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Profile and determinants of treatment failure among smear-positive pulmonary tuberculosis patients in Ebonyi, Southeastern Nigeria

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ABSTRACT

Background: Early identification of determinants of tuberculosis (TB) treatment failure is urgently needed in resource-limited settings. This study describes the profile and determinants of TB treatment failure in a high-incidence setting where patients were managed at a TB control program with significant resource limitations.

Methods: This was a retrospective case-control study carried out in one tertiary and one secondary hospital in Southeastern Nigeria. Cases were adult (⩾15 years) TB patients with a positive sputum smear after 5 months of treatment (treatment failure). Controls were adult TB patients whose sputum smear was positive at the beginning of the treatment but who were smear-negative in the last month of treatment and on at least one previous occasion (cured). Cases were compared with controls to assess determinants of treatment failure.

Results: Of the 1668 TB patients registered during the study period, 985 (59%) had smear-positive pulmonary TB. Of these, 694 (70.5%) were aged ⩽40 years, 602 (61.1%) were males, 707 (71.8%) were rural residents, and 898 (91.2%) received care at the private facility. The prevalence of treatment failure was 2.5%. Significant determinants of treatment failure were: older age (>40 years) ($P < 0.001$), male gender ($P = 0.04$), previous treatment for TB ($P = 0.045$), and positive sputum smears after two month of anti-tuberculosis treatment (0.001).

Conclusion: This study showed that the treatment failure rate among smear-positive TB patients is low in Nigeria. Education and improved clinical and laboratory interventions for the identified at-risk groups may reduce TB treatment failure in resource-limited settings.

Introduction

Tuberculosis (TB) control remains a global challenge especially in high-burden countries where resources are limited, human immunodeficiency virus (HIV) co-infection is high, and control efforts are being threatened by drug-resistant TB [1,2]. The World Health Organisation (WHO) currently recommends a case detection rate of 70% and a treatment

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success rate of 85% for all TB cases [1]. It is believed that achieving these targets will lead to a reduction in TB prevalence, incidence, transmission and drug resistance to TB [3].

An important indicator recommended by the WHO for the monitoring of TB control efforts is the proportion of pulmonary TB patients whose sputum smear or culture are positive after 5 months or later during treatment [4]. These individuals are classified as treatment failure cases. Treatment failure is a serious problem for National TB control programs because cases tend to have higher morbidity and mortality compared with those who are cured [5]. Also, they remain infectious for prolonged periods of time; hence, affected patients continue to transmit the disease in the community [5]. In addition, very high rates of multidrug-resistant TB have been found among treatment failure cases in resource-limited settings [6].

The identification of factors associated with treatment failure is a priority for TB control programs because this may help in the early institution of interventions for at-risk TB patients in order to improve treatment targets [4]. Few studies done in other settings have shown that predictors of treatment failure may include social, radiological, laboratory and treatment-related factors [7–10]. As these factors can vary in different populations and health systems, it is important to assess the situation in specific settings. No study has been carried out to identify the determinants of treatment failure in this setting. This study is aimed at determining the burden and predictors of TB treatment failure in smear-positive pulmonary TB patients in Southeastern Nigeria.

Materials and methods

Study design and setting

The study was conducted in one tertiary (public) and one secondary (private/not-for-profit mission) hospital in Ebonyi State, Southeastern Nigeria. A retrospective unmatched case-control study design was used to assess adult smear-positive pulmonary TB patients who registered for treatment at the study sites between 1 January 2011 and 31 December 2012. Cases were smear-positive pulmonary TB aged $\geqslant$15 years who had a positive sputum smear at 5 months and were classified as treatment failure after treatment (cases). Controls were adult pulmonary TB patients whose sputum smear was positive at the beginning of the treatment, but who were smear-negative in the last month of treatment and on at least one previous occasion [11,12].

Diagnosis and treatment of TB and HIV

Adult patients suspected of having TB undergo sputum acid-fast-bacilli (AFB) microscopy [11,12]. Patients with AFB in at least one of the three smears submitted are registered as smear-positive pulmonary TB. All adults suspected of having TB undergo HIV counseling and testing at the time of submission of sputum for AFB [12]. The NTP in Ebonyi State phased out the 8-month anti-TB regimen (consisting of 2 months of rifampicin [R], isoniazid [H], pyrazinamide [Z] and ethambutol [E]/6 months of ethambutol and isoniazid [2RHZE/6EH]) in the 2011 cohort [12]. All adult TB patients diagnosed in 2012 were treated using the 6-month anti-tuberculosis regimen consisting of: 2-month RHZE/and 4-month RH [2RHZE/4RH]. All the patients receive community directly observed treatment short course (DOTS). All HIV-infected TB patients are offered trimethoprim/sulfamethoxazole (cotrimoxazole prophylactic treatment [CPT]) to prevent other opportunistic infections. HIV treatment follows national and WHO guidelines with antiretroviral therapy initiated between two weeks and two months of commencing anti TB treatment [12].

Data collection and analysis

Using a standardized form, data about all smear-positive TB patients treated at the participating centers were extracted. Information collected included: registration status; age; gender; residence; regimen received; and treatment outcome. The standard WHO definitions were used for TB disease classification, registration and treatment outcome categories (cured, completed treatment, failure, defaulted treatment, died and transferred out) [11,12]. TB registration status was divided into 'new' or 'previously treated'.

Statistical analyses were performed using Epi Info (Epi Info version 3.4.1; Centers for Disease Control and Prevention, Atlanta, GA, USA). Univariate analyses were performed to describe the baseline characteristics of the participants and were reported as proportions and means. Categorical groups' comparisons were performed using the Chi-square tests, and the Fisher's exact test was used for an expected cell value frequency less than five. Multivariable logistic regression analysis showed unstable models and were therefore excluded. AP value of <0.05 was considered significant.

The study was approved by the Ethics and Research Advisory Committee of the National Tuberculosis and Leprosy Control Programme, Ministry of Health, Ebonyi State.

Results

Of the 1668 TB patients registered during the study period, 985 (59%) had smear-positive pulmonary TB. Of these, 694 (70.5%) were aged $\leqslant$40 years, 602 (61.1%) were males, 707 (71.8%) were rural residents and 898 (91.2%) received care at the private facility. Also, 928 (94.2%) of the cases were registered as new cases, 470 (47.7%) were treated with the current 6-month rifampicin containing regimen, and 136 (13.8%) were HIV positive (Table 1). Overall, 797 (80.9%) of the participants were cured, 98 (9.9%) defaulted, 57 (5.8%) died, 25 (2.5%) had treatment failure, and 8 (0.8%) were transferred out.

Serial sputum AFB results of the study participants are shown in Table 2; 985 patients were sputum smear-positive at entry, and of these, 187 (19%) were smear-positive after intensive treatment with RHZE for two months, and 25 (2.5%) remained positive after 5 months of treatment. Therefore, the prevalence of treatment failure was 2.5% (proportion with a positive sputum smear after 5 months of treatment). The treatment failure rate among patients who were HIV positive was 5/131 (3.7%) compared with 20/849 (2.4%) among those that were HIV negative ($p = 0.36$).

The analysis of factors associated with treatment failure is as shown in Table 3. The predictors of treatment failure were: