ABSTRACT

Objective: The World Health Organisation marked ten years of implementation of Directly Observed Treatment short course (DOTS). One key factor affecting the success of the DOTS strategy is the rising HIV prevalence among TB patients. The study was embarked upon to compare the treatment outcome of TB/HIV positive and TB/HIV negative patients in Sagamu, Nigeria.

Methods: A prospective study of 353 smear positive TB patients aged 15 years and above who were registered for 8 months anti-tuberculosis (DOTS) therapy between January 2001 and December 2003 at the Olabisi Onabanjo University Teaching Hospital, Sagamu, Nigeria. Treatment outcome indicators of cure, default, transfer to another district and death were assessed in relation to the HIV status of the patients.

Results: There were 353 eligible patients of which 58 (16.4%) were HIV positive. The clinical symptoms and signs of TB were similar in both HIV positive and negative TB patients. The cure rate was 76.8%, patients. The cure rate was significantly lower in HIV infected compared with non-HIV infected TB patients (60.3% v 80.0%; p=0.0001). However, among survivors it was not significant (71.4% v 82.5%; p=0.07). Overall mortality was 5.1% which was significantly higher in HIV positive compared to HIV negative TB patients (15.5% v 3.1%; p=0.0007). On the whole, 17% defaulted treatment and 1.1% failed treatment. These were however not significantly related to HIV status.

Conclusion: The cure rate in this study is still lower than the recommended 85% target by the WHO. Mortality rate in TB/HIV positive patients was higher than in HIV negative patients. The option of a community based TB programme using volunteers or family members to supervise administration of anti-TB drugs so as to ensure adherence to TB treatment may be considered.

KEYWORDS: HIV; Tuberculosis; Outcome; Nigeria.

INTRODUCTION

The World Health Organisation (WHO) marked ten years of successful Directly Observed Treatment Short course (DOTS) implementation for the control of tuberculosis in the year 2003. The DOTS strategy aims at curing the individual patient, interrupts transmission of TB to other persons, and preventing the emergence of drug-resistant TB. In spite of the proven efficacy of this strategy only 27% of the world's TB patients are currently receiving DOTS. The WHO set a global target of 85% cure rate and 70% case detection rate for TB control. In pursuance of this objective the Federal Ministry of Health through the National tuberculosis and leprosy control programme (NTBLCP) introduced the DOTS strategy for TB control in 1994. Currently, a total of 432 of the 774 local government areas are implementing the DOTS programme in Nigeria through substantial donor support.

One of the major challenges facing TB control globally is the HIV epidemic. Presently up to 70% of patients with sputum positive pulmonary tuberculosis are HIV positive in some countries in Sub Saharan Africa. The increasing frequency of TB/HIV co-infection has had considerable impact on TB control programmes in sub-Saharan Africa making the achievement of the 85% cure rate a big challenge. We have also observed an increasing prevalence of HIV infection among TB patients receiving the DOTS treatment programme in our centre. The study was embarked upon to compare the treatment outcome of TB/HIV positive and TB/HIV negative patients in Sagamu within the current routine DOTS treatment programme for TB control in Sagamu, Nigeria.

MATERIALS AND METHODS

Study Population and Setting

This is a prospective study of patients admitted into the DOTS treatment programme at the department of community medicine Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu. The study participants were recruited between January 2001 and December 2003. The study was carried out in Sagamu Local Government area in Ogun State. The town is a semi-urban area with an estimated population of 200,000 people. It is located about 50km from Lagos and Ibadan, Nigeria. The German Leprosy Relief Association (GLRA) was responsible for the provision of

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free drugs for the programme. The centre provides DOTS for the treatment of tuberculosis on out-patient basis.

**TB Control Programme**

All tuberculosis patients who satisfied the inclusion criteria which consist of clinical symptoms suggestive of pulmonary tuberculosis such as cough, fever, haemoptysis, weight loss and night sweats; positive sputum smear for acid and alcohol fast bacilli by the Ziehl Neelson staining method, at least two times in line with the WHO recommendation; new cases (i.e. a patient who has never used anti-TB drugs before or used it for less than a month); adult patients aged 15 years and above: were included in the study. All patients were commenced on Short Course Chemotherapy (SCC) for a total duration of eight months. The SCC consists of two phases namely the intensive and the continuation phases. Four drugs namely, rifampicin, ethambutol, isoniazid and pyrazinamide were administered daily under supervision by a nurse during the intensive phase of two months. Patients were followed up monthly as out-patients for six months on ethambutol and isoniazid during the continuation phase. Any patient who failed to receive his/her treatment as scheduled was traced home by Community Health Extension Workers.

**Laboratory Methods**

All patients enrolled in the study were offered voluntary counselling and confidential testing for HIV screening by trained counsellors. The HIV antibody screening was done using two methods namely the immunocomb II HIV 1&2 Bispot test kit (Orgenics, France) and the Capillus HIV-1/HIV-2 kit(Cambridge diagnostics, Ireland). A positive test is considered only when the blood sample is positive for the two test kits. Sputum microscopic examination for Acid Fast Baccilli (AFB) was carried out at end of the 2nd, 5th and 8th months of chemotherapy.

**Treatment Outcomes**

The treatment outcome categories defined in the study was in line with the NTBLCP guidelines. These include:

**Died:** death during TB treatment.
**Cured:** proven sputum smear negative after 8 months of therapy.
**Default:** failed to collect medication for more than 2 consecutive months after the date of the last attendance during the course of treatment.
**Treatment failure:** Sputum smear positive at five months or more after the commencement of anti-TB chemotherapy.

**Ethical approval**

The approval for this study was obtained from the OOUTH ethical committee for approval before the commencement of the project. Verbal informed consent was obtained from each patient before inclusion in the study.

**Data analysis**

Data analysis was done using standard statistical procedures with Epi info 2002 statistical soft wares. Differences between data were considered significant at P = 0.05. The differences between categorical variables were tested by Chi squared analysis. Survival analytical techniques were used to examine the effect of HIV sero-positivity on death rate. For analysis of death rate, survival rate curve was created to compare HIV positive and negative patients using the method of KAPLAN-MEIER (1958). Cox proportional hazards regression was used to calculate the hazards ratio. Confidence interval at the 95% level was determined and statistical significance was at the 5% level.

**RESULTS**

Table I presents the socio-demographic characteristics of TB patients by their HIV status. A total of 353 sputum positive pulmonary TB patients were enrolled into the study. The male: female ratio was 1:0.99. Majority of the participants in the study had secondary school education and were Christians. Fifty-eight patients tested HIV positive (16.4%). In all, 24 men (41.4%) were HIV positive compared with 34 women (58.6%), the association was not statistically significant (p =0.13). The mean age of the HIV positive and negative men were similar (32.3 ±8.4 and 32.57 ± 13.7; p= 0.93). The mean age of HIV positive women was similar to HIV negative women (32.4±8.4 v 30.8±12.3;p=0.48). The mean weight at presentation was similar between HIV positive and HIV negative patients (48.8±7.1kg v 50.6±9.0kg;p=0.16).

Table II presents the symptoms of tuberculosis in relation to the HIV status. There was no significant difference in the distribution of clinical symptoms of TB such as cough, fever, weight loss, haemoptysis and chest pain in relation to HIV status. Table III shows the treatment outcome in the patients under study according to HIV status. The overall cure rate was 76.8%.There was a strong association between HIV status and cure rate (60.3% v 80.0%;p=0.0001). However among survivors at the end of treatment the cure rate was no longer significantly
related to the HIV status (71.4% v 82.9%; p=0.07).

Figure 1 shows the age distribution of the study population according to their HIV status. Eighty-one percent of HIV positive and 67.8% of HIV negative TB patients were in the age group 20-39 years while the least frequency was in the age group of =60 years which consist of 1.7% of HIV positive and 7.1% of HIV negative TB patients.

Overall, 60 (16.7%) TB patients did not complete treatment. This was not related to their HIV status (22.4% v 15.9%; p=0.22). Forty (66.7%) were men while 20 (33.3%) were women. There was no significant age difference between HIV positive and negative patients who defaulted treatment (p=0.49). Four patients (1.1%) experienced failure of TB treatment, one (1.7%) HIV positive and three (1.0%) HIV negative the relationship was not significant.

Overall 18 (5.1%) patients died during treatment. Mortality was significantly higher in HIV positive compared to HIV negative TB patients (15.5% v 3.1%; p=0.00007). HIV positive patients who died during treatment were significantly younger than HIV negative patients that died (30.8±7.1yrs v 50.3±19.7yrs; p=0.01). HIV positive patients who died were of similar age to the HIV positive patients who survived (30.78±7.14yrs v 32.31±8.5yrs). There was no significant age difference between HIV negative patients who died and those who survived. After 8 months of follow-up, 71.4% of HIV positive and 82.5% of HIV negative tuberculosis patients were still alive.

The cure rate of 76.8% observed in this study is below the 85% recommended by the World Health Organisation. Similar studies have documented cure rates of between 80-85% 11-13. In many of the studies with high success rate, several reasons such as the widespread use of voluntary lay supervisors to administer DOTS and the use of incentives to patients may have contributed to the high rates of treatment completion 12,14,15. However, the cure rate was higher than the 43.7% reported in a hospital based study in Northern Nigeria 16. The disparity could be due to the late presentation of patients, fee charged for diagnosis and drug therapy and the absence of DOTS in the latter
study. This underscores the importance of the DOTS strategy in the control of tuberculosis in Nigeria. There is therefore a need for the decentralisation of TB treatment so that people infected with TB will have access to DOTS. Unlike previous studies however, the cure rate was significantly related to HIV positive status. The finding is similar to what was reported in South Africa gold miners17. HIV positive status is still a major factor contributing to the low level of treatment success in Nigeria.

It was observed that case fatality rate was higher in HIV positive patients compared to HIV negative patients. This is consistent with similar studies conducted in Africa18-20. The cause of death could not be immediately ascertained because most of the patients that died during the study period died at home. This was mainly due to inability to afford hospital admission fee. Other studies have shown that the increased mortality during TB treatment was as a result of other bacterial infections12,21 and the severe immunosuppression22 experienced by these patients before commencement of treatment. Hence some African researchers have advocated the use of co-trimoxazole prophylaxis to coinfected patients during TB treatment to reduce mortality and improve survival.23 Also, concurrent administration of antiretroviral and anti-TB treatment in patients who meet criteria for the initiation of antiretroviral therapy have been associated with improved survival in TB/HIV coinfected patients24.

The rate of default from treatment by the patients in this study was 17.0%. Default from treatment was higher in TB/HIV coinfected patients though the relationship was not statistically significant. We observed some reasons for default in this study. HIV patients who are severely ill tend to return to their home town to receive care and support from their extended family members. Secondly, some of the HIV patients leave the area to consult traditional and spiritual healers who advertise their infallible ability to cure HIV infection. Also, patients who were seriously ill could not come to collect their drugs personally and had no alternative arrangements available under the present government programme. Furthermore issues of stigma and discrimination forced some HIV positive patients to relocate especially those with HIV wasting syndrome and other obvious HIV related symptoms. Lastly, incorrect contact addresses or names made it extremely difficult to trace some of the patients who defaulted. The issues of discrimination and stigmatisation of HIV patients need to be addressed so as to ensure adherence to their TB treatment to improve survival. Family members can be used to as treatment partners to administer and monitor treatment especially when such patients are too ill and cannot come to collect their drugs personally. The provision of adequate logistic support to adequately trace defaulting patients is important to ensure success of the programme.

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