J Microbiol Immunol Infect.
2007;40:116-122

Original Article

Coinfection and clinical manifestations of tuberculosis in human immunodeficiency virus-infected and -uninfected adults at a teaching hospital, northwest Ethiopia

Afework Kassu[1,2], Getahun Mengistu[3], Belete Ayele[4], Ermias Diro[4], Firew Mekonnen[5], Dereje Ketema[4], Feleke Moges[1], Tsehay Mesfin[4], Assefa Getachew[6], Bahiru Ergicho[7], Daniel Elias[1,8], Abraham Aseffa[8], Yared Wondmikun[9], Fusao Ota[2]

[1]Department of Microbiology and Parasitology, University of Gondar, Gondar, Ethiopia; [2]Department of Preventive Environment and Nutrition, Institute of Health Biosciences, The University of Tokushima, Tokushima, Japan; [3]Department of Internal Medicine, Addis Ababa University, Addis Ababa; Departments of [4]Internal Medicine, [5]Community Health, [6]Radiology, and [7]Pathology, University of Gondar, Gondar; [8]Armauer Hansen Research Institute, Addis Ababa; and [9]Department of Physiology, University of Gondar, Gondar, Ethiopia

Received: January 10, 2006 Revised: April 3, 2006 Accepted: May 13, 2006

Background and Purpose: The pattern of clinical presentations of tuberculosis (TB) is reflected in the microbiological, radiological, and histological characteristics of the disease. However, coinfection with human immunodeficiency virus (HIV) poses special diagnostic and therapeutic challenges. This study was aimed at assessing the clinical manifestations of TB in patients with or without HIV coinfection in a hospital-based cross-sectional study in Gondar, Ethiopia.

Methods: TB was diagnosed following standard clinical, bacteriological, radiological, and histological procedures. HIV serostatus was checked by enzyme-linked immunosorbent assay.

Results: This study included 257 TB patients, of whom 52.1% were coinfected with HIV. Pulmonary TB and extrapulmonary TB were diagnosed in 64.2% and 35.8% of the patients, respectively. No significant association was found between sputum smear positivity and HIV serostatus. One-fifth of the patients reported hemoptysis. More than one-third had chest pain, and >90% reported fever and weight loss. Night sweats and cough were reported by 86% and 82.5%, respectively. Coarse crepitations were the most frequent auscultatory finding (33.9%). Sputum smear positivity rate was 26.8%. Cavitation was significantly associated with sputum smear positivity (odds ratio = 9.0, 95% confidence interval = 2.4-34.1). Wasting, cough of ≤5 months' duration, crepitation, chronic diarrhea, and herpes zoster scar were significantly associated with HIV-positive serology.

Conclusion: Coinfection with HIV was very high in patients with TB. The presence of herpes zoster scar, chronic diarrhea, coarse crepitations, and cough of ≤5 months' duration may assist in identifying TB patients with HIV infection.

Key words: Comorbidity; Ethiopia; HIV; Tuberculosis

Introduction

About one-third of the world's population suffers from *Mycobacterium tuberculosis* infection. Tuberculosis (TB) continues to be the most important cause of morbidity and mortality worldwide, killing approximately 2 million people each year [1]. Fuelled by the high prevalence of human immunodeficiency virus (HIV) infection, the incidence rate of TB is very high in sub-Saharan Africa [2]. In some areas of this region, TB and HIV coinfection rates have reached 60% to 70% [3].

M. tuberculosis infection develops into full-blown active disease when the immune system weakens as a

Corresponding author: Afework Kassu, Department of Preventive Environment and Nutrition, Institute of Health Biosciences, The University of Tokushima, Tokushima 770-8503, Japan.
E-mail: afeworkkassu@yahoo.com

result of HIV infection, malnutrition, or other pathologies [4]. The patterns of clinical presentations of TB depend on the hosts' immune status, which is reflected in the microbiological, radiological, and histological characteristics of TB. HIV-related pulmonary TB (PTB) can present across a wide range of immune status, and its clinical presentation also varies accordingly [4,5]. In the early stage of HIV infection, manifestations of TB are quite similar to that in HIV-negative patients. However, at a later phase, atypical pulmonary, extrapulmonary, and disseminated diseases are common [5]. TB and HIV coinfection presents special diagnostic and therapeutic challenges and constitutes an immense burden on the healthcare systems of heavily infected countries [2,3].

Among the countries with a high burden of coinfection, Ethiopia has the highest burden of both TB [2] and HIV [6] infection in sub-Saharan Africa. Notwithstanding the very rampant HIV pandemic [7] and the associated resurgence of TB [8], studies assessing the clinical issues of TB in coinfected patients are very scarce. Therefore, this study was aimed at assessing the clinical features of TB in HIV-seropositive and -seronegative TB patients at a university hospital in Gondar, Ethiopia.

Methods

Subjects and study area

Subjects examined were consecutive patients visiting the Gondar University Hospital between January 2003 and August 2003 for work-up of TB. The hospital is a tertiary level teaching and referral hospital with 400 beds for inpatients, and renders referral health services to over 4 million inhabitants in northwest Ethiopia. Informed consent was obtained from all patients and the study was approved by the research ethics committee of the University.

Diagnosis

A specialist medical doctor working in the TB clinic performed the necessary clinical and diagnostic work-up. Diagnosis of TB was made based on the combined evaluation of clinical, radiological, histopathological, and laboratory features of the patients in accordance with the protocol established by the National Tuberculosis and Leprosy Prevention and Control Program [8]. All relevant X-ray films were analyzed for the radiological features of TB and were interpreted by a consultant radiologist. Three consecutive sputum samples (spot, morning, and morning) were obtained from eligible patients using the standard procedure and microscopically examined for acid-fast bacilli (AFB) on direct smears using Ziehl-Neelsen staining. Fine-needle aspiration specimens collected from extrapulmonary TB (EPTB) cases were examined cytologically by a pathologist in keeping with the standard procedures. After diagnosis of TB, all patients were classified into treatment categories based on the World Health Organization (WHO) criteria and received appropriate anti-TB chemotherapy [8]. The following operational definitions were used in the diagnoses and classification of TB [8-11]. Smear-positive PTB (PTB+): 2 AFB+ sputum smears or 1 AFB+ sputum and chest X-ray abnormalities consistent with active PTB, even if they have other tissue/organ involvement. Smear-negative PTB (PTB–): at least 2 sputum smears negative for AFB, radiologic abnormalities consistent with active PTB, and a decision by a clinician to treat with a full course of anti-TB chemotherapy. EPTB: patients with histological and/or clinical evidence consistent with active TB and a decision by a physician to treat with a full course of anti-TB chemotherapy. Disseminated TB: involvement of 2 or more sites. Classical chest X-ray pattern: upper lobe infiltrates, bilateral infiltrates, cavitations, pulmonary fibrosis, and shrinkage. Atypical chest X-ray pattern: interstitial infiltrates, especially lower lobe infiltrates, intrathoracic adenopathy, pleural effusion, and no abnormalities. Category I TB: new PTB+ patients, new PTB patients who are seriously ill, and seriously ill EPTB patients. Category II TB: PTB+ relapses, PTB+ treatment failures, and PTB+ returns after default. Category III TB: new adult patients with PTB and new adult patients with EPTB.

Blood collection and screening for HIV

After informed consent and appropriate pretest counseling, about 5 mL of venous blood was collected from each patient. Serum was separated by centrifugation within 2 h of collection and kept at –20°C until use. The presence of HIV antibodies was determined by an enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions (Vironostica HIV Uni-Form II plus O; Organon Teknika, Boxtel, The Netherlands). The following testing algorithm was used to determine the serostatus of patients. Specimens that gave a negative result for HIV antibodies in ELISA were considered HIV negative. However, samples that tested positive in ELISA were tested for a second time and were considered positive if found to be positive in the

second ELISA. The HIV serology test was carried out anonymously with all clinical and laboratory data being identified by a code number. Patients were informed of the results of the HIV serology test after appropriate post-test counseling.

Statistical analysis

Data entry and analysis were performed using the Statistical Package for the Social Sciences (SPSS) for Windows (Version 10.0; SPSS, Chicago, IL, USA). The chi-squared (χ^2) test was used to compare categorical data, and logistics regression was used to avoid the confounder effect and to calculate risk ratio. Odds ratio (OR) and 95% confidence interval (CI) were used to measure the strength of an association. *p* Values of <0.05 were considered statistically significant.

Results

This study included 257 patients (105 males and 152 females) with a mean age of 32.7 years (range, 15-80 years). The total seroprevalence of HIV infection in the study population was 52.1% (134/257). There was no statistically significant difference in HIV infection rate between males and females. Analysis of body mass index (BMI) indicated that 67.3% of the patients had a BMI of <18.5 kg/m^2. This was more pronounced and frequent among HIV-positive TB patients as compared to HIV-negative ones. Severe malnutrition (BMI <15.9 kg/m^2), moderate malnutrition (BMI = 16-16.9 kg/m^2), and mild malnutrition (BMI = 17-18.4 kg/m^2) were observed in 20.6%, 17.1%, and 29.6% of the patients, respectively.

Table 1 shows clinical symptoms and physical findings of the patients by HIV serostatus. The common clinical symptoms were low-grade fever in 93%; weight loss, 90.3%; night sweating, 86%; and cough, 82.5% with productive sputum in 180 patients (70% of all TB cases). History of chest pain was found in 94 (36.6%), hemoptysis in 52 (one-fifth of all cases), and chronic diarrhea in 27 patients (10.5%). The most common clinical signs were coarse crepitations, lymphadenopathy, hydrothorax, consolidation, cavitations, post-herpes zoster scar, and organomegaly in decreasing order (Table 1). Patients with herpes zoster skin scar were 16.4 times more likely to have HIV than those without infection with zoster. Those with coarse crepitations in the chest were 2.2 times more likely to have HIV coinfection than those without crepitations. Chronic diarrhea and duration of cough for ≤5 months were significantly associated with HIV. Irrespective of the HIV serostatus, most patients had fever, weight loss, night sweats, and anorexia. This was true for patients with PTB and EPTB.

Out of 180 patients who had productive sputum, 38.3% (69/180) were found to be positive for AFB.

Table 1. Frequency distribution of clinical features of tuberculosis (TB) patients by human immunodeficiency virus (HIV) serostatus

Clinical features	HIV positive No. (%)	HIV negative No. (%)	Odds ratio (95% CI)
Fever	127 (53.1)	112 (46.9)	1.8 (0.6-4.6)
Weight loss ≥5 kg	67 (69.1)	30 (30.9)	3.1 (1.8-5.3)
Night sweats	120 (54.3)	101 (45.7)	1.8 (0.9-3.6)
Cough	114 (53.8)	98 (46.2)	1.4 (0.8-2.8)
Cough ≤5 months	97 (61.0)	62 (39.0)	3.3 (1.7-6.4)
Loss of appetite	106 (54.6)	88 (45.4)	0.7 (0.4-1.2)
Sputum production	98 (54.4)	82 (45.6)	1.2 (0.6-2.5)
Chest pain	49 (52.1)	45 (47.9)	0.9 (0.6-1.7)
Hemoptysis	28 (53.8)	24 (46.2)	1.1 (0.6-2.0)
Coarse crepitation	54 (62.1)	33 (37.9)	1.8 (1.1-3.1)
Lymphadenopathy	44 (56.4)	34 (43.6)	1.3 (0.8-2.2)
Pleural effusion	26 (59.1)	18 (40.9)	1.4 (0.7-2.7)
Signs of cavitation	15 (68.2)	7 (31.8)	2.1 (0.8-5.3)
Signs of consolidation	13 (61.9)	8 (38.1)	1.4 (0.6-3.3)
Hepatomegaly	11 (64.7)	6 (35.3)	1.7 (0.6-4.9)
Splenomegaly	11 (64.7)	6 (35.3)	1.7 (0.6-4.9)
Chronic diarrhea	20 (74.1)	7 (25.9)	2.9 (1.2-7.1)
Herpes zoster scar	17 (94.4)	1 (5.6)	17.7 (2.3-135.3)
History of TB treatment	24 (58.5)	17 (41.5)	1.4 (0.7-2.7)

Abbreviation: CI = confidence interval

Table 2. Clinical features associated with sputum smear-positive pulmonary tuberculosis

Clinical feature	AFB+ No. (%)	AFB– No. (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Signs of cavitation	17 (77.3)	5 (22.7)	12.0 (4.2-34.0)	9.0 (2.4-34.1)
Signs of consolidation	11 (50.0)	11 (50.0)	3.1 (1.3-7.4)	2.2 (0.8-6.6)
Coarse crepitations	41 (47.1)	46 (52.9)	4.5 (2.5-8.1)	2.4 (1.2-4.7)
Cough	67 (31.6)	145 (68.4)	9.9 (2.3-42.2)	8.5 (1.8-40.0)
Hemoptysis	21 (40.4)	31 (59.6)	2.2 (1.2-4.2)	1.8 (1.0-3.4)
Herpes zoster scar	0	18 (100.0)	0.0 (0.0-1.3E+7)	0.0 (0.0-1.3E+7)

Abbreviations: AFB+ = acid-fast bacilli-positive; AFB– = acid-fast bacilli-negative; OR = odds ratio; CI = confidence interval

Among these, 52.2% (36/69) were HIV-seropositive and 47.8% (33/69) were HIV-seronegative TB patients. The sputum smear positivity did not show statistically significant association with HIV serostatus ($\chi^2 = 0.011$, df = 1, p=0.52). Similarly, cavitary signs on examination did not differ significantly by HIV serostatus ($\chi^2 = 2.48$, df = 1, p=0.087), although they were significantly associated with sputum smear positivity for AFB in 80% (12/15) and 71% (5/7) of HIV-positive and HIV-negative TB patients, respectively ($\chi^2 = 31.14$, df = 1, p=0.000). History of cough and hemoptysis and sign of cavitations as well as coarse crepitations in the chest were independent predictors of sputum smear-positive TB, whereas history of herpes zoster attack predicted sputum smear negativity (Table 2).

Table 3 shows the relationship between HIV serostatus and site of TB. The lungs were the most common site of the disease in both HIV-positive and -negative patients. The most common extrapulmonary involvements were lymph nodes and pleura. PTB and EPTB were diagnosed in 62.4% (165/257) and 35.8% (92/257) of the patients, respectively. The overall sputum smear-positive rate was 26.8% (69/257) and the sputum smear-negative rate was 37.4% (92/257) [Table 4]. HIV seroprevalence was not significantly different between PTB (53.3%, 88/165) and EPTB (50.0%, 46/92) patients.

Table 3. Anatomical sites of tuberculosis (TB) by human immunodeficiency virus (HIV) serostatus

Site of TB	HIV status		Total (n = 257) No. (%)
	Positive (n = 134) No. (%)	Negative (n = 123) No. (%)	
Lung	94 (51.9)	80 (50.9)	174 (51.5)
Lymph node	44 (24.3)	34 (21.7)	78 (23.1)
Pleura	26 (14.4)	18 (11.5)	44 (13.0)
Peritoneum	5 (2.8)	7 (4.5)	12 (3.6)
TB spondylitis	2 (1.1)	8 (5.1)	10 (2.9)
Miliary	6 (3.3)	3 (1.9)	9 (2.7)
Pericardium	1 (0.5)	2 (1.3)	3 (0.9)
Others	3 (1.7)	5 (3.2)	8 (2.4)

Chest X-ray examinations were carried out for a total of 185 patients. Classical pattern was seen in 52.4% (97/185) of the patients out of which 28.6% (53/185) were coinfected with HIV. Atypical chest X-ray pattern was observed in 88 (47.6%) patients, of whom 27% (50/185) and 20.5% (38/185) were found to be HIV-seropositive and HIV-seronegative, respectively.

Of the total number of TB patients, 161 (62.6%) fall under category I, 6 (2.3%) under category II, and 90 (35.9%) under category III based on the WHO treatment categorization criteria [8,10,11]. TB category did not show any significant association with HIV serostatus ($\chi^2 = 1.93$, df = 2, p=0.38) [Table 4]. Among category I TB patients, 63 (39.1%) were PTB+ patients.

Discussion

Diagnosing active TB in people with HIV is a challenge in the developing world where resources, laboratory facilities, and technical expertise are often limited. Most of the symptoms of TB and X-ray findings are indistinguishable from those caused by other respiratory conditions. In addition, HIV pandemic poses a serious diagnostic and therapeutic challenge as a coinfection in high-burden countries [3].

This study demonstrates that the symptoms and clinical signs of TB were comparable in HIV-seropositive and -seronegative TB patients, as both groups had similar complaints of fever and weight loss, night sweats, cough, loss of appetite, chest pain, and hemoptysis. Coarse crepitations, lymphadenopathy, pleural effusion, and chest cavitations and consolidation were the common physical findings in decreasing order

Table 4. Type and frequency of tuberculosis (TB) diagnosis and treatment categorization by human immunodeficiency virus (HIV) serostatus

Diagnosis of tuberculosis	HIV status		Total No. (%)
	Positive No. (%)	Negative No. (%)	
Type			
Smear-positive PTB	36 (26.9)	33 (26.8)	69 (26.8)
Smear-negative PTB	52 (38.8)	44 (35.8)	96 (37.4)
EPTB	46 (34.4)	46 (37.3)	92 (35.8)
Category			
I	89 (55.3)	72 (44.3)	161 (62.6)
II	4 (66.7)	2 (33.3)	6 (2.3)
III	41 (45.6)	49 (54.4)	90 (35.9)

Abbreviations: PTB = pulmonary TB; EPTB = extrapulmonary TB

of occurrence. The absence of any difference in most of the clinical features between the HIV-seropositive and -seronegative TB patients might be due to the chronic nature of TB, leading to protracted ill-health and wasting [12]. Hence, the mere presence of TB will not indicate the level of immunosuppression posed by HIV infection in countries such as Ethiopia where there is a high burden of TB. On the other hand, however, the presence of herpes zoster scar, chronic diarrhea, coarse crepitations, and cough of ≤5 months' duration showed significant association with positive HIV serology in the patients. These may assist in identifying TB patients with HIV infection.

The overall rate of sputum PTB+ in the present study was 27% of all forms of TB and 42% of PTB cases. This figure is much lower than the global target of 70.0% [13], and the national figure of 54.0% [2]. However, the rate is higher than that reported from Addis Ababa by Bruchfeld et al [14], where of all PTB cases, less than 20% were sputum smear-positive. The sputum PTB– cases in our study accounted for 37% of all forms of TB and for 58% of the PTB cases, whereas the EPTB cases were found in 36% of all forms of TB. The high number of PTB– and EPTB cases in our study could be partly due to the referral system adopted in the country, where health centers are allowed to treat only sputum PTB+ patients and must refer other suspected TB patients to hospitals such as ours. On the other hand, non-adherence to diagnostic algorithm, poor quality of sputum processing and microscopy, lack of culture facility as well as high HIV coinfection might contribute to such high sputum smear-negative rates. It is noteworthy that the clinical features and chest radiographic findings of HIV/acquired immunodeficiency syndrome patients are similar to that of PTB patients. This might artificially inflate the PTB– diagnosis short of other diagnostic methods in cases where patients have other pulmonary pathologies.

The findings from the northern part of Ethiopia also showed values far below the national and global targets [15]. In that study, 17.7%, 42.6%, and 39.7% of TB patients were diagnosed as having PTB+, PTB–, and EPTB, respectively. Another study from southwest Ethiopia showed the proportion of PTB+, PTB–, and EPTB as 34.1%, 24.2%, and 41.7%, respectively [16]. In Nigeria, sputum smear-positive rate in patients at a directly observed therapy-short course (DOTS) clinic was 21.3% in 2005 [17]. It should be mentioned that about 80% of the global new TB cases each year occur in 22 high-burden countries (and Ethiopia is among the top 6) where 75% of undetected smear-positive cases were living in 2000, which will remain undetected under full geographic DOTS coverage [18].

The HIV prevalence rate of 52.1% observed among the TB patients in this study is much higher than previous reports from Ethiopia which ranged from 0.6% to 45% [19-22] and a recent report from Gambia which was 8.3% [23]. However, it is lower than an earlier report from Tanzania where 65% of TB patients were also co-infected with HIV [24].

In this study, the lung was the most common site of TB in both HIV-positive and -negative patients. Lymph node and pleural involvement as well as miliary pattern were observed more often among HIV-seropositive than HIV-seronegative TB patients as was also reported earlier [12,21,25]. A lower BMI was found in more patients with dual infection, as seen in other African countries [25]. Significant weight loss is common with TB and is associated to a greater extent with HIV as a wasting syndrome [12,26].

Pulmonary cavitation in this study was observed more often in HIV-seropositive TB patients than in HIV-seronegative TB patients. This finding is in agreement with earlier reports [27,28]. There is an association between pulmonary cavitations (independent predictor) and sputum positivity, where 12 out of 15 HIV-seropositive and 5 out of 7 HIV-seronegative PTB patients with cavitations were found positive for AFB.

The correlation between chest radiographic manifestations with the degree of immunosuppression has been well established [5,12]. However, in this study, the classical chest X-ray feature was found more often in HIV-seropositive PTB patients; this is in conflict with the results of the study carried out in Addis Ababa [29]. This may be explained by the high prevalence of TB in the country which would allow the occurrence of TB at any stage of HIV infection [12]. Findings in Zaire and Cote d'Ivoire showed that HIV-related TB can present across a wide spectrum of immunodeficiencies and that the clinical presentation may vary among patients [12]. In countries with high TB prevalence such as Ethiopia, a high proportion of cases with active TB reactivate early in the spectrum of HIV disease with upper lobe fibrocavitary lesions on chest radiography and *M. tuberculosis* infection preceding HIV infection [30].

Although the present study provides important clinical aspects of TB and HIV coinfection in a resource-constrained set-up in a developing county with high prevalence of the 2 diseases, it has some drawbacks which are subject to future studies. These include: (1) the lack of mycobacterial culture, which would have helped in delineating infection by TB bacilli or *Mycobacterium avium* complex; (2) the diagnoses of HIV infections were made solely by enzyme immune assay due to lack of confirmatory test (Western blot); and (3) CD4 T cell count was not performed, which would have helped in the clinical staging of HIV infection.

In conclusion, the prevalence of HIV in TB patients was very high and the proportion of PTB+ is far below the target set by WHO. Except for herpes zoster scar, chronic diarrhea, coarse crepitations, and cough of ≤5 months' duration, which were significantly associated with HIV-positive serology, most of the clinical presentations of TB were comparable in both HIV-seropositive and -seronegative patients. The presence of such features may assist in identifying TB patients with HIV infection.

Acknowledgments

This study was financially supported by the Research and Publications Office of the University of Gondar. We would like to thank the study participants, without whom this study could not have been completed.

References

1. Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC. Consensus statement. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. WHO Global Surveillance and Monitoring Project. JAMA. 1999;282:677-86.
2. World Health Organization. Global tuberculosis control: surveillance, planning, financing. WHO/CDS/TB/2003.316. Geneva, Switzerland: World Health Organization; 2003.
3. Corbett EL, Watt CJ, Walker N, Maher D, Williams BG, Raviglione MC, et al. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. Arch Intern Med. 2003;163:1009-21.
4. Frieden TR, Sterling TR, Munsiff SS, Watt CJ, Dye C. Tuberculosis. Lancet. 2003;362:887-99.
5. Grant AD, Djomand G, De Cock KM. Natural history and spectrum of disease in adults with HIV/AIDS in Africa. AIDS. 1997;11(Suppl B):S43-54.
6. UNAIDS/WHO. Reports on the global AIDS epidemic: December. Geneva, Switzerland: UNAIDS/WHO; 2004.
7. AIDS in Ethiopia. 5th ed. Addis Ababa, Ethiopia: Ministry of Health; 2004.
8. Manual on tuberculosis and leprosy prevention and control program. 2nd ed. Addis Ababa, Ethiopia: Ministry of Health; 2002.
9. World Health Organization. TB/HIV: a clinical manual. Geneva, Switzerland; 1996.
10. World Health Organization. Treatment of tuberculosis: guidelines for national programmes, 3rd ed. WHO/CDS/TB/2003.13. Global tuberculosis programme. Geneva, Switzerland: World Health Organization; 2003.
11. World Health Organization. Administering treatment. Managing TB at the regional level, module 3. WHO/CDS/TB/2002.310. Geneva, Switzerland: World Health Organization; 2003.
12. Harries AD. Tuberculosis in Africa: clinical presentation and management. Pharmacol Ther. 1997;73:1-50.
13. World Health Organization. 44th World Health Assembly (WHA/1991/REC/1) Supplemented by 53rd World Health Assembly. Report by the Director General, Provisional Agenda Item 12.1, A53/5. Geneva, Switzerland: World Health Organization; 2000.
14. Bruchfeld J, Aderaye G, Palme IB, Bjorvatn B, Britton S, Feleke Y, et al. Evaluation of outpatients with suspected pulmonary

tuberculosis in a high HIV prevalence setting in Ethiopia: clinical, diagnostic and epidemiological characteristics. Scand J Infect Dis. 2002;34:331-7.
15. Mesfin MM, Tasew TW, Richard MJ. The quality of tuberculosis diagnosis in districts of Tigray region of northern Ethiopia. Ethiop J Health Dev. 2005;19:13-20.
16. Michael KW, Belachew T, Jira C. Tuberculosis defaulters from the "dots" regimen in Jimma zone, southwest Ethiopia. Ethiop Med J. 2004;42:247-53.
17. Bassey EB, Momoh MA, Imadiyi SO, Udofia EB, Miri FS, Anukam KC, et al. The trend of pulmonary tuberculosis in patients seen at DOTS clinics in the Federal Capital Territory, Abuja, Nigeria. Public Health. 2005;119:405-8.
18. Dye C, Watt CJ, Bleed DM, Williams BG. What is the limit to case detection under the DOTS strategy for tuberculosis control? Tuberculosis (Edinb). 2003;83:35-43.
19. Kefenie H, Zewdie D, Desta B, Mehari H, Fekede H. The prevalence of HIV-1 antibodies in 106 tuberculosis patients. Ethiop J Health Dev. 1990;4:197-200.
20. Mitike G, Kebede D, Yeneneh H. HIV infection and antituberculosis drug resistance among pulmonary tuberculosis patients in Harar Tuberculosis Centre, Ethiopia. East Afr Med J. 1997;74:154-7.
21. Gellete A, Kebede D, Berhane Y. Tuberculosis and HIV infection in southern Ethiopia. Ethiop J Health Dev. 1997;11: 51-9.
22. Demissie M, Lindtjørn B, Tegbaru B. Human immunodeficiency virus (HIV) infection in tuberculosis patients in Addis Ababa. Ethiop J Health Dev. 2000;14:277-82.
23. Rathman G, Sillah J, Hill PC, Murray JF, Adegbola R, Corrah T, et al. Clinical and radiological presentation of 340 adults with smear positive Tuberculosis in Gambia. Int J Tuberc Lung Dis. 2003;7:942-7.
24. Schoch OD, Rieder HL. Characteristics of sputum smear-positive tuberculosis patients with and without HIV infection in a hospital in Zimbabwe. Eur Respir J. 1996;9:284-7.
25. Kumar P, Sharma N, Sharma NC, Patnaik S. Clinical profile of tuberculosis in patients with HIV infection/AIDS. Indian J Chest Dis Allied Sci. 2002;44:159-63.
26. Bane A, Yohannes AG, Fekade D. Morbidity and mortality of adult patients with HIV/AIDS at Tikur Anbessa Teaching Hospital, Addis Ababa, Ethiopia. Ethiop Med J. 2003;41: 131-40.
27. Colebunders RL, Ryder RW, Nzilambi N, Dikilu K, Willame JC, Kaboto M, et al. HIV infection in patients with tuberculosis in Kinshasa, Zaire. Am Rev Respir Dis. 1989;139:1082-5.
28. Raviglione MC, Narain JP, Kochi A. HIV-associated tuberculosis in developing countries: clinical features, diagnosis, and treatment. Bull World Health Organ. 1992;70:515-26.
29. Aderaye G, Bruchfeld J, Assefa G, Feleke D, Kallenius G, Baat M, et al. The relationship between disease pattern and disease burden by chest radiography, *M. tuberculosis* load and HIV status in patients with pulmonary tuberculosis in Addis Ababa. Infection. 2004;32:333-8.
30. Abouya L, Coulibaly IM, Coulibaly D, Kassim S, Ackah A, Greenberg AE, et al. Radiologic manifestations of pulmonary of tuberculosis in HIV-1 and HIV-2-infected patients in Abidjan, Cote d'Ivoire. Tuber Lung Dis. 1995;76:436-40.