The impact of HIV syndromes on the treatment of TB cases in Gombe State, Nigeria

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Abstract

Tuberculosis (TB) is the leading cause of death among people living with HIV/AIDS worldwide. HIV fuels the TB epidemic in populations such as in Nigeria where there is overlap between those infected with HIV and those infected with *Mycobacterium tuberculosis*. To address the enormous challenges posed by the dual TB/HIV infection, the Nigerian National Tuberculosis and Leprosy Control Programme (NTBLCP) began collaborative TB/HIV services in Gombe State with some other selected states in 2006. The study looked at 300 new sputum smear-positive acetate-free biofiltration (AFB) patients that had tested positive to HIV screening between diagnosis and second month of follow-up, and were treated between January and December 2006 in the Gombe State TB control programme. The control for the study came from the same cohort of January to December 2006 of new sputum smear-positive AFB patients (595) who had tested negative to HIV screening. The cohort analysis looked at the HIV sero-prevalence and the treatment outcomes: cure rate, failure rate, death rate, default rate, and transfer out rate among new smear pulmonary tuberculosis (PTB) patients that are dually infected with HIV and TB as compared to those not dually infected. The majority of HIV-positive and HIV-negative PTB patients studied were aged 39 years and below. There was no statistically significant difference between the mean age of patients with co-infection and those without co-infection. The majority of the co-infected patients were aged up to 30 years. There was a statistically significant difference in the mean age of males and females. Of the 300 HIV co-infected patients in the study population that were HIV positive, males accounted for 58.3% compared with 41.7% females. This was not statistically significance. TB patients that were HIV positive had a cure rate of 12.7%, while those that were HIV negative had a cure rate of 31.8%. The death rate among dually infected patients was higher compared with the HIV-negative patients. The treatment completion and default rates were higher in the HIV co-infected patient.

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Introduction

The global tuberculosis (TB) and HIV/AIDS epidemic represents an enormous amount of human suffering, pain, and grief. The World Health Organization (WHO) describes the TB/HIV co-infection as two monsters working together against humanity. Over the past decades we have witnessed the re-emergence of TB as a result of the worsening dual epidemic of TB and HIV/AIDS in sub-Saharan Africa. Nigeria, being the continent's most populous country has the second highest burden of TB in Africa and the fifth in the world.[1] The 4.4% prevalence of HIV is ranked among the highest in the world and it is estimated that Nigeria accounts for about 20% of people living with HIV/AIDS in sub-Saharan Africa.[2] TB is the major opportunistic infection and leading cause of death among people living with AIDS.[3,4]

To tackle the impact of the dual infection of TB and HIV/AIDS, the National Tuberculosis and Leprosy Control Programme (NTBLCP) adopted the STOP TB strategy. This includes TB/HIV collaboration and aims to detect at least 70% of smear-positive PTB cases and treats at least 85% of them successfully to prevent new TB infections. However, considering the influence of the HIV epidemic on TB, it has become imperative to intensify case detection of TB among persons living with HIV/AIDS (PLWHA), prevent HIV infections in people already infected with TB, and reduce the likelihood of latent TB in PLWHA progressing to active disease.

A national TB/HIV strategic framework sets out a clear mechanism for collaborative TB/HIV activities. The two disease programmes, TB and HIV/AIDS, got tremendous support from the United States Agency for International Development (USAID) and the round 5 Global Fund to Fight AIDS TB and Malaria. HIV programme implementation is presently ongoing in some selected healthcare facilities in 12 states in Nigeria, including Gombe state. The goal of this TB/HIV strategy is to reduce TB/HIV-associated morbidity and mortality through collaboration between NTBLCP and the national AIDS and Sexually Transmitted Diseases Control Programme (NASCP) at national and state levels. This collaboration has clear set objectives ranging from the establishment of mechanisms of collaboration between the TB and HIV/AIDS programmes and decreasing the burden of TB among PLWHA, to decreasing the burden of HIV in TB patients.[5]

Some specific activities that are geared towards achieving these set objectives are as follows:

- The establishment of national and state TB/HIV

working groups.
- Conducting surveillance of TB/HIV prevalence.
- Carrying out joint TB/HIV planning and implementation.
- Strengthening monitoring and evaluation.
- Reducing the burden of TB in PLWHA.
- Providing isoniazid prophylactic therapy (IPT) for PLWHA.
- Ensuring TB infection control in healthcare and congregate settings.
- Reducing the burden of HIV in TB patients through treatment and care.
- Supporting HIV/AIDS patients including anti-retroviral therapy (ART).[5]

Implementation of these activities also addresses areas of mutual interest in the two disease programmes and ultimately contributes immensely to addressing this dual epidemic which has exacted a tremendously negative impact on treatment outcomes of TB cases.

Materials and methods

Research and design

This was an analytical retrospective case-control study to compare the treatment outcome of new sputum smear-positive pulmonary tuberculosis (PTB) patients co-infected with HIV with the new sputum smear-positive PTB patients without HIV co-infection.

Study population

The study looked at all new sputum smear-positive acetate-free biofiltration (AFB) patients that tested positive to HIV screening between screening and second month of follow-up, and who were treated between January and December 2006 in the Gombe State TB control programme. The control for the study came from the same cohort of January and December 2006 of new sputum smear-positive AFB patients that tested negative to HIV screening.

Survey instrument

The instrument that was used for the survey was a specially designed form for data collection. The information for the survey was collected from the tuberculosis laboratory register, the NTBLCP TB treatment card, the Local Government Authority (LGA) tuberculosis treatment register, and the State 2007 annual report.

Data analysis

Data were analysed with Statistical Programme for Social Sciences version 11.0 (SPSS) software. Graphs, bar diagrams, pie charts, frequency tables, ratio proportions and rates were used to review data. Student's t-test and the Chi-square test were used to verify the differences between means and proportions, respectively. The level of significance was set at 5%.

Ethical considerations

A draft research proposal was sent to the Director of Medical Services, Gombe State through the state TBL control officer for permission to access the state TB programme registers and TB patient cards at the DOTS (directly observed therapy, short course) centres. Confidentiality and anonymity were ensured as no name or any form of identity was used on the data collection tool.

Results

The majority of HIV-positive and HIV-negative PTB patients studied were aged 39 years and below. There was no statistically significant difference (p=0.506) in the mean age of patients with co-infection (34.6±10.0 years) and those without co-infection (33.9±16.8 years).

A greater number of females and males not co-infected in the study population were aged 30 years and below. There was a statistical significant difference (p=0.002) in the mean age of males (35.9±17.0 years) and females (30.7±16.1 years). Also there was an equally statistically significant difference (p=0.000) between the mean weight of male (45.7±14.3 kg) and female (40.3±14.5 kg) patients that were co-infected. The 30-year age group and below in both sexes were the majority in the co-infected patients in the study population. Out of the 300 HIV co-infected patients in the study population that were HIV positive, males accounted for 58.3% compared with 41.7% that were females. This was not statistically significant at a p value of 0.333.

TB patients that were HIV positive had a cure rate of 12.7% while those that were HIV negative had a cure rate of 31.8%. The difference in cure rate was statistically significant (p=0.002). The death rate among dually infected patients was 25.7% compared with the HIV-negative patients (15.5%). This was equally statistically significant (p=0.000). The treatment completion and default rates were higher in the HIV co-infected patients.

Discussion

The Gombe State TB programme offers TB/HIV collaborative services (screening of TB patients for HIV and DOTS services) in nine health facilities located in Akko (2), Biliri (1), Funankaye (1), Gombe (2), Kaltungo (1), Duku (1), and Yamalta-Deba (2). In 2006 these centres tested a total of 1694 TB suspects: 1418 were registered for DOTS and 1040 screened for HIV, out of which 450 were HIV positive and, therefore, dually infected with TB and HIV.

The study looked into only new smear-positive PTB patients enrolled for treatment between January and December 2006. Follow-up and re-treatment cases were left out of the analysis. Only 300 cases out the 450 that were dually infected and smear positive were matched with 595 smear-positive patients who were HIV negative as a control.

The HIV sero-prevalence rate among sputum smear-positive TB patients in Gombe State was 23%. This research, the Burkina Faso studies, and rural Haiti studies all confirm an alarming increase in HIV sero-prevalence rate among TB patients.[6,7]

The HIV sero-prevalence among TB patients increased in Nigeria from 2.2% in 1991 to 19.7% in 2000, and to 27% in 2003.[8] In Africa, ranking countries by the number of TB cases attributable to HIV (per 100 000 population), places Nigeria third at 49.9 after South Africa and Ethiopia.[9]

The rising TB/HIV epidemic no doubt impacts negatively on AIDS and TB control programmes in many ways. The impact ranges from increased caseload of active TB attributable to HIV, HIV-related morbidity and mortality in TB patients, higher default rates and low cure rates, high rate of adverse drug reactions, increased risk of TB transmission and delay of access to health services for TB suspects due to the stigma of HIV/AIDS.[10]

The percentage of male sputum smear-positive TB patients was 61%. This rate is similar to the national values for 2007 TB with up to 65% of males with sputum smear-positive results.[11] This value is expected as males in sub-Saharan Africa are more exposed to predisposing factors for infection than females, being more outgoing.

Fewer HIV-positive patients were female (41.7%) compared with 58.3% male patients. However, this difference was not statistically significant (p0.333). There were more males in the study population, with a male:female ratio of 3:2. In Nigeria attendance and utilisation of the health services depends on significant others. Females are more affected as they have to wait on their male counterparts for advice and funding before attending hospital. This result is similar to data from South Africa (male 19.1%, females 11.4%) and Burkina Faso (male 24%, females 20.1%).[12]

Social inequalities, including gender and power relations, have an important impact on HIV transmission.[13] Recent reviews also suggest that women in many parts of the developing world are less likely to control how, when, and where sex takes place thereby increasing the likelihood of HIV infection.[14] Although the result of this research showed a higher HIV prevalence among the male population, this may not be unrelated to the greater number of males in the study group.

The majority (39.3%) of all the HIV-positive patients were in the 30–39 year age group. The lowest HIV seropositivity rate was seen among the older age groups ≥60 years (2%) and 50–59 years (5.7%). This finding may be related to the fact that the older age groups are less likely to be involved in the risky behaviours that predispose individuals to IV infection.

Among HIV-negative patients, the <30 years age group constitute the majority (45%) with fewer in age groups ≥60 years (9.4%) and 50–59 years (11.3%). The mean age of patients with co-infection was 34.6 years (standard deviation 10.0 years) and that of patients without co-infection was 33.9 years (standard deviation 16.8 years); this was not statistically significant (p=0.506.) The HIV sero-prevalence of 39.3% among the age group 30–39 years is similar to other studies,[14,-16] which showed higher HIV sero-prevalence among a similar age group.

The HIV sero-positive patients were younger than HIV-negative TB patients, since the risky behaviour that often predisposes to HIV infection is more common among these younger age group. Most members of this age group are not married and are economically viable, often constituting a greater percentage of the work force. They are more exposed to multiple sexual partners and thus more predisposed to HIV infection.

The treatment success rate (cured + treatment completed) was higher (70%) among HIV-negative patients than in TB/HIV-positive patients (41%). HIV-positive patients had a cure rate of 12.7% while those that are HIV negative had a cure rate of 31.8%. The difference in cure rate was statistically significant (see Table 1). Some African studies[7,17] claimed there was no difference in the two cure rates while others[18] have shown clearly that TB patients co-infected with HIV had worse treatment outcomes. The Nigerian TB programme uses drug regimen 2RHZE/6EH, different from the standard regimen 2RHZE/4RH being used in the other studies from South Africa and Burkina Faso and other national TB programmes, especially in developed countries. This may not be unrelated to the poor treatment outcome in the dually infected patients observed in this study. Also, the availability of ART for the dually infected was limited thus increasing the impact of dual infection more on these patients and hence giving poor treatment outcome.

Other studies also observed that HIV-infected patients who received a 6-month rifampicin-based course of TB treatment, or who received intermittent therapy of anti-TB drugs, had a higher relapse rate than HIV-infected subjects who received longer therapy or daily therapy, respectively. This suggests that the standard 6-month therapy may be insufficient to prevent relapse in patients with HIV.[19,20]

Overall, the drug regimen used for treatment has an effect on the cure rate and the 6-month regimen is more effective than the 8-month regimen.[12,21] Advocates for a better TB cure rate in Nigeria and attainment of the WHO 70/85 targets for the TB programme strongly believe that a change from the 8-month 2RHZE/6EH to 6-month 2RHZE/4RH is imperative.

The treatment completion rate in HIV-positive patient was 28% compared to 38.2% in HIV-negative patients. This difference was statistically significant (p=0.002). HIV-positive patients often present with smear-negative PTB and productive cough often decreases with TB treatment as most patients at 7 months may actually not be able to produce sputum for smear examination. Also HIV-positive patients at diagnosis are mainly sputum smear-negative and often complete treatment without sputum follow-up examination.

The death rate among the dually infected patients was more (25.7%) compared with that in HIV-negative patients (15.5%); the difference was also highly significant (p=0.000). The result was actually similar to other researches that had shown higher mortality rates among TB patients co-infected with HIV than among TB patient that were not dually infected.

Increased incidence of adverse drug reactions leading

Table 1 Treatment outcome of pulmonary tuberculosis patients with and without HIV co-infection

Treatment outcome	HIV-positive frequency (%)	HIV-negative frequency (%)	χ^2	*p* value
Treatment completed	84 (28.0)	228 (38.2)	9.353	0.002
Transferred out	81 (27.0)	68 (11.4)	34.849	0.000
Died	77 (25.7)	92 (15.5)	13.559	0.000
Cured	38 (12.7)	189 (31.8)	30.427	0.000
Default	20 (6.6)	17 (2.9)	7.303	0.007
Failed	0 (0.0)	1 (0.2)	0.000	1.000
Total	300 (100.0)	595 (100.0)		

Definition of terms
Treatment completed: any patient who was smear positive at diagnosis and who completed treatment but in whom smear examination results were not available at end of treatment. This includes all smear-negative and extra-pulmonary patients who completed treatment.
Transferred out – a patient who was transferred to another treatment centre in another state and whose treatment result is not known.
Died – any patient who dies for any reason during the course of his or her treatment.
Cured – a TB patient who was smear positive at diagnosis, who completed 8 months of treatment and who was smear negative at the end of the 7th month of treatment.
Default – a TB patient who interrupted treatment for 8 consecutive weeks or more after the date of the last attendance during the course of treatment
Failed – a smear-positive TB patient who while on the first line of treatment remained or becomes smear positive again 5 months or later after commencement of treatment

to interruption of treatment and occasional fatality rates have risen; 20–30% of HIV smear-positive PTB patients die before end of treatment[22, 10] and recurrence rates are even higher.

The study confirms that the mortality of TB patients is higher among HIV-positive patients than among HIV-negative patients. The high mortality rate can be explained by the severity of the HIV infection, adverse drug reactions, and associated opportunistic infections. Also the effectiveness of both the anti-TB drugs and ART may also be diminished by malabsorption in HIV/AIDS, drug interactions, and immune reconstitution syndrome.

Accessibility to ARV treatment was often not guaranteed since the state has only three ARV sites and patients are often referred from remote areas for treatment. Most patients in the study were not adherent to ART and occasional out-of-stock situations recorded in the state in 2006 may have contributed to this effect.

Only one out of the 595 HIV-negative patients failed treatment and no failure was recorded among the 300 dually infected patients in the study. The difference in failure rate was not statistically significant (p=1.000).

This result is similar to the Burkina Faso studies[12] that also showed no significant difference in cure rate between the HIV-positive and HIV-negative patients. Failure rate, mortality, and recurrence rates were all found to be higher among HIV-positive patients in some other studies.[19] In this case the differences were thought to be related to the treatment regimen used and the treatment duration. A continuation phase of 4 months isoniazid and rifampicin was found to have better treatment outcomes (failure rate) compared with 6 months of isoniazid and ethambutol, which was found to have a higher failure rate in HIV-positive patients.[8]

The default rate among TB patients with HIV co-infection (6.6%) was higher than that of TB patients without HIV co-infection (2.9%) (see Table 1). The difference was statistically significant. Many studies showed a higher default rate among dually infected patients.[10] The higher default rate in this study may not be unrelated to limited accessibility to ART services for the TB patients. Dually infected patients in some centres are referred to distant ART centres for HIV treatment and care, leading to default in TB treatment.

Integrating TB and HIV services into the general healthcare system[23] and engaging the private health care providers in the provision of TB and integrated TB/HIV services[23] have been found to be very effective in addressing accessibility to TB/HIV services and thus ensuring lower default rates.

The availability of drugs and other supplies is paramount in all responses to the TB/HIV scourge. ARV drugs and anti-TB drugs should be made available to the patients who need them. Strategies to ensure an uninterrupted supply of anti-TB drugs and ARVs through the state programme to the facility levels must be put in place.

The present 8-month regimen (2RHZE/6EH) used in the Nigeria National TB programme should be changed to a 6-month regimen (2RHZE/4RH). The re-treatment regimen should also be changed to 2S3RHZE/5RHE. This change will in no small measure (as can be inferred from this study in comparison with other previous studies) lead to improved TB treatment outcomes in TB/HIV co-infected patients.

The strengthened capacity of the National and state TB and HIV control programmes in planning and coordina-

tion of joint TB/HIV activities, and greater numbers of all other personnel, including community-based workers involved in the provision of all TB/HIV services, will ensure improved TB/HIV services to the populace.

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