Tuberculosis in rural Uganda

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Abstract

Background: St Francis Hospital, a health facility in the rural district of Mayuge, Uganda.
Objectives: To evaluate the presentation, course and outcome of patients with tuberculosis hospitalized to receive the intensive phase of treatment.
Method: Observational analytical study of all patients admitted during June 2002-March 2005.
Results: There were 680 patients. Their median age was 31 years (range 2-75); 364 (54 %) were male. There were 564 (83 %) new patients; 60 (9 %) defaulters; 35 (5 %) relapses; 14 (2 %) transfers; four chronic patients; and three treatment failures. Three hundred and thirteen patients (58 %) had moderate or severe malnutrition on admission. Among 102 patients tested for the human immunodeficiency virus, 68 (67 %) were positive. At the end of hospitalization 593 patients (87 %) were to be followed-up at St Francis Hospital or were transferred to another health facility, 31 (5 %) had absconded and 56 (8 %) had died.
Conclusion: The severely limited resources of our patients and the human immunodeficiency virus co-infection are likely factors contributing to their late presentation and the severity of the disease. It is doubtful that in our setting tuberculosis can be effectively controlled without addressing and correcting these factors.
Keywords: tuberculosis, Uganda, control, HIV, nutrition.
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Introduction

Uganda is among the 22 countries concentrating 80 % of the tuberculosis (TB) burden in the world.[1] since 1995 the case notification rate has been increasing yearly by 10 %. Thirty-seven thousand new cases (all TB forms) were diagnosed in 2001 (132 per 100 000 inhabitants). It has been estimated though that the number of new patients detected with a positive smear for acid-fast bacilli (AFB) represents just over half of the existing cases. These numbers may be even higher: a household survey in the capital Kampala showed an unexpected high rate of TB; more than half of the cases found had not been detected before the survey.[2]

To evaluate the clinical presentation of patients with TB admitted to St Francis Hospital (SFH) to receive the intensive phase of treatment and to assess their course and outcome at the end of their hospitalization we conducted the present study.

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Methods

SFH in Buluba is located near Lake Victoria in the district of Mayuge (population: 326 839; census 2002) in the South-East zone of the Uganda National Tuberculosis and Leprosy Control Program (NTLP). SFH was originally a facility for the care of patients with leprosy but is at present a sub-district hospital (Bunya West) and a training centre for the NTLP. The District has 24 Health Units of which six are diagnostic and treatment centres for TB. Most of its inhabitants are subsistence farmers or cultivate sugar cane for a nearby factory.

All patients diagnosed with TB in the District were directed to SFH in order to receive the intensive phase of category I (2HRZE/6HE) or category II (2HRZES/1HRZE/5HRE) regimens supervised as in-patients. Category I regimen was administered to new patients and Category II to all others. When the intensive phase was completed patients were discharged and referred to their corresponding Health Units.

During the 34 months of the study period several demographic and clinical parameters were recorded for every patient; the clinical course was followed and the date and reason for ending the hospitalization were recorded. Patients' categories,

forms and outcomes were classified according to the NTLP guidelines.

Residence was classified as living in Mayuge District, in one of the Mayuge bordering districts, or in any other district. Malnutrition was defined according to the body mass index (BMI) on presentation: mild (BMI= 17.0-18.4), moderate (BMI: 16.0-16.9), and severe (BMI: <16.0).

Results

Presentation

A total of 680 patients were registered and evaluated. There were 364 males (54 %). The median age for males was 35 years (range: 1-75) and for females 29 years (range: 4-75). Two hundred and ninety-seven patients (44 %) lived in Mayuge District, 279 (41 %) were from bordering districts and 104 (15 %) from other districts. The BMI could be calculated on admission in 576 patients (297 males and 246 females); 169 males (57 %) and 144 females (59 %) had a moderate or severe degree of malnutrition. Patients' categories and clinical forms are shown in the Table. The anatomical sites of EPTB were: pleura: 53; lymph nodes: 29; larynx: 19; pericardium: 15; bone: seven; meninges: four; abdomen: two; psoas, kidneys, breast, endometrium, and preauricular and lumbar abscess: one each (several patients had more than one site involved). Forty-six (33 %) patients with EPTB had a biopsy compatible with TB or a positive AFB smear (among those also having PTB). Among patients with PTB who had a radiograph 113 (32 %) had cavitary lesions; 15 patients presented with a pneumothorax.

During the study period, testing for the human immunodeficiency virus (HIV) infection was not available at SFH. Among the 102 patients who had been tested in another facility, 68 patients (68 %) were infected. The rate of infection was not significantly different between sexes: 29 males (60 %) and 15 females (72 %) ($p > 0.05$). Among those not tested, clinical findings (oral thrush, herpes zoster, Kaposi's sarcoma, cryptococcal meningitis, prolonged diarrhoea, and acute respiratory distress responding to *Pneumocystis* pneumonia treatment) suggested HIV infection in an additional 45 patients (8 %).

Drug susceptibility testing (DST) was not performed in our laboratory but resistance to anti-TB drugs was demonstrated in 17 patients at the National Reference Laboratory: to E in three patients; to E and S, to H and E, and to H and S in one patient each; to H, E and S in two patients; nine patients harboured bacilli resistant to H, R, E and S. As second-line anti-TB medications were not available this last group of patients was advised not to return for treatment.[3]

Course and outcome

During hospitalization 53 patients (8 %) suffered adverse reactions from an anti-TB medication. More than half manifested as arthralgias due to Z. Five reactions were due to E, 4 to H, and 3 to R; in 14 patients (26 %) the cause could not be determined. Four patients died: two patients from unrelated causes (they had suffered arthralgias from Z). The other two deaths were: a 12-year-old boy who developed acute anaemia and renal failure and an 11-year-old girl who after several weeks of treatment developed persistent headaches and intermittent loss of vision; a complete physical examination was normal and she died five days later.

After two months of treatment 249 patients with new PTB submitted sputum samples: 90 (36 %) had a positive AFB smear and the intensive phase was prolonged for another month. Amongst these, 59 patients had their sputum examined at the end of the three-month intensive phase: 26 (44 %) were still AFB smear positive. No significant differences were found between categories in the rates of smear positivity at the end of the intensive phase, with the exception of the patients with treatment failure who were all AFB smear positive after three months of treatment.

The median (SD) number of days of stay in the hospital was 60 (26.1) for patients transferred; 60 (28.8) for patients to be followed-up in Buluba; 36 (26.4) for patients absconding; and 14 (24.0) for patients dying. The outcomes at the end of hospitalization are shown in Table 1.

Table 1: Categories, clinical forms and outcomes of 680 patients with tuberculosis

Categories, clinical forms and outcomes	Number (percentage)
Category	
New	564 (83)
Return after default	60 (9)
Relapse	35 (5)
Transferred	14 (2)
Chronic	4
Treatment failure	3
Clinical form	
PTB	555 (82)

continuation of table 1

Categories, clinical forms and outcomes	Number (percentage)
EPTB	95 (14)
PTB plus EPTB	40 (6)
Outcome	
Transferred	443 (65)
Follow-up at SFH	150 (22)
Dead	56 (8)
Absconded	31 (5)

PTB: pulmonary tuberculosis; EPTB: extra-pulmonary tuberculosis, SFH: St Francis Hospital
H: isoniazid; R: rifampicin; Z: pyrazinamide E: ethambutol, S: streptomycin

Several sub-groups of patients had higher case fatality rates. Patients with moderate or severe malnutrition had a higher rate (32/313: 10 %) than patients with no or mild malnutrition (7/230: 3 %) (p= 0.01). Patients suffering from EPTB +/- PTB had a higher rate (22/135: 16 %) than patients with only PTB (50/595: 9 %) (p< 0.01). Finally, patients HIV infected plus patients probably HIV infected had also a significant higher case fatality rate (24/113: 21%) when compared to all the other patients (32/567: 6 %) (p< 0.01).

Discussion

This study has major limitations mostly arising from the fact that it took place in a fairly isolated rural hospital with very limited means, especially of diagnostic equipment and trained staff. Several issues, though, merit discussion as they could be relevant to other areas with similar characteristics.

TB constitutes an important health problem in our area but the number of patients detected was well under the national yearly estimated incidence (132 x 10^5). If we take it into account, about 1 222 patients (132 x 326 839 / 10^5) should have been detected during the 34 months of the study period. Nevertheless, only 680 patients were diagnosed and of those 297 (44 %) came from our district. This suggests that there are major deficiencies in the detection of TB in our catchments' area. This seems to be confirmed when we verify that all the patients had been diagnosed in SFH, indicating that no other health centre in the district was performing the adequate diagnostic TB tasks (clinical and laboratory examinations). The fact that more than half of our patients came from other districts also suggests that there were diagnostic deficiencies in those districts.

Most of the patients diagnosed and started on treatment in our area were detected late in the course of their illness. This is shown by the severe malnutrition that they suffered on admission, by the large proportion of patients with PTB presenting with cavities and with severe complications (such as pneumothorax), and by the high case fatality rate occurring soon after starting treatment. Two factors, probably, contribute to this severe clinical status: firstly, the difficult living conditions suffered by our population which provokes that ill persons do not seek medical attention until they are unable to perform their daily cores effectively, and secondly, the diagnostic deficiencies mentioned above in the health units of our area.

Diagnosing EPTB is laid with difficulties, especially in centres such as ours with very limited diagnostic equipment[4]. Our proportion of patients with EPTB (20 %) is well above the national average and indicates that with a high degree of suspicion the detection of several forms of EPTB can be achieved.

The close relation between TB and HIV infection seems to be confirmed by the significant prevalence of HIV infection detected in our small non random sample of patients. If we take into consideration that in areas with high rates of both infections (as suffered by most sub-Saharan countries), they constitute different manifestations of one pathological complex, systematic testing to detect HIV infection in all TB patients and screening for TB disease in HIV infected persons should be promoted and urgently implemented in order to improve the control of these infections.[5,6]

No DSTs were obtained systematically but there was a number of patients found to have different degrees of resistance to the anti-TB drugs and, most worrisome, several patients with multidrug-resistance TB. It must also be noted that no patient admitted with treatment failure had a negative sputum smear after receiving the three-month intensive phase of Category II regimen, suggesting that these patients may have already been resistant to several or all first line medications. To avoid resistance amplification and in order to cure these patients a wider use of DSTs must be recommended and a programme to administer second-line drugs should be envisioned.[7]

The rate of adverse reactions to anti-TB medications was not exceptionally high.[8] Most

reactions were mild and easily manageable. A study from Canada identified Z as being associated with significant adverse reactions.[9] These reactions resolved with the addition of aspirin. Of the two deaths, one was most likely secondary to R (haemolysis and renal failure);[10] the cause could not be determined in the second one.

After two months of treatment about one third of patients were still AFB smear positive; the intensive phase was prolonged and among those tested at the end of three months almost half were still AFB smear positive. A study performed in our institution showed that smear conversion was delayed when the disease was due to *M. africanum* and among patients with large numbers of bacilli.[11] In the capital, Kampala, a study detected the *M. africanum* strain in over half of the patients.[12]

The intricate relationship between malnutrition and TB has not yet been fully clarified[13] but severe malnutrition has been shown to be a risk factor for an early demise after diagnosing TB.[14] It has also been shown that TB patients if also HIV infected have a poorer prognosis than those non infected.[15] Finally, as patients HIV infected have a higher rate of EPTB, the higher case fatality rate of non pulmonary forms could be explained by a higher prevalence of HIV amongst these patients.[16]

A number of patients absconded before completing the intensive phase. The addition of these patients (5 %) to the patients who died in the hospital (8 %) demonstrates the difficulties encountered in our district to reach the World Health Organization's target to cure at least 85 % of patients. Promoting an earlier presentation, shortening the intensive treatment phase in the hospital and bringing the treatment closer to the patient should improve these results in the short term.

Conclusion

In the long term though, we cannot ignore that TB does not constitute an isolated disease but that it forms part -at least in our area- of a triad composed of *Mycobacterium tuberculosis*, HIV and the poverty suffered by our patients. We will not be able to control one element of this deadly association unless we broaden our perspective and address simultaneously the other two.

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References

1. World Health Organization. Report 2004. Global tuberculosis control. Surveillance, planning and financing. WHO/HTM/TB/2004.331. Geneva, Switzerland: WHO, 2004.
2. Guwatudde D, Zalwango S, Kamya MR, et al. Burden of tuberculosis in Kampala, Uganda. Bull WHO 2003; 81:799-805
3. Ollé-Goig JE. Nasira's story. Int J Tub Lung Dis 2006; 10:1420.
4. Richter C, Ndosi B, Mwammy AS, Mbwambo RK. Extrapulmonary tuberculosis –a simple diagnosis? A retrospective study at Dar es Salaam, Tanzania. *Trop Geo Med* 1991; 43:375-378
5. Godfrey-Faussett P, Ayles H. The impact of HIV on tuberculosis control-towards concerted action. Lep Rev 2002; 73:376-385
6. Corbett EL, Marston B, Churchyard GJ, de Cock KM. Tuberculosis in sub-Saharan Africa: opportunities, challenges, and change in the era of antiretroviral treatment. *Lancet* 2006; 367:926-936
7. Ollé-Goig JE. Editorial: The treatment of multidrug-resistant tuberculosis: a return to the pre-antibiotic era? *Trop Med Int Health* 2006; 11:625-628
8. Javada MR, Shalviri G, Gholami K, Salamzadeh J, Maghooli G, Mirsaeedi SM. Adverse reactions of anti-tuberculosis drugs in hospitalized patients: incidence, severity and risk factors. *Pharmacoepidemiol Drug Saf* 2007; 16:11 04-1110
9. Marra F, Marra CA, Bruchet N, Richardson K, Moadebi S, Elwood RK. Adverse drug reactions associated with first-line antituberculosis drug regimens. *Int J Tuberc Lung Dis* 2007; 11:868-875.
10. Girling DJ. Adverse effects of antituberculosis drugs. Bull Int Union Tuberc 1984; 59:152-162.
11. Bwire R, Borgdorff MW, Sticht-Groh V, et al. Tuberculosis chemotherapy and sputum conversion among HIV-seropositive and HIV-seronegative patients in South-Eastern Uganda. *East African Med J* 1999; 76:307-313.
12. Niemann S, Rusch-Gerdes S, Joloba ML, et al. *Mycobacterium africanum* subtype II is associated with two distinct genotypes and is a major cause of human tuberculosis in Kampala, Uganda. *J Clin Microbiol* 2002; 40:3398-3405.
13. Cegielski JP, McMurray DN. The relationship between malnutrition and tuberculosis: evidence from studies in humans and experimental animals. *Int J Tuberc Lung Dis* 2004; 8:286-298 .
14. Zachariah R, Spielman MP, Harries AD, Salaniponi FML. Moderate to severe malnutrition in patients with tuberculosis is a risk factor associated with early death. *Trans Roy Soc Trop Med Hyg* 2002. 96:291-294.
15. Whalen CC, Nsubuga P, Okwera A, et al. Impact of pulmonary tuberculosis on survival of HIV-infected adults: a prospective study in Uganda. *AIDS* 2000; 14:1219-1228
16. Raviglione MC, Harries AD, Msiska R, Wilkinson D, Nunn PL. Tuberculosis and HIV: current status in Africa. *AIDS* 1997; 11:S115-S123