 2012
- 25 Ukwaja K, Alobu I, Ifebunandu N, Osakwe C, Igwenyi C. From DOTS to the Stop TB Strategy: DOTS coverage and trend of tuberculosis notification in Ebonyi, southeastern Nigeria, 1998-2009. *Pan Afr Med J* 2011; 9: 12 [PMID: 22145056 DOI: 10.4314/pamj. v9i1.71187]
- 26 **Federal Ministry of Health**. National Tuberculosis and Leprosy Control Programme: workers manual. Revised 5th ed. Abuja, Nigeria: Federal Ministry of Health, 2010
- 27 World Health Organisation. Treatment of tuberculosis guidelines. 4th ed. Geneva, Switzerland: World Health Organization, 2010
- 28 Ukwaja KN, Alobu I, Ifebunandu NA, Osakwe PC. Trends in treatment outcome of smear-positive pulmonary tuberculosis in Southeastern Nigeria, 1999 - 2008. *Ital J Public Health* 2012; 9: e8860-1-7 [DOI: 10.2427/8660]
- 29 Abuaku BK, Tan H, Li X, Chen M, Huang X. A comparative analysis of tuberculosis treatment success between Hunan Province of China and Eastern Ghana. *Med Princ Pract* 2010; 19: 451-456 [PMID: 20881412 DOI: 10.1159/000320303]
- 30 Barker RD, Nthangeni ME, Millard FJ. Is the distance a patient lives from hospital a risk factor for death from tuberculosis in rural South Africa? *Int J Tuberc Lung Dis* 2002; 6: 98-103 [PMID: 11931423]
- 31 Muñoz-Sellart M, Cuevas LE, Tumato M, Merid Y, Yassin MA. Factors associated with poor tuberculosis treatment outcome in the Southern Region of Ethiopia. *Int J Tuberc Lung Dis* 2010; 14: 973-979 [PMID: 20626941]
- 32 Ukwaja KN, Ifebunandu NA, Osakwe PC, Alobu I. Tuberculosis treatment outcome and its determinants in a tertiary care setting in south-eastern Nigeria. *Niger Postgrad Med J* 2013; **20**: 125-129 [PMID: 23959354]
- 33 World Health Organization. Interim policy on collaborative TB/ HIV activities. Geneva: World Health Organization, 2004

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