Factors associated with nonadherence of tuberculosis treatment in the state of Paraná*

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ABSTRACT

Objectives: To describe the profile of tuberculosis reported cases and analyze the factors associated with treatment nonadherence in the state of Paraná. Methods: Ecological study that presented the TB cases reported between 2006 and 2010, using descriptive statistics and binary logistic regression, with significance level of 5%. Results: During this period, 15,077 cases were reported, of which 84.2% were new cases. The majority of patients were male, skin color/ethnicity white, and more than half were less than 40 years old with low education. Incidence rates and treatment nonadherence were higher than national rates. Less than half had directly observed therapy. Young, alcoholics, unemployed individuals with low education and previous treatment nonadherence were more likely not to adhere to treatment. Conclusion: The knowledge of these aspects can support a more effective strategy in combating tuberculosis treatment nonadherence.

Keywords: Tuberculosis/epidemiology; Treatment refusal; Public health

RESUMO

Objetivos: Descrever o perfil epidemiológico e clínico dos casos de tuberculose notificados no Estado do Paraná e identificar fatores associados ao abandono do tratamento. Métodos: O estudo do tipo ecológico que levantou os casos de tuberculose notificados no período entre 2006 e 2010, com uso da estatística descritiva e regressão logística binária, com nível de significância de 5%. Resultados: Nesse período, foram notificados 15.077 casos, dos quais 84,2% eram novos. A maioria dos doentes era do gênero masculino, de cor/etnia/etnia branca, e mais da metade tinha menos de 40 anos e baixa escolaridade. As taxas de incidência e de abandono do tratamento foram maiores que as taxas nacionais. Menos da metade fez tratamento diretamente observado. Indivíduos jovens, etilistas, desempregados, de baixa escolaridade e com abandono do tratamento anterior tiveram mais chances de abandonar o tratamento. Conclusão: O conhecimento desses aspectos pode subsidiar uma atuação mais efetiva no combate ao abandono do tratamento da tuberculose.

Descritores: Tuberculose/epidemiologia; Recusa do paciente ao tratamento; Saúde pública

RESUMEN

Objetivos: Describir el perfil epidemiológico y clínico de los casos de tuberculosis notificados en el Estado de Paraná e identificar factores asociados al abandono del tratamiento. Métodos: Se trata de un estudio de tipo ecológico en el que se levantó los casos de tuberculosis notificados en el período comprendido entre 2006 y 2010 y usó la estadística descriptiva y regresión logística binaria, con nivel de significancia del 5%. Resultados: En este período, fueron notificados 15.077 casos, de los cuales el 84,2% eran nuevos. La mayoría de los enfermos era del género masculino, de color/etnia/etnia blanca, y más de la mitad tenía menos de 40 años y baja escolaridad. Las tasas de incidencia y de abandono del tratamiento fueron mayores que las tasas nacionales. Menos de la mitad hizo tratamiento directamente observado. Individuos jóvenes, etílicos, desempleados, de baja escolaridad y con abandono del tratamiento anterior tuvieron más oportunidades de abandonar el tratamiento. Conclusión: El conocimiento de esos aspectos puede subsidiar una actuación más efectiva en el combate al abandono del tratamiento de la tuberculosis.

Descriptores: Tuberculosis/epidemiología; Negativa del paciente al tratamiento; Salud pública
INTRODUCTION

Tuberculosis (TB), a disease of global scale, is preventable and treatable with low cost and high efficiency medication, provided by the Unified Health System. Despite of this, there is no prospect, in the near future, of its elimination as a public health problem in Brazil because 80% of cases of the disease worldwide, representing 50 million people, are concentrated in our country and in 23 other developing countries(1,2).

In the State of Parana in 2010, 2415 new TB cases were registered and 125 deaths from the disease(5). Treatment nonadherence is one of the difficulties facing the State, which cannot meet the target of 85% cure rate of new cases. In 2009, for instance, the cure rate was 70% and treatment nonadherence of 7.2%(4), while the Ministry of Health recommendation is a maximum of 5%(6).

Treatment nonadherence is characterized by the treatment non-attendance of the individual to the clinic for over 30 consecutive days after the due date for return(3). Besides causing individual harm, nonadherence put the public health in risk; it may prolong the infectivity and increase the likelihood of disease transmission. Moreover, the correct treatment requires the use of special treatment regimens with other antibiotics for longer periods, making it more expensive and reducing the chances of cure(1,5).

Systematic assessment of TB treatment should be encouraged, as it helps to identify the main barriers to successful treatment and favors the surveillance of vulnerable groups to medication nonadherence(6).

Despite the epidemiological data presented, few studies have been conducted on the topic in the State of Parana. Particularly, there is a gap regarding factors related to nonadherence with TB treatment in the State, although knowledge of the dynamics related to these factors is essential to subsidize health actions for effective disease control. Given this situation, the present study aimed to describe the profile of tuberculosis reported cases and analyze the factors associated with treatment nonadherence in the state of Parana.

METHODS

This is an ecological and descriptive study which analysis consisted of all TB cases in people living in the State of Parana, reported between 2006 and 2010. The choice of this period was due to the fact that it was, from 2006, noted that the reduction in the number of missed or blank records. Data were collected in October 2011, based on consultation with the Information System for Notifiable Diseases (SINAN).

The State of Parana is administratively divided into 22 health districts, with a population estimated in 2011 of 10,512,349 inhabitants. It has 399 cities, of which 80% have population of less than 20,000 inhabitants and are home to 28% of the total population of the State(6).

For analysis we used data from the following sociodemographic variables: age, gender, skin color/ethnicity, education, employment, and epidemiological and clinical variables: type of admission, type of the disease, institutionalization, indication of supervised treatment, recorded and examined contacts, discharged reason and comorbidities. For the incidence calculation, we used data from the Brazilian Institute of Geography and Statistics, for the period studied and the number of new cases reported.

In the analysis of factors associated with treatment nonadherence, it was considered as the dependent variable treatment nonadherence (yes or no), excluding those who died of TB cases or other causes, and the following explanatory variables: age, number of contacts registered, gender, skin color/ethnicity, comorbidities, supervised treatment performed, unemployment, institutionalization, new case, recurrence, readmission after nonadherence, and education.

A descriptive analysis was performed using the SPSS software for Windows, version 18.0. To estimate the factors associated with treatment nonadherence, we used binary logistic regression, adopting a significance level of 5%. To calculate the odds ratio in percentage terms, the OR(b) skin color/ethnicity of this analysis was submitted to the formula: OR(b) -1*100.

The study was conducted in accordance with the guidelines established by Resolution No. 196/96 of the National Health Council. The request permission to perform it was made at the 15th Regional Health of Parana, and the research project was approved by the Permanent Committee of Ethics in Research of Worker Hospital, Curitiba (Parana) (Protocol 438/2011).

RESULTS

During the study period, there were 15,077 reported cases of TB in the state of Parana, with mean incidence of 23.5 per 100,000 inhabitants. The highest rate was observed in 2007 (24.77) and the lowest in 2009 (22.5), and, in 2010, it was 22.9 per 100,000 inhabitants.

Regarding age, it was observed that the age groups with the highest number of cases were 15-39 years and 40-59 years (49.1% and 34.2%, respectively). Together, the cases found in these two groups skin color/ethnicity corresponded to 85% of the total (Table 1).
Furthermore, white, male individuals, with low education and employed were the most affected. One aspect that drew attention concerns the missing data, such as education (20.8%) and employment (44.1%).
Regarding the epidemiological profile of patients, it was verified that most new cases were reported, however, in 8.5% of cases there was nonadherence. Regarding other characteristics, 80% of the cases were pulmonary tuberculosis, 6% of institutionalized individuals were in prisons and supervised treatment was indicated in 44% of the cases. During the study period, the percentage of cases that resulted in cure was 68%, 3.3% died of tuberculosis and 6.2% died of other causes. This category includes, for example, the deaths of individuals with AIDS (Table 2).

The data show that 5 variables together are able to explain 90.8% of cases of treatment nonadherence of tuberculosis in the State of Parana (Table 3).

**Table 3. Binary analysis of factors associated with tuberculosis treatment nonadherence of patients in State of Parana – 2006 to 2010**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exp(b)</th>
<th>RC%</th>
<th>Valor de p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.967</td>
<td>3.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender</td>
<td>0.685</td>
<td>31.5</td>
<td>0.066</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>0.365</td>
<td>63.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.953</td>
<td>4.7</td>
<td>0.898</td>
</tr>
<tr>
<td>Mental disorder</td>
<td>1.055</td>
<td>5.5</td>
<td>0.886</td>
</tr>
<tr>
<td>HIV positive</td>
<td>0.817</td>
<td>18.3</td>
<td>0.244</td>
</tr>
<tr>
<td>Supervised treatment performed</td>
<td>1.208</td>
<td>20.8</td>
<td>0.177</td>
</tr>
<tr>
<td>Number of contacts registered</td>
<td>0.968</td>
<td>3.2</td>
<td>0.111</td>
</tr>
<tr>
<td>Education</td>
<td>0.890</td>
<td>11</td>
<td>0.038</td>
</tr>
<tr>
<td>Skin color/Ethnicity (white)</td>
<td>1.000</td>
<td>0</td>
<td>0.999</td>
</tr>
<tr>
<td>Unemployment</td>
<td>1.805</td>
<td>80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Institutionalized</td>
<td>1.234</td>
<td>23.4</td>
<td>0.357</td>
</tr>
<tr>
<td>New case</td>
<td>0.706</td>
<td>29.4</td>
<td>0.162</td>
</tr>
<tr>
<td>Recurrence</td>
<td>1.014</td>
<td>1.4</td>
<td>0.968</td>
</tr>
<tr>
<td>Readmission after nonadherence</td>
<td>2.707</td>
<td>170</td>
<td>0.002</td>
</tr>
</tbody>
</table>


Data show that a significant correlation exists between the treatment nonadherence and the variables age, alcoholism, education, unemployment and readmission after nonadherence. Thus, the odds ratio or OR(b) proved to be more common treatment nonadherence of alcoholics (63%), unemployed (80%) and those who have not previously adhered to treatment (170%). Moreover, as each year goes by, the chance of nonadherence decreases in 3.3% and for each level of education increases 11% the chance of adherence to the treatment of tuberculosis.

**DISCUSSION**

The incidence of TB in the state of Parana in 2010 indicated lower rates than the national (37.9 per 100,000 inhabitants), although occupying a very comfortable position compared to the incidence, for example, in the state of Rio de Janeiro, which was 71.8 per 100,000 inhabitants (the highest number in the country), Parana was almost twice the percentage found in the Federal District (11.7 per 100,000 inhabitants)\(^7\).

Nevertheless, it must be noted that, in recent years, there has been a decrease in the incidence of the disease throughout the country\(^8\). In 2002, the rate was 44.4 new cases per 100,000 inhabitants; in 2008, it decreased to 37.4, representing a reduction of 15.6% in the period. As for absolute numbers, there were 77,493 new cases in 2002, but it was reduced to 70,989 in 2008\(^7\).

This reduced numbers were possible due to investments by the Ministry of Health over the years to combat the disease. In order to have a better picture, these investments in 2010 were 14 times higher than in 2002\(^7\). Nevertheless, the country still occupies the 19th position in number of cases, and the 108th place in the incidence\(^7\). These investments skin color/ethnicity regarding the directly observed treatment expansion and laboratory diagnosis with quality control and coinfection diagnosis of TB-HIV.

Thus, the fact that TB is the third leading cause of death from infectious diseases, the leading cause of death in AIDS patients and one of five priority diseases from the Ministry of Health\(^9\), constitute an important condition for investments in this area to present the expected effects.

Regarding age, individuals from the economically productive class were the most affected, which corroborates with findings from other studies\(^5,8\). The existence of bacilliferous young adults indicates the occurrence of recent transmission\(^5\). This epidemiological pattern differs from that found in European countries, where the disease has been better controlled and reach a different segment of the population: the elderly\(^8\).

The majority of patients were male, which was also identified in other studies\(^5,8-10\); but regarding skin color, the condition is different in Brazil, where TB is most prevalent in not white people. The prevalence of people of skin color/ethnicity not white was also identified in the Southeast and Midwest\(^5,8\), but also in the state of Rio Grande do Sul was found higher frequency of reported cases of tuberculosis in individuals of skin color/ethnicity white\(^11\). Probably the fact is related to the colonization of the southern region of the country, whose population mostly consists of European descendant people\(^12\).
Regarding education, there was missing data, which compromises epidemiological analysis of this population in Paraná, it has been identified that the disease affects, in most cases, people on social vulnerability, i.e. those with poor socioeconomic conditions that due to overpopulation and poor distribution of income are living below the poverty line, with low education and suffering from malnutrition and lack of basic sanitation\textsuperscript{(13,14)}.

Currently, there are indicators that fighting TB requires investment not only in the diagnosis and medical treatment, but also into effective actions on the social determinants of the disease. In this sense, one must remember that knowledge of patients’ sociodemographic profile provides subsidies to developing a more effective control plan against TB.

The employment was the variable with the highest percentage of missing data that may be related to the time spent by professionals to identify some occupations in the Brazilian Code of Occupations, used in the notification of SINAN. It should be noted that employment may present different names from those reported by the patient, but this does not justify the lack of filling of this information in the system, because there is a specific code to record unemployment and no classified occupation.

It is worth noting that there is need for greater attention in filling TB notifications and the various documents that are processed on epidemiological data, which are important for a more careful analysis of the population affected by TB, because they reflect their reality and constitute subsidies for planning actions to be implemented in many different sectors.

About the epidemiological profile of patients, it was found that the rate of nonadherence was higher than recommended by the Ministry of Health (5\%\textsuperscript{(1)}) and that the pulmonary TB, i.e. one that can transmit TB, affects most patients, indicating the urgency of implementing more effective actions to break the chain of transmission of the disease in the state of Paraná.

High rate of prisoners’ notification was also observed, which was expected, since this population is more vulnerable to contamination by the TB bacillus given the very nature of the confinement, which suffers from lack of sanitary conditions, number of people greater than the capacity of the jail, lack of places for sun, inadequate ventilation and other deficiencies.

Supervised treatment was indicated for 44\% of cases. It is noteworthy that not all cities in the state have adopted the new model proposed by the Ministry of Health, the Directly Observed Treatment (DOT), which provides observation of medication intake five times a week in the intensive phase of treatment, which the objective is to stimulate and ensure greater medication adherence\textsuperscript{(7)}. Still, according to the Ministry of Health, when it is not possible to adopt this strategy daily, for reporting purposes, DOT are considered the cases where the supervision of medication occurred in at least 24 doses in the initial phase (in the first two months) and 48 doses in the maintenance phase (4 months later). DOT enables the healthcare team to be closer to the patient and their contacts, which allows identifying symptomatic respiratory problems and hence diagnose them and treat them early. These aspects can help to reduce transmission of the disease and encourage adherence to treatment.

Regarding the situation of discharged cases, it was observed that during the period under study, the mean of cases discharged with cure (68.4\%) is below that recommended by the Ministry of Health, which is 85\%\textsuperscript{(1)} and that the death index cases by TB (3.3\%) was higher than the national mean (2.5\%) over the same period\textsuperscript{(7)}, as well as the nonadherence rate of TB treatment, which was 8.5\%. Although there is technology able to extinguish the Mycobacterium tuberculosis, this is still primarily responsible for transmission and infection of humans, especially in developing countries, where people intimately live with the social determinants of disease. Moreover, treatment nonadherence allows the bacteria to become multiresistant, which is a serious problem to be faced by the National Program to Control TB.

Just like this, results from other studies\textsuperscript{(5,9-12,16)} demonstrate that social and demographic factors are those that most influence the treatment nonadherence, so it is up to the professionals who work in the fight against TB to organize partnerships with other sectors, such as the Center for Social Assistance Reference – CRAS and Psychosocial Care Center – CAPS, so that these patients needs can be attenuated, thus increasing the chances of treatment adherence.

Besides age, illiteracy and low education (the latter characterized by incomplete elementary and high school), are related to greater likelihood of treatment nonadherence\textsuperscript{(5,10,15)}. These factors are associated with less understanding and access of these individuals to information about the disease and also access to health services. Thus, it is duty of health professionals, especially nurses, to encourage them to ask questions about symptoms, type of transmission and treatment of disease, and also provide them with clear information about these aspects, besides reaffirming that in the initial phase of treatment, even if symptoms disappear, to heal at least six months of regular use of medication prescription are needed.

In other studies, unemployment has also been identified as a predictor of treatment nonadherence\textsuperscript{(11,16)}. Despite the need to attend to health services to withdraw the medication and perform exams, especially in early
treatment, people with employment bond have higher treatment adherence. This may be related to the fact that they can count on the support and encouragement of work colleagues, but also because they felt responsible for their work activities, they can go back to work, as soon as clinical improvement is observed. On the other hand, unemployment contributes a poorer economic condition which in this case, even transportation costs may be a reason for treatment nonadherence. Moreover, homeless people who usually call themselves unemployed are also more vulnerable to TB, also showing more risk of nonadherence because of poor living conditions and the use of legal or illegal drugs.

Chemical dependence is a worrying factor in the diagnosis and treatment of TB, because there is a tendency of the health team and the patient to underestimate the cough as a symptom, linking it only to chemical use. Moreover, after the diagnosis, treatment adherence is complicated by the need to establish a routine in medication, which is a concern in the case of homeless(5).

In this study, because secondary data was used, it was not possible to obtain information about the use of illicit drugs among reported cases; but it was found that even with the poor quality in filling this field, in 17.2% of cases alcohol consumption was reported. This is an aggravating factor, because the literature has pointed out that the use of alcohol and other drugs is a factor closely related to nonadherence to treatment(8,11,17,18).

The risk of active TB is significantly higher in people who ingest more than 40g of alcohol beverages per day and/or have some disorder due to alcohol consumption(17). Given this, the social services should pay special attention to TB patients who drink alcohol beverages, for their tendency to treatment nonadherence, leading to treatment failure(17).

Finally, the readmission after treatment nonadherence proved to be a strong predictor of treatment discontinuation, confirming the results of other studies(5,8). For example, in a study conducted in Cuba that aimed to investigate resistance to antituberculosis drugs in patients re-admitted to treatment, it was found that they had acquired resistance to two or more drugs, which makes treatment more expensive, and trigger greater risk to the general population(17).

A fact that has drawn attention is that DOT has not showed statistically significant difference to be constituted as a protective factor for treatment nonadherence, and yet, in the state of Parana most cities did not adhere to the proposal of the Ministry of Health to implement the DOT as a strategy to ensure the target of 85% cure and nonadherence of less than 5%(19). In the cities of the State in which DOT was implanted, there is a chance of its implementation is not taking place, as recommended by the Ministry of Health in the sense that health professionals observe the intake of medication five times a week. DOT enables the healthcare team to be closer to the patient, which favors interaction, responsibility and humane care. Moreover, if the observation of treatment occurs in the home environment, the professional has the opportunity to assess the contacts and diagnose cases of contagion, which favors treatment and prognosis of the disease.

In this sense, health services should be organized in such a way that the patient can receive the medication in the nearest unit to their residence. In case of impossibility, the team should assess together with the patient where the most appropriate place is for this procedure, which may be at their workplace or home. In either situation, the medication is the responsibility of the health professional that supervises daily and on weekends and holidays the professional will provide him/her the necessary medications, leaving the patient with the responsibility for its intake(19).

Studies conducted in three States where this treatment was implemented, showed that the effectiveness of DOT for declining the occurrence of treatment nonadherence is evident(11,18,19). Another contribution of such treatment is that it allows the direct supervision of the dietary intakes of antituberculosis drugs and thus can identify the nonadherence at the beginning, i.e. shortly after its occurrence, facilitating the implementation of immediate corrective action(18). The current strategy of DOT has the objective to ensure adherence to treatment, reducing the risk of disease transmission to the community(19). On the other hand, in unsupervised treatment nonadherence cases are difficult to be identified, which may only be evident when the patient does not attend the services to withdrawn medications or medical appointments, or even when he/she admits to not taking medications prescribed by delaying the start of interventions by the health team. Studies have shown that the expansion of decentralized care and the implementation of DOT favor tuberculosis control and, with incentives, ensure greater adherence to medication rather than self-administered treatment(18,19).

Finally, knowing the epidemiological and sociodemographic profile of patients reported with tuberculosis and the predictor factors of treatment nonadherence enables health professionals, especially nurses, plan and implement effective actions for the rapid diagnosis of infection and fighting the disease. This is consistent with the goals of cure and treatment nonadherence established by the Ministry of Health, since TB still has an important role in the morbidity and mortality of the population of the State of Parana, as well as across the country.
CONCLUSIONS

This study allowed us to outline the profile of TB cases registered in the State of Parana in SINAN and identify factors associated with treatment nonadherence. With regard to the sociodemographic profile of the patients reported with tuberculosis, it was found that the majority was constituted by youth, white, male gender with low education levels. Regarding the epidemiological characteristics, the majority of new cases were reported with pulmonary TB, in which the rate of nonadherence and alcoholic individuals are high and the cure rate is low. Furthermore, DOT was not performed in almost half of the cases.

Factors related to the possibility of nonadherence were young age, alcoholism, unemployment, low education and readmission after treatment nonadherence. Knowledge of these aspects is important so health professionals can fight against treatment nonadherence, implementing DOT especially for those individuals who have nonadherence factors identified in the study.

REFERENCES