



*Full Length Research Paper*

# Human immunodeficiency virus and pulmonary tuberculosis co-infection: Need for co-ordinated collaborative detection and treatment services

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**Abstract**

HIV and tuberculosis are still healthcare problems in sub-Saharan Africa, with co-infection being common and having varying rates across Africa. This study prospectively analyzed the prevalence of TB among subjects sent for TB screening, and the prevalence of HIV infection among these patients. Smears were prepared from sputum samples and stained by the Ziehl-Neelsen method to detect acid-fast bacilli (AFB). Patients were termed TB positive if at least two out of three smears were positive for AFB. HIV testing was offered to subjects who were unaware of their HIV statuses. Screening for HIV was done using ELISA kits and confirmed by Western blot. Out of 1047 subjects screened for TB, 126 subjects (12.03%; 95% CI: 10.06% - 14%) were positive for TB. There was a slight male preponderance of TB positive subjects. 61.1% of the AFB smear-positive subjects were between the ages of 21 and 40 years. Only 0.95% of the subjects were co-infected with HIV and TB, whilst 75.6% did not know their HIV statuses. Of the subjects who accepted HIV testing, 57 (8.66%) tested positive, and 36 of them were AFB smear-positive. With the additional HIV testing, the HIV-TB co-infection prevalence rose to 4.39%. HIV-TB co-infection rates are thus affected by the availability of opportunities for testing to the patients at risk; with a large proportion of TB patients unaware of their HIV statuses. There is an urgent need to institute integrated detection and treatment services for HIV and TB.

**Keywords:** HIV, TB, testing, co-infection, collaborative service.

## INTRODUCTION

Infections with the human Immunodeficiency virus (HIV) infection and Mycobacterium tuberculosis (TB) are major health problems globally. This is despite the fact that an effective cure for TB has been available for years. HIV epidemic drives rapid increases in the prevalence of Tuberculosis (TB). There were 34 million people living with HIV at the end of 2010 (UNAIDS 2011), with Sub-Saharan Africa bearing the brunt of HIV/AIDS infections. Although 63% of people living with HIV infection reside in this region, it accounted for 72% of deaths from HIV/AIDS infection in 2006 (UNAIDS 2007).

TB is the leading cause of death in HIV positive individuals (Corbett et al., 2007). At least one-third of the 34million people living with HIV worldwide are infected with TB, are 20-30 times more likely to develop TB than those without HIV and one in four people with HIV die due to TB. (WHO, 2009). In 2011, 8.7 million new cases of TB were recorded with 13% co-infected with HIV and 1.4 million deaths from TB. Of the deaths from TB, almost one million were HIV-negative and 430,000 were HIV-positive (WHO, 2012).

With no anti-retroviral therapy (ART) treatment, up to 50% of people living with HIV who are diagnosed with TB die during the 6 to 8 months of TB treatment (Mukadi et al., 1997; Lawn et al., 2005; Manosuthi et al., 2006). Multi-drug resistant tuberculosis (MDR-TB) is defined as TB that is resistant at least to isoniazid (INH) and rifampicin (RMP). Extensively drug-resistant

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tuberculosis (XDR-TB) is defined as TB that has developed resistance to at least rifampicin and isoniazid as well as to any member of the quinolone family and one 2<sup>nd</sup> line drug: kanamycin, capreomycin or amikacin. XDR-TB strains have emerged from the mismanagement of multidrug-resistant TB (MDR-TB). The proportion of deaths rises to 72 – 98% among those with MDR-TB or XDR-TB (Gandhi et al., 2006; Wells et al., 2007).

A complex interrelationship exists between TB and HIV infections. TB can occur at anytime in the course of HIV infection. The risk of TB increases 2-3 folds within the first 2 years of HIV seroconversion (Lawn et al., 2011).

HIV alters the pathogenesis of TB by producing a progressive decline in cell-mediated immunity. TB exacerbates HIV infection and accelerates HIV disease progression to AIDS (Whalen et al., 1995). It also increases the vertical transmission of HIV. Whilst the risk of developing active TB for an immunocompetent individual is 5%-10% during their lifetime, that for HIV-positive individuals is 5% - 15% annually (Raviglione M et al., 1997).

There are diagnostic and therapeutic challenges posed by HIV and TB co-infection. HIV infection causes a reduction of cell-mediated immunity which is critical for effective host response against infection with *Mycobacterium tuberculosis* and alters clinical and radiologic features of TB thereby making diagnosis of TB difficult (FitzGerald et al., 1999). There is thus, a greater proportion of smear-negative TB and extra-pulmonary TB among HIV-infected individuals.

The treatment of HIV-TB co-infection has been associated with drug toxicity, and immune reconstitution inflammatory syndrome is believed to occur in HIV-TB co-infected patients undergoing treatment for both TB and HIV and is associated with the CD4 cell count at the initiation of anti-retroviral therapy (Aaron et al., 2004; Müller et al., 2010).

With a population of 162 million people, Nigeria is one of five countries with high TB/HIV burdens contributing 60% of the global HIV-associated TB in 2011 (WHO, 2012).

Nigeria had a national HIV prevalence of 4.1%, whilst Bayelsa State had a prevalence of 9.1% (Federal Ministry of Health., 2011). There were 84,263 new TB case notifications in 2011, and 26% of TB patients were HIV positive (WHO, 2011).

There is limited knowledge about HIV-TB co-infection prevalence in Bayelsa State and records of HIV-TB co-infection are not readily available. This study was therefore put together to determine the HIV-TB co-infection by studying subjects presenting for TB screening only.

## MATERIALS AND METHODS

### Study design

This was a prospective study carried out between the 1st of June 2011 and 31st of May 2012 in which all subjects presenting at the Microbiology Department for sputum test for AFB were recruited. Subjects who had already been diagnosed with TB were excluded from the study.

### Study area

The study was conducted at the Niger Delta University Teaching Hospital, Okolobiri, Bayelsa State, Nigeria. Bayelsa state is situated in the Niger Delta region of Nigeria, and has a population of 1.2 million people. The people are mostly farmers, fishermen and civil servants. The prevalence rate of HIV infection was 9.1% for 2010 (Federal Ministry of Health., 2011).

### Ethical Approval

Ethical approval was obtained from the Ethics Review Board, and informed consent was obtained from all study subjects.

### Sample collection

Subjects were instructed on how to obtain sputum specimens in the morning. 3 first morning specimens were obtained after a deep, productive cough on non-consecutive days. Specimens were brought to the Microbiology Department on the day of collection.

### Acid-Fast Bacilli (AFB) test

For each sample, a slide was prepared and stained using the Ziehl-Neelsen method. Slides were examined under the microscope by microscopists trained to detect acid-fast bacilli and identify *Mycobacterium tuberculosis*. A patient was TB smear-positive if at least two out of three smears were positive for AFB.

### HIV

Blood samples were obtained by venepuncture and centrifuged, and the sera obtained were screened for antibodies to HIV-1 and HIV-2 using approved ELISA kits (Alere Determine™ and Double Check Gold™) (Alere

**Table 1.** Age and sex distribution of the study subjects.

Age group (years)	Male	Female	Total
<10	9	15	24
11 to 20	37	48	85
21 to 30	170	196	366
31 to 40	144	135	279
41 to 50	75	57	132
51 to 60	55	46	101
61 to 70	20	13	33
>70	11	16	27
Total	521	526	1047

**Table 2.** Frequency of AFB positive smears according to age and sex.

Age group (years)	Male	Female	Total
<10	0	0	0
11 to 20	6	10	16
21 to 30	24	23	47
31 to 40	22	8	30
41 to 50	3	9	12
51 to 60	5	3	8
61 to 70	8	2	10
>70	2	1	3
Total	70	56	126

industries, Japan), according to the manufacturer's instructions. HIV infection was confirmed by Western blot.

### Statistical analysis

Statistical analysis was performed with the Graphpad Prism version 4® (Graphpad software, San Diego, CA). Differences between groups were determined by the one-way analysis of variance (ANOVA) or paired t- test with the level of significance set at  $p < 0.05$ .

## RESULTS

Three specimens each for 1047 subjects were received at the Microbiology Department for sputum AFB test. There were 521 males and 526 females, with a male: female ratio of 0.99:1 (Table 1). The age range of the subjects was between 4years and 85 years, mean age 34.56 years.

### Prevalence of TB

12.03% of the subjects (126) had at least two positive

AFB smears out of three (95% CI: 10.06% - 14%) (Table 2). There was a male preponderance of TB, with 55.5% (70) of the AFB smear-positive subjects being male.

Generally, 61.1% of the AFB smear positive subjects were between the ages of 21 and 40 years of age, with the 21-30 years group being responsible for 37.3% of AFB smear-positive subjects.

### HIV status

Three-quarters of the subjects (792) had never been tested for HIV and were unaware of their HIV statuses (Table 3). 14.61% were HIV positive, whilst 9.74 were HIV negative. Therefore, only 0.95% were co-infected with HIV and TB.

### HIV testing

After counselling, HIV testing was offered to the 792 subjects who were unaware of their HIV statuses. 658 subjects accepted and were tested, whilst 134 subjects opted out of testing. 57 subjects (8.66%) of the 658 subjects tested were positive for antibodies against HIV (Table 4). Out of the 57 subjects positive for HIV, 36 were

**Table 3.** Frequency of HIV and AFB statuses.

HIV status	No. of subjects	AFB smear positive
unknown	792	102
HIV - negative	102	14
HIV - positive	153	10
Total	1047	126

**Table 4.** Results for subjects who accepted HIV testing.

No. Tested	HIV-positive	%	AFB smear-positive
658	57	8.66	36 (5.47%)

AFB smear-positive. The final HIV-TB co-infection prevalence was thus 4.39%, whilst the number of HIV-positive subjects became 210 (20.05%).

## DISCUSSION

TB/HIV co-infection places an immense burden on healthcare systems (Pawlowski et al., 2012) and the mortality rate of untreated HIV-associated TB is believed to be very high (Corbett et al., 2007).

In our study, we detected an HIV-TB co-infection prevalence of 4.39% after additional testing for HIV. Our result is much lower than the 10% to 41.2% obtained in other studies in Nigeria (Iliyasu et al., 2009; Erhabor et al., 2010; Onubogu et al., 2010; Azuonwu et al., 2011; Pennap et al., 2011), but close to the 5.91% obtained in another study also in the Niger Delta region of Nigeria (Nwabuko et al., 2012). Differences in the prevalent rates obtained could be as a result of differences in study designs.

We observed an increase in the prevalence of HIV-TB co-infection from 0.95% to 4.39% just by offering HIV testing to the subjects. This clearly demonstrates that the detection of HIV and TB infection among the population at risk could be improved by the provision of increased opportunities for HIV and TB testing.

In 2011 in Nigeria, 81% of notified TB patients tested for HIV, 26% of the tested TB patients were HIV-positive, whilst 224,000 HIV-positive people were screened for TB (WHO, 2012). These figures are higher than what we obtained in Bayelsa State in the Niger Delta region of Nigeria. This is suggestive of regional differences in the availability of testing in Nigeria.

The diagnosis of sputum smear-negative pulmonary TB is difficult and remains a challenge in resource-limited settings such as ours. There is therefore, a need to strengthen diagnostic facilities and development of simpler and cheaper TB diagnostic tools.

The survival rate of HIV-positive TB patients is higher for smear-positive than for smear-negative patients, as

the HIV-positive smear-negative TB patients are generally more severely immuno-compromised than those with smear-positive TB (Corbett et al., 2007). This underscores the need for early detection and treatment before they become severely immuno-compromised.

A comprehensive approach is therefore required to tackle detection and treatment of HIV-TB co-infection. Collaborative programs need to be instituted, if improvements in diagnosis, treatment and outcomes of treatment of patients are desired. Despite the WHO policy on collaborative TB/HIV activities since 2004, implementation has been far from perfect in some of the countries' worst affected by HIV/TB (WHO, 2012). The policy encourages testing TB patients for HIV, providing antiretroviral therapy (ART) and co-trimoxazole preventive therapy (CPT) to TB patients living with HIV, providing HIV prevention services for TB patients, intensifying TB case-finding among people living with HIV, offering isoniazid preventive therapy (IPT) to people living with HIV who do not have active TB, and controlling the spread of TB infection in health-care and congregate settings.

MDR-TB has emerged a global epidemic partly due to deficiencies in management of TB programs (Wells et al. 2007). With the advent of MDR-TB and XDR-TB, there is a great need for higher TB testing among HIV-infected patients and higher HIV testing among TB patients.

Baseline screening and rapid diagnosis of TB among patients commencing ART has been shown to reduce morbidity and mortality (Lawn et al., 2008; Lawn et al., 2010). Initiation of ART within six months of TB diagnosis is associated with greater survival of patients (Manosuthi et al., 2006). This also highlights the importance of early diagnosis and treatment of HIV-TB co-infection.

There is an urgent need for integrated counselling and testing centres. Physicians should be encouraged to order HIV screening for any suspected TB patient, and TB screening for any suspected or confirmed HIV case after proper counselling and informed consent.

A lot of education is also required among health workers and the general population on the relationship

between HIV and TB and the importance of increased testing, early diagnosis and treatment.

## CONCLUSION

Detection of HIV-TB co-infection is clearly affected by the availability of opportunities for testing for both TB and HIV. The integration of testing and treatment services for both HIV and TB would greatly impact on the morbidity and mortality of HIV and TB infections.

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