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Eight Months vs Six Months Anti-TB Regimen in the Treatment of Newly Diagnosed Pulmonary Tuberculosis Patients in Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Author OJD designed the study, wrote the protocol, and wrote the first draft of the manuscript. Author OAA was involved in data analysis and writing of the manuscript. Authors HA, MG and OO were involved in data collection, managed the literature searches and proof reading of the manuscript. Author GA wrote the introduction. All authors read and approved the final manuscript.

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ABSTRACT

Background: The eight month's treatment regimen (2RHZE/6EH) was used by the Nigerian National TB and Leprosy Control Programme for the management of tuberculosis cases since 2003 when they commenced operation until October 2010 when the six month's treatment regimen

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(2RHZE/4RH) was introduced. This study compared the treatment outcomes of patients managed with eight and six month's treatment regimen between October 2009 and December 2011.
Methods: A desk review was carried out on the programme data of the Lagos State Tuberculosis and Leprosy Control Programme (LSTBLCP). The treatment outcomes of new smear positive TB patients managed between October 2009 and September 2010 (the eight month's treatment regimen period) and January to December 2011 (six month's treatment regimen period) were compared using Epi Info 2007 statistical software.
Results: A total of 4249 and 4167 smear positive TB patients were registered during the eight and six month's treatment regimen period respectively. The prevalence of HIV among TB patients was significantly higher (14.4%) during the eight month's treatment regime period compared with the six month's (12.1%) treatment regime period (P = .02). The cure rate of patients managed during the eight month's treatment regimen period was significantly lower (67.2%) and defaulter rate significantly higher (16.7%) compared with the cure (73.9%) and defaulter rates (12.2%) of patients managed during the six month's treatment regimen period (P<.001). However the failure and death rates of patients managed during the eight and six month's treatment regimen periods were comparable (P>.05). Among TB/HIV co-infected patients, the death rate was significantly higher among patients managed during the six month's regimen period and the default rate was significantly higher in patients managed during the eight month's treatment regimen period (p<.05).
Conclusion: Patients had better treatment outcomes during the six month's treatment regimen period in Lagos State. Sustaining these gains will be essential in reaching the national and global targets.

Keywords: Tuberculosis; effectiveness; treatment; anti-TB regimen; Nigeria.

1. INTRODUCTION

The introduction of the directly observed treatment short course (DOTs) for the treatment of tuberculosis by the World Health Organization (WHO) was adopted by almost all national tuberculosis programmes. The short course regimen includes two months intensive phase of four drugs namely rifampicin, isoniazid, pyrazinamide and ethambutol and six months continuation phase of two drugs namely thiacetazone and isoniazid for newly diagnosed smear positive tuberculosis patients [1]. However, because of the HIV epidemic, the treatment regimen for TB was reviewed in the last decade resulting in some adjustment to the short course regimen [2]. Thiacetazone was replaced with ethambutol in the continuation phase of treatment due to severe complications observed in people living with HIV [3]. In addition, streptomycin was removed from the regimen for new patients to reduce the risk of HIV transmission. Thus in the last decade, the eight months treatment regimen consisting of rifampicin, isoniazid, pyrazinamide and ethambutol (RHZE) for two months and six months continuation phase of ethambutol and isoniazid (EH) was practiced in many countries including Nigeria [4]. The Nigerian national tuberculosis and leprosy programme (NTBLCP) piloted the six month's rifampicin based regimen which consists of two months intensive phase of rifampicin, isoniazid, pyrazinamide and ethambutol (RHZE) and four months continuation phase of rifampicin and isoniazid (RH) for treatment for new TB patients in 2010. This study compared the treatment outcomes of patients managed based on 8 months treatment regimen of 2RHZE/6EH and six months treatment regimen of 2RHZE/4RH.

2. METHODOLOGY

The study was a retrospective review of records of patients diagnosed as new smear positive pulmonary TB patients who presented at TB treatment centers in Lagos state. The Lagos state TB and Leprosy Control Programme (LSTBLCP) commenced operation in 2003 with support from partners such as USAID, WHO, CIDA and IUATLD. Until 2010 when the six months treatment regimen was introduced, patients were managed using the eight months treatment regimen. All smear positive TB patients during the eight month's treatment period received eight months of anti-TB drugs which include two months of rifampicin, isoniazid, ethambutol and pyrazinamide (2RHZE) in fixed dose combination followed by six months of ethambutol and isoniazid (6EH) also as fixed dose combination. During the six month's treatment regimen period, all smear positive TB

patients were commenced on two months rifampicin, isoniazid, ethambutol and pyrazinamide (2RHZE) followed by 4 months of rifampicin and isoniazid (4RH) in fixed dose combination. Follow up smear microscopy was conducted for patients during the eight month's treatment regimen period at the end of second, fifth and seventh month of treatment while TB patients registered during the six month's treatment regimen period were followed up with sputum AFB microscopy at the end of the second, fifth and sixth month of treatment. During the six month's treatment regimen period, treatment supporters (usually family members) were selected by the patients to observe their treatment and also assist in refilling of anti-TB drugs at the DOTS facilities.

For patients without treatment supporter, drug use was directly observed during the two months intensive phase by health care workers at the selected DOTS facilities, however during the continuation phase; the patients were given one month appointment. For patients with treatment supporter, drugs were given to cover for two weeks to the patient or the treatment supporter who also supervised the treatment at home and charted the drug intake on a card. Empty drug blisters and cards used for charting drug intake were presented at the DOTS facilities before drug refill.

Socio-demographic data were retrieved from the TB facility register. Patients were categorized into one of the following treatment outcomes in line with the National TB and leprosy control guidelines. These are

a). Cured: This was the proportion of patients among smear positive patients that complete treatment and had at least two negative smears sputum AFB examinations with an interval of at least one month, one of which should be obtained at the end of treatment.
b). Treatment completed: This was the proportion of patients that completed treatment but sputum examination results are not available.
c). Died: The proportion of patients that died before completion of treatment.
d). Default: This was the proportion of patients that did not take drugs for two consecutive months or more.
e). Treatment failure: This was the proportion of patients who are still sputum smear positive at five months or more after the commencement of chemotherapy, or who interrupted treatment for more than 2 months after completing one month of chemotherapy, returned to treatment and are found to be smear positive
f). Transferred out: This was the proportion recorded that moved out of the health facility catchment area.
g). Treatment success: Defined as the sum of the cases that were cured and that completed treatment.

Data analysis was performed with the use of Epi Info 2007 statistical software. The percentages mean and standard deviation of numerical variables were calculated. Chi square was used to compare categorical variables. The level of significance was set at $p<.05$.

3. RESULTS

A total of 4249 and 4167 smear positive TB patients were registered during the eight and six month's treatment regimen period respectively. In the eight month's treatment regime group there were 2495 males and 1754 females while in the six months treatment group, there were 2471 males and 1696 females. The majority of the patients managed were in the age group 25-40 years, while about 2.0% were below 15 years as shown in Table 1. The prevalence of HIV among the TB patients was significantly higher (14.4%) during the eight month's treatment regimen period compared with 12.1% during the six month's treatment regimen period ($P = .02$) (Table 2). The treatment outcome for the period under review is shown in Table 3. Comparing the treatment outcomes of patients managed during the eight month's treatment regimen with those managed during the six month's treatment regimen, there was a significant increase in the proportion of patients with treatment success from 73.0% to 80.4% and also a significant reduction in the default rate (from 16.7% to 12.2%) ($P<.001$). However, there was no significant difference in treatment failure (2.2% vs. 1.7%) and death rates (3.1% % vs. 3.3%) in patients managed during the eight and six month's treatment regimen periods respectively ($P>.05$).

Similarly among TB/HIV co-infected patients, there was a significant reduction in the default rate (16.75 vs. 11.3%) in patients managed during the eight months and six month's

treatment regimen period respectively. The death rate was significantly higher in patients managed with the six month's treatment regimen compared with those managed with the eight month's treatment regimen. There was an increase in the treatment success rate in patients with TB/HIV managed during the eight month's treatment regimen period (69.1%) compared with those managed during the six month's treatment regimen period (74.0%) (*P* =0.07) as shown in Table 4.

Table 1. Age distribution of respondents treated with six and eight month's anti-TB treatment regimen

Age (years)	Eight months treatment regimen freq (%)	Six months treatment regimen freq (%)
<15	83 (1.9)	84 (1.9)
15 – 24	989 (23.3)	970 (23.2)
25 – 34	1495 (35.2)	1563 (37.5)
35 – 44	1980 (46.6)	823 (19.8)
45 – 54	749 (17.6)	462 (11.1)
55 – 64	358 (8.4)	178 (4.3)
>65	90 (2.1)	87 (2.1)
Total	4249 (100.0)	4167 (100.0)

Table 2. HIV prevalence among TB patients in the six and eight months treatment regimen category

HIV status	Eight months treatment regimen freq (%)	Six months treatment regimen freq (%)	χ^2	p
Positive	612 (14.4)	530 (12.7)	4.95	0.024
Negative	3637 (85.6)	3637 (87.3)		
Total	4249 (100.0)	4167 (100.0)		

Table 3. Treatment outcome of patients on six and eight months anti-TB treatment regimen category

Treatment outcomes	Eight months regimen n = 4249 (%)	Six months regimen n = 4167 (%)	χ2	p
Cured	2854 (67.2)	3079 (73.9)	45.70	<0.001
Treatment completed	331 (7.8)	270 (6.5)	5.45	0.020
Died	134 (3.1)	139 (3.3)	0.22	0.637
Treatment failure	96 (2.2)	72 (1.7)	3.04	0.081
Default	708 (16.7)	508 (12.2)	34.03	<0.001
Transferred out	126 (3.0)	99 (2.4)	2.81	0.094
Treatment success	3185 (75.0)	3349 (80.4)	35.48	<0.001

Table 4. Treatment outcome among TB/HIV positive co-infected patients on six and eight months anti-TB treatment regimen category

Treatment outcomes	Eight months regimen n = 612 (%)	Six months regimen n = 530 (%)	χ2	p
Cured	382 (62.4)	370 (69.8)	6.90	0.009
Treatment completed	41 (6.7)	22 (4.2)	3.54	0.060
Died	43 (7.0)	56 (10.6)	4.50	0.034
Treatment failure	11 (1.8)	8 (1.5)	0.14	0.704
Default	102 (16.7)	60 (11.3)	56.67	0.010
Transferred out	33 (5.4)	14 (2.6)	5.45	0.020
Treatment success	423 (69.1)	392 (74.0)	3.26	0.071

4. DISCUSSION

This study was designed to compare the treatment outcomes of the eight month's regimen and the six month's treatment regimen under programmatic condition. The study showed that the treatment outcomes during the six month's treatment regimen period were better than the eight month's treatment regimen among new smear positive TB patients. The treatment success rate was significantly higher while the default rate and the treatment failure rate were significantly lower among patients that received the six month's treatment regimen compared with those that were managed with the eight month's treatment regimen. Similar findings of higher cure and lower treatment failure rates were observed in Brazil [5].

Studies have shown that ethambutol has antagonistic effect on the bactericidal activities of other anti-tuberculous drugs and also antagonizes the sterility activity during the first two weeks of anti TB treatment [6,7]. The addition of ethambutol to SHRZ (streptomycin, isoniazid, rifampicin and pyrazinamide) and its substitution for streptomycin in a four drug regimen has been found to increase the relapse rate though the difference was not statistically significant [8,9]. This may account for the poorer treatment outcomes observed during the eight month's treatment regimen compared with the six month's treatment regimen period. From a programmatic point of view, the shorter treatment duration of the six month's treatment regimen compared with the eight month's treatment regimen and the introduction of treatment supporter during the six month's treatment regimen period may be responsible for the decline in the default rate in patients managed during the six months treatment regimen period.

Contrary to an earlier study that reported higher mortality which was attributed to HIV infection in patients that received the eight month treatment regimen, our study showed that the death rate in patients managed during the eight and six month's treatment regimen periods were comparable [1].

Among TB patients with HIV infection, a significantly higher cure rate and lower default rate was observed in those managed during the six month's treatment regimen period. However, the treatment failure rate was similar in those managed during the eight and six month's treatment regimen periods. Similar findings have been reported in other studies [7,10-13]. Contrary to findings from similar studies [10-13], there was a significantly higher death rate among patients managed during the six month's treatment regimen period compared with those managed during the eight month's treatment regimen period. The reason for this difference is not known.

The study is not without limitation. The study was a before and after design in which the patients were not randomized to each of the treatment regimen category. The purpose of this study however was to compare the treatment outcomes of patients managed during the two treatment regimen under programmatic condition.

5. CONCLUSION

There was higher cure rate and lower default rate in patients managed during the six month's anti-TB treatment regimen compared with the eight month's regimen. Sustaining these gains will be essential in reaching the national and global targets.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Data for this study were retrieved from secondary data routinely collected by the Lagos State TB control programme and as such no ethical clearance was obtained.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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