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Social, clinical, and adherence factors in patients co-infected with HIV/ Tuberculosis: a descriptive study

Gabriela Souza Damásio¹, Heloisa Martins França¹, Isabelle Christine Marinho de Oliveira¹, Aryele Rayana Antunes de Araújo¹, Alexsandra Rodrigues Feijão¹

¹ Federal University of Rio Grande do Norte

ABSTRACT

Aim: To evaluate the influence of social and clinical aspects in terms of medication adherence of patients co-infected with HIV/Tuberculosis. **Method:** This is a descriptive cross-sectional study using a quantitative approach, performed in a public institution in the state of Rio Grande do Norte, Brazil, in the period from August 2014 to January 2015, with 34 users co-infected with HIV/TB. The instruments used were: sociodemographic and clinical assessment; the Morisky-Green test and evaluation of the difficulty level for adherence. **Results:** adherence to treatment was significantly associated with the time of diagnosis for HIV over five years, with moderate difficulty regarding medication adherence ($p=0.019$). **Conclusion:** professionals need to consider the compliance with treatment in the general context in which users are found, including the associated factors and the actions planned by the service significantly influencing the treatment outcome.

Descriptors: Medication Adherence; HIV; Tuberculosis.

INTRODUCTION

The World Health Organization (WHO) estimates that 36.9 million people live with the human immunodeficiency virus (HIV) globally⁽¹⁾. In this population, the risk of developing tuberculosis (TB) is increased compared to those without the virus, due to the decrease of the defenses, which constitutes a condition of great impact on mortality rate in developing countries⁽²⁾.

Thus, with respect to the co-infection by HIV/TB, of the 9.6 million people who have developed TB, 1.5 million died of the disease; of these, 0.4 million were HIV positive in 2014⁽¹⁾. In Brazil, the numbers have reached 798,000 reported cases of people living with HIV/AIDS (PLWHA) and 63,189 new cases of TB, resulting in a co-infected rate of 9.7%⁽³⁻⁴⁾. In the Northeast of Brazil this rate reaches 7.9%, with the dynamics of internalization of the disease, showing how social factors, such as poverty and lack of investment in effective prevention programs and treatment, influence and hinder coping with both pathologies, especially TB which is the leading cause of death among infectious diseases defined in patients with HIV/AIDS⁽²⁻³⁾.

The early initiation of antiretroviral therapy (ART) for the treatment of TB is related to a reduction of all causes of death in this group⁽⁵⁻⁶⁾, and the early initiation of ART in HIV patients reduces the risk of developing TB in approximately 65%⁽¹⁾. However, recent studies indicate that only a third of patients co-infected with HIV/TB worldwide receive ART in a timely manner. The barriers in different parts of the treatment highlight the need for commitment of health services targeted to these patients through the integration of care and services at all levels⁽⁷⁾.

Considering that adherence to antiretroviral and tuberculostatic therapies is an important measure to reduce and control HIV/TB cases, the difficulty of adherence to treatment is an

important factor for the persistence of high rates of incidence and prevalence of infection in the country, impacting heavily on the epidemiological behavior⁽⁸⁾.

A review study shows that the available literature on adherence to treatment is practically restricted to Brazil⁽⁹⁾. According to the epidemiological control bulletin of TB in 2015, 12,337 cases of retreatment of TB were registered in Brazil, representing 16.3% of the 63,189 new cases reported in Brazil. With an unsatisfactory rate of TB cure below 80% and 11% therapy abandonment, it appears that, although the treatment is offered by the public and is a free service in Brazil, dropout rates and inadequate use of medication are significant⁽³⁾.

Thus, knowing the relationship between social and clinical difficulty of medication adherence for patients co-infected with HIV/TB will provide evidence of a health service planning in order to cope with such problems. Thus, the aim of this study is to evaluate the influences of social and clinical aspects of medication adherence by patients with co-infected HIV/TB.

METHOD

This is a descriptive transversal study using a quantitative approach, performed in outpatient care and treatment of patients co-infected with HIV/TB in the Hospital Giselda Trigueiro (HGT), a leading public institution in the state of Rio Grande do Norte (RN).

In Rio Grande do Norte, Brazil, from 2008 to 2012, 382 cases of TB associated with HIV were reported, an average of 76.4 cases per year. Based on this average, the sample was calculated, considering the period from August 2014 to January 2015, corresponding to six months. Thus, a sample of 38 subjects was estimated.

Inclusion criteria were: individuals seropositive for HIV diagnosed with TB, aged 18 years and over, and under treatment with a basic scheme established by the National Program to Combat Tuberculosis. Exclusion criteria were: users with some understanding and verbal expression difficulty; institutionalized or homeless individuals; patients who were hospitalized and discontinued treatment for TB due to serious side effects.

Participants were selected by convenience, that is, as they attended the consultation service. The approach to the subjects was performed before the medical consultations, in a private room. Data collection was carried out after signing Informed Consent, through interviews by the application of three instruments. The first was a sociodemographic and clinical evaluation form, in order to create a characterization of subjects, including gender, age, marital status, education level, monthly income, origin, time of diagnosis of HIV infection, category of exposure to HIV, partner serology, the beginning of antiretroviral treatment regimen, time in the tuberculostatic regimen, type of tuberculosis, examinations performed, and symptoms reported in attendance.

The second instrument was the Morisky-Green Test (MGT), a simple scale validated in Brazil, which aims to identify attitudes and behaviors against the adherence to treatment, consisting of four questions: 1- Have you ever forgotten to take your medicine? 2- Are you sometimes careless regarding the time you take your medicine? 3- Do you sometimes stop taking your medicine when you feel good? 4. Do you sometimes stop taking your medicine when you feel bad? The form of assessment was through dichotomous answers: YES is worth 0 and NOT is worth 1. According to the MGT Protocol, patients considered adherent to treatment are the ones who obtain the maximum score of four points and non-adherent those who get three points or less.

The third instrument was used to assess the degree of difficulty for adherence, based on the study of Marques (2006)⁽¹¹⁾. The instrument originally included 17 questions; however, in this study, only 10 items were used, according to its purpose. The answers were given on a five-level Likert scale: totally agree; partially agree; indecisive; partially disagree; totally disagree, and the respective values were 5, 4, 3, 2, and 1. The result is provided by the sum of the responses values, using scores equivalent to the original instrument, as follows: patients totaling 10 to 20 points, no difficulty adhering to treatment; 21 to 30 points, little difficulty adhering to treatment; 31 to 40 points, moderate difficulty adhering to treatment; and 41 to 50 points, severe difficulty adhering to treatment.

Data were analyzed using the Statistical Package for Social Sciences software (SPSS), version 20.0 and the free software R, version 3.0. Initially, it was checked whether the data in the study had normal distribution using the Shapiro Wilks test, necessary precondition for the application of parametric test for average comparison, the Student t test. As the data normality was not met, the non-parametric Mann-Whitney and chi-square tests were applied. Correlations in $p < 0.05$ were considered statistically significant. For data reliability, the statistical test of Cronbach's alpha was used.

The study followed the ethical precepts of the National Health Council Resolution 466/12, and was approved by the Ethics Committee of the Federal University of Rio Grande do Norte (UFRN), under opinion no. 650,693, CAAE: 27939814900005537.

RESULTS

Thirty-four subjects co-infected with HIV/TB were interviewed. Most of the interviewees

in this study were male (85.29%); the average age was 37.24 years, ranging between 23 and 61 years. As for marital status, 50% were married or in a stable relationship, and the average number of children was 1.94 children. Most were originally from a rural region of the State (61.77%), 44.12% had not completed elementary school, and 85.19% had a family income between one and two minimum wages.

As to the other data, 51.52% of patients received a diagnosis of HIV infection more than five years prior to the study, and 54.94% were infected through exposure through sexual intercourse. Regarding TB, 90.01% predominantly had the pulmonary form, highlighting the symptoms of cough (73.53%) and fever (61.76%). The average time of diagnosis of TB was 3.25 months, and the X-ray and acid-resistant bacilli (AFB) were the main examinations performed for diagnosis and follow-up treatment, as shown in Table 1.

Table 1 - Sociodemographic and clinical characterization of patients co-infected with HIV/TB. Natal/Brazil, 2014-2015

Variables	N (%)
Sex	
Male	29 (85,29%)
Female	5 (14,71%)
Age Group	
21 to 30 years	8 (23,53%)
31 to 40 years	15 (44,12%)
Above 40 years	11(32,35%)
Marital Status	
Single	17 (50,00%)
Married	8 (23,53%)
Stable union	9 (26,47%)
Schooling	
Illiterate	2 (5,88%)
Incomplete primary education	15 (44,12%)
Complete primary education	5 (14,71%)
Incomplete high school	5 (14,71%)
High school	7 (20,58%)
Monthly household income	
Up to 1 minimum wage	11 (14,81%)
1 to 2 minimum wages	23 (85,19%)

HIV exposure category	
Sexual	18 (54,54%)
Not known	15 (45,46%)
Time of diagnosis of HIV infection	
Up to 5 years	16 (48,48%)
Over 5 years	17 (51,52%)
Partner Serology	
No partner	18 (56,26 %)
Positive	9 (28,12%)
Negative	5 (15,62 %)
Type of TB	
Pulmonary	30 (90,91%)
Extrapulmonary	4 (9,09%)
Exams performed	
Radiograph	30 (90,91%)
AFB Research	12 (35,29%)
CD4 +	8 (28,57%)
PPD	7 (26,92%)
Viral charge	6 (23,08%)
Symptoms reported in care	
Cough	25 (73,53%)
Fever	21 (61,76%)
Dyspnoea	8 (23,53%)
Asthenia	4 (11,76%)
Anorexia	3 (8,82%)

Through the statistical test Cronbach's Alpha, which verifies the reliability of the data, it can be observed that the Moriski-Green instruments and evaluation of the level of adherence, evaluated in patients with HIV and TB, ranged from 0.729 and 0.755, respectively. Thus, data consistency is classified as satisfactory.

According to Moriski-Green test items, 73.53% of patients were classified as non-adherent to therapy (Table 2), this condition related to carelessness regarding the right time to take the medications and sleep.

Table 2 - Morisky-Green Test ranking. Natal/Brazil, 2014-2015

Classification	N (%)
Adherent	9 (26,47%)
Nonadherent	25 (73,53%)

It was found that 38.24% and 35.29% of the patients respectively presented low and

moderate difficulty adhering to treatment (Table 3). These degrees of difficulty for adherence can be evidenced by the following data: 32.35% reported having many medicines to take; 23.53% had difficulty swallowing medicines; 29.41% reported that the drugs caused side effects; 23.53% classified the treatment as complicated; and 26.47% have partial trouble remembering the time to take the medicine.

Table 3 - Classification of the degree of difficulty for adhesion of people with co-infected HIV/TB assisted in the outpatient clinic of the HGT. Natal/Brazil, 2014-2015

Classification of difficulty level for adhesion	N (%)
No difficulty adhering to treatment	8 (23,53%)
Little difficulty adhering to treatment	13 (38,24%)
Moderate difficulty adhering to treatment	12 (35,29%)
Much difficulty adhering to treatment	1 (2,94%)

Regarding the association of sociodemographic and clinical aspects with the classification of the degree of difficulty for the adherence of patients co-infected with HIV/TB (Table 4), it is observed that the association with the time of diagnosis for HIV over five years was significant, with moderate difficulty in terms of medication adherence ($p=0.019$). Therefore, the time of HIV diagnosis is directly proportional to the difficulty of accession.

DISCUSSION

This study shows the superiority of males in relation to females in terms of the co-infection with HIV/TB. The prevalence in patients co-infected with HIV/TB was also found in studies conducted in Brazil, South Africa, and Portugal.

Therefore, the male vulnerability to co-infection with HIV/TB is emphasized⁽¹²⁻¹⁴⁾.

The findings have also indicated that sexual intercourse is the main vector identified by patients for HIV infection. Despite all the HIV prevention work by WHO and other non-governmental organizations around the world since the 1980s, sexual transmission remains responsible for over 75% of new infections in the countries of the Americas⁽¹⁵⁾, which shows the difficulty in the implementation of measures such as condom use.

Concerning the clinical picture, the most frequent symptoms were cough (73.53%) and fever (61.76%), which are among those used for tracking cases of pulmonary TB recommended by the Ministry of Health and used as a parameter worldwide⁽¹⁶⁾. However, a Belgian study points to the need for health professionals be alert in order to track non-pulmonary forms of tuberculosis, which are also predictors of poor prognosis and require timely treatment^(9,16).

The need for treatment in a timely manner of both infections for patients co-infected with HIV/TB is determining in the prognosis and reduction of deaths among these patients⁽¹³⁾. In this study, 73.53% of respondents were classified as noncompliant, condition caused mainly by the lack of care with regard to taking the drugs at the right time.

The literature is quite diverse as to the time of HIV diagnosis and treatment adherence. Considering adherence as something complicated and difficult for many patients, it can be seen that the time of diagnosis for HIV above five years is related to lower adherence. Studies show that the negative influence of the accession can be explained by the chronic profile, by the healing impossibility of HIV, as well as the therapeutic difficulties, bringing uncertainty and causing psychological stress and disbelief in an effective outcome of treatment, and encouraging the abandonment of therapy^(12, 17).

Table 4 - Association between the sociodemographic and clinical characterization and classification of the degree of adherence to the treatment of people co-infected with HIV/TB assisted in the outpatient clinic of the HGT. Natal/Brasil, 2014-2015.

Variables	Adhesion degree classification				p-value
	Without difficulty	Little difficulty	Moderate difficulty	Much difficulty	
Sex					
Male	5 (17,24%)	12 (41,38%)	11 (37,93%)	1 (3,45%)	0,223 (1)
Female	3 (60%)	1 (20%)	1 (20%)	0 (0%)	
Age Group					
Up to 37 years	5 (25%)	7 (35%)	8 (40%)	0 (0%)	0,591 (1)
Over 37 years	3 (21,43%)	6 (42,86%)	4 (28,57%)	1 (7,14%)	
Marital Status					
Married	4 (23,53%)	5 (29,41%)	8 (47,06%)	0 (0%)	0,388(1)
Single	4 (23,53%)	8 (47,06%)	4 (23,53%)	1 (5,88%)	
Schooling					
Unschooling	0 (0%)	2 (100,00%)	0 (0%)	0 (0%)	0,658(1)
Incomplete Elementary School	6 (40%)	4 (26,67%)	4 (26,67%)	1 (6,66%)	
Complete Primary Education.	0 (0%)	2 (40%)	3 (60%)	0 (0%)	
Incomplete Medical Education.	1 (20%)	2 (40%)	2 (40%)	0 (0%)	
Complete Medical Education.	1 (14,28%)	3 (42,86%)	3 (42,86%)	0 (0%)	
Income					
Up to 1 SM	1 (25%)	2 (50%)	1 (25%)	0 (0%)	0,899(1)
Between 1 and 2 SM	5 (21,74%)	8 (34,78%)	9 (39,13%)	1 (4,35%)	
HIV diagnosis time					
Up to 5 years	7 (43,75%)	6 (37,50%)	3 (18,75%)	0 (0%)	0,019(1)
Over 5 years	1 (5,88%)	6 (35,29%)	9 (52,94%)	1 (5,88%)	
HIV exposure category					
Sexual	4 (22,22%)	7 (38,89%)	6 (33,33%)	1 (5,56%)	0,784(1)
Not known	4 (26,67%)	5 (33,33%)	6 (40%)	0 (0%)	
Cough Symptom					
No		3 (33,33%)	1 (11,11%)	0 (0,00%)	0,050 (1)
Yes		10 (40,00%)	11 (44,00%)	1 (4,00%)	

It was expected that patients with higher diagnosis times would demonstrate greater commitment to treatment by observing clinical improvements with it; however, a significant relationship between these variables was observed in patients with up to three years of diagnosis who presented little or no difficulty adhering to treatment⁽¹⁸⁾.

Statistically, the patients who had not cough symptoms were also those who had little to moderate difficulty in adherence to tuberculostatic treatment. This goes against the findings of national and international studies in which, commonly, asymptomatic patients

prefer to abandon treatment, deeming it not to be necessary, since they are asymptomatic for TB⁽¹⁹⁾.

Concerning the difficulties in terms of compliance to the treatment, the condition of having many remedies to take, the need to be assisted to make use of medications, which are complicated and difficult to swallow and, especially, the undesirable adverse effects were the main difficulties pointed out by patients. A study published in England emphasizes that few studies have pointed to the difficulty of treatment and the duration and number of doses, indicating that shortening treatment strategies tend to

get better response from users. Furthermore, it addresses socio-economic aspects as relevant⁽²⁰⁾. This study also points out that, in addition to adherence to TB treatment being critical to the success of treatment, noncompliance or poor adherence can promote the development of multidrug-resistant TB.

TB multidrug resistance causes a negative impact on treatment adherence, for further aggravate the patient's condition with HIV/AIDS and the necessity to make changes in the HAART regimen because of medications interactions and the increased number of drugs taken and adverse reactions⁽¹⁰⁾.

As a coping strategy, we can point out the Directly Observed Treatment (DOT), already developed in Brazil for TB patients in treatment in the Family Health Strategy. The nurse, as an important enabler of these actions, must be able to ensure hosting, connection, comprehensive care, planning and implementation of educational groups in the waiting room, and ensure supervised treatment to patients who present greater vulnerability to abandonment⁽⁹⁾.

CONCLUSION

The study showed a significant relationship between the classification of adherence to treatment and the time of HIV diagnosis. In the sample, the time of diagnosis for HIV above five years prior has moderate difficulty in terms of medication adherence.

Thus, professionals such as nurses directly related to patients co-infected with HIV/TB should intervene before the difficulties in terms of compliance to the treatment of patients in its general context, especially those with factors associated with them such as the time of diagnosis for HIV, because they significantly influence the treatment outcome.

It is pertinent to emphasize that strategies have been addressed in several countries with a view to increasing adherence to therapy and to promote a good prognosis. However, because of the lack of studies that address the relationship of the factors associated with the treatment of the coinfection HIV/TB, further studies in different populations are necessary so that new actions can be planned.

Among the limitations of this study are the time for restricted achievement, the small number of patients co-infected with HIV/TB under treatment during the collection period, and the non-probability sampling employed, in which the selection of subjects for accessibility does not guarantee the representativeness of the sample, making it difficult to generalize the results.

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