DOI: 10.1590/1980-5497201500040011

ORIGINAL ARTICLE / *ARTIGO ORIGINAL*

Delays in tuberculosis suspicion and diagnosis and related factors

Atrasos na suspeita e no diagnóstico de tuberculose e fatores relacionados

Natália Sperli Geraldes Marin dos Santos Sasaki[I], Maria de Lourdes Sperli Geraldes dos Santos[II], Silvia Helena F. Vendramini[II], Antonio Ruffino-Netto[III], Teresa Cristina Scatena Villa[IV], Francisco Chiaravalloti-Neto[V]

ABSTRACT: ***Objective:*** To measure the delays in tuberculosis (TB) suspicion and diagnosis and to identify factors related. ***Methods:*** We defined the delay in TB suspicion as the time between the perception of the symptoms by the patient and the search for health-care service and the diagnosis, as the time between the first visit to the health-care service and the diagnosis. We interviewed 100 patients treated at the health services in São José do Rio Preto that were diagnosed and reported/notified in 2008 and 2009, and the delays were quantified. We obtained the possible explanatory variables from interviews and secondary information available in the surveillance system. The addresses of TB patients and health-care services were geocoded. Variables were assessed by multiple linear regression analysis and, when spatial dependency was detected, by spatial regression. ***Results:*** The median values for the delays in TB suspicion and diagnosis were both 15 days. The first was modeled by linear regression and a positive relationship was found with the distances covered by the patients in order to get primary health-care service. The last was modeled by spatial regression and a positive relationship was found with the age and the frequency with the patients sought health-care services and a negative relationship with the pulmonary clinical form. ***Conclusion:*** The study revealed the existence of gaps in TB control activities related to the patients and the organization of the health-care services and showed the importance of taking into account the spatial dependence of the phenomena analyzed.

Keywords: Tuberculosis. Diagnosis. Health care (public health). Accessibility. Geographic information systems. Spatial analysis.

[I]*União das Faculdades dos Grandes Lagos* – São José do Rio Preto (SP), Brazil.
[II]School of Medicine of São José do Rio Preto – São José do Rio Preto (SP), Brazil.
[III]School of Medicine of Ribeirão Preto, *Universidade de São Paulo* – Ribeirão Preto (SP), Brazil.
[IV]Nursing School of Ribeirão Preto, *Universidade de São Paulo* – Ribeirão Preto (SP), Brazil.
[V]School of Public Health of *Universidade de São Paulo* – São Paulo (SP), Brazil.
Corresponding author: Francisco Chiaravalloti-Neto. Avenida Doutor Arnaldo, 715, CEP: 01246-904, Cerqueira César, São Paulo, SP, Brasil. E-mail: franciscochiara@usp.br
Conflict of interests: nothing to declare – **Financial support:** FAPESP (process No. 2008/07904-4) and CNPQ — Edital MCT/CNPq/CT-Saúde/MS/SCTIE/DECIT (process No. 034/2008).

RESUMO: ***Objetivo:*** Medir os atrasos na suspeita e no diagnóstico de tuberculose (TB) e identificar fatores relacionados. ***Métodos:*** O atraso na suspeita foi definido como o tempo entre a percepção, pelo doente, dos sintomas até a procura pelo primeiro atendimento e no diagnóstico, como o tempo entre o primeiro atendimento até a realização do diagnóstico. Foram entrevistados 100 doentes, diagnosticados e notificados em 2008 e 2009, atendidos em serviços de saúde (SSs) de São José do Rio Preto, para os quais foram quantificados os atrasos. As possíveis variáveis explicativas foram obtidas das entrevistas e de informações secundárias disponíveis no sistema de vigilância. Os endereços dos casos e dos serviços de saúde foram geocodificados. As variáveis foram analisadas por regressão linear múltipla e, quando da identificação de dependência espacial dos seus resíduos, por regressão espacial. ***Resultados:*** As medianas, tanto para o atraso na suspeita como no diagnóstico, foram 15 dias. O atraso na suspeita foi modelado por regressão linear e mostrou-se associado positivamente com as distâncias percorridas pelos doentes para obter o primeiro atendimento e negativamente com a religião (não cristã). O atraso no diagnóstico foi modelado por regressão espacial e mostrou-se associado positivamente com idade e número de vezes que o doente procurou o SS e negativamente com a classificação do caso (TB pulmonar). ***Conclusão:*** O estudo revelou lacunas nas ações de controle da TB relacionadas aos doentes e à organização dos serviços e mostrou a importância de se levar em conta a dependência espacial dos fenômenos analisados.

Palavras-chave: Tuberculose. Diagnóstico. Atenção à saúde. Acesso aos serviços de saúde. Sistemas de informação geográfica. Análise espacial.

INTRODUCTION

Early diagnosis and appropriate treatment are essential to reduce the spread of tuberculosis (TB). The detection of cases depends on the passive search for respiratory symptoms, the visit by the patient to the health-care service (HCS), and on the fast suspicion by the service so that they ask for a smear for the diagnosis[1]. The effective control of the disease depends on the search for primary health care (PHC), by the patient, within the period of 2–3 weeks[2,3] and the action of the PHC as a gateway for the services; facilitating the access and promoting full quality care; aiming at promoting, protecting, and recovering health[4].

Accessibility, understood as the adjustment degree between the HCS and the population in search for health care, is connected to the conception and the way of coping with the disease, defined by different dimensions: organizational, sociocultural, economical, and geographical[5]. The inequalities of access, the behavior of the population, the lack of professional qualification, and the structural problems of the HCSs are factors that interfere in the effectiveness of policies in the fight against TB[6] and delay the suspicion and diagnosis of TB to beyond what is considered appropriate for an effective control[7].

The access to diagnosis depends on the access to the HCSs[4,5], which are under the influence of the infrastructure, transportations and distances traveled by the patients, resulting in delays in the suspicion by the patients (delay in suspicion) and in the suspicion and confirmation by the service (delay in diagnosis), both being important aspects of accessibility[8]. The measuring of these delays and the identification of factor that act on them may contribute for the understanding of the phenomenon and the improvement of access to the services.

Thus, the objectives of this study were to measure the delays in suspicion and diagnosis of TB and to identify factors related to those.

METHODS

The study about the factors involved in the delayed suspicion and diagnosis of TB was carried out in São José do Rio Preto, using a cross-sectional design. The city located in the northwest region of the state of São Paulo, had, in 2010, 408,258 inhabitants, with good socioeconomic conditions[9] and is classified as a priority in the state for the control of TB[10].

A sample of 100 patients was taken among all diagnosed and notified cases, December 2008 onward, living in the municipality, who sought for health care in the HCS, older than 18 years of age, out of the prison system, without mental disorders, and according to participate in the research. Abandonment, death, and change of diagnosis were exclusion criteria.

The data were obtained through the use of a structured questionnaire based on the instrument proposed by Villa and Ruffino-Netto[11], previously tested and validated. The patients were selected based on information from the Notifiable Diseases Information System (*Sistema de Informação de Agravos de Notificação* – SINAN). Secondary sources were used based on the medical records and data from SINAN.

The analysis of the accessibility to the diagnosis was performed through geocoding of the addresses of the TB cases and of the HCSs. The distances traveled by the patients between their residence to the first HCS sought, after the perception of the disease until the diagnosis in the service, were obtained.

It was identified, based on the clinical form of the disease[10] and on the areas covered by the PHC, the service the patient should look for, which was compared to the services sought for the first time and the one that made the diagnosis. These comparisons produced dichotomous variables representing the care provided, or not, in the recommended locations and in or out of the areas covered by the PHC.

The classification of the TB case was used in order to define the ideal path to be taken by the patient, compared to the path taken in various situations (first service sought when one felt sick, diagnosis service), calculating the real (RD) and ideal distance (ID). The RD is the one that the patient traveled for the first service care and for the diagnosis of the TB. It was considered as the ID that should be traveled taking into account the territory which the patient belonged to and the classification of the case. For the coinfected patients with the human immunodeficiency virus (HIV), the specialized care service, which conducts the monitoring of the HIV, was considered the gateway to the service and, for the rest of them, the PHC. In performing the diagnosis, for extrapulmonary cases, the secondary services were also considered.

The RD and ID values were obtained by the ArcGIS 10.1 software. The difference between them represented the variables "difference of the traveled distances in regarding the first care and diagnosis," categorized in: negative or null difference (RD ≤ ID: the patient traveled a shorter or equal distance to the ideal one) and positive difference (RD > ID: the traveled distance was further than the ideal one).

The delays in suspicion and diagnosis of the TB were considered dependent variables. The independent variables considered in the analysis are presented in Tables 1 to 4, hierarchically classified into distal, medial, and proximal[12]. Initially, a bivariate analysis was performed relating dichotomized dependent variables in lower or higher or equal values to the respective medians, once these last ones are a sign of excessive delay in the suspicion by the patient and in the diagnosis of TB[1,2].

In the multiple linear regression analysis, dependent variables were considered as continuous (days of delay) and their normality was assessed through the Komolgorov–Smirnov test. The distal variables of gender and age were considered control variables and the others independent variables were included in the models when the respective p-values were lower or equal to 0.05.

Once obtained the models of multiple linear regression for the delays, their respective residues, and overall Moran indexes were calculated, using the neighboring matrix obtained by the GeoDa software (four closest neighbors). The regression model of delays, which showed a significant result for the overall Moran index ($p < 0.05$), was tested based on the following spatial model:

$$Y = X\beta + \lambda WY + u, \text{ sendo } u = \rho Wu + \varepsilon \text{ e } \varepsilon \sim N^{*}(0,\sigma^2)$$

where Y is the dependent variable; *X*, the matrix with the values of the independent variables; β, the vector with the regression coefficients; *W*, the neighbor matrix; λ and ρ are the spatial autocorrelation coefficient; *u* is the noise or disruption; and ε, the random error. The existing spatial dependency may be attributed to Y and to be included in the model with the term λWY. Another possibility, which may be considered along with the first one, is to treat the spatial effects such as the noise to be removed, which may be associated to the error and represented by ρWu[13].

One approach, to this model, based on estimators of generalized moments and semi parametric methods for the estimation of coefficients of the variance–covariance matrix, allowing at the same time the testing of hypothesis that the dependent variable (spatial lag model) and that the error term (spatial error model) are spatially correlated[13]. This modeling was carried out in the *sphet* Pack of the R program[14].

This research was evaluated and approved by the Research Ethics Committee of the School of Medicine of São José do Rio Preto (FAMERP).

RESULTS

For the study of the delay in the suspicion and diagnosis, 224 patients confirmed by the SINAN between December 2008 and November 2009 were selected for the interviews. From these, 12 underaged patients were excluded, along with 3 detainees, 1 admitted in a intensive care unit, 8 diagnosis changes, 68 not-found individuals, 19 deaths, 1 in another municipality, 2 psychiatric patients, 1 transference, and 9 refusals. After these exclusions, interviews with the 100 remaining patients were conducted between July and December 2009.

Of the 100 patients, 3 were excluded from the analysis about the delays: 2 for not remembering the time of delay in the suspicion and 1 who informed 10 years of delay in the diagnosis (outlier). Among the 97 patients analyzed, it was verified that 50% of them had delays in the suspicion of up to 15 days, and 25%, of more than 45 days. The maximum delay was 365 days, and the mean, 34.4 days (95%CI 23.8 – 45.1). About the delay in the diagnosis, 50% patients had a delay of up to 15 days, and 25% had delay of 30 days or more. The maximum delay was 365 days and the mean was 45.2 days (95%CI 29.9 – 60.8). The HCS was more sought was the urgency unit (50%), followed by the PHC (31%), and

Table 1. Bivariate analysis of the relation between the distal explainable variables of age, gender, professional activity and marital status and delay in the suspicion and diagnosis of tuberculosis longer or equal to 15 days, São José do Rio Preto, São Paulo, 2009.

Distal variables	Delays*	
	Suspicion ≥ 15 days	Diagnosis ≥ 15 days
	n (%)	n (%)
Age range		
18 to 29 years old	11 (64.7)	9 (52.9)
30 to 49 years old	22 (44.0)	28 (56.0)
50 years old or older	17 (56.7)	17 (56.7)
p-value	0.268	0.9677
Gender		
Female	18 (51.4)	20 (57.1)
Male	32 (51.6)	34 (54.8)
p-value	0.8461	0.9947
Professional activity		
Yes	18 (45.0)	24 (60.0)
No	32 (56.1)	30 (52.6)
p-value	0.3819	0.609
Marital status		
Single	19 (54.3)	15 (42.9)
Separated/divorced	6 (60.0)	6 (60.0)
Married/stable union	22 (51.1)	28 (65.1)
Widow/widower	3 (33.3)	5 (55.6)
p-value	0.6647	0.3238

*Percentages calculated on the total lines and refering to the delays ≥ 15 days.

the HCS that performed the most diagnosis of the disease was the hospital (46%), followed by the PHC (38%).

Tables 1 to 4 presented the results for the bivariate analysis between the two dichotomized dependent variables (delays < 15 days and ≥ 15 days) and the possible explanatory

Table 2. Bivariate analysis of the relation between the distal explanatory variables of religion, education and income and the delay in the suspicion and diagnosis of tuberculosis longer or equal to 15 days, São José do Rio Preto, São Paulo, 2009.

Distal variables	Delays*	
	Suspicion ≥ 15 days	Diagnosis ≥ 15 days
	n (%)	n (%)
Religion		
Without	4 (40.0)	5 (50.0)
With	46 (52.9)	49 (56.3)
p-value	0.5162	0.7466
Education		
Until the 1st phase of incomplete ES	18 (46.2)	15 (38.5)
1st phase of incomplete ES up to the 2nd phase of incomplete ES	19 (63.3)	23 (76.7)
2nd phase of ES up to CD	13 (46.4)	16 (57.1)
p-value	0.2987	0.0065
Income in MW (1 MW = R$465,00)		
0 to 1 MW	9 (42.9)	11 (52.4)
> 1 to 2 MW	14 (45.2)	14 (45.2)
> 2 up to 4 MW	18 (62.1)	18 (62.1)
> 4 MW	9 (56.3)	11 (68.8)
p-value	0.4339	0.381
Mean income		
< 0.4 MW	12 (46.1)	13 (50.0)
0.4 to < 0.9 MW	14 (48.3)	17 (58.6)
0.9 to < 1.5 MW	17 (60.7)	15 (53.5)
≥ 1.5 MW	7 (50.0)	9 (64.3)
p-value	0.7096	0.8225

*Percentages calculated on the total line and regarding the delays ≥ 15 days.
MW: minimum wage; ES: elementary school; CD: college degree.

Table 3. Bivariate analysis of the relation between medial explanatory variables and the delay in the suspicion and diagnosis of tuberculosis longer or equal to 15 days, São José do Rio Preto, São Paulo, 2009.

Medial variables	Delays*	
	Suspicion ≥ 15 days	Diagnosis ≥ 15 days
	n (%)	n (%)
Tests performed in the location		
Yes	31 (47.7)	33 (50.8)
No	19 (59.4)	21 (65.6)
p-value	0.3862	0.2430
Nº of times one sought for the HCS		
1	–	8 (26.7)
2	–	8 (42.1)
3 and 4	–	13 (61.9)
5 or more	–	25 (92.6)
p-value	–	0.0000
Type of HCS to be sought**		
Polyclinic	8 (34.8)	–
SCS/TCP/UU	7 (50.0)	–
PHC	17 (58.6)	–
PHC-F	8 (66.7)	–
p-value	0.2330	–
First care in the recommended HCS**		
Yes	5 (31.3)	–
No	35 (56.5)	–
p-value	0.1291	–
Difference of the traveled distances in relation to the first**		
RD ≤ ID	17 (42.5)	–
RD > ID	23 (60.5)	–
p-value	0.1721	–
Diagnosis in the recommended HCS**		
Yes	–	15 (53.6)
No	–	28 (56.0)
p-value	–	0.9757
Difference in the distances traveled for the diagnosis**		
RD ≤ ID	–	19 (57.5)
RD > ID		24 (53.3)
p-value	–	0.8873

*Percentages calculated on the total lines and refering to the delays ≥ 15 days; **Tabulation based on the 78 cases of geocoded TB.
HCS: health care services; SCS: Specialized Care Service; TCP: Tuberculosis Control program; UUA: urgency unit; PHC: Primary health Care ; PHC-F: Primary Health Care–Family ; RD: real distance; ID: ideal distance.

variables according to the classification into distal, medial, and proximal. To save space, only the results referring to the category ≥ 15 days for both types of delay are presented. For the distal and proximal variables, 97 patients were considered. For the medial ones, with the exception of the variable "number of times one sought for a HCS," only 78 (80.4%)

Table 4. Bivariate analysis of the relation between proximal explanatory variables and delay in the suspicion and diagnosis longer or equal to 15 days, São José do Rio Preto, São Paulo, 2009.

Proximal variables	Delays*	
	Suspicion ≥ 15 days	Diagnosis ≥ 15 days
	n (%)	n (%)
HIV		
Negative	42 (51.9)	45 (55.6)
Positive	8 (50.0)	9 (56.3)
p-value	0.8551	0.7825
Diabetes		
Yes	5 (45.4)	6 (54.5)
No	45 (52.3)	48 (55.8)
p-value	0.9113	0.7825
Alcohol/drugs		
Yes	12 (60.0)	10 (50.0)
No	38 (49.4)	44 (57.1)
p-value	0.551	0.7487
Classification of the case		
Extrapulmonary	6 (40.0)	12 (80.0)
Pulmonary	37 (55.2)	34 (50.8)
HIV	7 (46.7)	8 (56.3)
p-value	0.5204	0.1171
Type of case		
New	45 (50.0)	51 (56.7)
Reccurrence	3 (60.0)	3 (60.0)
Re-treatment	2(100.0)	0 (0.0)
p-value	0.6784	0.3917

*Percentage calculated on the total lines and refering to the delays ≥ 15 days.
HIV: human immunodeficiency virus.

patients whose address could be geocoded were considered. The reasons for non-geocoding were living in the rural area or invalid address.

The Kolmogorov-Smirnov normality test showed that the delay in the suspicion and diagnosis do not show normal behavior. After transformation by the use of the neperian logarithm plus one-tenth, due to some null values, they have presented normal approximate behavior (Kolmogorov-Smirnov tests, p = 0.1107 and p = 0.3453, respectively).

Table 5. Model of multiple linear regression and spatial regression of the delay in the suspicion and diagnosis of tuberculosis, global Moran índex, medians and normality tests of the regression residuals, São José do Rio Preto, São Paulo, 2009.

Variables	Linear regression		Spatial regression	
	Coefficients	p-value	Coefficients	p-value
Delay in the suspicion of TB				
Intercept	2.460	0.0006		
Age	-0.005	0.6596		
Gender (Male)*	-0.144	0.7087		
Difference in the distances traveled regarding the first care (> 0)	0.823	0.0218		
Global Moran indexes of residuals	I = 0.056	0.1637		
Mean of residuals	0.0000			
Normality test of the residuals	D = 0.072	0.8020		
Delay in the diagnosis of TB				
Intercept	2.159	0.0098	-0.737	0.5252
Age	0.021	0.0733	0.023	0.0419
Gender (Male)*	0.030	0.9333	-0.033	0.9402
No. of times one sought for the HCS	0.116	0.0000	0.115	0.0000
Classification of the case (pulmonary)**	-1.257	0.0078	-1.597	0.0005
Classification of the case (co-infection with HIV)**	-0.970	0.102	-1.537	0.0026
Global Moran indexes of residuals	0.128	0.0225	-0.067	0.8959
Auto-regressive spatial coefficient			1.194	0.0000
Mean of the residuals			0.0000	
Normality test of the residuals			0.074	0.7542

*Gender Female as category base; **extrapulmonary TB as category base.
TB: tuberculosis; HIV: human immunodeficiency virus; HCS: health care service.

Table 5 presented the multiple linear regression models obtained and the overall Moran indexes calculated for the residue of both models (suspicion and diagnosis), considering it was not significant for the delay in the suspicion, but it was significant for the diagnosis. Once obtained the linear regression model for the delay in the diagnosis and identified the need of considering the existence of spatial dependency, the tests of hypothesis performed showed that there was a need of considering in the regression model a spatial lag term ($\lambda = 1.194$; $p = 0.000$), but there would be no need to consider a representative term of spatial error ($p = 0$; $p > 0.05$).

The model obtained for the delay in suspicion has shown that the distance traveled by the patient (controlled by age and gender) was higher than the ideal one, with an increase of this type of delay. The residuals of this model presented mean equal to zero, normal distribution and constant variance. The model obtained to the delay in the diagnosis showed that the number of times a patient sought for the HCS and having pulmonary TB (in relation to extrapulmonary TB) presented, respectively, positive and negative relation with this delay, with results also controlled by age and gender. After the introduction of the spatial lag term in the model (1.194 Wy), its residuals presented mean equal to zero, normal distribution, and constant variance. Comparing this spatial model to the multiple linear regression model, alterations in the values of the coefficients of regression of some of the variables were verified (Table 5).

DISCUSSION

The early detection and the efficient treatment of pulmonary TB represent the main measure in order to interrupt the transmission chain of the disease[1,3] and are indicatives of a successful program[15]. An acceptable recommended time interval for the onset of symptoms up to the diagnosis was not found in the literature; however, some authors considered the reported mean or median of the times of delay for the diagnosis as a parameter[2,16-22]. This study considered the median, given that "time" is an asymmetric variable[1,20,22]. In relation to the suspicion by the patient and the operational aspects (diagnosis), in this study, both medians were 15 days.

The delay in the suspicion of TB by the patient may be influenced by the organization of different systems of health care, being lower when easily accessible and provided for free[1]. Despite the global availability of care in HCS, negative social factors tend to constrain the access to less favored segments of the community[8,20,22,23]. Patients spend a great deal of time and money searching for alternative solutions in order to alleviate the signs and symptoms before starting the treatment, and, many times, they do not get an effective diagnosis or tretament[19].

The decision of patients to search for health care depends on several factors, common to a lot of countries and scenarios, which may result in delays on TB suspicion and this is a reflection, among many things, of social, economic, cultural and geographic factors, such as poverty, the lack of knowledge about TB, education, and distance from the residence to the HCSs[19,21].

The time of delay must be considered for the diagnosis in a few days, once that the smear microscopy must be performed immediately. Literature shows that it revolves around 3–4 weeks, being three the maximum recommended time[3,21,24], and studies show a delay in the diagnosis, after the search by the patient in the first care unit[3,19,24].

The HCSs must be organized for one of the main challenges in the control of TB, which is to improve the detection of cases, through the active search for respiratory symptoms, despite the usual practice, which is using passive search. In this sense, it is noteworthy the importance of the PHC in this early diagnosis, by being the main gateway for the Unified Health System (*Sistema Único de Saúde* – SUS) and using health technologies that are able to solve the higher frequency and relevant problems in their territory. The literature shows flaws in the structure and functioning of the current health model, situations that represent the most important factor in the delay of the diagnosis of TB, and attributes this fact to the dysfunctions in the levels of health care, having a strong impact on the access of patients to these places. The great barriers are identified in the access to health care, in the relation between the team and the patient and in the organization of the services for the control of TB[3,8,24].

The variable "difference of the traveled distances related to the first care," positively and significantly associated in this study to the delay in the suspicion with the "first care in the recommended HCS," even if not considered as a model. The negative response means higher proportions in the delay of suspicion and probable larger traveled distances. Traveling a distance farther than the ideal one may also be related to geographic barriers that interfere in the search and choice for the first care[3,19].

Among those who traveled a farther distance than the ideal one, we may identify the search for an urgency unit instead of a PHC and the search for another PHC service other than the recommended one (by higher affinity, greater proximity to the workplace, easier to access in relation to the recommended PHC, schedule, availability for appointments, among others). Even among those in which the traveled distance was the same as the ideal one, when searching for polyclinics (PHC and urgency unit), they preferred the urgency unit as a gateway. Many studies with similar results have attributed this reality to the lack of comprehension of the patient about the entry door and the factors related to the organization of the PHC services, with a restricted schedule, scheduling criteria, and lack of classification of urgency and emergency risk[25,26].

From the variables associated to the delay in the diagnosis, the "classification of the case" is related to the fact that the diagnosis of extrapulmonary forms is made from clinical evidences and laboratory findings suggesting active forms in patients with at least one positive culture for *Mycobacterium tuberculosis* in extrapulmonary material[27]. There is difficulty in the clinical diagnosis, once that the symptoms are not specific and insidious, being, many times, made by exclusion of other diseases[23,28,29]. Another important factor is related to the search for the patient after worsening of the clinical condition[23,29]. Both situations correspond to the increased time of diagnosis.

In relation to the "number of times the patient sought for the HCS," the many visits made, by the patient, to the HCSs until they got the diagnosis may be related to the difficulty by the health professional in dealing with TB, with few diagnoses made in the first consultation[28]. This situation produces the worsening of the clinical condition and results, many times, in the hospitalization of the patient, whose diagnosis is made in hospitals, as shown in the result of this research.

Once that the TB cases are in the geographic space and the variables related to them may have spatial autocorrelation, the evaluation of the factors related to the delays demands the use of spatial analysis technology which, along with the Geographic Information Systems (GIS), contribute to the evaluation and planning of health actions in order to identify access difficulties to the HCSs[30].

The knowledge and understanding of the spatial distribution of phenomena, especially for diseases and illnesses which affect human beings, and the incorporation of space in the analysis to be performed have always been on the agenda, as demonstrated by the studies of John Snow, in the nineteenth century, in order to elucidate the mechanisms of cholera transmission[31,32]. However, the speed of this merger has been different in the areas of knowledge; in health, its implementation in the studies of diseases and conditions has been happening in a slower speed than in other areas[33]. Another important matter to be considered, even with the advances in the use of GISs and spatial analysis, is that not all studies dealing the space information take into account the possibility of the analyzed information being spatially autocorrelated[34].

In this sense, 12 studies on the occurrence of TB were selected in the literature in geographic locations of different scales (place of residence, census sectors, neighborhoods, districts, municipalities, regions, and countries), which used some kind of regression analysis. Of these, nine did not consider in the modeling the possibility of spatial autocorrelation of the dependent variables and/or resulting residuals[35]. Only in the studies developed by Ng et al.[36], Liu et al.[37], and Antunes and Waldman[30], there was this concern. In the remaining[38-46], this possibility was not considered and models with non-independent residuals may have been produced, with not properly estimated regression coefficients (super- or sub-dimensioned, or even with sense inversion)[35].

In the study developed by Ng et al.[36], the procedures used were the same as the ones in the delay study. The authors, after the carrying out a OLS (Ordinary least squares) model, identified the spatial dependency of the residuals. After modeling by spatial regression, a spatial lag parameter was introduced in the model and the regression coefficients suffer changes in their values. Ng et al.[36] concluded that the incidence of TB of a determined municipality suffered the influence of these rates observed in their neighbors. A similar approach was used by Antunes and Waldman[30] in order to study the relation between mortality by TB in the districts of São Paulo municipality.

The studies developed by Liu et al.[37] combined models of regression by minimum squares with a geographically weighted regression model (GWR) in order to study the multiresistant TB and its possible risk factors. This approach has taken into account the possible existence of spatial dependency in the variables involved in the multiresistant phenomenon.

In the study of the delay in the TB suspicion, the OLS model was proven adequate, once that its residuals were independent, with mean equal to zero and constant variance[35]. In the delay of the TB diagnosis, after the detection of spatial dependency in the residuals of OLS regression and the performing of the spatial regression analysis, it was obtained, as seen, a new model. In the case of this model, the spatial dependency found may be related to endogenous factors, once that it was assigned to the dependent variable[35].

The results obtained in this study and in the studies developed by Ng et al.[36], Liu et al.[37], and Antunes and Waldman[30] showed that, in studies evaluating phenomena that occur on the space, the use of modeling by regression without considering the spatial dependency of the dependent variables or the regression residuals may not be appropriate, resulting in models that violate the assumptions of this kind of modeling[34,35].

CONCLUSION

It is concluded in this study that in the municipality of São José do Rio Preto (SP), the median time in delay in the suspicion and diagnosis of TB was, for both aspects, equal to 15 days and the factors that contributed for the increased delays were, in case of suspicion, the patient traveling a distance farther than the ideal one (difference of the traveled distances in relation to the first care) and, in case of diagnosis, the patient having sought for the HCS for more than once and having extrapulmonary TB extrapulmonar, revealing gaps in the control actions of TB related to patients and the organization of the services.

The consideration of the spatial dependency of the phenomena studied and the use of modeling by spatial regression contribute for obtaining of more accurate models in an attempt of finding explanatory factors of the variability of the delays, which allows properly directing of resources in order to improve the TB control actions.

REFERENCES

1. Van Der Werf MJ, Chechulin Y, Yergorova OB, Marcinuk T, Stopolyanskiy A, Voloschhuk V, et al. Health care seeking behavior for tuberculosis symptoms in Kiev City, Ukraine. Int J Tuberc Lung Dis 2006; 10: 390-5.
2. Sreeramareddy CT, Panduru K, Menten V, Joris, Van den Ende J. Time delays in diagnosis of pulmonary tuberculosis: a systematic review of literature. BMC Infec Dis 2009; 9: 91.
3. Yimer S, Bjune G, Alene G. Diagnostic and treatment delay among pulmonary tuberculosis patients in Ethiopia: a cross sectional study. BMC Infect Dis 2005; 5: 112.
4. Starfield B. Atenção primária: equilíbrio entre necessidades de saúde, serviços e tecnologia. Brasília: UNESCO/Ministério da Saúde; 2002.
5. Fekete MC. Estudo da Acessibilidade na Avaliação dos Serviços de Saúde. In: Santana JP, Santos I, Fekete MC, Galvão EA, Mandelli MJ, Penna MFL, et al. Desenvolvimento Gerencial de Unidades Básicas do Sistema Único de Saúde (SUS). Brasília: OPS; 1997.
6. Lienhardt C, Ogden JA. Tuberculosis control in resource-poor countries: have we reached the limits of the universal paradigm? Trop Med Int Health 2004; 9: 833-41.

7. Sá LD, Rodrigues DCS, Barrêto AJR, Oliveira AAV, Pinheiro PGOD, Nogueira JA. A organização da estratégia saúde da família e aspectos relacionados ao atraso do diagnóstico da tuberculose. Cogitare Enferm 2011; 16: 437-42.
8. Hane F, Thiam S, Fall AS, Vidal L, Diop AH, Ndir M, Lienhardt C. Identifying barriers to effective tuberculosis control in Senegal: an anthropological approach. Int J Tuberc Lung Dis 2007; 11: 539-43.
9. São José do Rio Preto. Secretaria Municipal de Planejamento e Gestão Estratégica. Conjuntura Econômica; 2008.
10. Brasil. Secretaria de Vigilância em Saúde. Departamento de Vigilâncias das Doenças Transmissíveis. Programa Nacional de Controle da Tuberculose. Nota técnica 15 CGPNCTIDEVEP/SVS/MS. Brasília: Secretaria de Vigilância em Saúde; 2011.
11. Villa TCS, Ruffino-Netto A. Questionário para avaliação de desempenho de serviços de atenção básica no controle da tuberculose no Brasil. J Bras Pneumol 2009; 35: 610-12.
12. Victora CG, Huttly SR, Fuchs SC, Olinto MT. The role of conceptual frameworks in epidemiological analysis: a hierarchical approach. Int J Epidemiol 1997; 26: 224-7.
13. Kelejian HH, Prucha IR. Specification and estimation of spatial autoregressive models with autoregressive and heteroskedastic disturbances. J Econometrics 2010; 157: 53-67.
14. Piras G. Estimation of spatial autoregressive models with and without heteroskedastic innovations; 2013. Available from: https://cran.r-project.org/web/packages/sphet/sphet.pdf. (Acessado em 8 de julho de 2014).
15. Ibrahim S, Van der Loeff MS, Mubiru M, Konde-Lule J, Cobelens F. Long delays and missed opportunities in diagnosing smear-positive pulmonary tuberculosis in kampala, uganda: a cross-sectional study. PLoS ONE 2010; 5: 14459.
16. Maior ML, Guerra RL, Cailleaux-Cezar M, Golub JE, Conde MB. Tempo entre o início dos sintomas e o tratamento de tuberculose pulmonar em um município com elevada incidência da doença. J Bras Pneumol 2012; 38: 202-9.
17. Silva-Sobrinho RA, Andrade RLP, Ponce MAZ, Wysocki AD, Brunello ME, Scatena LM, et al. Retardo no diagnóstico da tuberculose em município da tríplice fronteira Brasil, Paraguai e Argentina. Rev Panam Salud Publica 2012; 31: 461-8.
18. Souza KMJ de, Villa TCS, Assolini FEP, Beraldo AA, França UM, Protti ST, et al. Atraso no diagnóstico da tuberculose em sistema prisional: a experiência do doente apenado. Texto Contexto - Enferm 2012; 21: 17-25.
19. Bawankule S, Quazi SZ, Gaidhane A, Khatib N. Delay in DOTS for new pulmonary tuberculosis patient from rural area of Wardha District, India. Online J Health Allied Scs 2010; 9(1): 5.
20. Chang CT, Esterman A: Diagnostic delay among pulmonary tuberculosis patients in Sarawak, Malaysia: a cross-sectionalstudy. Rural Remote Health 2007; 7: 667.
21. Mesfin MM, Newell JN, Walley JD, Gessessew A, Madeley RJ. Delayed consultation among pulmonary tuberculosis patients: a cross sectional study of 10 DOTS districts of Ethiopia. BMC Public Health 2009; 9: 53.
22. Pehme L, Rahu K, Altraja A. Factors related to helath system delays in the diagnosis of pulmonary tuberculosis in Estonia. Int J Tuberc Lung Dis 2007; 7(3): 687-707.
23. Leung ECC, Leung CC, Tam CM. Delayed presentation and treatment of newly diagnosed pulmonary tuberculosis patients in Hong Kong. Hong Kong Med J 2007; 13: 221-7.
24. Gaviria MB, Henao HM, Martínez T, Bernal E. Papel del personal de salud en el diagnóstico tardío de la tuberculosis pulmonar en adultos de Medellín, Colombia. Rev Panam Salud Publica 2010; 27: 83-92.
25. Oliveira LH, Mattos RA, Souza AIS. Cidadãos peregrinos: os "usuários" do SUS e os significados de sua demanda a prontos-socorros e hospitais no contexto de um processo de reorientação do modelo assistencial. Ciênc Saúde Colet 2009; 14: 1929-38.
26. 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: 63-8.
27. Bianco SR, Gurgel RL, Tavares MA. Aspectos radiológicos da tuberculose primária da mama: relato de caso e revisão de literatura. Rev Soc Bras Med Trop 2009; 42: 203-5.
28. Bento J, Silva AS, Rodrigues F, Duarte R. Métodos diagnósticos em tuberculose. Acta Med Port 2011; 24: 145-54.
29. Odusanya OO, Babafemi JO. Patterns of delays amongst pulmonary tuberculosis patients in Lagos, Nigeria. BMC Public Health 2004; 4: 18.
30. Antunes JLF, Waldman EA. The impact of AIDS, immigration and housing overcrowding on tuberculosis deaths in São Paulo, Brazil, 1994-1998. Soc Sci Med 2001; 52: 1071-80.
31. Snow J. Sobre a Maneira de Transmissão do Cólera. São Paulo: HUCITEC-ABRASCO; 1990.

32. Câmara G, Monteiro AM, Druck S, Carvalho MS. Análise Espacial e Geoprocessamento. In: Druck S, Carvalho MS, Câmara G, Monteiro AMV. Análise espacial de dados geográficos. Planaltina: Embrapa; 2004. p. 21-52.
33. Hino P, Santos CB dos, Villa TCS. Evolução espaço-temporal dos casos de tuberculose em Ribeirão Preto (SP), nos anos de 1998 a 2002. J Bras Pneumol 2005; 31: 523-7.
34. Bailey TC, Gatrell AC. Interactive Spatial Data Analysis. Harlow: Prentice Hall; 1995.
35. Bivand RS, Pebesma EJ, Gómez-Rubio V. Applied Spatial Data Analysis with R. Lexington: Springer; 2008.
36. Ng IC, Wen TH, Wang JY, Fang CT. Spatial dependency of tuberculosis incidence in Taiwan. PLoS ONE 2012; 7: e50740.
37. Liu Y, Jiang S, Liu Y, Wang R, Li X, Yuan Z, et al. Spatial epidemiology and spatial ecology study of worldwide drug-resistant tuberculosis. Int J Health Geogr 2011; 10: 50.
38. Hawker JI, Bakhshi SS, Ali S, Farrington CP. Ecological analysis of ethnic differences in relation between tuberculosis and poverty. BMJ 1999; 319: 1031-4.
39. Parslow R, El-Shimy N A, Cundall DB, McKinney PA. Tuberculosis, deprivation, and ethnicity in Leeds, UK, 1982–1997. Arch Dis Child 2001; 84: 109-13.
40. Baker M, Das D, Venugopal K, Howden-Chapman P. Tuberculosis associated with household crowding in a developed country. Epidemiol Community Health2008; 62: 715-21.
41. Quijano ED de, Brugal MT, Pasarín MI, Galdós-Tangüís H, Caylà J, Borrell C. Influencia de las desigualdades sociales, la conflictividad Social y la pobreza extrema sobre la morbilidad por Tuberculosis en la ciudad de Barcelona. Rev Esp Salud Pública 2001; 75: 517-27.
42. Culqui D, Zavaleta C, Romero J, Bonilla C, Trujillo O, Cueva N. Tuberculosis en poblaciones indígenas del Perú: Los Aimaras del Perú, 2000-2005. Rev Peru Epidemiol 2009; 13: 1-6.
43. Kistemann T, Munzinger A, Dangendorf F. Spatial patterns of tuberculosis incidence in Cologne (Germany). Soc Sci Med 2002; 55: 7-19.
44. Ponticiello A, Sturkenboom MCJM, Simonetti A, Ortolani R, Malerba M, Sanduzzi A. Deprivation, immigration and tuberculosis incidence in Naples, 1996 –2000. Eur J Epidemiol 2005; 20: 729-34.
45. Myers WP, Westenhouse JL, Flood J, Riley LW. An ecological study of tuberculosis transmission in California. Am J Public Health 2006; 96: 685-90.
46. Manfré LA, Lourenço RW, Donalisio MR. Distribuição espacial da tuberculose no município de Sorocaba, São Paulo, Brasil, 2000 – 2007. Rev Caminhos Geogr 2010; 11: 29-43.

Received on: 12/18/2014
Final version presented on: 06/09/2015
Accepted on: 07/14/2015