Trends in treatment outcome of smear-positive pulmonary tuberculosis in Southeastern Nigeria, 1999 - 2008

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ABSTRACT

BACKGROUND: the Directly Observed Treatment Short Course (DOTS) strategy was introduced into the tuberculosis control programme of Ebonyi, Southeastern, Nigeria in 1996. The impact of the programme on the treatment outcomes for smear-positive tuberculosis has not been assessed ever since. We assessed the trends in treatment outcome for new smear-positive pulmonary tuberculosis between 1999 and 2008.
METHODS: we conducted a retrospective analysis of the Ebonyi state Ministry of Health quarterly smear-positive tuberculosis statistical returns. Patients were treated and treatment outcome categories computed according to the WHO/National Tuberculosis Control Programme's guidelines. Chi-square for trends was used to determine significance.
RESULTS: the number of smear-positive cases who registered for treatment fell from 1 361 patients in 1999 to 977 in 2008 (Trend χ^2=349; P<0.001). The follow-up smear results at month two were not available for 16% of the patients in 1999; this unavailability decreased to 1.7% in 2008. The negative conversion rate at month two increased from 77.5% in 1999 to 95.9% in 2008 (Trend χ^2=16.5; P<0.001). Treatment success rose from 74.9% in 1999 to 88.7% in 2008 (Trend χ^2=12.8; P<0.001), whilst default rate declined from 12% to 4.3% (Trend χ^2=55.6; P<0.001). Though decreasing (Trend χ^2=4.64; P=0.031), the annual death rate remained at around 5% during the study period.
CONCLUSIONS: monitoring, supervision and home visits have improved, and our DOTS programme has achieved an 85% treatment success and declining default rates. However, with the current low case notification and high mortality rates, alternative mechanisms are needed to achieve global stop-TB targets in the State.

Key words: Tuberculosis; Smear-positive; Treatment outcome; DOTS; Tuberculosis control; Nigeria

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INTRODUCTION

Tuberculosis (TB) is one of the leading infectious causes of death globally (1). According to the 2010 World Health Organization (WHO) report, in 2009, there were an estimated 9.4 million incident cases (85% of these were in Asia and sub-Saharan Africa), and the annual number

of deaths due to TB was 1.7 million, including 400 000 patients infected with HIV (1). Key challenges for TB control in Sub-Saharan Africa are poverty, weak political will, weak health systems, drug resistant TB and, in the last two decades, the HIV/AIDS pandemic (2).

Nigeria ranks fourth among the world's 22 countries with a high tuberculosis burden (1). Based on the 2009 WHO estimates, the incidence of all forms of TB in Nigeria stands at 295/100 000 population (1). The Nigerian National Tuberculosis and Leprosy Control Programme (NTBLCP) was started in 1991. Its key strategies have been early case detection and treatment in order to interrupt transmission, reduction of morbidity/mortality and prevention of TB drug resistance (3). Nigeria also adopted the Directly Observed Treatment Short Course (DOTS) strategy in 1993, and by 2008 its geographic coverage had reached 99% (3).

The DOTS strategy was introduced through the tuberculosis control programme of Ebonyi state since its creation in 1996. The State Tuberculosis Control Programme and the German Leprosy Relief Association initially introduced DOTS in only two local government areas (LGAs) followed by a systematic scale-up, introducing more public and private health facilities in urban and rural areas of other LGAs into the programme every year. Full geographic (LGA) coverage in the state was achieved in 2005.

Treatment outcome remains an important indicator for assessing the quality of a tuberculosis control program. Standardized treatment outcome categories were outlined by the WHO in order to identify the proportion of patients who are at risk of future relapse and drug resistance (4) and to give immediate suggestions to the NTBLCP as to the areas where improvements needed to be made. Although population based case notification and treatment outcome for smear-positive tuberculosis are published annually by the WHO for each country, such figures may mask regional differences in case notification rate (5) and treatment outcome.

For example, the DOTS strategy was introduced in southern Nigeria about a decade before it reached the north (6). Since the expansion of DOTS into northern Nigeria, about 65% of the total national TB case notification during 2002 to 2007 came from the region (6). This probably accounted for differences in case notification trends for tuberculosis reported recently in southeast Nigeria (5). Thus, there is a need to document regional trends in population-based treatment outcomes for tuberculosis,

but this has not yet been assessed in Nigeria. Therefore, this study aimed to assess the trends in treatment outcomes for smear-positive pulmonary tuberculosis cases notified in Ebonyi state, southeast Nigeria, between 1999 and 2008.

METHODS

Study setting

Ebonyi state is one of the 36 states of the Nigerian federation located in the southeastern geopolitical zone with an estimated population of over 2.5 million people (7). The state had a high notification rate of new TB cases, with 77/100 000 in 2009 (5). In addition, it has 13 LGAs with 130 health care facilities currently providing DOTS services. All treatment units have standard unit registers from the NTBLCP. Tuberculosis and Leprosy control activities in each LGA are coordinated by a Tuberculosis and Leprosy control supervisor who is also responsible for monitoring, supervision, home visits and keeping up-to-date record of activities. These supervisors also provide a monthly report to the State Tuberculosis and Leprosy control officer who undertakes monthly monitoring and supervision, pools and analyses data from the state, and disseminates reports to the Federal Ministry of Health.

Design and data collection

We undertook a retrospective analysis of the trends in treatment outcome of new smear-positive pulmonary TB cases registered in all the LGAs in the state of Ebonyi between 1999 and 2008. Quarterly TB statistical returns deposited at the Ebonyi State Ministry of Health during the study period were reviewed.

Definitions

The NTBLCP uses the WHO-recommended recording/reporting guidelines and forms for the monitoring and evaluation of programme activities (3). Pulmonary tuberculosis (PTB) suspects submit three sputum samples (spot-morning-spot). Smears are graded according to the guidelines of the International Union against Tuberculosis and Lung Disease adopted in the National Workers Manual (3). Patients with at least two positive smears are considered smear-positive. Smear-positive patients

are treated for eight months (2-month intensive and 6-month continuation).

The treatment outcome was divided into seven categories according to WHO/NTBLCP guidelines (3). These categories were: *cured* (finished treatment with negative bacteriology result at the end of treatment), *completed treatment* (finished treatment, but without bacteriology result at the end of treatment), *failure* (remaining smear-positive at five months despite correct intake of medication), *defaulted treatment* (patients who interrupted their treatment for two consecutive months or more after registration), *died* (patients who died from any cause during the course of treatment), *transferred out* (patients whose treatment results are unknown due to transfer to another health facility) and *not evaluated* (any patient who was notified but the treatment outcome was not known because he was not registered for treatment). A successfully treated patient is one who was categorized as cured or completed treatment.

Statistical analysis

The collected data were recorded and analyzed using Microsoft Excel Templates for the analysis and presentation of tuberculosis epidemiologic data provided by the WHO-TB Epidemiology and Surveillance Virtual Workshop (8). Further statistical analyses were performed using Epi Info 3.4.1 software. Chi-square test for linear trends was used to assess for significant changes in trends of treatment outcome variables over time and Pearson's product-moment correlation coefficient was used to assess for the linear correlation between continuous variables.

Ethical Approval

Ethical approval was not required as the survey was based on retrospective data and the report is part of standard public health practice. Permission to publish this report was granted by the National Tuberculosis and Leprosy Control Programme office, Ministry of Health, Ebonyi State, Nigeria.

RESULTS

12 031 new patients with smear-positive tuberculosis were registered for treatment between 1999 and 2008. Although this number varied during the study period, the number of smear-positive PTB cases who registered for treatment fell from 1 361 patients in 1999 to 977 in 2008 and the decreasing trend was statistically significant (Trend χ^2=349; P<0.001). The follow-up smear results at month 2 were not available for 16% of the patients in 1999; this "unavailable" proportion had decreased to 1.7% by 2008 (Trend χ^2=16.6; P<0.001) (Table 1). A significant increase in trend (Trend χ^2=16.5; P<0.001) was also observed for the negative conversion rate at month 2 for patients who completed a follow-up smear testing – this total increased from 77.5% in 1999 to 95.9% in 2008. There was a strong correlation between this value and treatment success rate (R^2=0.45).

Overall, the average treatment success rate recorded in the State during the study period was 80%. The treatment success rate increased from 74.9% in 1999 to 88.7% in 2008, though treatment completion contributed less than an average of 4% to this proportion annually (Table 1). The increase in treatment success rate over the study period was statistically significant (Trend χ^2=12.8; P<0.001). In Figure 1, we compared the treatment success rate of Ebonyi State compared to Nigerian national figures. During the period from 1999 to 2008, smear-positive treatment success rate for Nigeria increased from 75% to 78%. Comparing Ebonyi to Nigeria, the difference in the trend of treatment success rate over the period was of clinical importance but not statistically significant (Trend χ^2=0.94; P=0.33).

Furthermore, a significant decrease in trend (Trend χ^2=55.6; P<0.001) was observed for the default rate – decreasing from 12% in 1999 to 4.3% in 2008 (Table 1). The treatment failure rate, which was initially 0.8% in 1999, increased gradually to reach a peak of 2.1% between 2001 and 2004 and then subsequently leveled-off at 1.1% in 2008. However, this trend was not statistically significant (Trend χ^2=0.232; P=0.63). Also, the average proportion of registered smear-positive pulmonary TB patients who died annually during the study period was 5%. Annual death rate ranged from 3.4% to 6.2% during the study period but, overall, a significant decrease in mortality trend occurred (Trend χ^2=4.64; P=0.031) (Table 1).

DISCUSSION

The results of our study show that there has been an increase in treatment success for smear-positive TB cases in Ebonyi state, in parallel to

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FIG. 1

TRENDS IN TREATMENT SUCCESS RATE FOR SMEAR-POSITIVE PULMONARY TUBERCULOSIS IN EBONYI STATE AND NIGERIA
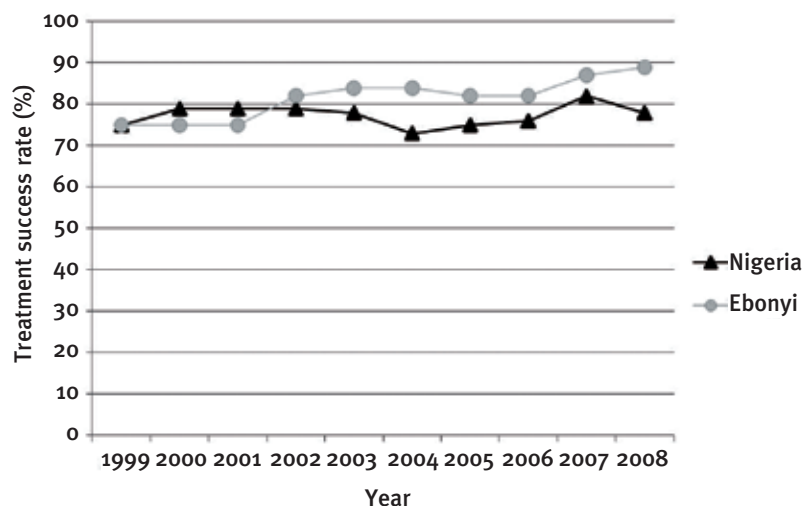
the expansion and the decentralization of the DOTS to rural public and private health facilities. Treatment with short course chemotherapy (SCC) increased from 1999 to 2008 partly due to the expansion of DOTS services, and partly due to the commitment of the NTBLCP of Ebonyi state to providing quality DOTS services to rural districts. However, trends in default and treatment failure showed inconsistencies over the years.

The proportion of smear-positive patients with a negative smear result after two months of anti-tuberculosis treatment is a known predictor of a favourable treatment outcome (9). Except for 2005, with data not available for almost half of the patients, the proportion of patients who did not have a sputum test result after two months of treatment decreased consistently from 16.9% in 1999 to 1.7% in 2008. Concurrently, the smear conversion rate increased by 18%, and this testifies the positive role that supervised DOTS services have played, using SCC in the rapid clearance of acid-fast bacilli during the first two months of treatment. Similar findings have been observed in other settings (10-12).

The treatment success rate showed a significant increase, surpassing the 85% target in 2007. The 2008 treatment success in this study (88.7%) was slightly higher than the average 87% observed among the twenty-two high tuberculosis-burden countries (1). This agrees with the finding of previous studies that the DOTS strategy works well in poor-resource settings with low overall

health coverage (10, 11). Better monitoring and supervision, increased coverage by SCC, strict DOTS, improved access to care, improved patient follow-up and overall better recording systems with the introduction of DOTS were factors that most likely played a significant role in improving the treatment outcomes in our region. Some of these factors have also been found to play a role elsewhere (10, 12).

The failure rate was below 1% for new smear-positive cases treated by SCC before 2000. Increased failure rate may be due to co-existing HIV infection and primary drug resistance. In parallel to the increase in incidence of HIV in Nigeria, the failure rate has also increased, reaching and maintaining a peak of 2.1% between 2001 and 2004, during which period HIV prevalence in Nigeria also reached a peak of 5.8% (13). Nevertheless, the current prevalence of HIV is 3.6% (14), and with improved case finding of TB among HIV infected patients and vice versa, as well as improved case holding by the NTBLCP, the failure rate has leveled-off to 1.1% currently. The low failure rate may have contributed to the overall low prevalence of multidrug-resistant tuberculosis (MDR-TB) in Nigeria, which was 1.8% for all new and 7.7% for all previously treated cases (1). Furthermore, we found that the death rate in smear-positive pulmonary tuberculosis patients remained at around 5% across the years. This suggests that the NTBLCP should focus on the reduction of case fatalities as the proportion

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TABLE 1

TREATMENT AND FOLLOW-UP OF NEW SMEAR-POSITIVE COHORT NOTIFIED THROUGH THE DOTS STRATEGY IN EBONYI SOUTHEASTERN NIGERIA, 1999 - 2008										
YEAR	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
NOTIFIED NUMBER (N)	1 429	1 496	1 341	1 348	1 312	1 247	1 193	1 105	781	927
SPUTUM TESTED AT MONTH 2, n (%)										
POSITIVE	93 (6.5)	102 (6.8)	93 (6.9)	121 (9.0)	149 (11.4)	130 (10.4)	70 (5.9)	85 (7.7)	25 (3.2)	21 (2.3)
NEGATIVE	1 108 (77.5)	1141 (76.3)	1 119 (83.5)	1 098 (81.5)	1 088 (82.9)	1 082 (86.8)	550 (46.1)	945 (85.5)	710 (90.2)	889 (95.9)
NOT AVAILABLE	228 (16.0)	253 (16.9)	129 (9.6)	129 (9.5)	75 (5.7)	35 (2.8)	573 (48.0)	75 (6.8)	52 (6.6)	17 (1.7)
TREATMENT OUTCOME, n (%)										
REGISTERED NUMBER[a]	1 361 (95.2)	1 419 (94.9)	1 289 (96.1)	1 335 (99.0)	1 328 (101.2)	1 247 (100.0)	1 183 (99.2)	1 105 (100.0)	787 (100.8)	977 (105.4)
CURED	1 033 (72.3)	1 090 (72.9)	990 (73.8)	1 079 (80.0)	1 084 (81.6)	1 010 (81.0)	965 (81)	884 (80)	664 (84.4)	835 (85.5)
TREATMENT COMPLETED	37 (2.6)	29 (1.9)	18 (1.3)	21 (1.6)	33 (2.5)	36 (2.9)	12 (1.0)	20 (1.8)	22 (2.8)	31 (3.2)
DIED	80 (5.6)	51 (3.4)	51 (3.8)	72 (5.3)	64 (4.8)	54 (4.3)	73 (6.1)	58 (5.3)	49 (6.2)	49 (5.0)
FAILED	12 (0.8)	14 (0.9)	28 (2.1)	28 (2.1)	21 (1.6)	26 (2.1)	16 (1.3)	17 (1.5)	10 (1.3)	11 (1.1)
DEFAULTED	171 (12.0)	173 (11.6)	174 (13.0)	128 (9.5)	114 (8.6)	118 (9.5)	115 (9.6)	123 (11.1)	35 (4.5)	42 (4.3)
TRANSFERRED OUT	28 (2.0)	62 (4.1)	28 (2.1)	7 (0.5)	12 (0.9)	3 (0.2)	2 (0.2)	3 (0.3)	7 (0.8)	9 (0.9)
NOT EVALUATED	68 (4.7)	77 (5.2)	52 (3.9)	13 (1.0)	0 (0)	0 (0)	10 (0.8)	0 (0)	0 (0)	0 (0)
TREATMENT SUCCESS RATE (%)	74.9	74.8	75.1	81.6	84.1	83.9	82.0	81.8	87.2	88.7

Cohort: cases diagnosed during a year and treated/followed-up through the following year.

a = for each year, if the number of patients registered was greater than the number notified, this was used as the denominator for calculating treatment outcome categories. If the number registered was smaller than the number notified, then the number notified was used as the denominator.

is declining slowly despite all the efforts made by the programme.

The default rate in this study was high initially but fell to 4.3% in 2008. This compares with a default rate of 6% observed nationally in the same year (1). Our study suggests that there is a need to sustain low default rates in our TB control programmes. The current reduction in

default in our programme occurred due to a new approach that was started in 2006, where patients who interrupted treatment within two weeks are visited at home, counseled and re-educated about the pitfalls of abandoning treatment by the LGA TB control supervisors. In other settings, counseling (15), home visits and motivation (16), and health education (17) have been used

successfully as interventions to reduce default rates in tuberculosis patients.

Since our study was based on the quarterly reports provided by the NTBLCP office in Ebonyi State, we cannot exclude the possibility of poor recording and reporting systems that may produce discrepancies between the notified and registered cases. However, this has been reduced via several recording and reporting training sessions organized by the NTBLCP for staff working in the public and private health sectors. Also, since not all cases that were notified actually registered for treatment within the same year, this may also have accounted for differences between cases notified and registered.

Another important limitation of this study is the lack of information on HIV co-infection rates and smear-negative treatment results. Data on HIV rates were not reported because such information was not routinely collected during the study period and because TB/HIV collaborative activities have only been recently started in the State. Furthermore, data on smear-negative TB treatment results were not included because, using the National TB Treatment guidelines, the diagnosis of smear-negative TB is subjective and treatment can go on for as long as 24 months. We believe that the evaluation of treatment outcome of smear-positive TB cases would be a more objective basis for assessing the performance of our TB control program aimed at managing susceptible PTB in our region.

In conclusion, through improved monitoring, supervision, home visits, better reporting systems, and the introduction and expansion of DOTS in Ebonyi, southeast Nigeria, the program's conditions has led to a significant increase in treatment success rate for smear-positive tuberculosis – over 10% better than national figures and surpassing the 85% target. The success was consolidated by declining default rates. However, a high proportion of patients consistently died across all the study years. This is a serious public health problem that needs to be addressed urgently. There is also the need to further decrease default and failure rates, as well as to sustain progress made in order to achieve the current global target of eliminating tuberculosis.

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