Original article

Tuberculosis and HIV infection in southern Ethiopia

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Abstract: A health institution-based cross-sectional study was carried out in Shashemene town, southern Ethiopia, between September, 1993 and January, 1994 to determine the sero-prevalence and the clinical impact of HIV among newly diagnosed tuberculosis patients. The HIV-antibody was determined using the two ELISA procedures (Wellcozyme, Wellcome Diagnostics, Dartford Kent England, and Du-pont assay, Singapore). A total of 450 tuberculosis patients aged 15 years and above were enrolled in the study. The overall HIV-seroprevalence rate was 44.4%. The highest rate was observed in the age group 20-39 years. A slightly higher HIV-infection rate was found in males (46%) than in females (41%). Those divorced and widowed patients had higher proportion of HIV sero-positivity. The HIV positivity rate was higher for extra-pulmonary than pulmonary form of tuberculosis (OR = 3.80; 95% CI: 1.49, 9.7). Higher proportions of sputum positive patients were HIV-positive compared to the sputum negative pulmonary tuberculosis patients (OR=1.09; 95% CI: 0.64,1.85) though they manifested typical radiographic features (OR = 7.87; 95% CI: 4.39, 14.21). Significant differences were noted among HIV positives than HIV negatives in manifesting herpes zoster, lymphadenopathy, oral candidiasis, peripheral paraesthesia and chronic diarrhoea. An alternative diagnostic approach is required to avoid missing HIV-related tuberculosis which is communicable to the general population. Other findings are discussed and recommendations made. [*Ethiop. J. Health Dev.* 1997;11(1):51-59]

Introduction

Tuberculosis remains a health problem of enormous dimensions, particularly in the developing world, affecting millions of people each year. The pandemic of the acquired immunodeficiency syndrome (AIDS) and the evidence of an association between TB and HIV, which causes AIDS is now a further cause for world-wide concern (1-4).

Considering that the great majority of HIV infections occur among the 15-49 year-old,(5,6) and assuming that the risks of infection with HIV and tuberculosis are independent, it has been estimated that world wide more than 4 million persons, again mostly in the developing countries, have been infected with both HIV and Mycobacterium tuberculosis.

The most important risk factor yet identified for the development of tuberculosis following infection is human immunodeficiency virus infection. Very high incidence rates of TB in dually infected individuals have been reported in both industrialized and developing countries (7).

In the developing countries, the overlap between HIV infection and tuberculosis is shown by the high HIV sero prevalence among patients presenting with active tuberculosis. Data from a number of African countries and Haiti show that sero-prevalence ranges between 17% and 66% (2, 8-12). Developing countries are also faced with the problem of the increased cost of tuberculosis treatment brought about by the increase in numbers of cases (13).

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The HIV pandemic will worsen the TB situation in developing countries in three ways over and above the existing situation by (a) reactivation of a latent TB infection among dually infected persons

(b) new infection with tubercle bacilli and rapid progression to active disease in HIV infected persons and (c) increasing the number of cases in the general population whose infection and disease is the result of transmission from HIV positive individuals developing TB by either reactivation or recent infection (14-16).

The influence of HIV-infection on the clinical picture of tuberculosis has been examined by studies in Africa (2) and elsewhere (17,18). In Ethiopia one study, conducted among 106 soldiers in 1988, has reported a 6.6% seropositivity among TB patients (19). Although a 1990 national tuberculin survey has shown an annual tuberculosis infection rate of 1.4%, and the disease is ranked first as cause of death for adults admitted to health care units (20), its relationship to HIV infections has not been well studied. The present study was thus undertaken to assess the magnitude of HIV infection in tuberculosis patients and describe the clinical manifestation of tuberculosis in HIV infected individuals.

Methods

This health institution-based cross-sectional study was conducted in Shashemene, a town located in southern Ethiopia, between September, 1993 and January, 1994. The town is found 250 kms along the main road from Addis-Ababa to Moyale-Kenya. It has a wide communication network connecting more than four regions of the country.

The sources of the study subjects include both inpatient and outpatient departments of Shashemene General Hospital, one Health Centre and another two health institutions (Gambo Catholic Hospital and Awassa Health Centre) which frequently refer patients to the Shashemene Hospital for the antiTB treatment. All new tuberculosis patients who came seeking the services of the health institutions were included in this study. New patients with a suspected and/or confirmed diagnosis of tuberculosis between September 5, 1993 and January 10, 1994 at the local hospital and health centre were entered in the study.

The purpose of the study was explained to the heads of health institutions in the study areas and to the clinicians who work there. Physicians in the health centres and hospitals were asked to refer all suspected TB cases to the research team for further investigation of the patient. Accordingly a total of 450 newly diagnosed TB patients were enrolled in the study.

To maximize efficient utilization of the ELISA reagent, patients' sera were stored at 20°C in Shashemene General Hospital and later analysed according to the Kit manufacturer's instructions.

The following operational definitions of tuberculosis were used: *confirmed TB diagnosis*: Pulmonary TB was diagnosed when there are two Acid Fast Bacili(AFB) positive results of sputum specimen; or a patient with one sputum specimen positive for AFB and radiologic abnormalities consistent with active pulmonary tuberculosis. *Suspect case*: patient in whom presumptive diagnosis is made on the basis of radiological or other clinical evidence and with negative AFB smear. *New case*: patient who was diagnosed with tuberculosis for the first time. *Disseminated TB*: there are more than two organs, other than pleural and lymph node, affected by the lesion. *HIV-Positivity* was defined to occur when patients tested positive to the combination of Wellcozyme and Dupont assays. A standardized questionnaire was used to collect demographic and clinical information. Physicians from each health institution filled out the questionnaires. In this questionnaire, information relating to their history and clinical examination was completed for each patient, radiological and laboratory results were recorded and blood samples taken by laboratory technicians. All patients with pulmonary tuberculosis had a chest X-ray. Radiological features, including the zones involved and the presence or absence of cavities, were recorded by the physician at the time of recruitment.

Seroprevalence was determined for all new TB patients who were 15 years of age and above, irrespective of the lesion site. All patients with suspected/confirmed TB were enrolled for the analysis of clinical presentations. Patients seen at the health institutions were treated according to the national guidelines by the respective health units. Serum samples were analysed for the HIV antibody by a competitive recombinant enzyme linked immunosorbent assay (Wellcozyme,

Welcome Diagnostics, Dartford, Kent UK) and antiglobulin recombinant ELISA assay (Dupont, Singapore). There are as yet, no reports of HIV-2 in Ethiopia. Throughout this text HIV-1 seropositivity is referred to as HIV-seropositivity.

Procedures were performed according to the kit manufacturer's instructions. Only those seropositive on both assays were considered HIV-positive. Studies in Addis Ababa (21), Kenya (22), and Zambia (2,23) showed this definition to be concordant with Western-Blot for HIV-1. This examination strategy is also supported by a recent WHO report (24). Sputum was examined for acid fast bacilli on direct smear using Ziehl-Neelsen stain and fluorescence microscopy with a 25 x objective and 6.5 x eye pieces. Serological testings were carried out anonymously, with all clinical and laboratory data being identified only by a code number.

A chest X-ray was performed for all pulmonary tuberculosis patients and read by three general practitioners (with similar year of experience) who have undertaken special training on the radiology of the chest to run the tuberculosis follow-up clinics.

Data entry and analysis were done using EPI INFO and SAS computer statistical packages. Initial analysis of the association between HIV seropositivity and various variables were performed using standard 2 x 2 tables. Further analyses were carried out using logistic regression. Where appropriate, Maentel Haenszel Chi-square methods were applied to test for trends. The odds ratios (OR) presented are the antilogs of the logistic regression co-efficient. Ninety-five percent confidence intervals were calculated and statistical significance was designated at $P < 0.05$. Patients were informed of the study procedures and the tests to be made during the investigation. Informed verbal consent was obtained from each participant. TB treatment was free for all study participants and anti-TB drug stock adequate for full course was secured for both study centres. Counselling service to be offered to HIV positive patients was organized in collaboration with the Zonal Health Department prior to the initiation of the study. The study was approved by the ethical committee of both the Department of Community Health and Faculty of Medicine, Addis Ababa University.

Results

Between September, 1993 and January, 1994, a total of 450 tuberculosis patients were enrolled in the study. Of the 450 patients there were 269 (60%) males and 181 (40%) females. The mean age of the patients was 30 years. Most patients 254 (56%) were from Shashemene, 97 (22%) were students. Farmers and housewives accounted for 17% each. The remaining 203 (45%) belonged to different other occupations. (Table 1).

Overall, 199 (44%) of the patients were positive for HIV. There were nine indeterminate results who were negative by Wellcozyme and positive by the Du-pont assay. These patients were considered as HIV negatives.

As indicated in Table 1, there was no statistical difference in HIV sero-prevalence with regard to age and sex. However, in the age group of 20-39 and in male patients HIV positivity was found to be higher. The peak sero-prevalence occurred in the age group 20-29 years. Sex was not associated with HIV status in these patients when adjusted for age. The adjusted odds ratio (OR) and 95% confidence interval (95% CI) were 0.84(0.57, 1.21).

There was a statistically significant association between marital status and HIV positivity.(OR=0.60, 95% CI :0.40,0.88 $p<0.05$).The association persisted even after adjusting for age and sex. Patients who were widowed/separated or divorced had higher prevalence of HIV positivity. Occupational categories which were significantly associated with HIV positivity were government employees, prostitutes, merchants, ex-soldiers, and daily labourers.

Table 1: **The socio-demographic distribution of HIV positives among tuberclosis patients, southern Ethiopia, 1994.**

	HIV Status		
Age	Posititve	Negative	Adjusted OR (95% CI)
15-19	27(40.9)	39(59.1)	1[2]
20-29	76(47.8)	83(52.2)	1.48 (0.86, 2.56)
30-39	62(46.6)	71(53.4)	1.56 (0.92, 2.64)

≥40	34(36.9)	8(63.1	1.18 (0.61, 2.25)
Sex			
Male	24(46.1)	45(53.9)	0.84 (0.57, 1.2)
Female	75(41.4)	06(58.6)	1.00 [2]
Marital Status			
Single	00(50)	03(41)	1[2]
Married	79(40)	35(54)	0.60 (0.40, 0.88)
Other	20(10)	13(5)	1.56 (0.73, 3.3)
Occupation			
Farmer	25(33)	50(67)	1[2]
Student	32(33)	65(67)	1.98 (0.51, 1.86)
Driver	9(35)	17(65)	1.05 (0.40, 2.7)
Hous-wife	27(36)	48(46)	1.12 (0.57, 2.2)
Daily labourer	13(52)	12(48)	2.15 (0.85, 5.4)
Ex-Soldier	26(55)	21(45)	2.46 (1.16, 5.2)
Merchant	22(59)	15(41)	2.91 (1.28, 6.59)
Prostitute	9(60)	6(40)	2.97 (1.94, 3.4)
Gov't employee	23(64)	13(36)	3.50 (1.50, 8.1)
Other	13(76)	4(24)	6.5 (1.92 , 22.1)
	27(40.9)	39(59.1)	1 [2]

[1]Adjusted odds ratio and 95% confidence interval. The logistic regression model included age (4 levels), sex, marital status (3 levels) and occupation (10 levels).
[2]Referenc category

Two hundred sixty nine patients were diagnosed as having pulmonary disease on the basis of clinical findings, radiographic and/or sputum smear results. In 128 (48%) of them tubercle bacilli were identified by the Ziehl Neelson stain method. In this study, patients with extrapulmonary tuberculosis were more likely to be HIV sero-positive than were patients with pulmonary lesions. Table 2 shows the relationship between HIV status and site of tuberculosis. Extrapulmonary disease (pleural, lymph node, disseminated), both alone and in combination with parenchymal lung disease, was strongly associated with HIV infection (OR = 3.92; 95% CI: 1.54, 9.9) $P < 0.05$. The association persisted when adjusted for age and sex (OR = 3.80 95% CI: 1.49, 9.7) $P < 0.05$. The lungs were, however, the commonest site of the disease in both HIV positive and negative patients.

The overall proportion of hospitalized tuberculosis patients was 29%. Out of these 41% were positive for HIV infection, while 46% of the ambulatory TB patients were sero-positive. The seroprevalence of HIV infection in hospitalized TB patients was not significantly different from those who attended the out-patient department. No significant association between HIV status and sputum examination result for AFB was observed in this study.

Table 2: **Association between sites of tuberculosis and HIV sero-positivity, southern Ethiopia, 1994.**

	HIV Status			OR (95% CI)
	Positive N=199	Negative N=251		
Pulmonary	95	174	1[1]	1[2]
Pleural	12	6	3.66(1.33, 10.0)	3.45(1.24
Disseminated	28	27	1.89(1.05, 3.40)	2.02(1.11
Lymph node	49	37	2.42(1.47, 3.97)	2.48(1.40
Pulm + EP	15	7	3.92(1.54, 9.9)	3.80)1.49

[1]Adjusted for age and sex by logistic regression.
[2]Reference category

Chest X-rays were available for all pulmonary TB patients (Table 3). The chest X-rays showed pulmonary cavitation in 79 (55%) of the HIV negative, but in only 65 (45%) of those HIV-positives. (OR = 2.61; 95% CI: 1.49, 4.56, $P < 0.05$). In seventy six (52%) of the 174 HIV negative pulmonary TB patients upper zone lesions predominated compared with 70 (48%) among the 95 HIV positive cases. (OR = 3.61; 95% CI: 2.02, 6.48, $P < 0.05$). When the association between HIV status and AFB sputum smear were positivty stratified for the presence of cavitation and superior segment involvement, trends were still present, but were less marked and were not statistically significant. As shown in Table 4, patients who had upper lobe infiltration appear to be nearly equally divided

between sputum smear positives and negatives; and most sputum positives appeared to have pulmonary cavitation (OR = 7.87; 95% CI: 4.39, 14.21).

Table 3: **Radiographic findings in cases with pulmonary tuberculosis in relation to HIV infection, southern Ethiopia, 1994.** X-ray findings HIV Positive No (%) HIV Negative No (%) Adjusted[2] OR (95% CI)

	n=95	n=174	
Upper zones only			
Yes	70(48)	76(52)	1.00[2]
No	25(20)	98(80)	3.61(2.02, 6.48)
Middle/Lower Zone			
Included	35(30	80(70)	1.00[2]
Not Included	60(39)	94(61)	0.69(.40, 1.18)
Cavitation			
Present	65(45)	79(55)	1.00[2]
Absent	30(24)	95(76)	.61(1.49, 4.56)

[1]Adjusted for age and sex by logistic regression.
[2]Reference category

Table 5, shows the relationship between symptoms and signs at presentation and HIV status. A significant number of sero-negative TB patients had complained of cough and fever. Prolonged history of cough and fever was also reported by a large proportion of TB patients. There was no significant difference in the history of marked weight loss and organomegaly among the HIV positive and negative patients. A large proportion of patients who presented with lymphadenopathy were positive for HIV.

Clinical signs and symptoms which showed an association with HIV infection were generalized lymphadenopathy, oral candidiasis, herpes zoster, chronic diarrhoea and paraesthesia. Sputum positive tuberculous patients showed a slight difference from sputum negatives in the development of fever. Most sputum negative patients had a more prolonged fever than the others. Large numbers of sputum negative patients tended to manifest with chronic cough than smear positive patients ($x^2 = 29.15$; df = 2, P <0.001).

Discussion

The sero-prevalence rate of 44.4% in this study is consistent with other studies conducted in Sub-Saharan Africa, the Caribbean and in some urban areas of the United States that have shown 2060% of tuberculosis patients to be HIV sero-positive (3,4). However this rate is much higher than that previously reported from testing of 106 Ethiopian soldiers in 1990

(19). This marked difference could be attributed to study size differences and to the rapid dissemination of HIV infection over time, with essential consideration of the time of introduction of the virus in the country and the level of immune compromise. Although evidence on the proportion of HIV/AIDS patients who developed tuberculosis is required this study partly supports the new HIV/AIDS case definition for Ethiopia which considers TB as a major criterion.

Table 4: **Association between sputum smear positivity and radiographic appearances among pulmonary TB patients, southern Ethiopia, 1994.**

	Sputum for AFB		Adjusted[1] OR (95% CI)
	Positive	Negative	
Cavity			
Present	00(69)	44(31)	1[2]
Absent	28(22)	97(78)	7.87(4.39, 14,21)
Upper zone involvement			

[1] Adjusted for age and sex by logistic regression. [2]Reference category

The sero-prevalence of HIV-infection in hospitalized TB patients was not significantly different from those attending the out-patient department. However, inferences regarding the prevalence of

Yes	52(52)	48(48)	1[2]
No	76(44)	93(56)	.33(0.78, 2.24)

[1]Adjusted for age and sex by logistic regression.
[2]Reference category

The findings in this study are also in conformity with the other observations that have been noted in the USA, Europe and Africa (1,2,5-12).

The higher sero-positivity observed in this study among the age group 20-39 years is comparable with other African studies (2,6,8,13). The younger ages at which sero-reactive persons developed tuberculosis probably reflects the age prevalence of HIV sero-positive persons in the community, as it is similar to that reported from the surveillance data in this country (21).

Distribution of HIV positivity across the various occupatons in this study indicates the wider distribution of the infection in the community. Accordingly, the practice of concentrating on specific groups of the population while addressing health education deserves re-consideration.

The association of HIV infection with marital status is compatible with the known transmission dynamics of HIV. Being single has a higher risk of acquiring the infection.

Table 5: **HIV sero-positivity and selected clinical findings among tuberculosis patients, southern Ethiopia, 1994.**

Clinical Findings	HIV +ve No (%) (n=199)	HIV -ve No (%) (n=251)	Adjusted[1] OR (95% CI)
Candidiasis			
Present	12(6)	5(2)	3.16(1.02, 10.4) 0.02
Absent	187(94)	246(98)	1 [2]
Lymphadenophaty			
Absent	58(29)	51(20)	1.61(1.02, 2.55) 0.03
Present	141(71)	200(80)	1.00 [2]
Herpes Zoster			
Absent	14(7)	6(2)	3.46(1.21, 10.3) 0.008
Present	185(93)	245(98)	1.00 [2]
Hepatomegaly			
Present	35(18)	52(21)	0.82(0.49, 1.35) 0.40
Absent	164(82)	199(79)	1.00 [2]
Splenomegaly			
Present	164(15)	199(79)	1.22(1.74, 2.03) 0.40
Absent	35(85)	52(21)	1.00 [2]
Paraesthesia			
Present	30(15)	17(7)	2.44(1.25, 4.80) 0.004
Absent	164(85)	234(93)	1.00 [2]
Marked weight loss			
Present	124(62)	155(62)	1.02(0.69, 1.53 0.09
Absent	75(38)	96(38)	1.00 [2]
Fever			
None	8(4)	10(4)	1.00[2]
< one month	67(34)	92(36)	0.91(0.34, 2.4) 0.5
≥One month	124(62)	149(59)	1.04(0.39, 27)
Cough			
None	40(20)	40(16)	1.00[2]
<one month	35(18)	42(17)	0.83(0.44, 1.56) 0.45
≥one month	124(62)	196(67)	0.73(0.44, 2.04)
Diarrhea			
None	53(77)	221(88)	1.00[2]
<one month	32(16)	18(7)	2.56(1.39, 4.74) 0.008
≥one month	14(7)	12(5)	1.68(0.75, 3.74)

HIV infection in hospitalized TB patients depends on many factors that may have changed over time, such as HIV specific mortality rates and criteria for hospital admission and discharge. Examination of this variation between the two sources of TB patients is required through further study.

In this study 29% of the patients with tuberculosis were admitted to the hospital for anti-TB treatment. This indicates the effect of HIV on work load of hospitals. The impact of HIV on resource utilization like hospital beds, diagnostic investigations and therapies has been studied elsewhere (16). This also reinforces the importance of educating all personnel involved in health care to take precautions against occupational exposure to HIV with all patients and to avoid possible nosocomial infections. In the absence of rapid and effective interventions, increasing numbers of HIV/TB cases are likely to occur and affect hospital admissions in Ethiopia.

In this study the lung was the commonest site of disease in both HIV positive and negative patients. Only 23% of HIV positive patients had positive sputum smears. Even though the absolute number of 46 was much less than the number of sputum-positive HIV negative cases, the role of HIV for the spread of the disease in the community should not be underestimated. Since pulmonary disease is probably more important in the transmission, the contribution of HIV positive TB patients to the spread of the disease is likely to be greater despite this association of HIV with extrapulmonary disease.

The proportion of HIV positive TB patients who had extrapulmonary infection alone (35%) was similar with that reported in a cohort study in Zambia (23), but was higher than other studies done in Zaire, Haiti and Ivory coast (2,11,12). This difference could have resulted from bias towards pulmonary disease during recruitment in those studies which were conducted at TB referral centres. Lymphadenopathy remains the most frequent form of extrapulmonary TB as reported from Central Africa Republic, Kenya, Zambia and Brazil (6). A study from Zaire also showed that patients with suspected TB and with extrapulmonary TB had higher HIV seropositivity rates than patients with sputum confirmed TB (2). This fact should be seen in the light of an essential consideration; i.e., a general shift of trend from pulmonary to extrapulmonary tuberculosis in the present HIV/AIDS era, thus leading to diagnostic difficulties by challenging/impeding the available diagnostic possibilities. Similar to other evidences obtained (2,11,22), there was no appreciable difference in HIV seropositivity among sputum smear positive and negative pulmonary TB patients. Similar findings were reported elsewhere (2,11,22), although others have reported a tendency for HIV positive patients to have a negative sputum smear (9). This variation may account for the level of immuno-deficiency posed by HIV infection and prior exposure to TB. The negative sputum smear among HIV positive patients probably indicates that HIV positive TB patients may frequently have dry cough. The TB detection rate based on sputum smear examination may thus be comparable to that described for HIV sero- negative patients, at least during the early stages of HIV disease (6).

The classic form of TB, with cavitating, upper zone, pulmonary lesions, is known to be determined by the interaction between the bacillus and the host's immune system so that, in the presence of immuno-deficiency, a different outcome may be expected (8).

In this study pulmonary cavitation was observed more often in HIV sero-negative TB patients when compared with HIV sero-positive TB patients. This finding is incompatible with other reports (2,6), and could be explained by the low grade immuno-depression in the study subjects, leading to the typical cavitary lesion. Similar findings have been reported (26,27) attributing the lesion to the interaction between the bacillus and the host's immune system.

In contrast to other evidence elsewhere (6,26,27) this study revealed that most HIV negative patients with pulmonary tuberculosis tend to have the classic upper lobe involvement. However, a large proportion of HIV positive patients had atypical presentation having supplementary middle/lower zone involvement and non cavitary appearance. These findings further strengthen the distorted radiographic appearance of TB patients which was established elsewhere (6).

A discrepancy between pulmonary cavitation, sputum positivity and upper lobe involvement was observed in this study. All sputum positive cases did not show cavitation and /or upper segment involvement. It has been observed that even in the absence of cavitation the profound impairment of the immunity seen in HIV infection may permit tubercle bacilli to multiply in such large numbers

as to become visible on smear examination (11). Therefore the above finding could probably be a reflection of this phenomenon.

Both tuberculosis and HIV infection lead to chronic ill-health and wasting, and both are associated with persistent cough and fever. These characteristics were also seen in this study, illustrating the difficulties in clinical diagnosis. Patients with tuberculosis, with or without HIV infection, might be diagnosed as having HIV/AIDS alone and might therefore fail to receive the anti-TB treatment. This study examined the impact of HIV on the process of diagnosis of TB. Symptoms of TB were comparable in both groups. HIV positive and negative patients, had similar complaints of cough, although fever was more frequent and of longer duration in HIV positives.

The presence of generalized lymphadenopathy, peripheral paraesthesia, herpes zoster, oral candidiasis and diarrhoea may assist in identifying patients with dual infection with tuberculosis and HIV but do not contribute to the diagnosis of TB itself. The lack of association between HIV and prolonged diarrhoea in this study could be attributed to possible recall bias. The tendency of sputum smear negative patients to manifest with prolonged cough and fever further threatens the sputum detection rate, thus compounding the difficulty of clinical diagnosis of pulmonary tuberculosis. In the absence of a quick and cheap diagnostic test, physicians may be obliged to treat patients with prolonged fever, cough, weight loss, negative sputum smear for acid fast bacilli and failure to respond to standard antibiotics, as tuberculosis cases without confirmation of the diagnosis. It is worth mentioning that this cross-sectional study lacks information about the role of HIV infection on tuberculosis relapse. A longitudinal design is required to address this issue.

It is to be noted that there are certain limitations to the study. The nature of the study itself has limited the collection of complete information from the patients regarding the clinical signs and symptoms. Nevertheless, since all new tuberculosis patients seen at the health institutions during the study period were included in the study, and the physicians involved in clinical examination of patients were the same, it is assumed that in general, the information obtained was comparable for all patients. Confirmation of TB diagnosis was not possible because of the inherent limitation of the diagnostic tests. Lymph node biopsy could not be done for logistic reasons. But it is unlikely that the limitations pointed out would compromise the main findings of the study.

The urban-rural mix of the study subjects and uniformity of the selection criteria used for enroling new TB patients with adequate sample size permits the internal validity and wider generalizability of the study findings.

In conclusion, the results show a high prevalence of HIV infection among tuberculosis patients. The results also show the difficulties of clinical diagnosis of co-infected patients who manifested unusual clinical, laboratory and radiographic features. A diagnostic approach with a higher degree of diagnostic ability is requ ired to avoid missing HIV-related tuberculosis which is communicable to the general population.

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