Diagnosis of tuberculosis in developing countries in the era of high HIV transmission; alternative approaches
Yassin, M.A.

Citation for published version (APA):
Yassin, M. A. (2005). Diagnosis of tuberculosis in developing countries in the era of high HIV transmission; alternative approaches Amsterdam: Rozenberg
Chapter 11

HIV and Tuberculosis co-infection in the Southern Region of Ethiopia: A prospective epidemiological study.
HIV and Tuberculosis Coinfection in the Southern Region of Ethiopia: A Prospective Epidemiological Study

MOHAMMED AHMED YASSIN1,2, LUELSEGED TAKELE1, SAHLEMARIAM GEBRESENBET1, EMEBET GIRMA1, MESKELE LERA1, ERSIDO LENDEBO1 and LUIS E. CUEVAS2

From the 1Southern Region Health Bureau, Awassa Ethiopia, 2Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, UK, 3Bethuho Major Health Centre, Awassa, Ethiopia, and 4HIV/AIDS Secretariat Council, Awassa, Ethiopia

HIV has played a key role in TB, modifying its incidence and clinical presentation. This study describes the prevalence of HIV among TB patients attending health facilities in the southern region of Ethiopia. The HIV prevalence was 18% for female and 21% for male TB patients. 15% and 30%, respectively, of the rural and urban patients with TB were HIV positive (p < 0.05). 19% (51/261) smear-positive PTB, 26% (36/137) smear-negative PTB and 11% (10/94) of the extrapulmonary TB patients were HIV positive. The proportion of patients with extra-PTB varied from 11% to 38% across the centres and was highest in the zones with the lowest HIV prevalence. In the light of limited diagnostic facilities, clinicians often make a clinical diagnosis of TB without laboratory confirmation. The increase in the number of TB cases could be due to HIV. However, the number of health facilities offering TB treatment in the area also increased (from 53 to 236) during the same period and the increase in TB is likely to be the result of a combination of factors, including improved detection and HIV. It is important to consider this multi-factorial phenomenon when interpreting the increase of TB in a geographical area.

M. A. Yassin, Liverpool School of Tropical Medicine, Pembroke Place, L3 5QA, Liverpool, UK (E-mail: muyassin@liverpool.ac.uk)

INTRODUCTION
Tuberculosis (TB) is a leading cause of adult morbidity and mortality in the world. In sub-Saharan Africa, the incidence of pulmonary TB (PTB) has doubled over the past few years (1, 2) and Ethiopia has an estimated TB incidence of 292 per 100,000 population (3). In the southern region of Ethiopia, the number of registered TB patients has increased by 214% from 8339 cases in 1997 to 17,885 in 2001. This increase could be due to the spread of HIV in the last 2 decades. However, during this period the number of facilities under the TB control programme has increased from 53 in 1997 to 236 in 2002 (4) and the increased number of cases could be due to improved detection and reporting.

The proportion of TB infections due to HIV varies between countries and has reached levels above 80% in some African countries (5, 6). In Ethiopia, the prevalence of HIV among TB patients can be as high as 57% (7). However, most Ethiopian studies are based in urban areas and there is scanty information from rural areas. This study describes the prevalence of HIV infection and the clinical presentation of patients with TB attending 5 predominantly rural health locations of Ethiopia.

MATERIALS AND METHODS
The study was based in 5 rural hospitals of the Southern Region of Ethiopia which have sputum microscopy, X-ray facilities and participate in the HIV sentinel surveillance system. HIV surveillance is conducted among pregnant women attending the antenatal clinics (8).

All TB patients attending the TB clinics were included consecutively until 100 patients had been recruited from each site. Patients were classified as smear-positive PTB if they had at least 2 positive sputum smears or 1 positive smear and chest X-ray findings suggestive of TB, and as smear-negative PTB if they had cough for more than 3 weeks, did not respond to a course of antibiotics and the chest X-ray was suggestive of PTB but the routine smears were negative. Patients were considered to have extrapulmonary TB if they had chronic symptoms suggestive of TB (i.e. chronic lymphadenitis with or without suppuration and sinus, pleural effusion or involvement of vertebral bones) and did not respond to a course of antibiotics (9). Although it is recommended to obtain a biopsy for these patients, this is rarely done in rural areas and the diagnosis is often made clinically. The diagnosis of TB in children was based on the presence of suggestive symptoms, a history of close contact with another person with TB, the presence of suggestive chest X-ray findings and failure to respond to antibiotics.

Blood samples were obtained for routine investigations at the time of enrolment of all TB patients and the serum remaining on completion of all tests was anonymously tested for HIV using an ELISA test (Vironistica® HIV Uni-form II plus 0 microelisa). Although a single positive ELISA is considered as HIV-positive for surveillance purposes, samples giving indeterminate results were re-tested using a rapid HIV test (Determine® HIV-1/2, Abbott Laboratories). All TB patients who were diagnosed and treated during the study period were tested for HIV and none of them rejected anonymous testing, and patients requesting HIV testing were referred for voluntary counselling and testing.

Ethical approval was obtained from the Health Bureau of the Southern Region. Data were entered into Epi-info 2002 and serological results were cross tabulated with demographic and clinical variables. p values <0.05 were considered significant.

DOI: 10.1080/00365540410020848
CHAPTER 11

Scand J Infect Dis 36

HIV and TB in southern Ethiopia 671

### Table I. Demographic characteristics and disease classification of the study population by HIV status

<table>
<thead>
<tr>
<th>HIV-positive n=97 (%)</th>
<th>HIV-negative n=403 (%)</th>
<th>Odds ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>56 (21)</td>
<td>214 (79)</td>
<td>1.2 (0.7-1.9)</td>
</tr>
<tr>
<td>Female</td>
<td>41 (19)</td>
<td>181 (81)</td>
<td></td>
</tr>
<tr>
<td>Residency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>45 (30)</td>
<td>105 (70)</td>
<td>2.6 (1.6-4.2)</td>
</tr>
<tr>
<td>Rural</td>
<td>47 (14)</td>
<td>282 (86)</td>
<td></td>
</tr>
<tr>
<td>New diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>93 (19)</td>
<td>389 (81)</td>
<td></td>
</tr>
<tr>
<td>Relapse/defaulter</td>
<td>4 (36)</td>
<td>7 (64)</td>
<td>2.4 (0.5-9.6)</td>
</tr>
<tr>
<td>Smear positive PTB</td>
<td>51 (19)</td>
<td>210 (81)</td>
<td></td>
</tr>
<tr>
<td>Smear negative PTB</td>
<td>36 (26)</td>
<td>101 (74)</td>
<td>1.5 (0.9-2.5)</td>
</tr>
<tr>
<td>Extra-pulmonary</td>
<td>10 (11)</td>
<td>84 (89)</td>
<td>0.5 (0.2-1.1)</td>
</tr>
</tbody>
</table>

n. Number; 95% CI, 95% confidence interval.

* Data were incomplete for some variables: gender was not recorded for 8 (2%), residence for 21 (4%) and disease category for 8 (2%) of the patients.

RESULTS

500 patients were enrolled from September to November 2002 and their general characteristics are described in Table I. 269 (53.8%) were male and 223 (44.6%) female. Age was not recorded for 8 (1.6%) of the patients, but the mean age was 28 y (range 1-73 y) and 80% were between 15 and 44 y. Most participants (332, 69%) lived in rural settings. 261 (53%) had smear-positive PTB, 137 (28%) smear-negative PTB, and 94 (19%) extrapulmonary TB. There was a strong association between area of residence and HIV, with 15% (47/329) of the rural patients and 30% (45/150) of the urban patients being HIV positive (p <0.001). HIV prevalence was also associated with age. Although only 39 children <15 y old were enrolled, 9 (23%) were HIV positive. The highest number of TB cases occurred in the 15 to 24-y-olds. TB-HIV coinfections however peaked in children and in the 25 to 34-y-old adults (Fig), which was later than the peak for TB. 489 (98%) patients were new and 11 (2%) had re-registered for treatment. HIV infection in this latter group was more frequent (36%) than in newly diagnosed cases (19%), although this was not statistically significant. The HIV prevalence was 19% and 26% among smear-positive and smear-negative PTB cases, respectively. These prevalences were higher than in patients with extrapulmonary TB (11%), although this was only marginally significant.

The prevalence of HIV among the mothers attending the hospitals ranged from 2.3% to 12% and was significantly lower than the prevalence among TB patients (19%, range 15% to 25%), (p <0.01). The prevalence of HIV among TB patients was not associated with the prevalence of HIV among the mothers attending each hospital. The clinical presentation of TB varied across the centres and with the prevalence of HIV, although sometimes in unexpected directions. The proportion of patients with smear-negative PTB was higher in HIV-positive than in HIV-negative patients in all the centres. However, the proportion of cases with smear-positive PTB among HIV-negative cases was higher in the centres with the highest maternal HIV prevalence, and the hospital with the lowest maternal HIV positivity (2.3%) had the highest proportion of HIV-negative extrapulmonary TB.

DISCUSSION

HIV has played a key role modifying the incidence (10, 11) and clinical presentation of TB (12-14). However, the changes in the epidemiology of TB in Africa are likely to be due to a combination of factors, including drought, famine, overcrowding and changes in the implementation of TB control programmes. These factors compound the interpretation of the role that HIV has played. In the southern region the TB control programme started as a pilot programme in 3 health facilities in 1995 and rapidly expanded with an exponential increase in the number of registered patients (4). At the same time, patients with HIV-TB coinfection were increasingly seen at the health facilities.
Although the proportion of TB patients with HIV is high (19%), it is lower than in Addis Ababa, where more than 50% of the patients are coinfected (3, 7). The proportion of patients coinfected often correlates with the prevalence of HIV and duration of the introduction of the infection in a population. HIV prevalence in the southern region is 3.7% (8), compared to 16% in Addis Ababa (9) and 26% in Malawi (15–18). The proportions of TB patients with HIV in these areas are 19%, 56% and 87% respectively, suggesting that a relatively small increase in the prevalence of HIV results in a disproportionate increase in the proportion of TB patients coinfected with HIV.

The differences in the proportion of HIV-TB coinfection across the centres could be explained by the characteristics of their catchment population. Centres serving a predominantly urban population have a higher proportion of TB-HIV coinfections than centres serving rural populations as urban areas have a higher HIV prevalence (8).

The overall low HIV prevalence among patients with extrapulmonary TB could partially be explained by the recent introduction of HIV infection among these communities, as workers elsewhere have documented an increase in extrapulmonary TB with increasing HIV prevalence (19); extrapulmonary TB usually occurring later than PTB in the course of HIV. One area in the region has a high incidence of extra-pulmonary TB among the HIV-uninfected population (18). This finding however does not explain the high proportion of extrapulmonary TB reported from other areas, and it might be that there are important differences in the diagnostic skills of the staff, the methods used for diagnosis and/or the pattern of the population to seek medical advice across the study sites.

As expected, the highest HIV prevalence was documented among TB patients with smear-negative PTB (12). HIV-infected patients with advanced immunosuppression are unable to form cavities in their lungs and expectorate fewer bacilli in sputum (12, 20). Clinicians are aware that the clinical presentation of TB changes with HIV and that chest X-ray anomalies could be due to other opportunistic infections. However, in the light of limited diagnostic facilities, there is a tendency to make a clinical diagnosis of PTB without confirmation from the laboratory (6). Further studies are thus necessary to investigate if these are truly infected TB patients or if the clinical practices of the staff are changing with increased awareness of HIV.

The information on the proportion of TB patients coinfected with HIV and the changing clinical presentation of TB could help planning prevention and control programme efforts. This planning however needs to consider that other factors also influence the epidemiology of TB.

ACKNOWLEDGEMENTS

We are grateful to the staff of the TB clinics and laboratories of Atatt, Dilla, Hossana and Soddo hospitals and Bushullo Major Health Centre for their involvement during data collection and the National TB and leprosy control programme of Ethiopia for supporting the operational costs.

REFERENCES


Submitted February 16, 2004; accepted June 7, 2004