Nonadherence in Tuberculosis Treatment Among HIV Patients Attending Bamrasnaradura Hospital, Nontha-buri

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Abstract

Objective - To determine the clinical manifestations, outcome and nonadherence, in tuberculosis (TB) among HIV patients in Bamrasnaradura Hospital, Nonthaburi.

Design - A retrospective cohort study; hospital record files were reviewed over 11 months. A total of 200 consecutive HIV patients were entered and followed for a 6 months period of their TB treatment. Sociodemographic data, symptoms and signs and results of investigation tests were recorded at the time of presentation, while diagnosis, and clinical outcome were done at the end of the follow-up time.

Results - Extrapulmonary tuberculosis (58%) was more common than pure pulmonary involvement (42%). Lymphadenopathy (52%) was the commonest sign on physical examination. Chest X-rays were positive in 55 per cent cases, while AFB examination was positive in 48.5 per cent from the sputum and 46 per cent from lymph node aspirate specimens. After 6 months of treatment, 30 per cent patients were still alive, 12 per cent had died, and 50 per cent were lost to follow-up. Factors such as low socioeconomic status ($p<0.001$), being newly diagnosed with TB ($p<0.001$), past history of TB ($p<0.003$), etc., were statistically significant in predicting the likely nonadherence in TB treatment among HIV patients.

Conclusion - In HIV-infected individual, tuberculosis presents more often with extrapulmonary involvement, and the diagnosis is not difficult. While treatment of tuberculosis is successful, patients' compliance is the biggest problem in managing them.

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For over 10 years, HIV has been a major public health problem in Thailand despite the government's efforts to stop its spread.

Tuberculosis has an estimated prevalence of PPD positivity >10 mm among adults aged 20-39 years of about 20-33 per cent according to Stewart[1]. This makes it another public health problem.

Poldeh[2] reported an increasing number of tuberculosis cases (up to 61% in HIV/AIDS patients). TB, thus, is probably one of the most common opportunistic infections.

Nonadherence to the therapy in tuberculosis is possibly one of the most important factors which interferes in successfully by combating this disease among HIV infected patients. Frieden et al[3] believes it leads to further problems such as emergence of resistance.

PATIENTS AND METHOD

This retrospective cohort study was performed at Bamrasnaradura Hospital, which is a Ministry of Public Health facility to treat infectious diseases. Nonthaburi province provides a mix of both rural and city patients to represent the population of HIV patients.

Patients

HIV patients more than 14 years of age, who attended either inpatient or outpatient departments in the hospital were selected. The tuberculosis diagnostic criteria were the acid fast bacilli present on at least one specimen (CSF, sputum, etc.) obtained at the time of presentation, with or without culture confirmation.

Method

A total of 200 consecutive patients were entered into the study between January and November 1997. A list of positive AFB smear results in HIV patients was obtained from the Microbiology Department, and inclusion criteria checked against the record files from the Records Department. Information from the time of their presentation with tuberculosis until 6 months into their treatment was studied. This information was recorded on the standard study case record form for each subject. Data on clinical outcome was recorded including treatment regimens, adverse drug reactions, etc. At 6 months of therapy, patients were either alive, dead or lost to follow-up.

Death and the cause of death were obtained from hospital records or death certificates. Nonadherence was determined as loss of follow-up. This was in cases where a subject missed an appointment or absconded from hospital, and did not return to continue his/her treatment.

Data Analysis

On completion of data collection, it was entered onto the computer and analyzed using the EPI INFO 6 system.

For categorical variables, per cent calculations were done to obtain exact values for each of the subgroups. For continuous variables, analysis gave means with standard deviation or medians with 95 per cent confidence intervals.

Nonadherence or loss of follow-up analysis was done by correlation of two variables using the two by two tables (the chi - squared test) and statistical significance was found where the p - value < 0.05.

RESULTS

84.5 per cent were male subjects with a mean age +/- SD of 32.5 +/- 10 years. 46.5 per cent patients stated they came from Bangkok, 15 per cent from Nonthaburi, and other rural areas consisted of 38.5 per cent. Only 45 per cent were married. The largest occupational groups were laborers (57%) and the unemployed (25.5%)

Past history of tuberculosis was found in 23.5 per cent cases. Opportunistic infections prior to this presentation were found in 43.5 per cent subjects, 19.5 per cent of which were cryptococcal meningitis.

Lymphadenopathy was the commonest sign (52%) shown in the record files in physical examination notes; 29.5 per cent and 14.5 per cent were at the cervical and supraclavicular region respectively.

Only 54.5 per cent of chest radiographs showed signs consistent with tuberculosis.

Examination for acid fast bacilli gave positive results in 46 per cent of lymph node aspirates and 48.5 per cent sputum specimens as shown in Table 1.

Extrapulmonary tuberculosis was seen in 58 per cent of all subjects, as shown in Fig. 1.

Outcome

Only 100 patients completed the 6 months' follow-up, the other 100 failed. After 6 months

Table 1. Investigation results at time of presentation (N = 200)

Clinical investigation	Positive cases	Negative cases	Cases not recorded
CD4+count	36	-	164
- Median (95% CI)	32 (0-25)	-	-
Chest X-ray	109	15	76
- Infiltrates	71	-	-
- Cavity	9	-	-
- Pleural effusion	12	-	-
- Miliary	4	-	-
- Other	13	-	-
Sputum AFB exam	97	23	80
TTA AFB exam	9	2	189
LN aspirate AFB exam	92	6	102
LN biopsy AFB exam	9	1	190
Blood culture AFB	6	4	190
Stool AFB exam	5	3	192
Skin AFB exam	3	0	197
CSF AFB exam	3	13	194
Pleural effusion AFB	4	1	195

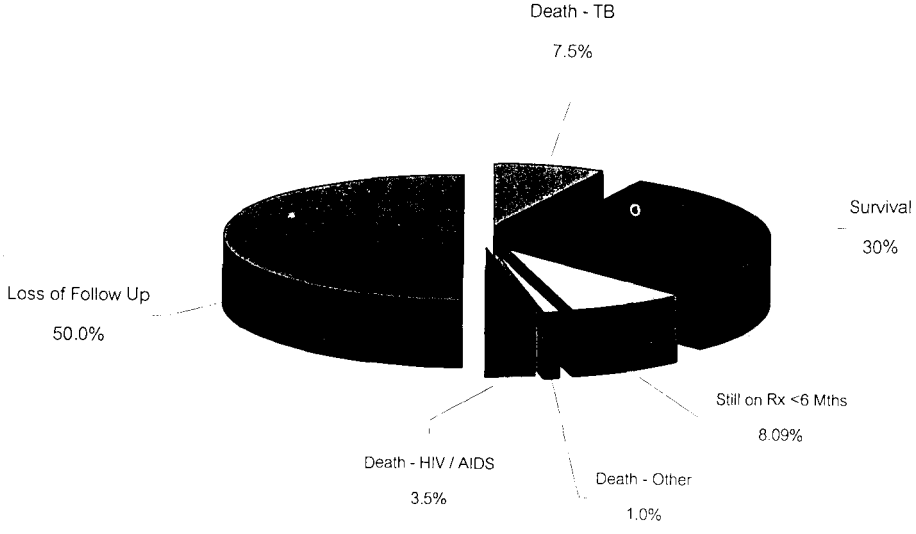

Fig. 1. Clinical outcome.

from the time of commencement of antituberculous therapy, 79.5 per cent patients were on the four drug (IRZE), 6 months regimen. Adverse drug reactions were recorded in the hospital record files in 10.5 per cent of cases. There were 3 cases which resulted from isoniazid, 16 cases from rifampicin, and 2 from other adverse drug reactions.

The clinical outcomes is described in Fig. 1. There were 30 per cent of subjects, who were alive and either completed or were still continuing their therapy. 12 per cent of patients died during the follow-up time. Of these, 15 subjects were recorded to have died due to tuberculosis infection itself.

Table 2. Loss of follow-up, comparison between 100 subjects lost to follow-up, and 100 other subjects. (N = 200)

Variable	P-value
Sex (M/F)	0.002
Nonmarried *vs* married	0.01
Low socioeconomic status	0.001
Residence to hospital distance group	0.65
Past history of tuberculosis	0.003
Time from diagnosis (4 weeks)	<0.001
Tuberculosis diagnostic subgroups	0.675
IRZE (*vs* other RX) regimen	<0.001

Loss of follow-up examination due to their HIV infection.

During 6 months follow-up there were 50 per cent subjects who exhibited nonadherence to TB therapy as show in Table 2

On further analysis of this group, there were 88 males (52% of all males) and 12 females (39% of all females), (p=0.002). 47 (55% of all singles) were single patients, 40 per cent of all married (36 subjects) compared to 10 (66%) were either single or not married were found significant.

As for the occupations, 22 (43%) were unemployed, 64 (56%) were laborers and only 7 (32%) belonged to the higher income group (p= 0.001). Residential areas had almost equal representation (p=0.65).

The past history of tuberculosis on obtaining the patient's clinical information, showed 20 (43%) of all subjects with a past history of TB were lost to follow-up, but only 1 (6%) of those with no past experience of TB dropped out (p=0.003).

Looking at the diagnostic subgroups, 23 (46%) of all patients with disseminated disease, 45 (54%) of all pure pulmonary cases, and 32 (48%) of all pure TB lymphadenitis were subsequently lost to follow-up (p=0.675).

There were 92 (58%) of all the patients on the four drug regimen in this category, but only 8 (20%) patients on other drug regimens stopped their therapy prematurely (p<0.001).

Analysis of their management showed, most were lost early on in their treatment, and this decreased with time of management (p<0.001) ; 60 subjects did not come back within the first 4 weeks of treatment onset, another 18 in the second month, and only 4 subjects in the 5th and 6th's months of therapy.

DISCUSSION

This retrospective cohort study showed that the sample obtained was representative of HIV patients in Thailand which was similarly reported by Ruxrungtham et al[4] and Nelson et al[5]. Also the symptoms and signs at the time of presentation showed similar findings with the studies done by Raviglione et al[6] and Kramer et al[7].

The diagnostic criteria for this study was the examination of specimens for presence of acid fast bacilli, and not the culture for *Mycobacterium tuberculosis*, which is the gold standard in diagnosis of TB. As cultures take 4-6 weeks, and the need for therapy in HIV patients is imperative, there was a requirement for a quick, and inexpensive test, which would yield a high proportion of positive results. Thus, the AFB test was chosen as it fulfilled these criteria.

As stated above, lymph node aspirate was diagnostic in 46 per cent cases, and sputum in 48.5 per cent of cases. This is supported by the results of Rieder et al[8].

Chest X-rays, while positive in only 54.5 per cent patients, is still a useful initial investigation. It is noninvasive, quick, inexpensive, and as stated by Perriens et al[9] has a role as an additional tool in a physician's armamentarium of diagnostic techniques.

Looking at the diagnoses, extrapulmonary involvement was more common. Even though Ruxrungtham et al found only about 20 per cent of extrapulmonary cases in Thailand, other studies, such as by Lupatkin et al[10] and Shafer et al[11] support the higher percentages.

The standard regimen for TB therapy at Bamrasnaradura Hospital is the four drug, six months one. The other 20.5 per cent of cases on different regimens were either due to resistance to one or more agents, or due to therapy for cryptococcal meningitis with imidazole group agents.

The rate of side effects (10.5%) was lower than data shown by Chaulk et al[12]. This may be due to limitations of this study, such as recall bias or lack of notification by the patients, who were lost to follow-up.

While the 30 per cent of subjects who completed 6 months of therapy is low, it is consistent with studies in Thailand by Punnotok et al[13]. This may well be due to treatment not being given by the direct therapy (DOT) regimen, whereas

Sribhaya was able to achieve a 90 per cent success rate.

The nonadherence group was by far the largest (50%). Pablos - Mendez et al[14] supports the findings of significance with being male (p= 0.002) and having a low socioeconomic status (p= 0.001). Subjects, who were not married appear to be lost from clinics more easily (p=0.01), and this may be due to lack of support from relatives and spouses.

Presence of TB on taking the patient's past medical history seems to be significant (p= 0.003) in the rate of nonadherence, and is also seen in Pulido's work[15].

A significant finding (p<0.001) was that patients on other drug regimens tended to adhere to therapy better. It may be due to the presence of other coexisting opportunistic infections, and thus, more frequent contact with physicians and more support from health professionals in general, which seems to increase compliance according to Hodgkin[16]. This will need further evaluation in future studies.

SUMMARY

Despite the limitations of this study, the above findings indicate that tuberculosis as an opportunistic infection in HIV/AIDS requires prompt diagnosis and treatment. This process is further made difficult by extrapulmonary involvement, and thus, often nonspecific presentations. The AFB examination of specimens proved to be a quick method of diagnosis for tuberculosis infection with good positive yields.

Once the diagnosis is made and therapy is commenced, though success in eradication of the disease is possible, the biggest problem is the nonadherence of HIV patients and loss of their follow-up Factors that seem to appear in the nonadherence group, have been identified in this study, and may prove to be helpful in reducing nonadherence.

Further work needs to be done to evaluate this, and whether increased counseling and support by physicians of these patients has the desired effect.

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การไม่กลับมาติดตามผลการรักษาของผู้ป่วยเอดส์ที่เป็นวัณโรค ณ โรงพยาบาลบำราศนราดูร

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วัตถุประสงค์ เพื่อศึกษาอาการทางคลินิกและการไม่กลับมาติดตามผลการรักษาในผู้ป่วยเอดส์ที่เป็นวัณโรค ณ โรงพยาบาลบำราศนราดูร

วิธีการวิจัย การศึกษานี้เป็นการศึกษาย้อนหลังโดยศึกษาข้อมูลจากเวชระเบียนของผู้ป่วยเอดส์ที่ได้รับการวินิจฉัยว่าเป็นวัณโรคและได้รับยาต้านวัณโรคจำนวน 200 ราย เป็นระยะเวลา 11 เดือน ข้อมูลเหล่านี้ได้แก่ ข้อมูลทางด้านสังคม สิ่งแสดงและสิ่งตรวจพบ ตลอดจนผลการรักษาทางคลินิกของผู้ป่วยและวิเคราะห์ การที่ผู้ป่วยไม่มาติดตามผลโดยใช้ Chi square test

ผลการศึกษา พบว่า 58% ของผู้ป่วยเอดส์มักจะมาด้วยอาการวัณโรคที่ไม่ใช่ในปอด เมื่อเปรียบเทียบกับวัณโรคปอด (42%) สิ่งตรวจพบที่สำคัญคือมีต่อมน้ำเหลืองโต (52%) มีผลเอกซเรย์ปอดเข้าได้กับวัณโรคปอด เพียง 55% ในขณะที่การตรวจพบ AFB ในเสมหะและน้ำจากต่อมน้ำเหลืองมีจำนวน 48.5% และ 46% ตามลำดับ หลังจากการรักษา 6 เดือน 30% ผู้ป่วยยังมีชีวิต, 12% เสียชีวิต และ 50% ไม่กลับมารับการรักษาต่อในระหว่างที่ได้รับยารักษา ปัจจัยที่พบว่ามีส่วนทำให้ผู้ป่วยไม่กลับมาติดตามผลการรักษาได้แก่ ผู้ป่วยที่มีรายได้ต่ำ ผู้ป่วยที่พึ่งได้รับการวินิจฉัยว่าเป็นวัณโรคเป็นครั้งแรกและผู้ป่วยที่เคยมีประวัติเป็นวัณโรค ($P < 0.001$)

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