HIV and TB co-infection among patients on directly observed treatment of short course in Abeokuta, Ogun State, Nigeria

Okonko IO[1], Soleye FA[2], Adeniji FO[3], Okerentugba PO[1]

[1]Medical Microbiology Unit, Department of Microbiology, University of Port Harcourt, East-West Road, P.M.B. 5323, Choba, Port Harcourt, Rivers State, Nigeria.
[2]Medical Laboratory Unit, Department of Health Services, University of Agriculture, Abeokuta, Ogun State, Nigeria.
[3]Department of Preventive and Social Medicine, College of Health Sciences, University of Port Harcourt, East-West Road, P.M.B. 5323, Choba, Port Harcourt, Rivers State, Nigeria.
mac2finney@yahoo.com; iheanyi.okonko@uniport.edu.ng; Tel.: +234 803 538 0891

ABSTRACT: This study aimed to determine the prevalence of HIV and TB among patients on directly observed treatment of short-course (DOTS) in Abeokuta, Nigeria. Two hundred DOTS attendees (124 males and 76 females, age range: 16 to 75 years of age) at the Department of Health Services, UNAAB were randomly recruited for this study from January 1999 to July 2010. Samples of sputum and blood were collected and processed using standard laboratory procedures. All the patients' sera were screened for antibodies to HIV-1/2 using two rapid ELISA kits. Sputum was examined for presence of *Mycobacterium tuberculosis* using Ziehl-Nelson's staining method. The results showed that of the 200 patients enrolled in the DOTS, 30 (15.0%) patients were only acid-fast bacilli positive, 3 (1.5%) were only positive for anti-HIV antibodies and none (0.0%) was positive for both HIV antibody and TB. We observed that patients ≥ 40 years had higher infection rate for TB (21.5%) and HIV antibody (3.1%). Statistically, there was no significant difference in the distribution of HIV and TB infections with respect to age ($P>0.05$). Males and females appeared comparable in either infection rate ($P = 0.05$). Students had higher infection rate for TB (16.7%) and non-student had higher rate for HIV (1.6%); these differences were not statistically significant ($P > 0.05$). Those in the urban area had higher infection rate for TB (17.2%) while those in the rural area had higher infection rate for HIV (1.9%). Statistically, there was no significant difference between these values with respect to residential areas. The findings of this study have further confirmed that TB and HIV infections are common in Abeokuta, an urban area of Ogun State, Nigeria.
[Okonko IO, Soleye FA, Adeniji FO, Okerentugba PO. **HIV and TB co-infection among patients on directly observed treatment of short course in Abeokuta, Ogun State, Nigeria.** Nat Sci. 2012; 10(6):10-14]. (ISSN: 1545-0740). http://www.sciencepub.net/nature. 3

Key words: DOTS centre, blood, ELISA, HIV, *Mycobacterium tuberculosis*, Nigeria

Abbreviations: DOTS: directly observed treatment of short course; **HIV:** Human immunodeficiency virus; **TB:** tuberculosis; **SIV:** Simian immunodeficiency virus; **HAART:** highly active anti-retroviral therapy; **UNAAB:** University of Agriculture, Abeokuta; **MDR:** multidrug-resistance; **XDR-TB:** extensively resistant form of TB.

1. INTRODUCTION

Africa is facing the worst tuberculosis (TB) epidemic since the advent of the antibiotic era. Driven by a generalized human immunodeficiency virus (HIV) epidemic and compounded by weak health care systems, inadequate diagnostic laboratories and conditions that promote transmission of infectious agents, the devastating situation has become exacerbated by the emergence of drug-resistant strains of *Mycobacterium tuberculosis* (*M. tuberculosis*) (Chaisson and Martinson, 2008). HIV and TB are the two leading causes of death and continue to be a serious problem in developing countries (Baltussen et al., 2005). It is estimated that these countries account for about 35% of all reported HIV cases in the world (Haskins et al., 2009). It is now the leading cause of death in Africa replacing malaria and other communicable diseases (Umolu *et al*., 2005).

The TB epidemic is on the rise in most countries, including Nigeria. Over the past decades, TB incidence has increased in several countries in Africa. Available data suggest that this increase is mainly as a result of the burden of HIV infection in those countries because HIV infection induces immunosuppression. The epidemic of *M. tuberculosis* has affected about one-third of the world's population creating an adverse impact socially and economically in developing countries (Malen et al., 2006). TB, caused by the bacterium *M. tuberculosis,* is believed to enhance the progression of the HIV disease (Haskins et al., 2009). This enhancement of the virus has been suggested to be a result of the generalized immune activation in tuberculosis patients (Paton et al., 2005). Chaisson et al. (2004) reported that HIV infection appears to be a key component in the development of active TB by rapidly increasing its progression. Although very little

substantial evidence is currently available, *in vitro* studies have shown that *M. tuberculosis* induces HIV replication thereby increasing the viral load in patients with TB (Chaisson et al., 2004). The frequency with which HIV and *M. tuberculosis* infection occur together is determined by the epidemiology of each disease in a given population. The incidence of TB in HIV-infected persons is more than 100 times that of the general population. In untreated HIV-infected persons who have positive tuberculin skin test, the risk of active TB is about 8% per year (Coico et al., 2003).

The effectiveness of TB therapy is significantly lower among patients with HIV and AIDS (Vihrova et al., 2007). The World Health Organization (WHO) estimates that a person with both HIV and TB infection is thirty times more likely to become ill with TB than a person with *M. tuberculosis* infection alone (Reid et al., 2006). *M. tuberculosis* strains that are resistant to an increasing number of second-line drugs for treating multidrug-resistant tuberculosis (MDR-TB) are becoming a threat to public health worldwide (Shah et al., 2007). Drug resistance accompanied by HIV-associated immunodeficiency is the main cause of treatment failure (Vihrova et al., 2007). The first line of TB drugs includes isoniazid (H), rifampicin (R), ethambutol (E), pyrazinamide (Z), and streptomycin (S). MDR-TB is diagnosed when *M. tuberculosis* is resistant to at least isoniazid (H) and rifampicin (R), the two most powerful, first line drugs. The extensively resistant form of TB (XDR-TB), in addition to lack of sensitivity to H and R, is also resistant to any of fluoroquinolones, and at least one of second-line injectable drugs e.g. kanamycin and amikacin (Migliori et al., 2007).

In Abeokuta, Ogun State, Nigeria, there is dearth of literature on prevalence of HIV and TB co-infection and associated risk factors to the best of our knowledge. This study was undertaken to determine the prevalence of HIV and TB co-infection among patients in Abeokuta, Southwestern Nigeria from 1999-2010.

2. MATERIALS AND METHODS

2.1. Study area: This study was conducted from January 1999 to July 2010 in the Department of Health Services, University of Agriculture, Abeokuta (UNAAB), Ogun State, Nigeria.

2.2. Study population: A total of 200 patients suspected of having TB (124 males and 76 females) in DOTS centre at the Department of Health Services, UNAAB were enrolled in this study. They were of different ages and socioeconomic status. These patients were consecutively recruited after giving consents to participate in the study. Other relevant information of all participants was obtained using a Performa specially designed for this purpose. The age of the DOTS attendees ranged from 16 to 75 years of age. The male to female ratio was 1.7:1. Table 1 summarizes the demographic characteristics of the study patients. Active pulmonary TB was certified by a medical history and clinical findings compatible with pulmonary TB, a chest X-ray showing lung involvement, and positive sputum smear for acid-fast bacilli (AFB) or the culture of *M. tuberculosis* (Vihrova et al., 2007).

Table 1: Demographic characteristics of DOTS attendees in UNAAB, Abeokuta, Nigeria from 1999-2010

Parameters	No. Tested (%)	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Age Group (years)													
Less than 40	135 (67.5)	11	10	4	7	2	2	5	2	12	34	26	20
40 and above	65 (32.5)	7	7	3	5	2	2	9	0	5	8	5	12
Sex													
Males	124 (62.0)	13	11	6	7	2	2	5	1	10	24	19	24
Females	76 (38.0)	5	6	1	5	2	2	9	1	7	18	12	8
Occupation													
Students	78 (39.0)	7	4	0	0	2	2	4	2	4	16	18	19
Non-students	122 (61.0)	11	13	7	12	2	2	10	0	13	26	13	13
Area (residential location)													
Rural	107 (53.5)	12	7	3	4	2	2	5	0	3	29	19	21
Urban	93 (46.5)	6	10	4	8	2	2	9	2	14	13	12	11
Total	**200(100.0)**	**18**	**17**	**7**	**12**	**4**	**4**	**14**	**2**	**17**	**42**	**31**	**32**

2.3. Assay for HIV-1 and 2 Antibodies

From each study participant, about 5 ml blood sample was collected by venipuncture into plain tubes. The samples were transported in a commercially available collection and transport system for TB and HIV to the Medical laboratory unit, Department of Health Services, UNAAB for analysis and processed using standard laboratory procedures. The blood samples were centrifuged and the sera were used for the analysis. All the sera were screened for antibodies to HIV-1/2 using WHO-approved kits, the DETERMINE® HIV-1/2 (Abbott laboratories) and

HIV-1/2 STAT-PAK® (Chembio Diagnostic Systems, Inc.). The sensitivity and specificity of both kits ranged from 99.0%-100.0%. The test and interpretation were carried out according to the manufacturer's specifications. Both positive and negative control plasma were run along with the test samples, using the same procedure.

2.4. Sputum Analysis

Sputum was examined for presence of *M. tuberculosis* using Ziehl-Nelson's staining method as described by Cheesbrough (2006). Further confirmation of a positive sample was done by microscopy.

2.5. Statistical analysis

All data generated were presented with descriptive statistics; in order to establish relationship between infection rate and factors such as age and gender, $\chi 2$ statistical test was used (level of significance set at $p < 0.05$). SPSS 15.0 for Windows was used for the analysis. We also calculated trends in reporting rates for 1999–2010 by age, sex, and setting (urban and rural) and expressed as average percentage.

3. RESULTS ANALYSIS

Table 2 shows the groupings and group-specific prevalence rates of the study patients. Of the 200 suspected TB patients in the DOTS, 30(15.0%) patients were AFB positive, 3(1.5%) were positive for HIV antibodies and none (0.0%) was positive for dual TB and HIV infection. There were 124 (62.0%) males and 76 (38.0%) females, their age ranged from 16 to 75 years. Statistical analysis however, showed no significant difference in the prevalence of HIV or TB with respect to age, sex, occupation and locations (P> 0.05).

Table 2: Group-specific prevalence rates and risk factors for TB or HIV infection among attendees of DOTS in Abeokuta, Ogun State, Nigeria from 1999-2010.

Factors	No. tested (%)	No. positive for AFB (%)	No. positive for HIV (%)	No. positive for TB and HIV (%)
Age Group (years)				
Less than 40	135 (67.5)	16 (11.8)	1 (0.7)	0 (0.0)
40 and above	65 (32.5)	14 (21.5)	2 (3.1)	0 (0.0)
Sex				
Males	124 (62.0)	19 (15.3)	0 (0.0)	0 (0.0)
Females	76 (38.0)	11 (14.5)	3 (3.9)	0 (0.0)
Occupation				
Students	78 (39.0)	13 (16.7)	1 (0.9)	0 (0.0)
Non-students	122 (61.0)	17 (13.9)	2 (1.6)	0 (0.0)
Area (residential location)				
Rural	107 (53.5)	14 (13.1)	2 (1.9)	0 (0.0)
Urban	93 (46.5)	16 (17.2)	1 (1.1)	0 (0.0)
Total	**200(100.0)**	**30 (15.0)**	**3 (1.5)**	**0 (0.0)**

Table 3: Annual distribution of TB and HIV infections among DOTS attendees in Abeokuta, ogun State, Nigeria, 1999-2010.

Year of study	No. Tested (%)	No. Positive for AFB (%)	No. Positive HIV (%)	No. Positive for TB & HIV (%)
1999	18 (9.0)	4 (22.2)	0 (0.0)	0 (0.0)
2000	17 (8.5)	3 (17.6)	0 (0.0)	0 (0.0)
2001	7 (3.5)	1 (14.3)	0 (0.0)	0 (0.0)
2002	12 (6.0)	1 (8.3)	0 (0.0)	0 (0.0)
2003	4 (2.0)	1 (25.0)	0 (0.0)	0 (0.0)
2004	4 (2.0)	2 (50.0)	0 (0.0)	0 (0.0)
2005	14 (7.0)	2 (14.3)	0 (0.0)	0 (0.0)
2006	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
2007	17 (8.5)	1 (5.9)	0 (0.0)	0 (0.0)
2008	42 (21.0)	3 (7.1)	2 (4.8)	0 (0.0)
2009	31 (15.5)	3 (9.7)	1 (3.2)	0 (0.0)
2010	32 (16.0)	9 (28.1)	0 (0.0)	0 (0.0)
Total	**200(100.0)**	**30 (15.0)**	**3(1.5)**	**0 (0.0)**

Table 3 shows the annual prevalence rates of TB and HIV antibody among DOTS attendees in Abeokuta, Ogun State, Southwestern Nigeria from 1999 to 2010. HIV antibodies were detected only in samples collected in 2008 (4.8%) and 2009 (3.2%) with higher rate of infection occurring in year 2008 than in 2009. The annual distribution of TB showed a decreasing trend from 4 patients in 1999 to zero in 2006, after which it rose from 1 in 2007 to 9 in 2010.

4. DISCUSSION

This study was carried out to determine the prevalence of HIV and TB co-infection among patients in Abeokuta, Southwestern Nigeria from 1999-2010. A total of 200 samples of sputum and blood were collected from DOTS center attendees between January, 1999 and July, 2010; of which 30 (15.0%) were positive for AFB and 3 (1.5%) were positive for antibodies to HIV. The 15.0% AFB positivity reported in this study is lower than the 23.0% reported for AFB by both microscopy and culture in a study by Idigbe et al. (1998) among prison inmates in Lagos. However, it is higher than the 7.0% recorded in the general population in Lagos (Idigbe et al., 1998).

From this study, the age range of DOTS attendees was 16 to 75 years of age. The study showed that TB infection was relatively high in age group 40 years and above compared to subjects in age group less than 40 years. Previous studies have reported highest prevalence of HIV infection and TB in age group less than 40 years of age (Nnorom et al., 1996; Bruchfeld et al., 2002; Obiora et al., 2004). Obiora et al. (2004) also reported higher infection rate for TB among <20 years and 21–30 years old subjects in Benin and Irrua, Nigeria. Nnorom et al. (1996) reported higher infection rate for TB among 16-30 age group in urban and rural communities in Nigeria.

In this study, the male:female ratio was 1.63:1 with comparable 15.3% and 14.5% TB prevalence respectively for male and female participants (Table 2). This somewhat disagrees with the Mota et al. (2006) who reported that TB infection was more in males (80.0%) than females. The higher rates of TB reported by Nnorom et al. (1996) and Obiora et al. (2004) were also contrary to our observation in this study. The prevalence of TB without HIV coinfection was higher in males than females, though the difference was not statistically significant; this is consistent with other studies (Bruchfeld et al., 2002; Akpaka et al., 2006).

Also, a look at the occupational distribution revealed that non-students had the higher proportion of patients (Table 2). However, higher prevalence of TB was found among students than the non-students, while higher seroprevalence of HIV antibody was found among non-students compare with the students. Interestingly, none of these differences were statistically significant. The high prevalence of TB among these occupational groups underscores the need for intervention strategies that are focused, gender-sensitive and culturally appropriate. Obiora et al. (2004) reported no significant difference in the prevalence of TB and HIV-PTB infection rate in Benin and Irrua when sex and occupation of the subjects are considered.

From Table 3, it can be observed that there was a decrease form 1999 to 2003, then a rise in 2004 and 2005 with no reported AFB positivity in 2006. An increase was also observed from 2007 to 2010 (Table 3). A similar result was reported in Ibadan by Ige et al. (2006). Also, the number of TB patients decreased from a total of 4 in the year 1999 to 1 in 2003 and from 2 in 2004 to 0 in 2006. The decrease in number was most likely due to the fact that directly observed therapy short-course (DOTS) are now available at other centres within the city and its environs. A similar assertion was also made by Ige et al. (2006) in their study at Ibadan. Our study differs slightly from Ige et al. (2006), in that no HIV/TB coinfection was reported.

The limitation of the study is that it was conducted using one tertiary institution, and located in the rural area of Abeokuta city; these results may reflect what is happening in other similar heath institutions in the metropolis. The generalizability of our findings is also limited because participants were voluntary and self-selected. The power to observe statistically significant findings is limited because the study included only small numbers of cases of suspected TB infection.

In conclusion, the study showed no significant difference in the prevalence of HIV or TB with respect to age, sex, occupation and locations (P> 0.05). However, the results of this study have further highlighted the fact that TB and HIV infections are common in Abeokuta, an urban area of Ogun State, Nigeria.

ACKNOWLEDGEMENTS

We thank all participants who volunteered and those who participated in this study. The authors express their sincere appreciation to the management of Department of Health Services, University of Agriculture, Abeokuta, Nigeria for the assistance received from the Staff of Medical Laboratory Unit during this research. We would like to particularly thank Dr. WF Sule of the Department of Biological Sciences, Osun State University, Osogbo, Osun State, Nigeria for assisting us in data and statistical analysis.

Correspondence to:
Iheanyi O. Okonko
Department of Microbiology, University of Port Harcourt, Choba, PMB 5323 Port Harcourt, Rivers State, Nigeria; E-mail: mac2finney@yahoo.com;

iheanyi.okonko@uniport.edu.ng. Tel.: +234 803 538 0891

REFERENCES

1. Akpaka PE, Tulloch-Reid M, Justiz-Vaillant A, Smikle MF. 2006. Prevalence of human immunodeficiency virus infection in patients with pulmonary tuberculosis at the National Chest Hospital in Jamaica. Rev Panam Salud Publication; 19(1): 38–43.
2. Baltussen R, Dye C, Floyd K (2005). Cost effectiveness analysis of strategies for tuberculosis control in developing countries. Brit. Med. J. 10: 1136.
3. Bruchfeld J, Aderaye G, Palme IG, Bjorvatn B, Ghebremichael S, Hoffner S, et al. 2002. Molecular epidemiology and drug resistance of Mycobacterium tuberculosis isolates from Ethiopian pulmonary tuberculosis patients with and without HIV infection. Journal of Clinical Microbiology; 40:1636–1643.
4. Chaisson RE, Martinson NA. 2008. Tuberculosis in Africa — Combating an HIV-Driven Crisis. The New England Journal of Medicine 358 (11):1089-1092
5. Chaisson R, Charalambous S, Churchyard G, Cock K, Day J, Fielding K, Grant A, Hayes R, Moloi V, Morris L, Puren A (2004). Does tuberculosis increase HIV load? J. Infect. Dis. 190: 1677-1684.
6. Cheesebrough M (2006). District Laboratory Practice in Tropical Countries, part 1. University Press, Cambridge, pp. 239-258.
7. Coico R, Sunshine G, Benjamini E (2003). Immunology: A short course; 5th edition. John Wiley & Sons, Inc., Hoboken, New Jersey. pp. 245-247.
8. Haskins JL, Ladapo J. Nwosu VC. 2009. Human immunodeficiency virus (HIV) and *Mycobacterium tuberculosis*: A collaboration to kill. African Journal of Microbiology Research Vol. 3(13) pp. 1029-1035.
9. Idigbe O, Sofola T, Odiah F, Oyewole F, Okoye R, Giwa-amu J, Akinosho R; International Conference on AIDS. Pulmonary tuberculosis and HIV infections among prison inmates in Lagos, Nigeria. *Int Conf AIDS*. 1998; 12: 137 (abstract no. 13256).
10. Ige OM, Sogaolu OM, Ogunlade A. 2006. Pattern of presentation of tuberculosis and the hospital prevalence of tuberculosis and human immunodeficiency virus co-infection in University College Hospital, Ibadan: a review of five years (1998–2002). Abstract printing supported by Nonin Medical, Inc. Visit Nonin Medical, Inc. at stand C09 Poster Discussion Room C1c - 10:45-12:45; MONDAY, SEPTEMBER 4TH 2006; P2258.
11. Malen H, Mustafa T, Riise AMD, Wiker HG (2006). Vaccine approaches to prevent Tuberculosis. Scandinavian J. Immunol. 64: 243-250.
12. Migliori GB, Besozzi G, Girardi E, Kliiman K, Lange C, Toungoussova OS, Ferrara G, Cirillo DM, Gori A, Matteelli A, Spanevello A, Codecasa LR, Raviglione MC; SMIRA/TBNET Study Group (2007). Clinical and operational value of the extensively drug-resistant tuberculosis definition. Eur. Respir. J. 30: 623-626.
13. Mota P, Diogo N, Pina J. 2006. Multidrug-resistant tuberculosis in a tuberculosis unit–results of five years. Epidemiology of susceptible, resistant and multidrug-resistant tuberculosis (MDR-TB), P2244. MONDAY, SEPTEMBER 4TH 2006/
14. Nnorom JA, Esu-Williams E, Tilley-Gyado A; 1996. HIV, tuberculosis and syphilis in Nigeria: a descriptive study. International Conference on AIDS. *Int Conf AIDS*. 1996 Jul 7-12; 11: 138 (abstract no. Mo.C.1479).
15. Obiora G, Nwobu and Marcellinus Aigbokhan, Okodua and Mirabeau Youtchou, Tatfeng (2004) *Comparative Study Of HIV Associated Pulmonary Tuberculosis In Chest Clinics from two Regions Of Edo State, Nigeria.* Online Journal of Health and Allied Sciences [Journal (On-line/Unpaginated)]
16. Paton NI, Chua YK, Earnest A, Chee CB (2004). Randomized controlled trial of nutritional supplementation in patients with newly diagnosed tuberculosis and wasting. Am. J. Clin. Nutr. 80: 460-465.
17. Reid A, Scano F, Getahun H, Williams B, Dye C, Nunn P, De Cock KM, Hankins C, Miller B, Castro KG, Raviglione MC (2006). Towards universal access to HIV prevention, treatment, care, and support: the role of tuberculosis/HIV collaboration. Lancet Infect. Dis. 6:483-95.
18. Shah NS, Wright A, Bai G-H, Barrera L, Boulahbal F, Martín-Casabona N, Drobniewski F, Gilpin C, Havelková M, Lepe R, Lumb R, Metchock B, Portaels F, Rodrigues MF, Rüsch-Gerdes S, Van Deun A, Vincent V, Laserson K, Wells C, Cegielski JP. 2007. Worldwide emergence of extensively drug-resistant tuberculosis. Emerging Infectious Diseases, 13(3): 380-388.
19. Umolu PI, Okoror LE, Orhue P. 2005. Human immunodeficiency virus (HIV) seropositivity and hepatitis B surface antigenemia (HBsAg) among blood donors in Benin City, Edo state, Nigeria. *African Health Sciences; 5(1)*: 55–58.
20. Vihrova LA, Pylypchuk VS, Kutsyna GA. 2007. Open label trial of adjuvant immunotherapy with Dzherelo, Svitanok and Lizorm, in MDR-TB, XDR-TB and TB/HIV co-infected patients receiving anti-tuberculosis therapy under DOTS. Journal of Medicinal Plants Research 1(5): 117-122.

3/22/2012