Abandonment of previous treatment and case of resistant multidrug tuberculosis in a tertiary institution in the city of Rio de Janeiro

Abandono de tratamento anterior e caso de tuberculose multidroga resistente em uma instituição terciária na cidade do Rio de Janeiro

Abandono de tratamiento anterior y caso de tuberculosis multidroga resistente en una institución terciaria en la ciudad de Río de Janeiro

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ABSTRACT

Objective: The study's purpose has been to describe the characteristics of cases of tuberculosis treatment abandonment in patients who developed multidrug-resistant tuberculosis (MDR-TB). **Methods:** It is a descriptive study with a quantitative approach that was carried out in a tertiary referral institution for the treatment of MDR-TB, located in the *Rio de Janeiro* city. A structured instrument was used with information from forty medical records between August and December 2016. Data analysis was performed using SPSS software. **Results:** Considering the patients studied, 35% abandoned previous treatment of tuberculosis. **Conclusion:** It is necessary the early identification of patients who are at greater risk for treatment abandonment, as well as the creation of a model of assistance aimed at the profile of users who abandon treatment, with a participatory practice with educational groups that promote preventive actions, identifying and experimenting strategies for overcoming barriers linked to reality, in both individual and collective lives.
Descriptors: Tuberculosis resistant to multiple medications, drug therapy adherence, therapy.

RESUMO

Objetivos: Descrever as características dos casos de abandono do tratamento de tuberculose em pacientes que desenvolveram tuberculose multirresistente (TBMR). **Métodos**: Estudo descritivo de abordagem quantitativa, desenvolvido em uma instituição terciária de referência para tratamento de TBMR localizada na cidade do Rio de Janeiro. Foi utilizado instrumento estruturado com informações de quarenta prontuários entre os meses de agosto a dezembro de 2016. A análise dos dados foi realizada por meio do software SPSS. **Resultados**: Dos pacientes estudados, 35% abandonaram tratamento anterior de tuberculose. **Conclusão e implicação para a prática:** É necessária a identificação precoce de pacientes que apresentam maior risco para abandono do tratamento, bem como a criação de um modelo de assistência voltado ao perfil dos usuários que abandonam o tratamento, com uma prática participativa, com grupos educativos que

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promovam ações preventivas, identificando e estudando estratégias para a superação de barreiras ligadas à realidade de vida individual e coletiva.

Descritores: Tuberculose Resistente a Múltiplos Medicamentos, Adesão a Medicação, Terapêutica.

RESUMEN

Objetivos: Describir las características de los casos de abandono del tratamiento de tuberculosis en pacientes que desarrollaron TBMR. **Métodos:** estudio descriptivo de abordaje cuantitativo, desarrollado en una institución terciaria de referencia para tratamiento de TBMR, ubicado en la ciudad de Río de Janeiro. Se utilizó instrumento estructurado con informaciones de cuarenta prontuarios entre los meses de agosto a diciembre de 2016. El análisis de los datos fue realizado a través del software SPSS. **Resultados:** de los pacientes estudiados, el 35% abandonó el tratamiento anterior de la tuberculosis. **Conclusión e implicación para la práctica:** es necesaria la identificación precoz de pacientes que presentan mayor riesgo para el abandono del tratamiento, así como la creación de un modelo de asistencia orientado al perfil de los usuarios que abandonan el tratamiento, con una práctica participativa, con grupos educativos Que promuevan acciones preventivas, identificando, estudiando estrategias para la superación de barreras ligadas a la realidad, de vida individual y colectiva.

Descriptores: Tuberculosis Resistente a Múltiples Medicamentos, Adhesión a Medicación, Terapéutica.

INTRODUCTION

One of the main concerns regarding tuberculosis is reducing treatment cessation rates. In Brazil, the dropout rate is high, it is around 17%, but in many regions, it reaches higher levels. This leads to non-disruption of the transmission chain, as people with tuberculosis (TB) who do not adhere to therapy remain ill and continue as a source of contagion. Furthermore, treatment withdrawal leads to drug resistance and relapse of the disease, which imposes difficulties on the patient's healing process, increasing the time and cost of treatment.[1,2,3]

The abandonment of the treatment itself is described by the Health Ministry as the absence of the user for more than 30 consecutive days after the date due to return, at the national level, between the Federation Units of the country, the proportion of abandonment varied from 2.8 to 15.9% in 2014.[4] This rupture in adherence results in a marked impact on indicators of incidence, resistance to multiple drugs, diseases, associated diseases, and increased mortality rates.[5] Causes known to be associated with discontinuation of treatment involve factors intrinsic to the user, such as the use of alcohol and other drugs, false impression of healing and discomfort caused by lack of food and extrinsic factors as a modality of applied treatment and operationalization of health services.[6]

Still, as a potent ingredient for the challenge of tuberculosis control, multidrug resistance emerges for treatment. The World Health Organization estimates that around 480,000 people develop MDR-TB every year.[7] In 2013, only 20% of these people received recommended treatment regimens.[7]

Considering those patients who are actually treated, only 10% can heal. It may also present more resistant forms (XDR-TB) and with the possibility of improbable cure and consequent death.[8]

Nevertheless, the growth in the number of such cases is causing worldwide concern, and this clinical form of multidrug resistance has been increasingly linked to the deficiency of health systems and is nowadays a major global challenge of TB control.[9] The advent of antibiotics for the treatment of tuberculosis corresponds to a high advance in the fight against the disease. Nonetheless, since its first use, antibiotic therapy has been associated with the emergence of drug-resistant strains of Mycobacterium tuberculosis.[10]

XDR-TB is a major threat to public health. Its very existence is a reflection of the lack of control of TB and the lack of implementation of the measures recommended in the WHO's Stop TB Strategy, which should minimize the emergence of drug resistance.[8]

The number of multidrug-resistant tuberculosis (MDR-TB) cases and extensively drug-resistant tuberculosis (XDR-TB) has increased significantly in the world.[11] Recent data show that the number of MDR-TB cases has tripled between 2009 and 2013 in MDR-TB accounted for 3.5% of all new cases of tuberculosis and 20.5% of all TB cases previously treated, whereas cases of XDR-TB accounted for 9% of all cases of MDR-TB reported in 100 countries.[12]

Given the aforementioned, the study's goal was to analyze the occurrence of tuberculosis treatment abandonment and the subsequent complication for the development of Multidrug-Resistant Tuberculosis in a tertiary referral institution for the treatment of Multiresistant Tuberculosis, located in the *Rio de Janeiro* city.

METHODS

It is a descriptive study with a quantitative approach. This research was performed by considering the information obtained in 40 patients' medical records that were referred with MDR-TB, in the Tisiology Service of the *Hospital Universitário Clementino Fraga Filho (HUCFF). HUCFF* is a referral hospital for the treatment of multidrug-resistant tuberculosis, located on the campus of the *Universidade Federal do Rio de Janeiro (UFRJ)*, which currently receives patients diagnosed with multidrug-resistant tuberculosis related to program areas 2.2. At the time of collection, 40 patients had admitted to *HUCFF* for treatment of MDR-TB, and all records were used for data collection, since all met the criteria for inclusion of the study.

The study was carried out over the period from August to December 2016 and the data were obtained by analyzing the medical records.

The population was composed of patients belonging to Programmatic Area (PA) 2.2 who are referred to (*HUCFF*) for the treatment of MDR-TB. The PA 2.2 has the study hospital as a reference for the treatment of MDR-TB and covers 7 neighborhoods, as follows: *Praça da Bandeira, Tijuca, Alto da Boa Vista, Maracanã, Vila Isabel, Andaraí, Grajaú.*

The sample was delimited according to the following inclusion criteria: patients diagnosed with MDR-TB, age group of 18 years old or older, and treated with a basic regimen recommended by the *Programa Nacional de Controle da Tuberculose (PNCT)* [National Tuberculosis Control

Program]. As exclusion criteria, the medical records of users who presented incomplete information and difficulty understanding were not eligible.

For data collection, a structured questionnaire was used for the socio-demographic evaluation where the variables investigated were: gender, skin color, age, schooling, TB form, HIV test result, HIV-AIDS co-infection, and presence of other comorbidities.

We also searched for data on the form of entry into the program, whether they were treatment-naive patients (new case) or whether they were previously treated for tuberculosis (returns). In addition to data research as the predominant clinical form of tuberculosis and follow-up with the Directly Observed Treatment Short (DOTS) strategy.

The data obtained were coded and typed in Microsoft Excel 2010 spreadsheet and analyzed with the support of the statistical package for the social sciences SPSS version 22.0. They were treated with descriptive statistics and presented in frequency tables, with absolute values (n) and percentages (%) for the categorical variables.

All the ethical care that govern researches with human beings were observed and respected, according to the Resolution No. 466/2012, and in the Normative No. 001/2013 regulated by the National Health Council.

The study was approved by the Research Ethics Committee of the *Escola de Enfermagem Anna Nery (EEAN)* from the *Universidade Federal do Rio de Janeiro (UFRJ)*, on May 31st, 2016, having as protocol the *Certificado de Apresentação para Apreciação Ética (CAAE)* [Certificate of Presentation for Ethical Appraisal] No. 54091116.7.0000.5238.

RESULTS

Table 1 shows that among the 40 patients investigated, 67.5% were male and 32.5% female, with the majority being 42.5% brown skin color. When the level of schooling was analyzed, 40% of the total number of patients studied had between 4 and 7 years of schooling and 42.5% between 8 and 11 years of schooling. This time was also observed among those who have abandoned treatment.

Table 1 - Clinic and sociodemographic profile of the MDR-TB bearing patients.

Variable		Notified Cases		Abandonment Cases	
		n	%	n	%
Gender	Male	27	67.5	10	71.4
	Female	13	32.5	4	28.6
Skin color	White	12	30	5	35.7
	Brown	17	42.5	4	28.6
	Black	11	27.5	5	35.7
Age	0-20 years old	3	7.5	1	7.2
	21-40 years old	21	52.5	6	42.9
	41-60 years old	8	20	4	28.5
	61 years old or more	8	20	3	21.4
Schooling	0-3 years	4	10	1	7.2
	4-7 years	16	40	10	71.4
	8-11 years	17	42.5	3	21.4
	12 or more	3	7.5	0	0

Variable		Notified Cases		Abandonment Cases	
		n	%	n	%
Program entrance	New case	26	65	NA	NA
	Return	14	35	14	100
AIDS	Yes	9	22.5	0	0
	No	31	77.5	14	100
DOTS	Yes	10	25	1	7.2
	No	30	75	13	92.8
Tuberculosis form	Pulmonary	35	87.5	13	92.8
	Extrapulmonary	5	12.5	1	7.2

* NA - No applicable.

The average age was 43.6 years old with the variation between 18 and 77 years old. Considering the 40 patients, 35% have abandoned treatment. Of those, 10% dropped out more than six times. When analyzed the educational level of those who dropped out of treatment 71.4% had less than seven years of study and when analyzed the level of education of those who did not abandon treatment 40% had less than seven years of study. Of the patients who left the treatment only one had the extrapulmonary form. Observing the total number of patients investigated, 25% received the Directly Supervised Treatment. When the comorbidity data were analyzed, the most present comorbidity was HIV with 22.5% of coinfected patients. The BAAR test was positive in 82.5% of the patients and the Culture test was positive in 70% of the cases. Regarding the Antimicrobial Sensitivity Test, 45% presented resistance to at least two drugs: rifampicin and isoniazid.

DISCUSSION

There is a consensus in the current literature about associating the emergence of MDR-TB strains with failures in health services, especially regarding the appropriate treatment of reported cases, so leaving the natural chain of transmission of the bacillus flowing.[7] Several studies also point to the low adherence to treatment and/or inadequate pharmacological treatment as important factors for the emergence of MDR-TB.[9] In Brazil, in 2000, the dropout rate was considered high and was around 17% .[4] In this study, the dropout rate was considered high when compared to stipulated levels of 5% by WHO.[8]

Of the 35% patients who had abandoned treatment previously, 10% dropped out more than six times. In Brazil, 96% of the cases of resistance of the bacilli are of the acquired type, the infected patients present bilateral pulmonary cavitations in 65% of the cases, and HIV co-infection in 7%. For the treatment of these cases, it is necessary to use injectable drugs and reserve drugs, with a duration of 18 to 24 months, whose effectiveness is approximately 60%.[13] Another important fact is that drug resistance is an important risk of failure to institute treatment.[14]

In developing countries, such as Brazil, serious social inequalities, increased poverty and poor income distribution, when associated with poor medical and health conditions and, moreover, the difficulty in accessing health services, lead to higher rates of infection with the microorganism,

worsening of the disease, high frequency of comorbidities, co-infection as HIV/TB, and the development of multiple drug-resistant strains. Given this aforesaid context, one of the most serious problems today is undoubtedly multidrug-resistant tuberculosis (MDR-TB) and extensively resistant tuberculosis (XDR-TB).[15]

The multi-resistance issue in Brazil is also associated with non-compliance with the therapeutic scheme. This is a serious problem in the context of TB control actions, since patients who abandon TB treatment and/or irregular therapy favor the persistence of microorganism transmission in the community and drug resistance, then negatively impacting disease control.[4,7,9]

The predominance of tuberculosis in males, one of the findings of this research, is similar to that found in the literature, pointing out that the difference in TB involvement between the sexes may be due to several factors, such as economic, cultural and social factors related to exposure to the bacillus.[2,16,17]

Herein, 25% of the patients were black and 35% brown and corroborate with other studies that indicate that in Brazil, blacks and browns have lower schooling, lower wages, reside in peripheral neighborhoods of large cities and are excluded from various rights social policies. Consequently, it can be hypothesized that the health, disease and death process is socially constructed and demarcated by the territorial and social space that black and white men and women occupy in society.[18,19]

It is known that socio-cultural factors can make treatment difficult, such as low level of education, lack of knowledge about tuberculosis and non-acceptance of the disease, and the fact that some patients consider themselves cured before the effective cure since patients feel good.[20]

The rate of abandonment to tuberculosis treatment verified in the cases analyzed in this study was 35%. Studies conducted in Brazil show abandonment rates varying from 38% to 42%, and these rates are extremely high, since the Health Ministry recommends only 5% of abandonment as acceptable.[7] It is considered as abandonment, the patient who, once initiated the treatment stopped attending the Health Unit for more than thirty consecutive days, after the date set for the return.[21] High rates of treatment abandonment were also found in other studies conducted in the country, showing the need to implement actions aimed at their prevention, especially in those groups that are at greater risk for abandonment.[2,16]

Discontinuation of tuberculosis treatment contributes to the maintenance of transmission since patients who do not stick to it or use chemotherapy for insufficient time and/or incorrectly remain the source of contamination, increasing relapse rates and drug resistance. These factors impede healing since they increase the time and cost of treatment.[18,22]

In developing countries, 80.0% of those infected are between 15 and 59 years of age, considered to be the one with the highest social productivity, with economic and social implications for the individual and his family.[23,24] In this study, the most affected age group was from 21 to 40 years old (52.5%), the highest dropout rate in this range may be related to the lifestyle of this population, which normally uses

alcoholic beverages and has irregular feeding times, factors that may contribute to the interruption of treatment, these results were confirmed in several studies.[20,25,26,27]

Twenty percent of the disease cases were found in the range above 61 years, confirming that the increase in life expectancy of the population has changed the age profile of tuberculosis cases, increasing its occurrence among the elderly.[2,16,28] Pulmonary localization is the most common form of MDR-TB in the present study, where 87.5% of the patients who presented the disease were pulmonary.[29,30,31]

The Health Ministry estimates that in the general population, 80.0% of the TB cases present the pulmonary form.[32] When analyzed the educational level of those who left treatment, 71.4% had less than seven years of study and when analyzed the educational level of those who did not abandon the treatment 40% had less than seven years of study, confirming with data from the literature where San Pedro (2013) in an ecological study, discusses that it is possible to verify that indicators related to income, schooling, and population density are associated with tuberculosis at different levels of spatial aggregation.

Several factors may hinder the treatment and cure of tuberculosis, such as socio-cultural factors, low level of schooling, lack of knowledge about and acceptance of the disease, mistaken perception of being cured before effective cure, patients feel better after the first 15 days of treatment. The shorter the educational time, the greater the need of the special attention of the health professionals to the patient in treatment in the promotion of orientations of easy understanding for the patient, thus avoiding the abandonment.

According to the *Programa Nacional de Controle da Tuberculose (PNCT)* [National Tuberculosis Control Program], a prevalence of 50 million infected, 100,000 new cases and 4,000 deaths are estimated annually for Brazil and an incidence rate of 37.2/100,000 inhabitants.[33] The World Health Organization currently considers that TB occupies an important percentage of the use of resources in the health sector.[8]

Data from the State Department of Health of *Rio de Janeiro* State that in 2014, 155 multi-resistant cases occurred in the State capital.

In 2013, Brazil registered 503 cases of MDR-TB, while countries such as Bolivia recorded 72 cases, Argentina 116 cases of the disease, Paraguay only 6 cases of MDR-TB and 10 cases in Venezuela.[4] In 2014 Chile recorded 15 cases of MDR-TB in its country, where 9 of the cases of MDR-TB with Chilean nationality, 5 Peruvian cases and 1 Colombian case.[35]

When analyzing the data of cases of MDR-TB in Brazil in relation to the *Mercosul* countries, it is possible to observe a higher prevalence of MDR-TB cases in Brazil. This scenario can be justified because of the problematic of access to treatment, which is hampered by the current treatment regimens, which are long-term, poorly tolerated and difficult to administer in the places where the majority of patients reside, reasons that hinder adherence and the success of treatment, and these are one of the crucial factors for abandonment.[36] One way is to facilitate access to treatment and especially to Directly Observed Treatment, so that we could provide thousands of

lives in the next decades to be preserved. The decentralization of diagnosis and treatment to health centers in the periphery would also facilitate patient care and could contribute to an improvement in cure rates and a reduction in the chain of bacillus transmission.

Aiming to reduce treatment abandonment rates, it is a priority to know the factors associated with such abandonment, in order to reorient people in TB treatment to practices and health care.[28] In *Rio de Janeiro* city, forms of multidrug resistance have been established and disseminated among the various population groups, favored by the growth of community densities, is related to local "pockets of poverty" with a large concentration of housing units, without access to ventilation and lighting, which facilitates the spread of respiratory diseases.[13]

The increase in the rate of abandonment of treatment, the deterioration of health services due to the decrease of investments in the sector are also problems faced in the *Rio de Janeiro* city.[37,38]

In Brazil, the scarcity of recent studies on the epidemiology of MDR-TB in the country makes difficult the process of showing the real situation the disease in territory based on its determining and conditioning factors, be they social, cultural or clinical-epidemiological.

CONCLUSIONS

It is clear that in the 21st century, many patients suffer and die due to TB, although the disease is curable, and the treatment is fully funded by the *Sistema Único de Saúde (SUS)* [Unified Health System]. Involving cultural, economic, social and ideological dimensions, this scenario is related to several factors that are not restricted only to health policies, a reason that makes it difficult to control the disease.

The study found that the early identification of patients who are at greater risk for treatment abandonment justifies a careful approach to be defined according to the conditions of each location. Adherence to treatment, correct diagnosis, and appropriate therapy are not only important to the health status of the patients but are a public health problem.

The study confirms the need of creating a model of assistance focused on the users' profile who abandon treatment, by promoting a participative, collective practice with educational groups that promote preventive actions, identifying and studying strategies for overcoming barriers linked to the reality of life, individual and collective. Hence, it is expected that the results of this study may contribute to the improvement of health actions, providing subsidies for the teams to intensify educational and awareness actions about the need to follow the treatment until healing, then reducing cases of treatment abandonment, therefore, reducing cases of MDR-TB.

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