Noncompliance With Tuberculosis Treatment by Patients at a Tuberculosis and AIDS Reference Hospital in Midwestern Brazil

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Introduction: In developing countries, there is little information about the risk factors that predict noncompliance with tuberculosis (TB) treatment in hospitals. Objective: This study analyzes possible factors associated with noncompliance with TB treatment among patients treated at HAA. Design: A retrospective cohort study was made including all patients who initiated TB treatment at HAA, from January to December 1998. A standard form was used to review medical records and to collect data on each patient. This data was evaluated in comparison with data from the state TB control program. Results: Of the 341 patients included in the study, 186 (61.2%) were considered cured and 67 (22%) were non-compliant. The factors associated with noncompliance were: previous anti-TB treatment (RR = 1.95, 95% CI 1.29 to 2.93), prescription of drugs other than the standard first-line regimen proposed by the Brazilian Health Ministry (Rifampin + Isoniazide + Pyrazinamide) (RR = 0.54, 95% CI 0.35 to 0.83), the need for hospitalization (RR = 2.19, 95% CI 1.46 to 3.29) and non-inclusion in the hospital's TB Control Program for treatment follow up (RR = 0.54, 95% CI 0.35 to 0.82). Setting: Anuar Auad Hospital (HAA) – Goiânia, Goiás, Brazil. Conclusion: Our results indicate the importance of establishing Tuberculosis Control Programs in hospitals, while paying special attention to patients with risk factors for noncompliance with TB treatment.

Key Words: Tuberculosis, treatment, compliance, TB control program, Goiânia.

Although tuberculosis can be cured by regular intake of antimicrobial drugs, it continues to be a serious world public health problem. The World Health Organization (WHO) estimates that 8 million cases of tuberculosis were reported in 2000, of which 1.87 million were fatal due to late diagnosis or noncompliance with treatment [1].

In Brazil, it is estimated that nearly 50 million people have been infected by Koch's bacillus. According to Health Ministry data, approximately 90,000 new tuberculosis cases are reported annually, of which 10 to 30% are treated by secondary and tertiary Health Care Units and 6% are fatal [2,3]. In the state of Goiás, 1,052 new tuberculosis cases were reported in 1998, with an incidence coefficient of 22.2/100,000 and lethality of 10%. Of that total, 35% were treated at the HDTAA in the city of Goiânia [3].

TB/HIV co-infection is giving rise to fresh concerns regarding tuberculosis control due to the rising hospitalization rate and the need for new treatment strategies [4,5].

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One of the main difficulties involved in meeting the goals of tuberculosis control programs (TCP) is poor compliance with antimicrobial treatment [6-8]. Nationwide in Brazil, the noncompliance rate varies between 12% and 16%, although noncompliance among TB patients in major cities (usually state capitals) varies between 27% and 34% [9]. Some international studies have also investigated factors associated with noncompliance with treatment [10-15]. Most were carried out at primary or secondary health care units. However, few studies have evaluated patients who initiated tuberculosis treatment at a hospital, particularly in large urban centers [16-18].

In a meta-analysis of noncompliance with medication, Haynes et al. [18] found that it is common. Although there have been numerous studies on the efficacy of treatment with new drugs, most of which are clinical trials financed by the pharmaceutical industry (stage I, II and III trials), stage IV clinical trials are rarely financed by governmental organizations. Usually, stage IV trials evaluate the effectiveness of new antimicrobial treatments in different populations, the causes of noncompliance, and the cost effectiveness of the different strategies [19].

The objective of this study was to evaluate factors involved in noncompliance with tuberculosis treatment at HDTAA in the state of Goiás, a tertiary reference hospital for infectious and parasitic diseases – including AIDS and tuberculosis – in order to develop strategies for increasing the effectiveness of the treatment of this endemic disease.

Design

This study was carried out at the Anuar Auad Hospital for Tropical Diseases (HDTAA), a public hospital run by the State Health Department that is a regional reference for infectious and parasitic diseases. It has 126 beds and treats approximately 15,000 outpatients and 2,500 inpatients annually.

We analyzed a retrospective cohort study of all TB patients who initiated specific treatment at HDTAA between January and December 1998. Follow-up periods ranged between 6 and 24 months after the conclusion of treatment.

We identified patients by consulting records of notification forms. A standard form (annex 1) was used to collect data from each patient's medical records. Data was also recovered for the patients transferred to other health care units who were cured, noncompliant or who died, or whose treatment failed. The data was then analyzed and correlated with the final outcome of treatment. The final results were compared with data from the state TB control program.

The TB patients' diagnoses were obtained through bacilloscopy or microbacterial cultures, and some patients' attending physicians considered the probability of cure on the basis of clinical-epidemiological data and additional tests (PPD and chest X-ray). [3] The final outcomes of treatment included cure, noncompliance, death, transfer from health unit, change in diagnosis and treatment failure.

Definitions

Cure: Patients with negative bacilloscopy in clinical respiratory samples and/or who showed satisfactory clinical and X-ray improvement;

Noncompliance: Failure to appear at the health service for over 60 days after last treatment;

Death: Patients who died during treatment and follow-up, regardless of the cause of death;

Failure: Persistently positive sputum smears at the end of treatment or strongly positive patient at the onset of treatment who showed no improvement by the fourth month;

Change in diagnosis: Ruling out a diagnosis of TB after treatment has been initiated;

Transfer: Patients were transferred to another health unit and final results of treatment are unknown;

Retreatment: Prescription of drug regimen for patient already treated for over 30 days who required different therapy due to relapse after cure, return after noncompliance or due to failure of anti-TB treatment;

HIV infection: Record of positive HIV test (ELISA and/or Western Blott). HIV tests were only requested for patients with associated risk factors.

Patients were treated provided by a team of professionals trained to treat TB patients (1 doctor/one nurse) or by professionals who carry out routine hospital procedures without prior specific training in TB treatment. Patients were chosen at random for treatment by of these groups of health care workers. Depending on the day they were hospitalized or scheduled an outpatient consultation, possible TB patients or those with firm diagnoses were treated by the health workers on duty at that time. No financial incentives were given to these patients for participation in the treatment program.

Admission to HDTAA was decided on the basis of the seriousness of their clinical condition, the presence of side effects and, in some cases, due to social problems.

Data for noncompliant patients were compared with those for cured patients. In these two groups of patients, factors potentially associated with noncompliance with TB treatment were compared, such as gender, skin color, marital status, origin (place of residence), employment status, alcohol use, HIV infection, comorbidities, prior TB treatment, need for hospitalization, clinical form of the disease (pulmonary, extrapulmonary or disseminated), bacilloscopy results, type of antimicrobial regimen used, adverse effects of TB medication and type of health care given by the two teams of health care workers (with and without specific tuberculosis training).

The study was approved by HDTAA's Research Ethics Board.

To analyze the variables studied, we used the chi-squared test or Fisher's exact test., Statistically significance (alpha = 0.05) was determined through logistical regression in the multivariate analysis, and proximate values were included in the univariate analysis. Stata 5 statistical software was used.

Results

An evaluation of notification forms in medical records and the progress of patients registered with the State Tuberculosis Control Program enabled us to include in the final statistical analysis, 67 noncompliant patients and 186 patients considered cured, out of 341 patients who initiated TB treatment at HDTAA (Figure 1).

Tables 1 and 2 show the parameters for all 341 patients. They were predominantly male (67.4%), aged between 20 and 49 (68.9%), and resided in the city of Goiânia and neighboring municipalities (69.2%). TB/AIDS co-infection was 10.1% and alcohol consumption, 25.2%. Among other associated comorbidities, tobacco smoking, diabetes and epilepsy were the most prevalent, respectively 15.2%, 4.7% and 4.7%. The percentage of patients undergoing retreatment was 20.8% and 42.2% of those whose condition developed into an actual disease state were admitted to the HDTAA. Pulmonary tuberculosis was present in 80.7% of all cases and 84.3% showed a positive bacilloscopy at the beginning of treatment. The TB control program team treated only 30.2% of all patients. Of a total of 301 patients, the cure rate found was 61.8%, noncompliance, 22.2%, death, 12% and treatment failure, 4%. The rest were transferred or had a change in diagnosis.

Univariate analysis showed no significant difference between noncompliant and cured patients with regard to gender, age, color, marital status, origin, employment status or HIV co-infection, however alcohol consumption was a predictive factor for noncompliance (Table 3). The presence of adverse effects of treatment regiments also proved not to be significant.

Reported cases involving retreatment, the need for hospitalization or treatment by health care workers who were not trained to treat TB patients and the use of an antimicrobial regiment other than regimen I (Rifampin + Isoniazide + Pyrazinamide) were significantly associated with noncompliance (Table 4).

After multivariate analysis, it was found that treatment by health care workers who are not trained to treat TB patients, the need for hospitalization and non-use of

Table 1. Demographic data for 341 TB patients who initiated treatment at HDTAA

Variables	N	%
Gender		
Male	230	67.4
Female	111	32.6
Age group (years)		
0 – 9	14	4.1
10 – 19	23	6.7
20 – 29	83	24.3
30 – 39	78	22.9
40 – 49	74	21.7
50 – 59	20	5.9
60 – 69	31	9.1
> 70	18	5.3
Color*		
White	48	14.0
Black	10	2.9
Brown	205	60.1
Other	3	1.0
Marital status*		
Single	157	46.0
Married	134	39.3
Other	20	10.0
Origin		
Goiânia	125	41.0
Other cities in 1st region	86	28.2
Other cities in the state	61	20.0
Other states	33	10.8
Unemployed*		
Yes	15	4.4
No	296	86.8

*Numbers do not include all patients, due to a lack of specific information in some patient records.

Table 2. Epidemiological data for 341 TB patients who initiated treatment at HDTAA

Variables	N	%
HIV positive		
Yes	35	10.2
No	114	33.4
Not tested *	192	56.4
Alcohol drinker†		
Yes	87	25.5
No	1559	46.6
Other comorbidities		
Epilepsy	16	4.7
Diabetes	16	4.7
DPOC	6	1.8
Hansen's disease	5	1.5
Neoplasia	4	1.2
Paracoccidiodomycosis	4	1.2
Silicosis	3	0.9
Smoking history	52	15.2
Other	7	2.1
Retreatment		
Yes	71	20.8
No	270	79.2
Hospitalization required		
Yes	143	42.0
No	198	68.0
Forms of disease		
Pulmonary	275	80.6
Pleural	20	5.9
Ganglionic	30	8.8
Other	16	4.7
Bacilloscopy§		
Positive	230	83.6
Negative	45	16.4
Treatment		
Doctor on call	98	28.7
Regular doctor	140	41.1
TB program	103	30.2
Adverse effects		
Yes	62	18.0
No	279	82.0

* Patients without clinical-epidemiological reasons for requesting testing.
† Regardless of quantity or frequency. Figures do not include all alcohol drinkers due to lack of specific information in some records.
§ Only for pulmonary TB patients.

Table 3. Statistical analysis of data on noncompliant and cured TB patients, compared with social and demographic parameters

Variables	Noncompliant	Cured	Relative risk	CI 95%	P value
Gender					
Male	43	129	1.19	0.77<RR<1.81	0.45
Female	224	57			
Color					
White	10	24	0.79	0.45<RR<1.36	0.40
Non-white	40	126			
Marital status					
Single	43	97	0.67	0.46<RR<1.06	0.08
Not single	21	81			
Origin					
Goiânia	37	85	1.32	0.87<RR<2.00	0.18
Other cities*	30	101			
HIV positive					
Yes	6	18	0.94	0.45<RR<1.94	0.85
No	51	148			
Alcohol drinker †					
Yes	22	38	1.50	0.95<RR<2.38	0.08
No	29	90			
Unemployed					
Yes	4	7	1.32	0.58<RR<2.96	0.53
No	60	157			

* Other cities in rural Goiás State and other states.
†Regardless of quantity or frequency.

Table 4. Statistical analysis of data on noncompliant and cured patients, compared with previous history, diagnosis and treatment of TB

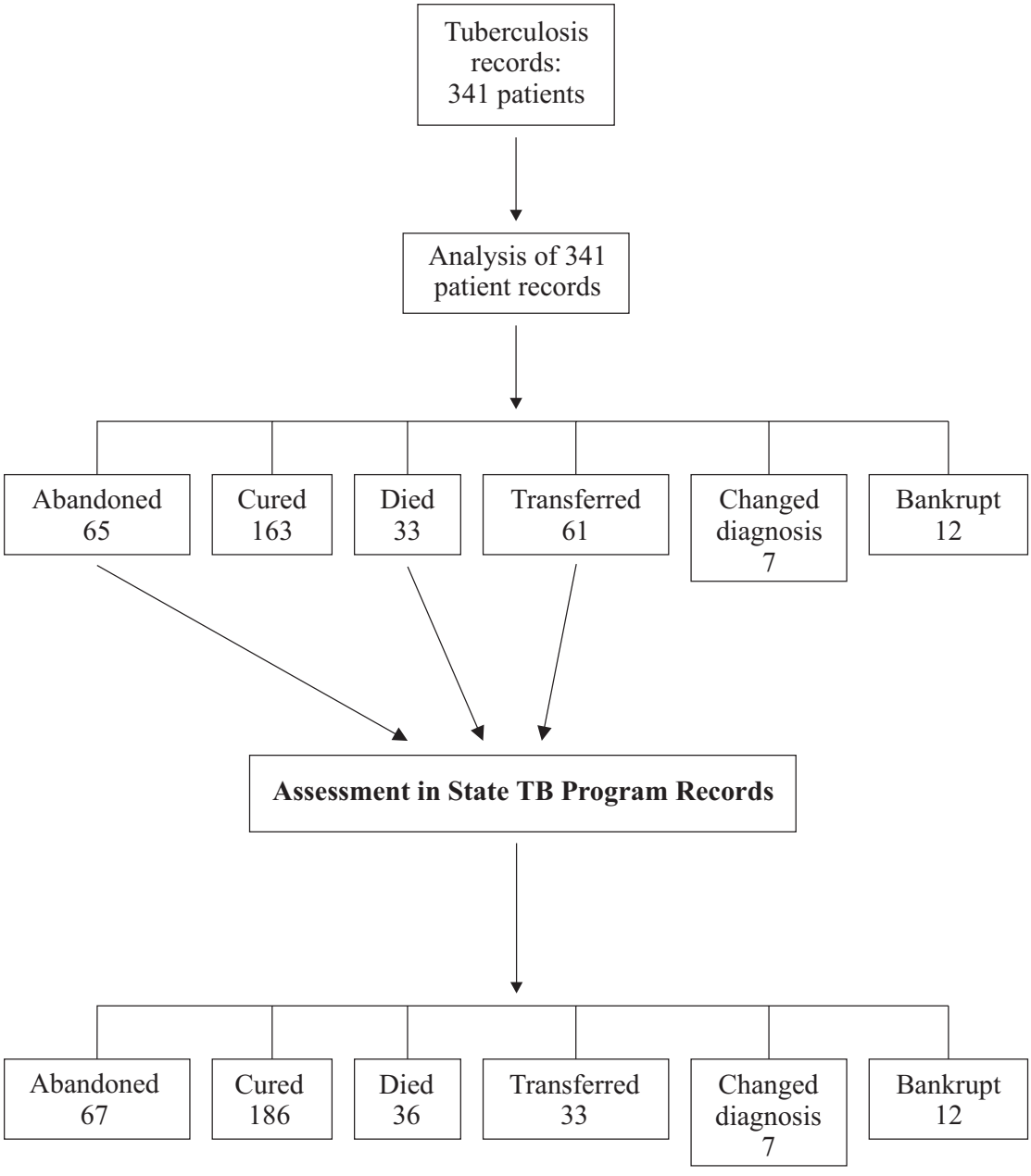
Variables	Noncompliant	Cured	Relative risk	CI 95%	P value
HIV Positive					
Yes	6	18	0.94	0.45<RR<1.94	0.85
No	51	148			
Alcohol Drinker					
Yes	22	38	1.50	0.95<RR<2.38	0.08
No	29	90			
Other comorbidities*					
Yes	20	63	0.87	0.55<RR<1.37	0.55
No	47	123			
Retreatment					
Yes	21	27	1.95	1.29<RR<2.93	< 0.001
No	46	159			
Needs hospitalization†					
Yes	37	54	2.19	1.46<RR<3.29	< 0.001
No	30	132			
Pulmonary TB					
Yes	56	146	1.29	0.73<RR<2.27	0.37
No	11	40			
Positive bacilloscopy‡					
Yes	46	123	0.89	0.51<RR<1.59	0.72
No	10	23			
Treated by professional trained in TB therapy					
Yes	10	72	0.54	0.35<RR<0.82	< 0.001
No	57	114			
Use of First-line regimen§					
Yes	49	162	0.54	0.35<RR< 0.83	< 0.001
No	18	24			
Adverse effects					
Yes	16	34	1.27	0.79<RR<2.04	0.32
No	51	152			

* Presence of comorbidities except AIDS and alcohol.
† Hospitalized for present disease.
‡ At time of present diagnosis.
§ Rifampin + Isoniazide + Pyrazinamide.

Table 5. Results of multivariate analysis of factors associated with noncompliance

	Adjusted RR	CI 95%	P
Treatment by TB program	0.29	0.13 – 0.64	< 0.001
Use of First-line regimen	0.37	0.17 – 0.78	< 0.001
Need for hospitalization	2.25	1.23 – 4.11	< 0.001

Figure 1. Flow chart – Progress analysis of 341 patients who initiated TB treatment at HDTAA



regimen I were significantly associated with the group of patients who were noncompliant with TB treatment (Table 5).

Discussion

The benefits of curing a tuberculosis patient go beyond the individual, since it is a significant step towards breaking the chain of transmission and consequently controlling this endemic disease. Thus, the low effectiveness of treatment shown in flow chart 1 is a cause for concern and closely related to noncompliance and outbreaks of multiresistant tuberculosis [20].

Poor compliance with the antimicrobial regimen has historically been cited as one of the most challenging problems for tuberculosis treatment [21]. It has become a focus of attention for national tuberculosis control programs in several countries, including Brazil, and has provoked the recent adoption of a strategy of establishing supervised treatment [22].

In Brazil, the average rate of noncompliance with TB treatment in the early 1980s ranged from 10% to 16% [6]. By the 1990s, particularly in large urban centers, a cohort study carried out in 12 major cities by CNPS/FNS/MS in 1992 reported 28% noncompliance among 2,054 patient records studied [9]. This was due to worsening socioeconomic conditions, the dismantling of the public health system, and an increase in HIV infection. These data are similar to those of an HDTAA study conducted in 1996 and 1997 [23] and the data in our study, carried out in 1998.

Countless factors have been associated with poor compliance with treatment, including its complexity and duration, adverse side effects, difficult access to health care services [15-17], alcohol consumption [8], lack of preventive treatment and unemployment [11]. Factors such as age, gender, color and educational level are usually not found to be predictors of poor compliance [11]. Studies that have evaluated factors associated with noncompliance with tuberculosis treatment using data gathered from patient records are usually limited. However, in this study, no significant difference was observed between data obtained at the hospital and those included from the analysis of the records of the state tuberculosis control program (unpublished data). Therefore, the data obtained from medical records probably provided good-quality information. Due to understaffing in the hospital's TB Program, there was no follow up for patients transferred to other health units.

We did not find some of the risk factors occasionally associated with increased noncompliance with TB treatment, such as being male, unemployed, and HIV-positive [11,13,16]. This may be due to the small sample size. However, other authors have also failed to confirm these associations [25,26]. Alcohol consumption and living alone can predict noncompliance. This has also been found in other studies [17,21]. Furthermore, an evaluation of supervised treatment found an 18% noncompliance rate, and alcohol consumption was one of the significant factors associated with noncompliance [26]. Most patients treated at HDTAA are residents of the city of Goiânia, however there was no significant variation regarding noncompliance when compared with patients from other cities in the State of Goiás. Preventive treatment has been cited as a factor associated with noncompliance [27]. However, we did not find such an association, probably because diagnosis had been confirmed before initiating treatment. Prior treatment and the need to use a form of drug therapy other than regimen I have also been reported as a predictive factor for noncompliance [8,10,16,28], which suggests that patients undergoing retreatment should be monitored more closely and, if possible, assigned to supervised treatment. The need for hospitalization was significantly greater for noncompliant patients, which demonstrates that hospitalization does not contribute to greater compliance and agrees with the analysis of Natal et al. [17].

In the multivariate analysis the parameters, type of treatment regime used, need for hospitalization and lack of treatment by health care workers trained to treat TB patients continued to be associated with poor compliance. Oliveira and Moreira-Filho [8] reported that isolated cases of drug resistance are directly affect the success of treatment and irregularities in health care services are responsible for their lack of success. In a

study of the results of tuberculosis treatment at 45 health care services in 14 Central American countries, Teixeira [29] reported that the main causes of noncompliance were a lack of sanitary education and a lack of organized health services. The First Brazilian Consensus on Tuberculosis (1977) concluded that the main factor responsible for noncompliance was problems in the structure and organization of health services, particularly poor or nonexistent tuberculosis control programs, which is the case with most general hospitals in the large urban centers of developing nations [6,26].

Conclusions

The degree of success of TB treatment in the city of Goiás observed in this study was not considered satisfactory. Factors associated with noncompliance with treatment, including the need for hospitalization for actual disease, specific treatment other than regimen I and treatment by unspecialized personel indicate a need to implement a tuberculosis control program in general hospitals and provide supervised treatment at least for patients with parameters considered predictive for noncompliance.

There should be more appropriate interaction with other primary and secondary health units and community programs established in the 1990s in Brazil, such as the Programa de Saúde da Família (Family Health Program).

If the results of this study are confirmed by other studies of patients treated by general hospitals, legislators responsible for public health policies should give priority to providing special treatment for tuberculosis patients at these units, particularly in large urban centers, establishing outpatient and hospital-based tuberculosis control programs.

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