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Determinants of non adherence to tuberculosis treatment in Argentina: barriers related to access to treatment

Determinantes da não adesão ao tratamento da tuberculose na Argentina: barreiras relacionadas com o acesso ao tratamento

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ABSTRACT: ***Objective:*** To identify the association between non-adherence to tuberculosis treatment and access to treatment. ***Methods:*** A cross-sectional study was carried out in the Metropolitan Area of Buenos Aires, Argentina. One hundred twenty three patients notified in 2007 (38 non adherent and 85 adherents) were interviewed regarding the health care process and socio-demographic characteristics. Factors associated to non-adherence were assessed through logistic regression analysis. ***Results:*** An increased risk of non-adherence with to treatment was found in male patients (OR = 2.8; 95%CI 1.2 – 6.7), patients who had medical check-ups at hospitals (OR = 3.4; 95%CI 1.1 – 10.0) and those who had difficulties with transportation costs (OR = 2.5; 95%CI 1.1 – 5.9). ***Conclusion:*** Risk of non-adherence increases as a result of economic barriers in accessing health care facilities. Decentralization of treatment to primary health care centers and social protection measures for patients should be considered as priorities for disease control strategies in order to lessen the impact of those barriers on adherence to treatment.

Keywords: Tuberculosis. Medication adherence. Therapeutics. Epidemiologic factors. Argentina. Decentralization

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RESUMO: ***Objetivo:*** Identificar a associação entre a não adesão ao tratamento da tuberculose e as características de acesso ao tratamento. ***Métodos:*** Um estudo transversal foi realizado na Região Metropolitana de Buenos Aires, Argentina. Cento e vinte e três pacientes notificados em 2007 (38 aderentes e 85 não aderentes) foram entrevistados sobre o processo de cuidados de saúde e características sócio-demográficas. Fatores associados a não adesão foram avaliados através da análise de regressão logística. ***Resultados:*** Foi encontrado um aumento do risco de não adesão ao tratamento em pacientes do sexo masculino (OR = 2,8, IC95% 1,2 – 6,7), pacientes que tiveram controles médicos em hospitais (OR = 3,4, IC95% 1,1 – 10,0) e aqueles que tiveram dificuldades com os custos de transporte (OR = 2.5, IC95% 1,1 – 5,9). ***Conclusão:*** O risco de não adesão aumenta como resultado de barreiras econômicas no acesso aos serviços de saúde. A descentralização do tratamento para os centros de atenção primária à saúde e medidas de proteção social para os pacientes devem ser considerados como prioridades para as estratégias de controle da doença, a fim de diminuir o impacto dessas barreiras na adesão ao tratamento.

Palavras-chave: Tuberculose. Adesão à medicação. Terapêutica. Fatores epidemiológicos. Argentina. Descentralização

INTRODUCTION

Despite the availability of a cost-effective treatment, tuberculosis (TB) is still a major public health burden in developing countries[1]. In Argentina, TB affects around 9,500 people (25 cases per 100,000 people) and causes 800 deaths every year[2].

Treatment adherence is considered a key component for disease control since treatment disruption may result in persistent infectiousness and higher rates of treatment failure, continued transmission, drug resistance, and death[3]. The World Health Organization (WHO) recommends that non-adherence should not exceed 5%[4]. Argentina showed a 13.8% non-adherence rate in 2010[5], being one of the highest figures in the last ten years[5].

Since 1994, Direct Observed Treatment Strategy (DOTS) has been recommended for treatment adherence and has been introduced in TB control programs in many countries with varying degrees of success[6,7]. Although it is widely recognized that DOTS is an important tool in disease control, results from different studies have shown that, both in DOTS and non-DOTS contexts, the patient demographic and socio-economic characteristics[8-20], and the availability and organization of health services are key factors influencing treatment adherence as well. In general, male patients, those with lower level of education, and those unemployed are less likely to comply with treatment[8-12]. Living conditions, social support, transportation costs, and distance to health facilities have also shown to influence treatment adherence, especially in more vulnerable groups[13-20]. This is mainly due to factors associated with poverty and underdevelopment, such as poor living conditions, underlying low health status, lack of money to pay for health care and inadequate access to health services[21].

Financial barriers to accessing TB treatment and factors related with the attention received have been identified as key factors in non-compliance and treatment default[10,22].

In Argentina, non-adherence rates greatly vary among provinces, from 0 to 27.3%[5]. Although the National Program for TB Control recommends DOTS as the main strategy for disease control, its utilization is heterogeneous due to local health systems´ capacities to guarantee patient supervision. From 2008 to 2010 we carried out a study to analyze how treatment modality (DOT *versus* no-DOT) and patients´ socio-demographic characteristics influence non-adherence to treatment[23] in municipalities of the Metropolitan Area of Buenos Aires (MABA), comprising approximately 10% of the country population. Results were published elsewhere[23] and showed that almost all patients received non-DOT treatment and poverty was the predominant social explanatory factor for non-adherence. The study also showed that, in comparison with patients receiving treatment at hospitals, those treated at primary health care centers (PHCs) were more likely to adhere to treatment. While there is some evidence showing that better adherence at PHCs might be related to characteristics of the health care process, like how health services are organized and the accessibility to health care services[21,22], in Argentina no previous study has analyzed this topic. We therefore carried out an analysis of the data, incorporating four variables to understand characteristics of the health care process that influence on the capacities patients to comply with tuberculosis treatment[23]: distance to the health facility, difficulties with transportation costs, difficulties with transportation time, and quality of care. The aim of our study was to identify the association between non-adherence to tuberculosis treatment and characteristics of access to treatment. In our view, this analysis will contribute to a deeper understanding of factors influencing non-adherence of TB treatment, thus providing evidence to improve treatment adherence in Argentina.

MATERIAL AND METHODS

SETTING

The study was carried out in the 6th Health Region (HRVI), located in the Southern area of MABA. This is the most populated region in Buenos Aires Province, and the region where the majority of TB cases are notified every year (13% of total notified cases in Argentina, and 30% of total notified in Buenos Aires Province).

This cross-sectional study was carried out between January-December 2007. Of the total 27 hospitals existing in the Region, seven hospitals from seven districts concentrate notification of approximately 80% of total notified regional cases. These are the hospitals that were included in the study, located in the following districts: Almirante Brown, Avellaneda, Berazategui, Esteban Echeverría, Ezeiza, Lomas de Zamora and Quilmes. During 2006-2007, the non-adherence rate for new smear-positive patients was 13.46% (range 5.45 – 19.16) in those districts.

STUDY POPULATION

Patients diagnosed with TB during 2007 who were eligible to participate in this study were identified through the registration records from the National Program for TB control (NPTB). Eligible cases were all patients with pulmonary TB, aged 18 years or older, who lived in any of the selected districts, and were under drug treatment in a participating hospital located in the same district where the patient lived. Non-eligible cases were patients younger than 18 years old, those who completed treatment in a non-participating hospital, and those who were in prison or mentally ill during the treatment period.

In this cross sectional study non-adherents were all eligible patients who did not adhere to their treatment. Following the definition used by the NPTB, a non-adherent patient was defined as not having received TB treatment for 60 consecutive days or more. Adherents were all eligible patients who completed the stipulated treatment.

STUDY DESIGN

The study protocol was approved by the Ethics Committee of the participating hospitals. Patients were called by telephone by a health team member. After obtaining a signed informed consent, patients were interviewed face-to-face, by an interviewer of our team using a structured questionnaire. A questionnaire was developed that included socio-demographic and socio-economic variables as well as variables related with characteristics of the treatment, of the health care attention received and about accessibility characteristics to the heath care service. Counseling about the importance of completing treatment was provided to non-adherent patients once the interview had finished. The questionnaire was pilot-tested with 10 patients (not included in the study) from the studied area.

STATISTICAL ANALYSIS

Stata/SE V9.0 (Stata Corp., College Station Tx, USA) was used for statistical analysis. The relation between health care characteristics and non-adherence to TB treatment (outcome) was investigated using stepwise multivariate logistic regression to control for potential confounding by background socio-demographic characteristics of patients (sex, age, level of education, social security, income level, occupation, head of household social security). Occupation was categorized as employed with social protection (the person works for a public or private company and benefits from social health insurance, retirement and paid annual-leave), employed without social protection (the person works freelance or for a public or private company and does not benefit from health insurance, retirement or paid annual-leave), unemployed or inactive. Variables used to analyze the influence of health care characteristics on treatment adherence were: type of health facility where treatment

was provided (primary health centre, referral hospital), type of health facility where control visits were carried out (primary health centre / others, referral hospital), difficulties in cost of transportation (yes, no), difficulties with transportation time (yes, no), distance to health care facility (less than 3.4 kilometers, more than 3.4 kilometers).

The significance of the observed associations was assessed through χ^2 tests; means were compared by independent sample t-tests. All variables with a p-value < 0.05 in univariate analysis were included in the multivariate logistic regression model. In the multivariate analysis, p-value ≤ 0.05 was considered as statistically significant. Results are presented in terms of risk for non-adherence (OR) with 95% confidence intervals (95%CI). In this analysis, the interpretation of the OR (measuring association) was the same as relative risk (comparison of risks, depending on the level of exposure).

RESULTS

Between January-December 2007, 193 patients were eligible for this study. Seventy-eight (40%) did not adhere to TB treatment and 115 (60%) patients adhered. One hundred twenty three (64%) patients were surveyed: 38 non-adherents and 85 adherents. Forty non-adherent patients (51%) and 30 adherent patients (26%) could not be reached due to death, wrong address or relocation to another district (Table 1).

Table 2 shows the socio-demographic characteristics of the 123 participant patients. Mean age was 39 (Standard deviation – SD 1.5). 33 (27%) had never gone to school or had up to primary level of education uncompleted. Ninety-eight (80%) had no health insurance, 63 (51%) had incomes lower than 750 $ and 77 (64%) were employed without social protection. Eighty nine (72%) belonged to households whose heads had not social security.

Prevalence of characteristics related to treatment and health care organization can be seen in Table 3. Most patients (98%) received no-DOT treatment. Eighty three (67%) were treated at referral hospitals and 41 (33%) had control visits at primary health care centers. Ninety-three (76%) reported delays of less than 30 minutes to receive health care in each visit to the health center, 62 (52%) reported difficulties in cost of transportation

Table 1. Treatment outcome in terms of participation in the survey. Adherent and Non-adherent Patients. HRVI, 2007.

Participation in the study	Non-adherents		Adherents		Total	
	n	%	n	%	n	%
Yes	38	30.9	85	69.1	123	100.0
No	40	57.1	30	42.9	70	100.0
Total	78	40.4	115	59.6	193	100.0

HRVI: 6th Health Region; RS6: Região de Saúde 6.

Table 2. Socio-demographic characteristics of patients and heads of households. Adherent and Non-adherent Patients. HRVI, 2007.

Characteristics	Non-adherents		Adherents		Total	p-value
	n = 38	%	n = 85	%	n = 123	
Sex						
Male	12	22.2	42	77.8	54	0.05
Female	26	37.7	43	62.3	69	
Age (years)						
18 – 24	11	37.9	18	62.1	29	ns
25 – 34	12	27.3	32	72.7	44	
35 – 64	13	35.1	24	64.9	37	
65 and more	2	15.4	11	84.6	13	
Mean age (SD)	37 (2.3)		41 (1.8)			ns
Educational level						
Never gone to school/ Primary Incomplete	8	24.2	25	75.8	33	ns
Primary Complete	12	37.5	20	62.5	32	
Secondary or more	18	31.0	40	69.0	58	
Social Security						
Yes	6	24.0	19	76.0	25	ns
No	32	32.7	66	67.3	98	
Head of household Social Security						
Yes	6	17.6	28	82.4	34	ns
No	32	36.0	57	64.0	89	
Type of occupation of patients*						
Employed with social protection	3	12.0	22	88.0	25	ns
Employed without social protection	27	35.1	50	64.9	77	
Inactive or Unemployed	8	40.0	12	60.0	20	
Household income level**						
More than 750 $	14	22.2	49	77.8	63	0.023
Up to 750 $	24	41.4	34	58.6	58	

*Missing data for one case; **Missing data for two cases; HRVI: 6th Health Region; RS6: Região de Saúde 6; SD: Standard deviation; ns: not significant; $: Argentine peso.

Table 3. Prevalence of characteristics of health care received by patients. Adherent and Non-adherent Patients. HRVI, 2007.

Treatment and health care characteristics	Non-adherents		Adherents		Total	p-value
	n = 38	%	n = 85	%	n = 123	
DOT status						
No	37	30.6	84	69.4	121	ns
Yes	1	50.0	1	50.0	2	
Type of health facility were treatment was provided						
Primary Health Centre	7	17.5	33	82.5	40	0.026
Referral hospital	31	37.3	52	62.7	83	
Type health facility where control visits were carried out						
Primary Health Centre/Others	7	17.1	34	82.9	41	0.022
Referral hospital	31	37.8	51	62.2	82	
Delays in health care attention						
Less than 30 minutes	30	32.3	63	67.7	93	ns
More than 30 minutes	8	26.7	22	73.3	30	
Difficulties in cost of transportation*						
Yes	25	40.3	37	59.7	62	0.020
No	12	20.7	46	79.3	58	
Difficulties with transportation time*						
Yes	13	41.9	18	58.1	31	ns
No	24	27.0	65	73.0	89	
Distance to the Health Care Facility						
Less than 3.4 kilometers	22	29.3	53	70.7	75	ns
More than 3.4 kilometers	16	33.3	32	66.7	48	
Media distance (in kilometers)						
All patients	3.4 (2.9 – 3.9)					
Among cases	4 (2.6 – 5.4)					
Among controls	3.1 (2.7 – 3.6)					

*Missing data for three cases; DOT: Direct Observed Treatment; ; ns: not significant; HRVI: 6th Health Region; RS6: Região de Saúde 6.

and 31 (25%) reported difficulties with transportation time. Most patients (61%) lived less than 3.4 kilometers far from the health care facility where they received treatment.

Table 4 presents the results of univariate and multivariate associations between health care characteristics and non-adherence, including socio-demographic characteristics of patients to control for potential confounding. Those patients who had their control visits at hospitals (OR = 3.4; 95%CI 1.3 – 9.0) and were supplied with TB drugs at hospitals (OR = 2.8; 95%CI 1.1 – 7.1) were three times more likely not to adhere to treatment. It was also observed that the risk of non-adherence to treatment was higher among those who had economic constrains to back transportation costs (OR = 2.6; 95%CI 1.1 – 5.8). Male patients (OR = 2.2; 95%CI 1.0 – 5.2) and those with the lowest household income (OR = 2.5, 95%CI 1.1 – 5.4) were at higher risk of non-adherence.

In multivariate analysis (Table 4), three variables remained significantly associated to non-adherence: sex, type of health service where patients had their control visit, and having difficulties with transportation costs. Male patients were 2.8 times more likely to non-adhere to treatment (95%CI 1.2 – 6.7). Patients who had medical check-ups at hospitals had almost a 3.4 times higher risk of non-adherence (95%CI 1.1 – 10.0). Patients who had difficulties with transportation costs had a 2.5 times higher risk of non-adherence (95%CI 1.1 – 5.9).

Table 4. Univariate and multivariate associations between socio-demographic, socioeconomic, treatment and health care characteristics and non compliance. Adherent and Non-adherent Patients. HRVI, 2007.

Characteristics	Univariate analysis			Multivariate analysis		
	OR	95%CI	p-value	OR	95%CI	p-value
Sex						
Female	1					
Male	2.2	(1.0 – 5.2)	0.05	2.8	(1.2 – 6.7)	0.020
Household level income						
More than $750	1					
Up to $750	2,5	(1.1 – 5.4)	0.025			
Type of health facility were treatment was provided						
Primary Health Centre	1					
Referral hospital	2.8	(1.1 – 7.1)	0.029			
Type health facility were control visits were carried out						
Primary Health Centre/Others	1					
Referral hospital	3.4	(1.3 – 9.0)	0.014	3.4	(1.1 – 10.0)	0.025
Difficulties with cost of transportation						
No	1					
Yes	2.6	(1.1 – 5.8)	0.022	2.5	(1.1 – 5.9)	0.042

HRVI: 6th Health Region; RS6: Região de Saúde 6; OR: Odds ratio; 95%CI: 95% Confidence interval.

DISCUSSION

To our knowledge, this is the first time that health care process characteristics are included in the analysis of the social determinants of adherence to tuberculosis treatment in Argentina. Our results showed that the burden of transportation costs and the type of health facility are major explanatory factors. Besides, results showed that in the Argentinean context, being male is an important risk factor for the treatment non-adherence.

In effect, patients with difficulties regarding transportation costs presented almost three times higher risks of non-adherence to treatment. Several studies have shown that costs related to treatment, such as transportation costs or costs associated to supplementary medication, negatively influences adherence[18-20]. They have also found that the provision of drugs free of charge is not enough to guarantee compliance, especially in lower-income sectors. A study in Nepal found that although the medication was provided free of charge, the burden of travel costs was a restricting factor in completing treatment[19]. In other study in Gambia, patients who spent more time travelling to the health center or had higher travel expenses were at higher risk of non adherence to treatment[24]. Although several studies have found that the association between non-adherence and cost of transportation is related to increasing travelling distances to receive health care[9,10,18,19,25-27], in our study the relationship between distance to health facilities and non-adherence was not statistically significant, thus suggesting that for the study population, cost of transportation is a barrier independently of the distance to health care centers.

These results confirmed our previous findings[23] that showed that for a self-administered treatment population, patients treated at hospitals (*versus* those who do so in PHCs) have an increased risk of non-adherence. In a study from Sudan[26], authors also found a higher rate of treatment success in PHCs than among patients treated at hospitals. In this context, decentralization to community-based tuberculosis services was highlighted as a key factor for treatment adherence and the lower default rate at PHCs was interpreted as an effect of better conditions for directly observed treatment and follow-up[26]. A study carried out in China evaluated whether decentralization results in access improvement to TB services and showed that patients in the decentralized group spent less on travel and treatment for TB, and that a higher quality of care was observed in this group as well as better treatment outcomes[28].

While several studies have analyzed how decentralization to PHC contributes to better outcomes by reducing distance between patient´s place and the health service[19,26,28], few studies have focused on the health facilities' characteristics and treatment outcomes. Results from a study in Peru[29] aimed at evaluating users' satisfaction with PHCs and hospitals showed that satisfaction was higher in PHCs. The association found in our study between the type of health facility where treatment was received and patient´s adherence could be related to different quality of care. However, delay in receiving health care (an indicator of quality of care) was not statistically significant with non-adherence to treatment. Further studies are needed to indentify other health facilities' characteristics that might influence non-adherence to TB treatment.

Our results showed that men were at higher risk of treatment non-adherence than women. Studies that analyzed the relationship between sex/gender and non-adherence showed that men´s breadwinner status as head of households explained their fewer adherences to treatment. A study conducted in India[30] found that being male and being employed implied twice the risk of abandoning treatment, mainly because workers have trouble in leaving their duties for a health care center visit. In proportion, in our study, the group of employed heads of household with social protection had higher levels of adherence than those with employment but with no social protection, or those who were unemployed or inactive.

Although these differences were not significant in our study, most likely due to the small sample size, the fact that the majority of patients who were heads of households were male (72%) supports this hypothesis. On the same line, a study conducted in Argentina[31] on treatment adherence of cancer patients showed that one main factor in reducing the adherence rate was the loss of income resulting from disruption of work activities during the treatment, especially when workers did not have any social protection. Consequently, household income decreases, and the capacity to afford the costs associated to treatment is threatened[31]. Another possible explanatory factor of the lower adherence among men is that, in general, they have fewer contacts with the health care system. In the above mentioned study from India a greater adherence to treatment was found among women. They concluded that this might be a consequence of women having more contacts with the health services given that they usually take care of their children´s health[31]. In a study conducted in Nicaragua[10] authors found that male patients had a risk to drop out from treatment nearly two and a half times higher than women, and that this risk was still higher after controlling for factors related with lifestyle behaviors, such as alcoholism, smoking and drug abuse.

This study has some limitations. Firstly, it may be affected by selection bias, as 51% of the non-adherent and 26% of the adherent patients were not contacted as a consequence of erroneous address information. Despite this limitation, no significant statistical difference was found in relation to age and sex between interviewed and non-interviewed cases (both non-adherent and adherent patients) (Table 5). This matches with other studies

Table 5. Socio-demographics characteristics and treatment outcome in terms of participation in the survey. Adherent and Non-adherent Patients. HRVI, 2007.

Socio-demographics Characteristics	Non-adherents (n = 78)		Adherents (n = 115)		p-value
	Participation in the Surrey		Participation in the Surrey		
	Yes n = 38	No n = 40	Yes n = 85	No n = 30	
Mean age (SD)	37 (2.3)	36 (2.5)	41 (1.8)	35 (2.3)	ns
Sex					
Female	54,5%	45,5%	70,5%	29,5%	ns
Male	46,4%	53,6%	77,8%	22,2%	

HRVI: 6th Health Region; RS6: Região de Saúde 6; SD: Standard deviation; ns: not significant.

that have also showed a greater difficulty in reaching patients who had not comply with treatment[18,32]. Secondly, only one patient refused to take part in this study, making the participation rate close to 100%. Therefore it can be concluded that this study has not been affected by selection bias due to participation refusal.

CONCLUSION

We believe that our study contributes to the identification of socio-economic factors related to non-adherence to TB treatment in Argentina. It also contributes to delineating the profile of non-adherent patients: male, having difficulties with transportation costs, and receiving treatment at hospitals. Decentralization of TB treatment to primary health care centers and social protection measures for patients in vulnerable social conditions should be considered priorities in TB control strategies.

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