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Treatment Outcome of Tuberculosis Cases and HIV Co-infected Patients. A Retrospective Study at a Federal Medical Centre of North Central Nigeria

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ABSTRACT

Background: Tuberculosis (TB) is the leading cause of death among people living with HIV/AIDS worldwide. Despite the availability of highly effective treatment for decades, Tuberculosis (TB) remains a major health problem in Nigeria due to the increasing association between HIV and TB observed over the past three decades when HIV was discovered. However, the proportion of TB and or TB/HIV co-infected patients who have successful TB treatment outcome is not well known. This study determined the treatment outcome of TB/HIV co-infected patients with HIV negative patients at Federal Medical Centre Makurdi, Benue State, Nigeria.
Methods: A retrospective study that used secondary data from Directly Observed Treatment Short (DOTS) course center (APIN Unit). 268 cases were considered and the period under review covers from January, 2019 to December, 2021.
Results: Out of the total 268 TB cases reviewed, the HIV prevalence rate was 28.7 %. More than two-third (78.4%) of HIV-negative patients had successful treatment compared to 68.9% of HIV positive patients that were treated successful. Out of the 77 HIV co-infected patients, 10.4% defaulted, 14.2% had died, and 6.5% failed treatment compared to HIV-negative patients amongst whom 15.2% defaulted, 4.8% died and 1.6% failed treatment. TB/HIV co-infection was significantly associated with poor treatment outcome (AOR: 1.158; 95 % CI 0.617-2.173; p = 0.648).
Conclusion: The favorable treatment outcome of HIV-negative patients is more than that of HIV-positive patients and the most probable predictable factor responsible is the CD4 count of patient; indicating that TB/HIV co-infection has remained a major public health problem in Benue state. Therefore, there is the need for sustained strengthening and expansion of the national TB/HIV programmes.

Keywords: Tuberculosis; HIV; Outcome; TB/HIV Co-infection; Nigeria.

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Introduction

Tuberculosis (TB) and human immune deficiency virus (HIV) co-infection is a serious public health challenge because of associated mortality globally[20]. 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 5th in the world[17]. 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. TB is the major opportunistic infection and leading cause of death among people living with AIDS[2,5].

It's already 28 years since Nigeria adopted the Directly Observed Treatment Short Course (DOTS) TB strategy in 1994 and is now implementing the STOP TB strategy which has as some of its targets to reduce the TB prevalence and death rates by 50% relative to 1990 level and to eliminate by 2050, TB as a public health burden.

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 Benue 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.

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 and supporting HIV/AIDS patients including anti-retro-viral therapy.

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

The number of TB/HIV related unfavorable treatment outcomes has reduced worldwide due to increased access to anti-retroviral (ARV) therapy[18]. However, in Nigeria the proportion of TB in comparison with TB/HIV co-infected patients who have successful TB treatment outcome is not well known or ascertained[3]. There is also paucity of data on how treatment outcomes among TB/HIV co-infected patients are influenced by TB/HIV

collaborative activities in the country. Therefore, the main goal of this research is to determine the treatment outcome of TB patients and compare the treatment outcomes between co-infected TB/HIV and TB patients at Federal Medical Centre, Makurdi, Benue State with high HIV burden and high TB burden in Nigeria. The success or otherwise of the implementation of the TB/HIV control strategies will determine whether the second objective of the STOP TB strategy (Protect vulnerable populations from TB, TB/HIV and multidrug-resistant TB) as well as Goal-3 of the Sustainable Development Goal (SDG) which emphasized healthy lives and well-being for all; could be achieved. Tuberculosis is almost always curable if patients with drug susceptible organisms are given sufficient uninterrupted therapy. If untreated, 50%–80% of patients with smear positive TB die and in a poorly implemented TB programme, as many as 30% of patients with smear positive TB die[10].

Despite the fact that TB is treatable and curable, it has proved impossible to eliminate and this has been worsened by the HIV/AIDS epidemic. Although there has been recent progress of global efforts, TB is still one of the leading causes of mortality and morbidity worldwide by an infectious agent and still remains a major public health burden globally and especially in developing countries like Nigeria.

Methods

Setting: Benue state is located in the north central geographic zone of Nigeria. Benue State has an estimated population of 4,712,020 in 2010 (i.e. 2.8% projection from 2006 National population figures of 4,219,244). There are two main ethnic groups, Tiv and Idoma. Other ethnic groups include Igede, Etulo and Jukun. The Benue people are mostly farmers engaged in subsistence and commercial farming. A small percentage of the populations are involved in petty trading and civil service jobs.

As at 2012, FMC Makurdi had achieved 100% DOTS coverage in all the registered TB patients. During the reviewed period, the national guidelines for ART for HIV/TB co-infection followed the 2006 World Health Organization Guidelines for ART. As per these guidelines, all HIV-infected persons with pulmonary TB, extra-pulmonary or disseminated TB with a CD4-lymphocyte count $\leq 350/mm^3$ were considered eligible for ART. The most common ART regimen initiated was Zidovudine or Stavudine plus Lamivudine plus Efavirenz.

Study Design: A retrospective study of all available secondary data of TB and TB/HIV co-infection cases registered annually by the Tuberculosis and Leprosy Control Programme (TBLCP) at Federal Medical Centre Makurdi, Benue state. The period under review covers from January, 2019 to December, 2021.The data collected for this study was limited to the scope, which is the proportion of TB and TB/HIV co-infected patients who have successful TB treatment outcome after TB treatment. It was not intended to show case the relationship between HIV patients and other co-morbid conditions or diseases. For this purpose, only the TB/HIV data was collected during the data collection exercise.

Eligibility Criteria: All individual registered for treatments that are eligible for both ART and TB treatment services were included for the study and persons whose test results were incomplete for HIV were excluded and patients with other co-morbidities aside HIV were also excluded. Being a retrospective study that made use of secondary data, unconfirmed diagnosis of HIV and those lacking proper documentation were also excluded. Only those with clear documentation were used.

This study was conducted at APIN unit, Federal Medical Centre Makurdi, with highest TB burden providing ART comprehensive services using outlier sampling methodology by first ranking the facilities with the highest notification data for Tuberculosis.

Data Collection: The main data source is from APIN unit where the routine NTBLCP standardized facility reporting and recording forms, and ART Patient Management Monitoring (PMM) registers. Information on the socio-demographic variables, type of TB patient, site of diagnosis, date of diagnosis, sputum smear results, HIV status, Co-

trimoxazole presumptive therapy, ART regimen, CD4 count (baseline and the most recent), duration of TB treatment and treatment outcome were extracted from the records. Data collection was done manually. The TB health facility registers and patient treatment cards were provided by the facility research participants and the information seen were exported to the extraction sheet.

Outcome Measurements: The Nigerian NTLCP guideline, adopted from WHO, was used for the clinical case and treatment outcome definitions[20]. These outcomes include:

1. Cured: TB patient who was smeared positive at diagnosis, who completed 6 or 8 months of treatment and who is smear negative at the end of 6th or 7th month of treatment and at least one previous occasion.

2. Treatment completed: TB patient who was smeared positive at diagnosis and who completed treatment but in whom smear examination results are not available at the end of treatment, or all smear negative and extra-pulmonary TB patients who completed treatment.

3. Successful Treatment: The sum of cured and treatment completed.

4. Failure: A smear positive patient who while on Category 1 treatment remained, or became smear positive again five months or later after commencement of treatment.

5. Defaulted: A patient who has been on treatment for at least four weeks and whose treatment was interrupted for eight or more consecutive weeks.

7. Died: TB patient who dies for any reason during the course of anti-tuberculosis chemotherapy.

It is worth mentioning that the regimen for the treatment of drug susceptible TB is for a period of six months and the treatment outcomes are given at the completion of the treatment regimen. TB Patients at the commencement of treatment are subjected to follow-up microscopy tests after diagnosis at month two, month five and month six during the period of treatment to confirm that there is a conversion of the TB patient status during that period. These laboratory tests are aimed to confirm whether or not a patient has been cured of the disease. Irrespective of the result of the outcomes of the microscopy tests, a TB patient cannot be declared cured or otherwise, until all the follow-up tests have been conducted till the end of treatment. On the other hand, for TB patients with smear negative result at diagnosis but who were confirmed to be symptomatic to TB by a medical officer, treatment outcome is also given at the end of the completion of the treatment regimen.

Data Analysis: Data was extracted, checked for errors and entered into IBM Statistical Packages for Social Sciences (SPSS) version 26.0. Descriptive statistics were used to summarize the independent variables. Logistic regression analysis was done to analyzed whether there is an association between TB treatment outcome and independent predictors. Crude and adjusted odd ratios were computed to see the strength of association.

Ethical Approval: The study protocol was submitted to the Federal Medical Center Makurdi's Ethics Committee for approval before data collection. To ensure confidentiality, anonymity was maintained from data entry into the data collection tool and into the computer before data analysis.

Results

Of the 268 records of patients reviewed, the majority 118 (44%) were between 20 – 39 years. Mean age was 19.4±11.0 years. The majority were males 158 (59%) while 205 (76.5%) were new cases. The percentage of TB/HIV co-infected patients was 28.7% and of the 238 (88.8%) were pulmonary TB, 186 (75%) were smear positive as shown in Table 1.

Table 1. Demographic and Tuberculosis profile of patients

Variable	**Frequency (n= 268)**	**%**
Age group (years)		
<20	42	15.7
20 – 39	118	44
40 – 59	77	28.7
≥ 60	31	11.6
Mean±SD	19.445	
Gender		
Male	158	59

Female	110	41
Type of TB		
Pulmonary	238	88.8
Extra-pulmonary	30	11.2
Treatment category		
New	205	76.5
Retreatment	63	23.5
Had treatment supporter		
Yes	174	64.9
No	94	35.1
HIV status		
Negative	191	71.3
Positive	77	28.7
Smear result	n = 248	%
Positive	186	75
Negative	62	25

The odds of having TB/HIV co-infection were 0.99 higher among extra-pulmonary TB patients), than pulmonary TB patients (AOR 0.988; 95% CI 0.453-2.158: p = 0.864). In addition, the chances of having treatment success outcome in HIV negative patients were more, than in HIV positive patients (AOR 0.445; 95%CI 0.237-0.838; p = 0.012) as shown in table 2.

Table 2. Associated Factors of TB/HIV co-infected and TB patients showing the Crude and Adjusted Odd Ratios

Variable	**TB/HIV n=77(%)**	**TB n=191 (%)**	**COR (95%) CI. *P***	**AOR (95%) CI, *P***
Gender				
Male	49 (27.3)	160 (72.7)	0.843 (0.494 - 1.440) 0.530	0.918 (0.531 - 1.587) 0.759
Female	28 (31)	82 (69)		
Type of TB				
Extra-pulmonary	16 (42.1)	22 (57.9)	0.909 (0.423 - 1.953) 0.807	0.988 (0.453 - 2.158) 0.977
Pulmonary	61 (26.5)	169 (73.5)		
Type of Patient				
Retreated	20 (32.8)	41 (67.2)	1.154 (0.620	1.158 (0.617
New	57 (27.5)	150 (72.5)	- 2.148) 0.650	- 2.158) 0.650
Treatment Outcome				
No Treatment Success	23 (43.4)	30 (56.6)	0.440 (0.236 - 0.822) 0.009	0.445 (0.237 - 0.838) 0.012
Treatment success	54 (25.1)	161 (74.9)		

Table 3 showed that a significantly higher proportion of TB patients were cured than TB/HIV co-infected patients (28.3% vs 23.4%; p = <0.001) however, more TB/HIV co-infected patients died than TB patients (14.2% vs 4.8%; p 0.655).

Table 3. Treatment outcome in TB/HIV co-infected and TB patients

Variable	**TB/HIV n=77(%)**	**TB n=191(%)**	**Statistical significance, *P***
Cured	18 (23.4)	54 (28.3)	<0.001
Treatment completed	35 (45.5)	96 (50.1)	<0.001
Treatment failure	5 (6.5)	3 (1.6)	0.489
Defaulted	8 (10.4)	29 (15.2)	<0.001
Died	11(14.2)	9 (4.8)	0.655
Treatment success	53 (68.8)	150 (78.5)	<0.001

Discussion

HIV is a major driving force for the persisting TB epidemic in sub-Saharan Africa. Hence there is a strong correlation between increment in the prevalence of HIV and the incidence of TB. This present study showed that all the patients treated for TB had HIV counseling and testing (HCT). This finding is lower than the Lagos state (92.4%) and national (92%) figures[12, 22]. This may be because the study was carried out at a very short duration.

The risk of developing TB is high in sub-Saharan Africa. This is partly due to high HIV prevalence. In 2014, an estimated 41% of African TB cases were HIV co-infected[19,16]. In this study, 28.7% had TB/HIV co-infection which is high compared to Lagos state (23%)

[16]. However southern Africa countries like Malawi and South Africa with high HIV prevalence reported TB/HIV co-infection rate between 56% – 62%[19]. The prevalence of TB/HIV co-infection was 43% in Africa and between 50 – 80% in parts of sub-Saharan Africa in 2012[21, 9]. The findings may be a reflection of the decline of HIV prevalence in the country as earlier studies showed that TB/HIV prevalence in Nigeria was between 32% and 43% [11,6].

This survey revealed that, TB/HIV co-infection was associated with age group 20 years and above. This was not in accordant to what was reported in similar studies from Nigeria and Ethiopia, where TB/HIV co-infection was associated with lower age groups[13]. TB and HIV are known to affect people in the reproductive age groups.

TB/HIV co-infected patients were three times likely to have extra-pulmonary TB (EPTB) than pulmonary TB in this study. Extra-pulmonary TB has been associated with HIV infection because there is increased susceptibility for reactivation and dissemination of TB in these patients[1,8.] HIV infection is recognized as the commonest risk factor associated with EPTB and the odds of having EPTB are increased in advanced HIV infection[3]. This study differs from what was obtained in a study from Ethiopia which showed that TB/HIV co-infection was associated with pulmonary TB, the study found those with CD4 count of 200-350 cells/μL had a lower occurrence of TB compared to those with count < 200 cells/μL. Similarly, in a meta-analysis to assess the protective effect of ART on the emergence of TB, a 65% reduction in the incidence of TB was seen across all CD4 cell counts. More so, reduction of 57% was shown in patients with CD4 counts of > 350 cells/μL, but above all the highest influence was seen in persons with CD4 counts of <200 cells/μL, in whom a decline in TB incidence of 84% was seen[15].

In this present study, TB/HIV co-infection was significantly associated with poor treatment outcome (AOR: 1.158; 95 % CI 0.617-2.173; p = 0.648). This is incongruent to a study from India that reported comparable treatment outcomes between TB/HIV co-infected patients and TB patients[14]. TB/HIV co-infection has been shown to be associated with poorer TB treatment outcomes than TB infection[13]. Decreased intestinal absorption of anti-tuberculosis drugs, TB and HIV drug interaction, pill burden, HIV related stigma, lack of disclosure of HIV status and cost of attending two clinics especially when both clinics are not the same day have been adduced as possible reasons for poor treatment outcome among TB/HIV co-infected patients[15]. Severe immune suppression which may increase difficulty of diagnosis and hence delay in treatment initiation may often result in higher mortality among TB/HIV co-infected patients[4].

Conclusion

This study demonstrates a favorable treatment outcome in HIV-negative patients compared to HIV-positive patients at FMC Makurdi, Benue state for the two years period reviewed; indicating that TB/HIV co-infection has remained a major public health problem. Therefore, TB/HIV co-infection in Nigeria should be jointly managed and collaboration between the two programs needs to be strengthened and the services should be coordinated. In the nearest future, other authors could build on the findings of this paper using more recent and primary data as a follow-up study, to confirm the findings of this paper and to indicate possible variations which this study could not present owing to the limitation and use of secondary data.

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