Factors associated with delayed diagnosis of pulmonary tuberculosis in the state of Rio de Janeiro, Brazil*

Fatores associados ao atraso no diagnóstico da tuberculose pulmonar no estado do Rio de Janeiro

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Abstract

Objective: To estimate the total time elapsed between symptom onset and diagnosis of pulmonary tuberculosis (patient delay plus health care system delay), analyzing the factors associated with delayed diagnosis in the state of Rio de Janeiro, Brazil. **Methods:** We conducted a questionnaire-based survey involving 218 pulmonary tuberculosis patients treated for two months at 20 health care clinics and 3 hospitals in eight cities within the state of Rio de Janeiro. We collected socioeconomic and demographic data, as well as data regarding the health care system and the medical history of the patients. **Results:** The median time elapsed from the onset of symptoms to diagnosis was 68 days (interquartile range [IQR]: 35-119 days). The median patient delay (time from symptom onset to initial medical visit) was 30 days (IQR: 15-60 days), and the median health care system delay (time from initial medical visit to diagnosis) was 21 days (IQR: 8-47 days). A cut-off point of 21 days was adopted. The factors independently associated with patient delay were female gender, cough, and unemployment [adjusted OR (95% CI) = 2.7 (1.3-5.6); 11.6 (2.3-58.8); and 2.0 (1.0-3.8), respectively], whereas only female gender was independently associated with health care system delay (OR= 3.2; 95% CI: 1.7-6.0). **Conclusions:** Delayed diagnosis of pulmonary tuberculosis remains a problem in Rio de Janeiro, increasing the risk of transmission and mortality, that risk being greater for women and the socioeconomically disadvantaged. Patients might not recognize the significance of chronic cough as a health problem. Tuberculosis education programs targeting women might improve this situation.

Keywords: Tuberculosis, pulmonary/diagnosis; Delayed diagnosis; Health care surveys.

Resumo

Objetivo: Estimar o tempo decorrido entre início dos sintomas e diagnóstico de tuberculose pulmonar (tempo do paciente, desde o início dos sintomas até a primeira visita médica, e tempo do sistema de saúde, desde a primeira visita até o diagnóstico) e analisar os fatores associados ao atraso no diagnóstico da tuberculose pulmonar no estado do Rio de Janeiro. Métodos: Inquérito baseado em questionário com 218 pacientes com tuberculose pulmonar, no 2º mês de tratamento, em 20 unidades de saúde e 3 hospitais de oito municípios do estado do Rio de Janeiro. Dados socioeconômicos, dados demográficos, dados sobre o serviço de saúde e história clínica foram coletados. **Resultados:** A mediana do tempo do início dos sintomas até o diagnóstico foi de 68 dias [intervalo interquartil (II): 35-119 dias]. A mediana do tempo dos pacientes foi de 30 dias (II: 15-60 dias) e a do tempo do sistema de saúde foi de 21 dias (II: 8-47 dias). Um ponto de corte de 21 dias foi adotado para atraso. Os fatores independentes associados ao atraso do paciente foram sexo feminino, tosse e desemprego [OR ajustada (IC95%) = 2,7 (1,3-5,6); 11,6 (2,3-58,8); e 2,0 (1,0-3,8), respectivamente], enquanto aquele associado ao atraso do sistema de saúde foi apenas sexo feminino (OR = 3,2; lC95%: 1,7-6,0). Conclusões: O diagnóstico tardio da tuberculose pulmonar continua sendo um problema no Rio de Janeiro, possivelmente colaborando para a transmissão e a mortalidade. Mulheres e desprivilegiados socioeconomicamente são mais vulneráveis. Tosse crônica talvez seja subestimada como um problema de saúde pelos pacientes. Campanhas educacionais sobre os sintomas da doença e direcionadas às mulheres podem colaborar para reduzir esse atraso.

Descritores: Tuberculose pulmonar/diagnóstico; Diagnóstico tardio; Pesquisas sobre serviços da saúde.

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Introduction

Delayed diagnosis of pulmonary tuberculosis (TB) can result in a more severe disease presentation, with more long-term sequelae, higher mortality, and perpetuation of the transmission chain.⁽¹⁾ Early diagnosis and prompt pharmacological treatment initiation are essential for effective disease control. ⁽¹⁾ Knowledge of the factors associated with delayed diagnosis can be important in order to indicate potential strategies to reduce this delay.

Although TB is an infectious disease that can be prevented and cured, it remains a public health problem worldwide.⁽²⁾ It is estimated that, every year, there are 9.4 million new TB cases and nearly 2 million people die from TB. The World Health Organization estimates that Brazil ranks 19th among the 22 countries that, together, account for 80% of all TB cases worldwide.⁽²⁾

Among all Brazilian states, Rio de Janeiro has the highest TB incidence rate (71.8/100,000 population in 2010)⁽³⁾ and the highest mortality rate (5.0/100,000 population in 2009),⁽³⁾ which are double the national averages, despite implementation of the directly observed treatment, short-course (DOTS) strategy in the state in 1999.⁽⁴⁾ In order to achieve TB control, one of the goals of the Brazilian National Ministry of Health is to decentralize TB treatment toward primary health care, in order to increase patient access to health care facilities and to establish a hierarchy in the complexity of care, among other reasons.⁽⁵⁾ The state of Rio de Janeiro has experienced a significant delay in expanding the DOTS strategy and the coverage of the Family Health Program.⁽⁶⁾ The cure rates in the state of Rio de Janeiro, including those among prison inmates, are among the lowest in the country.⁽³⁾ In addition, the state has the a higher number of cases of multi-drug resistant TB than does any other Brazilian state, accounting for 42.6% of all such cases nationwide.⁽⁵⁾ Among the priority cities, the Rio de Janeiro State Department of Health has identified 14 that are in a more serious situation, with higher disease burdens.⁽⁶⁾

The objectives of the present study were to estimate the total time elapsed between symptom onset and diagnosis of pulmonary TB-patient delay (time from symptom onset to initial medical visit) plus health care system delay (time from initial medical visit to diagnosis)and analyze the factors associated with delayed diagnosis in a sample of patients in the state of Rio de Janeiro.

Methods

This was a cross-sectional study conducted in the state of Rio de Janeiro between April of 2007 and May of 2008. Pulmonary TB patients enrolled in the Tuberculosis Control Programs of the 8 cities investigated in the present study were eligible for inclusion. The inclusion criteria were as follows: presenting with pulmonary TB confirmed by sputum examination (sputum smear microscopy, culture for Mycobacterium tuberculosis, or both); not being diagnosed with pulmonary TB until the beginning of month 2 of treatment (after 5-12 weeks of treatment); being under treatment and having been interviewed in one of 20 primary health care clinics (of which 11 provided DOTS and 9 did not) or in one of 3 hospitals. The 23 health care facilities involved are distributed across 8 cities (Rio de Janeiro, Belford Roxo, Itaboraí, Duque de Caxias, Nilópolis, Queimados, Niterói, and São Gonçalo) that are among the 14 cities where the disease burden is highest and that constitute the metropolitan area of Rio de Janeiro. Those cities account for 72% of the population of the state of Rio de Janeiro, as well as for 86% of all TB cases in the state.⁽⁴⁾ A convenience sample of the clinics was selected by the Rio de Janeiro State Department of Health. We excluded patients who had difficulty in speaking and those who were younger than 18 years of age.

We used a questionnaire to collect demographic and socioeconomic data, as well as data regarding health insurance, clinical history/previous comorbidities, days elapsed between symptom onset and diagnosis of pulmonary TB, time required to commute from the patient residence to the health care clinic, type of facility first sought by the patient, DOTS availability, and hospitalization. The instrument was administered by previously trained students. The time frames were classified as patient delay (time from symptom onset to initial medical visit) and health care system delay (time from initial medical visit to diagnosis). The instrument employed has been validated in various Englishspeaking and Spanish-speaking countries,^(7,8) and the Brazilian Portuguese-language version had been validated in a pilot study conducted

prior to the collection of the data presented here.

We categorized patient delay and health care system delay by arbitrarily using a cut-off point of 21 days. A time frame \geq 21 days was considered to constitute delayed diagnosis. The cut-off point for patient delay was established on the basis of the Brazilian National Tuberculosis Control Program definition of patients with respiratory symptoms, as well as of a systematic review,⁽⁹⁾ which recommended the use of that cut-off point for health care system delay. Other cut-off points were tested (data not shown), and the time frame of 21 days proved adequate to detect significant associations between delayed diagnosis and the independent variables.

The data collected by administering the questionnaires were double entered into a Microsoft Office Access 2007 database and exported to a Microsoft Office Excel 2007 spreadsheet. The data were analyzed with the statistical package Statistical Analysis System, version 9.1 (SAS Institute Inc., Cary, NC, USA). Associations between the outcome (delayed diagnosis) and the independent variables were analyzed by calculating the ORs and respective 95% Cls. Variables that showed marginal associations (p < 0.20) in the univariate analysis were included in a multivariate logistic regression analysis in order to calculate the adjusted OR.

The study was approved by the Brazilian National Research Ethics Committee (Ruling no. 235/2007). All patients who agreed to participate gave written informed consent.

Results

The characteristics of the 218 patients are presented in Table 1. The median time elapsed from the onset of symptoms to diagnosis (total time) was 68 days, the interquartile range (IQR) being 35-119 days. The median patient delay was 30 days (IQR, 15-60 days), and the median health care system delay was 21 days (IQR, 8-47 days). The factors independently associated with patient delay were female gender, cough, and unemployment (Table 2), whereas only female gender was independently associated with health care system delay (Table 3). We obtained consistent results using other cut-off points for patient delay and health care system delay (data not shown).

Characteristic	n (%)
Gender	
Female	79 (36)
Male	139 (64)
Age, years	
< 35	114 (52)
≥ 35	104 (48)
Level of education	
Illiterate	29 (13)
9 years of schooling	103 (47)
High school (incomplete)	21 (10)
High school (complete)	53 (24)
College	12 (6)
Number of residents per household	
1	25 (11)
2-4	143 (66)
≥ 5	50 (23)
Monthly individual income, US\$ ^a	()
< 55	132 (61)
55-222	51 (23)
222-444	15 (7)
> 444	20 (9)
Monthly family income, US\$ ^a	20 (5)
< 55	40 (18)
55-222	64 (29)
222-444	49 (23)
> 444	65 (30)
Employment status	(50)
Employed	118 (54)
Student	12 (5)
Unemployed	71 (33)
Retired	17 (8)
Comorbidities	17 (0)
No	145 (67)
Yes	73 (33)
Type of facility first sought by patients	
Primary health care clinic	72 (33)
Hospital	87 (40)
Private clinic/practice	36 (16)
Drugstore Other ^b	21(10)
	2 (1)
Time required to arrive at the clinic, min < 40	112 (E1)
< 40 ≥ 40	112 (51)
∠ 40 Health insurance	106 (49)
No	104 (04)
	184 (84) 34 (16)
Yes	34 (10)
Hospitalization	100 (07)
No Yes	189 (87)
	29 (13)
History of tuberculosis treatment	107 (00)
New case	187 (86)
Retreatment	31 (14)
DOTS available near the household ^c No	102 (40)
	102 (49)
Yes DOTS: directly observed treatment,	108 (51) short-course.
bors, uncery observed treatment,	short-course.

observed treatment, DOTS: directly short-course. ^aExchange rate (US dollars vs. Brazilian reals) on the day of the interview: US\$ 1.00 = R\$ 1.80. ^bFaith healer, in 1; and active surveillance, in 1. °At hospitals: 8.

Table 1 - Characteristics of the 218 pulmonary

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 Table 2 - Factors associated with patient delay. Metropolitan area of Rio de Janeiro, Brazil, 2008.

Factors	> 21	≤ 21	ORª (95% Cl)	р	Adjusted OF
	days	days	-		
Caradar	n (%)	n (%)			
Gender		10 (16)		0.000	
Female	66 (84)	13 (16)	3.0 (1.4-6.2)	0.003	2.7 (1.3-5.6)
Male	88 (63)	51 (37)	1.0		
Age, years		22 (22)		0 4 0 0	
< 35	76 (77)	23 (23)	1.7 (0.9-3.3)	0.100	-
≥ 35	78 (66)	41 (34)	1.0		
Level of education					
llliterate/9 years of schooling	94 (73)	38 (27)	1.1 (0.6-2.0)	0.939	-
High school or college	60 (65)	26 (35)	1.0		
Monthly individual income, prediagnosis, US\$ ^b					
< 223	123 (75)	41 (25)	2.2 (1.1-4.5)	0.022	-
≥ 223	31 (57)	23 (43)	1.0		
Monthly family income, prediagnosis, US\$ ^b					
< 223	80 (77)	24 (23)	1.8 (1.0-3.4)	0.072	-
≥ 223	74 (65)	40 (35)	1.0		
Employment status ^c					
Unemployed	80 (79)	21 (21)	2.2 (1.2-4.3)	0.015	2.0 (1.0-3.8)
Employed/retired	70 (63)	41 (39)	1.0		
Comorbidities					
No	101 (69)	45 (31)	0.8 (0.4-1.6)	0.605	-
Yes	53 (73)	19 (27)	1.0		
History of tuberculosis treatment					
New case	131 (70)	56 (30)	0.8 (0.3-2.1)	0.800	-
Retreatment	23 (74)	8 (26)	1.0		
Cough					
No	2 (18)	9 (82)	0.1 (0.0-0.4)	<	11.6 (2.3-58.8
Yes	152 (73)	55 (27)	1.0	0.001	
Sputum					
No	33 (60)	22 (40)	0.5 (0.3-1.0)	0.067	-
Yes	121 (74)	42 (26)	1.0		
Hemoptysis					
No	104 (68)	48 (32)	0.7 (0.3-1.4)	0.352	-
Yes	50 (76)	16 (24)	1.0		
Fever					
No	37 (71)	15 (29)	1.0 (0.5-2.2)	0.935	-
Yes	117 (70)	49 (30)	1.0		
Fatigue	. ,				
No	32 (67)	16 (33)	0.8 (0.4-1.7)	0.613	-
Yes	122 (72)	48 (28)	1.0		
Weight loss	(, _)	(20)			
No	22 (65)	12 (35)	0.7 (0.3-1.7)	0.534	_
Yes	132 (71)	52 (29)	1.0	0.007	_
Time required to arrive at the clinic, min	134 (11)	(ر ۵) ۵۰	1.0		
≥ 40	82 (77)	24 (23)	2.0 (1.0-3.6)	0.049	
				0.049	-
< 40 DOTS: directly observed treatment, short-cour	72 (64)	40 (36)	1.0	(1.0.1.1	

DOTS: directly observed treatment, short-course. ${}^{\circ}OR = 1.0$ (reference). ${}^{\circ}Exchange rate (US dollars vs. Brazilian reals) on the day of the interview: US$ 1.00 = R$ 1.80. <math>{}^{\circ}Students$ only: 6. ${}^{\circ}At$ hospitals: 8. ${}^{\circ}Faith$ healer, in 1; and active surveillance, in 1.

Table 2 - Continued	•••
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Factors	> 21	≤ 21	OR ^a (95% Cl)	р	Adjusted OR
	days	days		·	Ū
	n (%)	n (%)	-		
DOTS available near the household ^d					
No	73 (72)	29 (28)	1.1 (0.6-2.1)	0.852	-
Yes	75 (69)	35 (31)	1.0		
Health insurance					
No	133 (72)	51 (28)	1.6 (0.7-3.7)	0.302	-
Yes	21 (62)	13 (38)	1.0		
Hospitalization					
No	136 (72)	53 (28)	1.6 (0.6-3.8)	0.384	-
Yes	18 (62)	11 (38)	1.0		
Type of facility first sought by patients					
Hospital	56 (64)	31 (36)	0.6 (0.3-1.2)	0.843	-
Private clinic/practice	26 (72)	10 (28)	0.8 (0.3-2.2)		
Drugstore	16 (76)	5 (24)	(0.3-3.6)		
Primary health care clinic	55 (76)	17 (24)	1.0		
Other ^e					
Number of residents per household					
1	17 (68)	8 (32)	0.8 (0.2-2.4)	0.633	-
2-4	100 (70)	43 (30)	0.8 (0.4-1.8)		
≥ 5	37 (74)	13 (26)	1.0		

DOTS: directly observed treatment, short-course. ${}^{a}OR = 1.0$ (reference). ${}^{b}Exchange rate (US dollars vs. Brazilian reals) on the day of the interview: US$ 1.00 = R$ 1.80. <math>{}^{c}Students$ only: 6. ${}^{d}At$ hospitals: 8. ${}^{c}Faith$ healer, in 1; and active surveillance, in 1.

Of the 218 patients interviewed, the number of visits to the health care clinics before the diagnosis was as follows: one visit, in 45 patients (21%); two visits, in 78 (36%); three visits, in 62 (28%); four visits, in 24 (11%); and five visits, in 9 (4%). The type of facility first sought by patients was a hospital in 87 (40%) of the cases; a primary health care clinic in 72 (33%); a private facility (clinic or office) in 36 (17%); a drugstore in 21 (9%); and other (healer or active surveillance) in 2 (1%). The diagnosis was made at primary health care clinics in 178 (82%) of the cases; in hospitals in 29 (13%); and at private facilities in 11 (5%).

Discussion

There is no consensus regarding the acceptable time from the onset of symptoms to the diagnosis of TB. According to a recently published systematic review,⁽⁹⁾ the mean time elapsed between symptom onset and diagnosis, in developed countries, is 61.3 days, mean patient delay being 25.8 days and mean health

care system delay being 21.5 days, compared with 67.8, 31.7, and 28.4 days, respectively, in developing countries. In the present study, the mean total time elapsed between symptom onset and diagnosis of TB (68 days) and the mean patient delay (30 days) were similar to those found in developing countries, whereas the mean health care system delay (21 days) was similar to those found in developed countries,⁽⁹⁾ suggesting that access to the health care system is more limited in low- and middle-income countries. However, we found the mean total time to diagnosis in the metropolitan area of Rio de Janeiro to be shorter than that reported for other Brazilian capitals: 110 days for Vitória⁽¹⁰⁾; and 142 days for Recife.(11) Nevertheless, we deemed the time to diagnosis to be delayed in Rio de Janeiro. Although the health care system delay found in the present study was similar to that found in developed countries, it still needs to be drastically reduced. In order to circumvent such limitations, the scientific community has focused its efforts on finding rapid, inexpensive diagnostic tests that can be used at the various

Table 3 – F	actors associated	with health	care system	delay.	Metropolitan	area of Rio de J	Janeiro, Brazi	l, 2008.
	Factors			> 21	≤ 21	OR ^a (95% Cl)	р	
				days	days			

n (%)GenderFemale55 (70)Male58 (42)Age, years51 (52) ≥ 35 62 (52)Level of education66 (50)High school or college39 (45)Monthly individual income, prediagnosis, US\$ ^b 223 ≥ 223 26 (48)Monthly family income, prediagnosis, US\$ ^b < 223 55 (53) ≥ 223 58 (51)Employment status ^c UnemployedUnemployed53 (52)	days		
Female 55 (70) Male 58 (42) Age, years 51 (52) \geq 35 51 (52) \geq 35 62 (52) Level of education 66 (50) High school or college 39 (45) Monthly individual income, prediagnosis, US\$ ^b 26 (48) Monthly family income, prediagnosis, US\$ ^b 26 (48) Monthly family income, prediagnosis, US\$ ^b 55 (53) \geq 223 55 (53) \geq 223 58 (51) Employment status ^c 55 (53)	n (%)		
Male 58 (42) Age, years 51 (52) \geq 35 62 (52) Level of education 66 (50) High school or college 39 (45) Monthly individual income, prediagnosis, US\$ ^b 57 (53) \geq 223 26 (48) Monthly family income, prediagnosis, US\$ ^b 55 (53) \geq 223 58 (51) Employment status ^c 58 (51)			
Age, years< 35	24 (30)	3.2 (1.7-6.0)	< 0.001
< 35 ≥ 35 Level of education Illiterate/9 years of schooling High school or college 39 (45) Monthly individual income, prediagnosis, US\$ ^b < 223 223 Monthly family income, prediagnosis, US\$ ^b < 223 26 (48) Monthly family income, prediagnosis, US\$ ^b < 223 55 (53) ≥ 223 Employment status ^c	81 (58)	1.0	
≥ 35 62 (52) Level of education 66 (50) High school or college 39 (45) Monthly individual income, prediagnosis, US\$ ^b < 223 87 (53) ≥ 223 26 (48) Monthly family income, prediagnosis, US\$ ^b < 223 55 (53) ≥ 223 55 (53) ≥ 223 58 (51) Employment status ^c			
Level of education66 (50)Illiterate/9 years of schooling66 (50)High school or college39 (45)Monthly individual income, prediagnosis, US\$b87 (53) ≥ 223 26 (48)Monthly family income, prediagnosis, US\$b26 (48) < 223 55 (53) ≥ 223 58 (51)Employment status ^c 57 (53)	48 (48)	1.0 (0.6-1.7)	0.960
Illiterate/9 years of schooling66 (50)High school or college39 (45)Monthly individual income, prediagnosis, US\$b $<$ < 223	57 (48)	1.0	
High school or college39 (45)Monthly individual income, prediagnosis, US\$b <223 <223 87 (53) ≥223 26 (48)Monthly family income, prediagnosis, US\$b <223 <223 55 (53) ≥223 58 (51)Employment status ^c $<$			
Monthly individual income, prediagnosis, US\$ ^b < 223 87 (53) ≥ 223 26 (48) Monthly family income, prediagnosis, US\$ ^b < 223 55 (53) ≥ 223 58 (51) Employment status ^c	66 (50)	0.8 (0.5-1.5)	0.594
<pre>< 223 87 (53) ≥ 223 26 (48) Monthly family income, prediagnosis, US\$^b < 223 55 (53) ≥ 223 58 (51) Employment status^c</pre>	47 (55)	1.0	
≥ 223 26 (48) Monthly family income, prediagnosis, US\$ ^b < 223 55 (53) ≥ 223 58 (51) Employment status ^c			
Monthly family income, prediagnosis, US\$ b < 223	77 (47)	1.2 (0.6-2.4)	0.640
< 223	28 (52)	1.0	
≥ 223 58 (51) Employment status ^c			
Employment status ^c	49 (47)	1.1 (0.6-1.9)	0.872
	56 (49)	1.0	
Unemployed 53 (52)			
	48 (48)	1.0 (0.6-1.8)	0.916
Employed/retired 58 (52)	53 (48)	1.0	
Comorbidities			
No 78 (53)	68 (47)	1.2 (0.7-2.2)	0.600
Yes 35 (49)	37 (51)	1.0	
History of tuberculosis treatment			
New case 102 (55)	85 (45)	2.2 (0.9-5.2)	0.076
Retreatment 11 (35)	20 (65)	1.0	
Cough			
No 4 (36)	7 (64)	0.5 (0.1-2.0)	0.457
Yes 109 (53)	98 (47)	1.0	
Sputum			
No 31 (56)	24 (44)	1.3 (0.7-2.5)	0.534
Yes 82 (50)	81 (50)	1.0	
Hemoptysis			
No 83 (55)	69 (45)	1.4 (0.8-2.7)	0.274
Yes 30 (45)	36 (55)	1.0	
Fever			
No 31 (60)	21 (40)	1.5 (0.8-3.0)	0.259
Yes 82 (49)	84 (51)	1.0	
Fatigue			
No 22 (46)	26 (54)	0.7 (0.4-1.5)	0.436
Yes 91 (54)	79 (46)	1.0	
Weight loss	· · /		
No 16 (47)	18 (53)	0.8 (0.4-1.8)	0.675
Yes 97 (53)	87 (47)	1.0	
Time required to arrive at the clinic, min	<i>s.</i> (<i>n</i>)		
≥ 40 87 (56)	68 (44)	1.8 (1.0-3.4)	0.066
< 40 26 (41)	37 (59)	1.0	0.000
DOTS available near the household ^d	5, (55)		

DOTS: directly observed treatment, short-course. ${}^{\circ}OR = 1.0$ (reference). ${}^{b}Exchange rate (US dollars vs. Brazilian reals) on the day of the interview: US$ 1.00 = R$ 1.80. Students only: 6. <math>{}^{d}At$ hospitals: 8. ${}^{e}Faith$ healer, in 1; and active surveillance, in 1.

Factors	> 21	≤ 21	OR ^a (95% Cl)	р
	days	days		·
	n (%)	n (%)		
No	59 (57)	43 (43)	1.5 (0.9-2.7)	0.161
Yes	51 (47)	57 (53)	1.0	
Health insurance				
No	94 (51)	90 (49)	0.8 (0.4-1.8)	0.743
Yes	19 (56)	15 (44)	1.0	
Hospitalization				
No	96 (51)	93 (49)	0.7 (0.3-1.7)	0.558
Yes	17 (59)	12 (41)	1.0	
Type of facility first sought by patients				
Hospital	42 (48)	45 (52)	1.2 (0.6-2.3)	0.001
Private clinic/practice	23 (64)	13 (36)	2.2 (0.9-5.5)	
Drugstore	15 (71)	6 (29)	3.1 (1.0-10.3)	
Primary health care clinic	32 (44)	40 (56)	1.0	
Others ^e				
Number of residents per household				
1	19 (76)	6 (24)	4.8 (1.5-16.2)	0.350
2-4	74 (52)	69 (48)	1.6 (0.8-3.3)	
≥ 5	20 (40)	30 (60)	1.0	
Facility where the diagnoses was made				
Medical clinic/office	24 (60)	16 (40)	1.5 (0.7-3.2)	0.333
Primary health care clinic	89 (50)	89 (50)	1.0	

DOTS: directly observed treatment, short-course. ${}^{a}OR = 1.0$ (reference). ${}^{b}Exchange rate (US dollars vs. Brazilian reals) on the day of the interview: US$ 1.00 = R$ 1.80. 'Students only: 6. <math>{}^{d}At$ hospitals: 8. "Faith healer, in 1; and active surveillance, in 1.

time points in the care process. One such test, which has recently brought hope because it is highly accurate, easy to use, and rapid, is the GeneXpert test (Cepheid, Sunnyvale, CA, USA),⁽¹²⁾ a test that now requires implementation and cost-effectiveness studies in low- and middleincome countries, such as Brazil. Our finding that, despite the long time to the diagnosis of TB, over half of the patients visited the health care clinics twice or more before the diagnosis corroborates the impression that the greatest difficulty lies not only in the low diagnostic suspicion but also in the low speed at which the test results are obtained. However, a low index of suspicion of TB, principally in women, in whom the disease is less prevalent, can also explain, in part, the delay.

In Brazil and other countries, patient delay has been associated with various factors, including level of education, income, unemployment, gender, and limited access to the public health care system.⁽¹³⁻¹⁵⁾ The inequity between the genders, as well as among patients of different socioeconomic status, in terms of

access to diagnosis and of treatment outcomes has been reported by different studies.(16-21) Gender-related differences have been attributed to the fact that women have greater difficulty in producing sputum,⁽¹⁹⁾ greater fear of stigmatization, and greater difficulty in gaining access to the health care system.^(20,21) Another possible explanation for such findings is that women currently have to balance work and home duties, which results in less time for self-care. However, a study conducted in the city of Duque de Caxias, Brazil, which has one of the highest treatment abandonment rates in the state of Rio de Janeiro, reported different findings regarding gender. In that study, the diagnostic delay was greater (90 days) and was not associated with gender.⁽¹⁸⁾ This discrepancy might be related to differences in the study designs, given that the patients who were interviewed in that study had not been under treatment for long, whereas in the present study the patients had been under treatment for 2 months, on average. Unlike other authors, we found no association between income and time to diagnosis in our

sample. However, we found that unemployment, which can be considered a proxy measure for socioeconomic status, doubled the chance of delayed diagnosis. In fact, patient-reported income is not considered a satisfactory estimate of socioeconomic status.

We found that patients with cough were over 11 times more likely to delay seeking medical attention. This curious finding has previously been reported,⁽⁹⁾ and there are various possible explanations for it. It can take longer for patients with chronic cough to seek treatment for the condition. Unfortunately, we collected no data regarding smoking or other respiratory symptoms that might have indicated other reasons for chronic cough. On the other hand, it is possible that patients with cough do not consider it to be a serious condition. There are various possible anthropological and cultural explanations for that finding, including the way in which each individual defines the concepts of disease and symptom.^(22,23) Finally, the lack of information regarding TB and the significance of its symptoms can also explain that finding.⁽²⁴⁾ Our study does not allow us to determine which of these factors are in fact implicated in delayed diagnosis.

The fact that hospitals were the first point of care sought by a high number of patients reflects the poor quality of the primary health care system in the state of Rio de Janeiro. We find it interesting that, although most patients first sought medical attention at hospitals, more than 80% were diagnosed at a primary health care clinic. The diagnostic and practical shortcomings of the approach to TB in the emergency rooms of public hospitals in the state of Rio de Janeiro have previously been reported. ⁽²⁵⁾

Our study has some limitations. The questionnaire used did not address smoking, evaluate the degree of knowledge of TB, characterize beliefs regarding TB, or attempt to explain why the diagnosis was delayed; it only sought to find associated factors to be addressed in future qualitative studies. In addition, the study design did not allow us to evaluate patients who have no access to health care and consequently to the diagnosis of the disease. Finally, the fact that we began to collect information when patients had been under treatment for 2 months might constitute a recall bias. However, our study has certain strengths: it involved 8 of the 14 priority cities in the state of Rio de Janeiro; it included only patients in whom the diagnosis had been confirmed; the questionnaire employed had previously been used in a pilot study, which allowed us to improve the instrument for data collection; and the analysis of the data was consistent, despite the different cut-off points used for the outcome.

In conclusion, the diagnosis of TB is delayed in the state of Rio de Janeiro, and the delay is principally due to the time elapsed between the onset of symptoms and the first medical visit, especially among women, the unemployed, and individuals with chronic cough. Qualitative studies should be conducted in order to clarify the reasons for the delay in diagnosis. We recommend that the Brazilian National Ministry of Health strengthen the educational campaigns designed to provide information regarding the symptoms of TB, especially those that target women. Finally, we recommend that the Rio de Janeiro state health care system be streamlined in order to improve access to primary health care clinics and hasten the diagnosis of TB. We also recommend that active surveillance be performed among women. The implementation of such measures could reducing the delay in establishing a diagnosis of TB.

References

- 1. Golub JE, Bur S, Cronin WA, Gange S, Baruch N, Comstock GW, et al. Delayed tuberculosis diagnosis and tuberculosis transmission. Int J Tuberc Lung Dis. 2006;10(1):24-30.
- 2. World Health Organization. Global Tuberculosis Control: surveillance, planning, financing. Geneva: World Health Organization; 2010.
- 3. Ministério da Saúde [homepage on Internet]. Brasília: Ministério da Saúde. [cited 2010 Sep 03]. Série histórica da Taxa de Incidência de Tuberculose. Brasil, Regiões e Unidades Federadas de residência por ano de diagnóstico (1990 a 2009). [Adobe Acrobat document, 7p.] Available from: http://portal.saude.gov.br/portal/ arquivos/pdf/incidencia_tabela2.pdf
- Secretaria de Estado de Saúde e Defesa Civil [Homepage on the Internet]. Rio de Janeiro: Secretaria de Estado de Saúde e Defesa Civil. [cited 2010 Dec 15]. Plano Estratégico Para Controle da Tuberculose do Estado do Rio de Janeiro, 2003 a 2005. [Adobe Acrobat document, 30p.] Available from: http://portal.saude.rj.gov.br/ tuberculose/Artigos/plano%20estrat%E9gico%202003-2005.pdf
- Organização Pan-Americana da Saúde [homepage on the Internet]. Brasília: Organização Pan-Americana da Saúde. [cited 2010 Dec 15]. Plano Estratégico para o Controle da Tuberculose, Brasil 2007 a 2015 Available from:

http://new.paho.org/bra/index2.php?option=com_ docman&task=doc_view&gid=927<emid=614

- 6. Secretaria de Estado de Saúde e Defesa Civil do Rio de Janeiro. [homepage on the Internet]. Il Encontro de Atenção Básica para descentralização e controle da tuberculose no Estado do Rio de Janeiro, 11 de junho 2010 [cited 2010 Jan 03]. Available from: http://new. paho.org/bra/index.php?option=com_content&task=vi ew&id=1299<emid=259
- Aspler A, Menzies D, Oxlade O, Banda J, Mwenge L, Godfrey-Faussett P, et al. Cost of tuberculosis diagnosis and treatment from the patient perspective in Lusaka, Zambia. Int J Tuberc Lung Dis. 2008;12(8):928-35.
- Oxlade O, Vaca J, Romero E, Schwartzman K, Graham B, Hernandez L, et al. The long-term health and economic benefits of DOTS implementation in Ecuador. Can J Public Health. 2006;97(1):14-9.
- 9. Sreeramareddy CT, Panduru KV, Menten J, Van den Ende J. Time delays in diagnosis of pulmonary tuberculosis: a systematic review of literature. BMC Infect Dis. 2009;9:91.
- Maciel EL, Golub JE, Peres RL, Hadad DJ, Fávero JL, Molino LP, et al. Delay in diagnosis of pulmonary tuberculosis at a primary health clinic in Vitoria, Brazil. Int J Tuberc Lung Dis. 2010;14(11):1403-10.
- dos Santos MA, Albuquerque MF, Ximenes RA, Lucena-Silva NL, Braga C, Campelo AR, et al. Risk factors for treatment delay in pulmonary tuberculosis in Recife, Brazil. BMC Public Health. 2005;5:25.
- Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, et al. Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med. 2010;363(11):1005-15.
- Zerbini E, Chirico MC, Salvadores B, Amigot B, Estrada S, Algorry G. Delay in tuberculosis diagnosis and treatment in four provinces of Argentina. Int J Tuberc Lung Dis. 2008;12(1):63-8.
- Long NH, Johansson E, Lönnroth K, Eriksson B, Winkvist A, Diwan VK. Longer delays in tuberculosis diagnosis among women in Vietnam. Int J Tuberc Lung Dis. 1999;3(5):388-93.

- Long NH, Johansson E, Diwan VK, Winkvist A. Different tuberculosis in men and women: beliefs from focus groups in Vietnam. Soc Sci Med. 1999;49(6):815-22.
- Holmes CB, Hausler H, Nunn P. A review of sex differences in the epidemiology of tuberculosis. Int J Tuberc Lung Dis. 1998;2(2):96-104.
- Lawn SD, Afful B, Acheampong JW. Pulmonary tuberculosis: diagnostic delay in Ghanaian adults. Int J Tuberc Lung Dis. 1998;2(8):635-40.
- Belo MT, Luiz RR, Hanson C, Selig L, Teixeira EG, Chalfoun T, et al. Tuberculosis and gender in a priority city in the state of Rio de Janeiro, Brazil. J Bras Pneumol. 2010;36(5):621-5.
- Boeree MJ, Harries AD, Godschalk P, Demast Q, Upindi B, Mwale A, et al. Gender differences in relation to sputum submission and smear-positive pulmonary tuberculosis in Malawi. Int J Tuberc Lung Dis. 2000;4(9):882-4.
- Allebeck P. Delay in tuberculosis care: one link in a long chain of social inequities. Eur J Public Health. 2007;17(5):409.
- Gosoniu GD, Ganapathy S, Kemp J, Auer C, Somma D, Karim F, et al. Gender and socio-cultural determinants of delay to diagnosis of TB in Bangladesh, India and Malawi. Int J Tuberc Lung Dis. 2008;12(7):848-55.
- Hudelson P. Gender differentials in tuberculosis: the role of socio-economic and cultural factors. Tuber Lung Dis. 1996;77(5):391-400.
- Ruffino-Netto A, Pereira JC. O processo saúde-doença e suas interpretações. Medicina (Ribeirão Preto). 1982;15(1):1-4.
- 24. Brasil Tuberculose [homepage on the Internet]. Rio de Janeiro: The Global Found. [cited 2011 Jan 10]. Falta de informação ainda é o maior desafio. [Adobe Acrobat document, 8p.] Available from: http:// www.fundoglobaltb.org.br/download/Pesquisa_ FG-DATAUFF_tuberculose_jan-2010.PDF
- Selig L, Belo MT, Teixeira EG, Cunha AJ, Brito R, Sanches K, et al. The study of tuberculosis-attributed deaths as a tool for disease control planning in Rio de Janeiro, Brazil. Int J Tuberc Lung Dis. 2003;7(9):855-9.

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