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Profile of notified tuberculosis cases and factors associated with treatment dropout

ABSTRACT

OBJECTIVE: To describe the profile of notified tuberculosis cases and analyze the factors associated with treatment dropout.

METHODS: A total of 178 cases of tuberculosis notified in the western region of Belo Horizonte (Southeastern Brazil) in 2001 and 2002 and recorded in the National System for Notifiable Diseases were described. An unmatched case-control study was conducted, with data collected by means of interviews, to compare patients who dropped out of treatment with those who achieved cure. The following variables were analyzed: sociodemographic and behavioral characteristics, associations with AIDS, side effects, information on the disease and interest in treatment. Univariate analysis and unconditional logistic regression for multivariate analysis were used. Adjusted odds ratios with 95% confidence limits were used as the measurement for associations.

RESULTS: The coefficient of incidence was 56.6/100,000 inhabitants. There was predominance of men aged 30 to 49 years and of the pulmonary form (76.4%) and bacillary form (72.5%). Among the notified cases, 65.2% achieved cure, 12.4% dropped out of treatment and 9.6% died. Treatment location had no influence on the results. In the case-control study, there was no difference regarding gender, color, schooling, income, occupation, family support, association with AIDS and alcohol consumption. The use of drugs, interest in treatment and information about the disease were shown to be independently associated with dropout.

CONCLUSIONS: Adherence to treatment is a challenge in controlling tuberculosis. The protection factors (interest in treatment and information about the disease) and recognition that drug use is a risk factor must form part of the strategies for patient care in order to reduce dropout rates and restore health.

KEYWORDS: Tuberculosis, epidemiology. Disease notification. Incidence. Risk factors. Case-control studies. Tuberculosis, treatment dropout.

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INTRODUCTION

Although tuberculosis is preventable and treatable with low-cost and high-efficiency medications, it has been presenting resurgence, with repercussions on cure and mortality rates.

Brazil is in tenth highest place among national tuberculosis rates. In 2001, the incidence rate for the whole country was 46.5/100,000 inhabitants, and it was 34.6 for Minas Gerais and 53.2 for Belo Horizonte.*

*Ministério da Saúde. Série histórica de doenças de notificação compulsória por UF. 1980-2005. Available from: http://portal.saude.gov.br/portal/arquivos/pdf/tuberculose_2006.pdf [Accessed on Jan 15, 2006]

Treatment dropout and incomplete treatment¹⁸ favor drug resistance and are factors that have a negative impact on controlling this disease. In the different regions of Brazil, the dropout rate ranges from 4.5 to 20.3%.

In 2000, data from the *Sistema de Informação Nacional de Agravos de Notificação* (SINAN – National Information System for Notifiable Diseases)* showed that in the western region of Belo Horizonte only 57.2% of the cases achieved discharge because of cure, while 31.1% were notified as dropouts or remained without information regarding the conclusion of treatment. These rates are far from the national targets proposed by the Ministry of Health, of 85% cure and less than 5% dropout.

The present study aimed at describing the clinical-epidemiological characteristics of notified tuberculosis cases and identifying factors associated with treatment dropout, with the aim of providing backing for planning interventions and improving the adherence to treatment.

METHODS

The study was developed in the western region of Belo Horizonte, Southeastern Brazil, among an estimated population of 268,698 inhabitants that is characterized by marked social contrasts: 74.6% living in districts with better access to urban facilities and 25.4% living in shantytowns.**

To identify the outcomes among cases notified during the study period, the Monthly Tuberculosis Control Files were used initially. To obtain outcome information on the 18.5% of the notifications for which these files did not give this information, steps were followed that included crossing the SINAN data with data from the *Sistema de Informações sobre Mortalidade* (SIM – National Mortality Information System) for 2001, 2002 and 2003, consultation with the unit responsible for notifications and home visits made by community health agents. This process resulted in reducing the percentage of notifications without outcome information to 2.8%. The undernotification calculation was done according to the algorithm in the Technical Norms Manual of the Ministry of Health.

The case-control study included all the tuberculosis patients aged 15 years and over for whom notification was issued. The exclusion criteria were change of diagnosis and moving away to other municipalities.

Treatment dropout was considered to be situations in which the patient failed to attend a scheduled return visit and also did not appear during the next 30 consecutive days. In supervised treatment programs, the time limit is 30 days counting from when the drug was last taken.***

The cases were taken to be the tuberculosis patients for whom notifications had been issued who dropped out of treatment between July 2001 and June 2002. The controls were patients for whom notifications were issued during the same period who were discharged due to cure. The study had a total of 50 participants, of whom 20 were cases and 30 were controls, giving a ratio of 1:1.5.

The controls utilized were living in the same neighborhoods, i.e. in the same area of coverage and with the same case risk. The neighborhoods were identified by the vulnerability index of the Municipal Health Department of Belo Horizonte, by means of geocoding the addresses of cases and controls using the Mapinfo 5.0 software.

The cases and controls were directly interviewed by one of the authors, at the health unit or at home, using a semi-structured questionnaire that had previously been tested in a pilot study on four patients (two cases and two controls) for whom notifications were issued in July and August 2002. The interviews were arranged by telephone or by a community health agent who visited the subject at home.

The descriptive analysis of the SINAN data included epidemiological variables (age, sex and area where the home was located), clinical variables (disease type, sputum bacilloscopy and HIV serological test), treatment location and outcome.

This case-control study took the dependent variable to be treatment dropout and the following were explanatory variables: sociodemographic and behavioral data – sex, color, schooling, occupation, income and high alcohol use (weekly consumption of ethanol greater than 420 g); drug use; clinical history (side effects, association with AIDS, reports of associated diseases or previous treatment, symptomatology at diagnosis, or presence of another person with tuberculosis in the family); level of information about the disease; data on the organization of the health services (treatment location, availability of medications, access to consultations and time spent waiting to be seen); and variables relating to the patient's perception of his state of health, family

* Source: Gerência de Regulação, Epidemiologia e Informação do Distrito Sanitário Oeste/Secretaria Municipal de Saúde, Belo Horizonte, Minas Gerais, 2001.

** Prefeitura Municipal de Saúde de Belo Horizonte. Distrito Sanitário Oeste. Available from: http://portal2.pbh.gov.br/pbh/index.html?id_conteudo=4346&id_nivel1=-1 [Accessed on Apr 15, 2002]

*** Ministério da Saúde. Plano Nacional de Controle da Tuberculose. Manual de Normas Técnicas, Estrutura e Operacionalização. Brasília (DF). 2000.

support, interest in treatment, reason for dropping out and stressful situations.

To calculate the incidence in conformity with guidance from the Ministry of Health,* population data from the *Instituto Brasileiro de Geografia e Estatística* (IBGE – Brazilian Institute for Geography and Statistics) was utilized together with the new-case notifications in SINAN, excluding duplicated cases.

The statistical analysis on the data from SINAN and the case-control study involved frequency distributions, central trend measurements and investigation of associations between explanatory variables and the response variable (dropout or cure), using Pearson's Chi-square or Fisher's exact test for categorical variables and Student's t-test for continuous variables. Statistical decisions were made on the basis of the descriptive value of the test (p).

For multivariate analysis on the case-control study, to determine the independent effect of the associations, odds ratios (OR) with 95% confidence intervals and significance level of 0.05 were used. The modeling process, using non-conditional logistic regression, was performed in successive steps, beginning with the variables selected from univariate analysis ($p < 0.15$) and

the variables of epidemiological importance. Backward elimination (one by one) was used in the modeling. To evaluate the models, the Wald test, likelihood ratio and Hosmer-Lemeshow test were used. For variables that were not shown to be associated with the outcome, the statistical power was calculated.

The database for the case-control study was stored in EpiInfo, which was also used for the statistical analysis, plus the Minitab 12 software.

The study was approved by the Research Ethics Committee of the Universidade Federal de Minas Gerais (ETIC 136/03).

RESULTS

During the study period, 178 confirmed cases of tuberculosis were notified in the western region of Belo Horizonte. Among these individuals, 65.2% were cured, 12.4% dropped out of treatment, 9.6% died (Table 1) and 10% moved away, had their diagnoses changed or were still undergoing treatment. All the patients who dropped out were between 15 and 49 years old.

The incidence of tuberculosis was 56.6/100,000 inhabitants, with a range from 10.54 to 105.84 in the different

Table 1. Outcomes from notified tuberculosis cases according to sex, age group, clinical form and location of treatment. Belo Horizonte, Southeastern Brazil, 2001-2002.

Variable	Cure N=116		Dropout N=22		Death * N=17		p
	N	%	N	%	N	%	
Sex							
Male	83	71.6	13	59.1	13	76.5	0.14
Female	33	28.4	9	40.9	4	23.5	
Age group (years)							
<15	20	17.2	0	0.0	0	0.0	0.0
15-49	82	70.7	22	100.0	8	47.1	
50 and over	14	12.1	0	0.0	9	52.9	
Clinical form							
Pulmonary	88	75.9	20	90.9	12	70.6	0.23
Extrapulmonary	24	20.7	2	9.1	3	17.6	
Pulmonary + extrapulmonary	4	3.4	0	0.0	2	11.8	
Location of treatment							
Within the area of coverage	54	46.6	12	54.5	4	23.5	0.13
Outside of the area of coverage	62	53.4	10	45.5	13	76.5	

Source: SINAN (Sistema de Informação sobre Agravos de Notificação - National System for Notifiable Diseases) / Brazilian Ministry of Health - 2001/2002

* Death due to all causes

areas of coverage. The estimated undernotification was 7%. The cases notified to SINAN were predominantly among males (69.7%) with a mean age of 34.4 and median age of 32.5 years. The most frequent form of the disease was pulmonary (76.4%), accounting for 72.5% of the adults with the bacillus, followed by extrapulmonary forms (19.1%), which were seen particularly among individuals over the age of 50 years.

Among the 41% with blood tests for HIV, it was found that 12.9% were seropositive, without differences in the clinical form of tuberculosis ($p>0.05$).

Most of the notified cases (57%) were attended outside of the residential areas covered, mainly in reference hospitals (28.7%) and outpatient clinics (27.1%). The responsibility taken by the health centers for caring for tuberculosis was unequal, ranging from zero to 77% of the people living in their areas of coverage (Figure

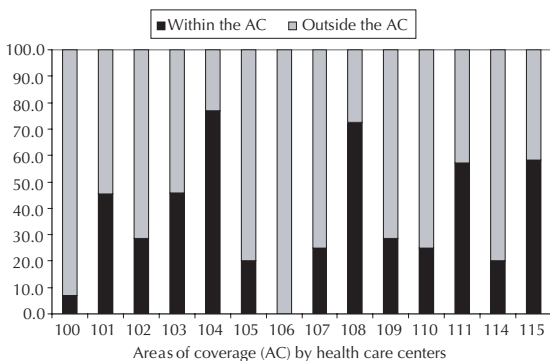


Figure 1. Distribution of notified tuberculosis cases undergoing treatment, according to residential areas covered by health care centers. Belo Horizonte, Southeastern Brazil, 2001-2002.

Source: SINAN/MS – 2001/2002

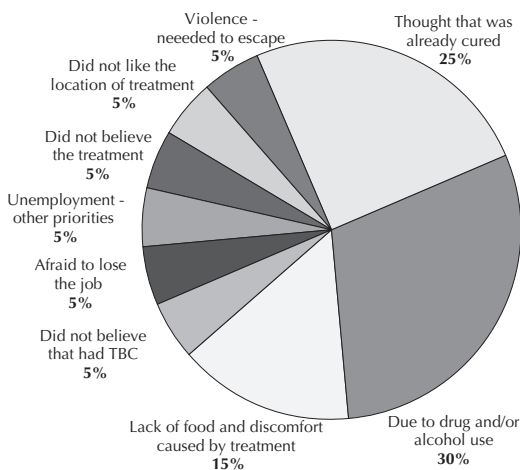


Figure 2. Main reasons for dropping out according to tuberculosis patient's perception. Belo Horizonte, Southeastern Brazil, 2001-2002.

1). The location of treatment had no influence on the outcomes of cure, dropout and death ($p>0.05$).

With regard to the case-control study, among the 22 patients (cases) who dropped out of treatment, 20 (91%) were interviewed. Two cases were not included in the study: one because this person was not known at the address on the notification record and the other by recommendation from the management of the primary health care unit, because this person was involved in drug trafficking. The 30 eligible controls all participated in the study.

Figure 2 shows that the main reasons for dropping out, according to the patients' perceptions, were drug or alcohol use (30%) and clinical improvement (25%).

The profile of the participants in the case-control study was similar to the profile of the cases notified in SINAN, with predominance of males (64%) of mean age 35.5 years and median age of 33 years; 88% of the cases were among individuals aged 15 to 49 years. The most frequent form of the disease was pulmonary (75%), accounting for 78.9% of the adult with the bacillus. Furthermore, the cases were seen to be predominantly among non-whites (78%) with less than eight years of schooling (74%), and half of them were living with a per capita income of less than or equal to half a minimum salary. It was observed that 36% were unemployed and almost all of them (92%) reported a family connection.

The mean age (31.1 years) and mean family income (2.3 minimum salaries) were lower among the cases ($p<0.05$). Univariate analysis (Table 2) indicated that self-reported occupation, interest in treatment, level of information about the disease, drug consumption and occurrence of side effects were shown to be associated with treatment dropout. Regarding the interviewees' perceptions about their state of health, it was found that those who considered their state of health to be bad were ten times more likely to drop out of treatment, with a dose-response gradient ($p=0.004$).

There was no difference between the cases and controls in relation to gender, color, schooling, alcohol use, stress, reports of associated diseases or previous treatment, symptomatology at diagnosis, presence of another person with tuberculosis in the family, or family support.

Among the variables related to the organization of the health services, it was found that the location of treatment, availability of medications, access to consultations and time spent waiting to be seen were not associated with dropout ($p>0.05$).

The modeling process was started with the variables selected from the univariate analysis: age, occupation,

Table 2. Personal characteristics, habits, association with AIDS, side effects, location of treatment, information and interest in treatment among the cases (patients who dropped out of tuberculosis treatment) and controls. Belo Horizonte, Southeastern Brazil, 2001- 2002.

Variable	Cases		Controls		OR	95% CI
	N	%	N	%		
Sex						
Male	13	65.00	19	63.30	1.08	0.28;4.13
Female	7	35.00	11	36.70	1.00	
Color						
Non-white	16	80.00	23	76.70	1.22	0.26;6.04
White	4	20.00	7	23.30	1.00	
Schooling						
< 8 years of schooling	16	80.00	21	70.00	1.71	0.38;8.16
> 8 years of schooling	4	20.00	9	30.00	1.00	
Occupation *						
With occupation	13	65.00	28	93.30	0.13	0.02;0.73
Without occupation	7	35.00	2	6.70	1.00	
Alcohol use						
Yes	5	25.00	2	6.70	4.67	0.67;40.14
No	15	75.00	28	93.30	1.00	
Drug use *						
Yes	11	55.00	5	16.70	6.11	1.66;22.50
No	9	45.00	25	83.30	1.00	
Side effects ***						
Yes	14	73.70	12	40.00	4.20	1.03;18.07
No	5	26.30	18	60.00	1.00	
Association with AIDS						
Yes	3	15.00	1	3.30	5.12	0.41;138.94
No	17	85.00	29	96.70	1.00	
Location of treatment						
Within the area of coverage	11	55.00	14	46.67	1.40	0.39;5.09
Outside of the area of coverage	9	45.00	16	53.33	1.00	
Interest in treatment *						
Yes	12	60.00	29	96.70	0.05	0.01;0.46
No	8	40.00	1	3.30	1.00	
Information about the disease *						
Yes	12	66.70	27	90.00	0.22	0.05;1.04
No	6	33.30	3	10.00	1.00	

* $p < 0.05$

** no response

alcohol use, drug use, family income, side effects from medications prescribed in the treatment, number of previous treatments, family support during treatment, interest in treatment, state of health and level of information about the disease. The association with AIDS ($p=0.20$) was included because of its relevance in other studies.

The variables that were shown to be significant ($p < 0.05$) were tested in a new model and, because of the epi-

demiological importance, it was decided to keep the variable of alcohol use in the model. This ended up excluded from the final model through the results from the Wald test ($p=0.184$).

The final model defined (Table 3) included the variables of drug use, interest in treatment and level of information about the disease, all of which showed statistical adequacy (Hosmer-Lemeshow test > 0.05).

Table 3. Final model for multivariate analysis on the outcome (cure or dropout) from tuberculosis treatment. Belo Horizonte, Southeastern Brazil, 2001-2002.

Variable	Case N	Control N	Unadjusted odds ratio	Adjusted odds ratio	95% CI	Wald Z
Drug use						
Yes	11	5	6.11	7.12	1.38;6.81	2.34
No	9	25	1	1		
Information about the disease						
Yes	12	27	0.22	0.11	0.02;0.69	-2.35
No	6	3	1	1		
Interest in treatment						
Yes	12	29	0.05	0.03	0.00;0.30	-2.93
No	8	1	1	1		

Calculation of the statistical power of the non-significant variables that nevertheless had epidemiological relevance indicated that the lack of association may have occurred because of the sample size (sample power for alcohol use = 45%; for association with AIDS = 31.7%; and for loss of employment or income = 45.1%).

DISCUSSION

The choice of the western region for this research was based on the relevance of this area regarding the occurrence of tuberculosis cases in Belo Horizonte (12% of the cases in 2001), the accessibility of the data and the feasibility of the fieldwork. Although the case-control study was performed with 91% of the treatment dropouts notified, it may not have had sufficient sample size to detect associations with some variables, among which alcohol use and association with AIDS. The care taken in qualifying the database, the search for information on outcomes and the application of a standardized form by a single interviewer contributed towards obtaining reliable data and internal validity for this study.

The high percentage of records without data on the outcome shows negligence in notifying this disease. On the other hand, the subsequent reduction to 2.8% proves that epidemiological surveillance cannot be passive: it requires systematic contacts with the units and sometimes patients need to be approached in their homes.

The rate of incidence was similar to what was estimated for Belo Horizonte in 2001. The wide variability in the distribution of cases, reaching levels of up to twice the coefficient of incidence for the region in the areas with

greater vulnerability indices, reveals coherence with the social causes of this disease.

Rich countries present coefficients of less than 10/100,000 inhabitants, with higher incidence among immigrants, people living in the streets, ethnic minorities, HIV-positive individuals, users of injectable drugs and elderly people, particularly those living in old peoples' homes.^{13,17,19,21} Russia, with a rate of 95/100,000 inhabitants in 2000,¹⁹ and Spain,⁵ with 38.5/100,000 inhabitants, present epidemiological patterns differing from other industrialized countries. In southeast Asia and India, the coefficient of incidence may reach 200-400/100,000 inhabitants.¹⁶

The treatment dropout in the study location was similar to the rate of 12.9% that was estimated for Brazil in 2001,¹ and does not meet the Ministry of Health's target. The organization of the health services and better quality of care have been indicated as factors of relevance for diminishing treatment dropout.* Greater care, both from the services and for the adults responsible for children may explain the absence of dropout among children under 15 years of age.

The predominance of cases among men confirms the profile observed in uncontrolled studies on tuberculosis.¹² The greater frequency of the pulmonary form coincides with findings from Brazil** and the United States.²¹

Almost all of the care was provided within the public network. However, a high percentage of the individuals were seen outside of the coverage area, despite the recommendations for decentralization of care. Such guidance is aimed particularly towards implementing supervised treatment. Although the literature has

* Ministério da Saúde e Sociedade Brasileira de Pneumologia e Tisiologia. Controle da tuberculose: Uma Proposta de Integração Ensino - Serviço. Rio de Janeiro (Brasil); 2002

** Dalcolmo MMP. Regime de curta duração, intermitente e parcialmente supervisionado, como estratégia de redução do abandono no tratamento da tuberculose no Brasil. [Doctoral thesis]. São Paulo (SP): Escola Paulista da Universidade Federal de São Paulo, 2000

indicated* that there is a lower dropout rate when the individuals live in an area linked to a health center, in the present study the location of treatment (within the coverage area or outside of it) did not influence the dropouts.

The differences in the responsibility and control over patients taken by the health centers, which theoretically have the same infrastructure available, indicate the difficulties of team working and suggest the need for better capacitation or performance among professionals with greater sensitivity and commitment, such that they would be able to care for almost all the local patients at that health care unit. Tuberculosis control could in this way function as a marker for the quality of the service provided at the unit, thus translating the compliance with the protocol and the team's competence level. The fragility of the care provided was also shown by the low percentage of patients who had undergone serological tests for HIV detection. Although well established,** the recommendation that HIV detection tests should be performed in tuberculosis cases was implemented in the cases of less than half of the patients, with the aggravating factor that AIDS was the principal cause of death among the patients.

Another fact that indicated inadequate control over the disease was the high percentage of young adults with the bacillus, which indicated the occurrence of recent transmission.*** This epidemiological pattern differs from what is found in countries where the disease is under better control and the elderly population is most affected, consequent to exposure in the past.¹⁷

To this end, the implementation of the Family Health Program in Belo Horizonte and the computerization of the healthcare units in the western region of the municipality are expected to improve the control over this endemic disease, thus facilitating effective implementation of supervised treatment. As recommended by the World Health Organization (WHO) and by the Ministry of Health, tuberculosis control has been taken up as a target by the Municipal Health Department of Belo Horizonte.

With regard to the case-control study, drug use was confirmed as an important factor associated with treatment dropout.^{3,*} The reasons for dropping out, as perceived by patients, that have been reported in the literature include the feeling that they are getting better, alcohol or drug use and discomfort with the treatment, including side effects in this.^{8,***}

The level of information about the disease and interest in treatment were shown to be protection factors. It is consistently reported in the literature^{2,11,***} that possession of information is an important factor in adhering to treatment and that lack of knowledge about the possibility of cure may stimulate dropout.⁴ However, even when the information is passed on, the process of transmission and incorporation of the knowledge is not always satisfactory and efficient for all patients*** and does not ensure changes in behavior.¹⁰ The verification of an association between interest in treatment and favorable evolution in the present study coincides with other authors' findings.^{8,20}

The influence of socioeconomic conditions on becoming ill and treatment dropout is already known.**** Both employment^{6,8} and unemployment appear as reasons for dropping out: the first for fear of losing it and the second because of prioritization of subsistence, which leads to postponement of seeking medical care. In the present study, the exclusion of the income and occupation variables from the multivariate analysis may be explained by the fact that both the cases and controls lived in areas of similar vulnerability. Schooling did not appear to constitute a risk factor for treatment dropout.^{1,6,****}

The occurrence of side effects from the medications used in the treatment was not confirmed as a risk factor for treatment dropout, even after adjustment of the analysis, which contradicts some qualitative studies.^{8,****}

In the unadjusted analysis, it was seen that there was a greater chance of dropping out from treatment among individuals who considered that their state of health was poor, with a dose-response effect. Nonetheless, this association did not remain in the final model. The patients' perception that they felt better after the initial phase of the treatment was the reason for dropping out that was indicated most.^{8,****}

There is controversy in the literature regarding greater likelihood of dropping out from treatment among men and non-white individuals.^{3,*}

The importance of family support in adhering to treatment that has been described in several studies,^{7,8,****} was not confirmed in the present study.

Although considered to be a factor classically associated with dropping out of treatment and becoming ill,^{1,3,15}

* Dalcolmo MMP. Regime de curta duração, intermitente e parcialmente supervisionado, como estratégia de redução do abandono no tratamento da tuberculose no Brasil. [Doctoral thesis]. São Paulo (SP): Escola Paulista da Universidade Federal de São Paulo, 2000

** Ministério da Saúde. Plano Nacional de Controle da Tuberculose. Manual de Normas Técnicas, Estrutura e Operacionalização. Brasília (DF). 2000.

*** Perini E. O abandono do tratamento da tuberculose: transgredindo regras, banalizando conceitos. [Doctoral thesis]. Belo Horizonte (MG): Escola de Veterinária da Universidade Federal de Minas Gerais; 1998

**** Oliveira HB. Estudo do reingressante no sistema de notificação: recidivas em tuberculose e seus fatores de risco em Campinas, 1993-1994. [Doctoral thesis]. Campinas (SP): Faculdade de Ciências Médicas da Universidade Estadual de Campinas; 1996

abusive alcohol intake was similar between the groups, probably because of the sample size. Nonetheless, in a randomized clinical trial with a large sample from an urban population, there was also no association.*

There are reports that patients undergoing retreatment drop out more often than do new cases.^{1,7} However, in the present study, the cases and controls did not differ regarding previous treatments, which is in agreement with other authors.^{3,*}

Comorbidities and association with AIDS were not shown to be factors associated with treatment dropout. There is controversy in the literature regarding the evolution of tuberculosis among HIV-infected individuals.^{1,3,11}

The groups were similar with regard to variables measuring stress: important events at the time of becoming ill, death or illness in the family and loss of employment or income. On the other hand, qualitative studies have shown that these tensions within a sociocultural context worsen when a threatening disease is diagnosed.**

As in other studies,^{6,8} no difference was detected in relation to the distance to the health service, thus verifying that some individuals feel more comfortable undergoing treatment far from home, because of the stigma of the disease, although some studies indicate distance to be a factor making adherence difficult.^{2,*}

Some studies have indicated irregularities in the distribution of medications, precariousness in the attendance and difficulties in accessing services as possible causes of patient loss,^{18,**} which were not confirmed in relation to the health service studied. The high rate of treatment dropout, even when standardized and funded by

the public system, indicates the involvement of other relevant questions⁸ that must be faced.

The results from the present study confirm that tuberculosis persists as an important public health problem. The Ministry of Health's cure and dropout targets are not being attained. Patient care is still not effectively decentralized and the units are seen to be very different from each other with regard to taking responsibility for care provision. The strategies for controlling this disease need to take into consideration the factors associated with dropout, which are closely related to patients' habits and the way in which they get hold of information on their disease and are motivated to complete their treatment.

The vulnerability of drug users indicates the need for urgent and specific priority interventions. Ignoring differences between patients' profiles signifies failing to reach good treatment results and effective control over tuberculosis transmission.

Tuberculosis control depends on improving the factors relating to health services: reliable information systems, expansion of decentralized care that enables the implementation of supervised treatment, capacitation of professionals and strengthening of the team-working, and optimization of references and contra-references. In addition to this, individualizing the approach and placing value on educational activities will provide decoded information on the disease and stimulate patients to undergo treatment. Establishment of interdisciplinary partnerships and intersectoral actions are powerful alternatives for acting on the whole set of factors relating to patients, thus seeking to make them co-responsible for facing up to their illness.

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