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Factors affecting successful antituberculosis treatment: a single-center experience

Marcella Cardoso Gonçalves[1], Amanda Aparecida Silva de Aguiar[2], Ana Paula Biadola[3], Paulo José Mascarenhas Mazaro[4], Marcus Vinícius Pimenta Rodrigues[3], Rosana Leal do Prado[3], Eliana Peresi-Lordelo[3]*

SUMMARY

OBJECTIVE: The identification of factors that influence a favorable antituberculosis treatment outcome could be of great use for the promotion of specific health actions to increase the success rate. Thus, the objective of this study was to investigate the factors affecting successful antituberculosis treatment in patients seen at a reference service in the Western region of São Paulo State/Brazil.

METHODS: A retrospective study was carried out from 2010 to 2016 based on the data obtained from the Notification Disease Information System of TB patients treated at a reference service in Brazil. The study included patients with treatment outcomes and excluded those from the penitentiary system or with resistant or multidrug-resistant TB. Patients were categorized as having a successful (cured) or unsuccessful (treatment default and death) treatment outcome. The association between TB treatment outcomes and social and clinical factors was analyzed.

RESULTS: A total of 356 cases of TB were treated between 2010 and 2016. Among the cases, the majority were cured and the overall treatment success rate was 85.96%, with a range between 80.33% (2010) and 97.65% (2016). After the exclusion of resistant/multidrug-resistant TB, 348 patients were analyzed. In the final logistic regression model analysis, education less than 8 years (OR 1.66; p<0.0001) and people living with human immunodeficiency virus/acquired immunodeficiency syndrome (OR 0.23; p<0.0046) were found to be significantly related to an unfavorable treatment outcome.

CONCLUSION: Low education and being a person living with human immunodeficiency virus/acquired immunodeficiency syndrome are vulnerability factors that can affect the successful outcome of antituberculosis treatment.

KEYWORDS: Tuberculosis. Antitubercular agents. Socioeconomic factors. HIV infections.

INTRODUCTION

Tuberculosis (TB) is still considered a major health problem worldwide. It is estimated that one-fourth of the global population is infected with the bacillus *Mycobacterium tuberculosis*, which is responsible for 1.3 million deaths[1]. Brazil is considered one of the 22 countries, with the highest number of TB cases, an overall number of newly diagnosed patients of 95,000, and 4,800 estimated deaths, of which 1,900 were human immunodeficiency virus (HIV)-associated[1].

Besides the highest number of TB cases in Brazil, there was a considerable reduction in cases in the past years due to strategic programs to control TB. Among these, the National Tuberculosis Control Program established priority municipalities to implement actions to reduce TB incidence and mortality[1,2]. The city of Presidente Prudente, which is located in the Western region of São Paulo State/Brazil, is considered one of the priority municipalities to control TB[3]. The average TB incidence rate of this city was 41.05/100,000 inhabitants between 2007 and 2015[4].

One of the strategic goals to eliminate TB is to increase the success rate of anti-TB treatment in the priority municipalities, which could be enhanced through the identification of factors that influence a favorable outcome, in order to guide the implantation of prevention health actions in the population. Thus, the objective of this study was to investigate the factors affecting successful anti-TB treatment outcomes in patients at a reference service in the Western region of São Paulo State/Brazil.

METHODS

Study design and setting

The city of Presidente Prudente, which is located about 560 km from the state capital São Paulo, is a mid-sized urban center.

[1]Estratégia Saúde da Família – Bauru (SP), Brazil.
[2]Universidade Estadual Paulista "Julio de Mesquita Filho" – Botucatu (SP), Brazil.
[3]Universidade do Oeste Paulista – Presidente Prudente (SP), Brazil.
[4]Setor de Tisiologia do Ambulatório "Profª Ana Cardoso Maia de Oliveira Lima" – Presidente Prudente (SP), Brazil.
*Corresponding author: elianaperesi@unoeste.br
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According to the recent census, in 2019, the estimated population was 228,743 inhabitants, with a population density of 368.89 inhabitants/km^2 [5].

A retrospective cross-sectional study was carried out based on the research of electronic data of patients with TB treated at the Tisiology Clinic of the Integrated Health Center of Presidente Prudente from 2010 to 2016. Patients with pulmonary and extrapulmonary TB were studied and divided according to the treatment outcomes.

The electronic data were obtained from the Notifiable Diseases Information System (SINAN), which is the Brazilian nationwide system responsible for notification, investigation, and, in the case of communicable diseases, follow-up and treatment[6]. Since we studied one single center, these specific data from SINAN were obtained with the staff of the Tisiology Outpatient Clinic of the Integrated Health Center of Presidente Prudente, which has exclusive access to the system and is responsible for uploading data from the patients attending the service.

Study groups

Patients were divided into two groups based on the treatment outcomes. The group with favorable treatment outcomes included patients defined as cured by the entry system. The unfavorable group brought together patients with an outcome of default, death from TB, and death from other causes.

In the SINAN, the TB outcomes are classified as follows: *Cure*: patients with two negative bacilloscopy, at any time of treatment and at the 5th or 6th month of treatment. For cases that need extension of the treatment time, the last 2 months will be considered. Discharge for cure will also be given to the patient who completed treatment without evidence of failure and was discharged based on the clinical and radiological criteria due to the impossibility of carrying out smear tests or culture; *Default*: patients who used the medication for 30 days or more and interrupted the treatment for more than 30 consecutive days; *Death by TB*; *Other causes of death* (died during TB treatment or another cause); and *MDR-TB/failure*[6].

To understand the factors associated with the general population, patients belonging to the penitentiary system were excluded to obtain the data. Patients with resistant or multidrug-resistant TB (DR/MDR-TB), associated with the MDR-TB/failure outcome category, were also excluded after obtaining data because of the type of anti-TB treatment regimen.

Variables

The characteristics selected for the study were as follows: Sociodemographic: gender (male and female), age (≤19 years; 20–49 years; 50–69 years; ≥70 years), skin color (white and non-white), education (<8 years and ≥8 years), and occupation (employed and unemployed); Clinics: bacteriological confirmation (no and yes) and bacilloscopy (negative and positive); Retreatment (no and yes); and Pulmonary form (no and yes). Patients diagnosed with both pulmonary and extrapulmonary TB were classified into the pulmonary TB group; Presence of cavitation (no and yes); Comorbidities: HIV/acquired immunodeficiency syndrome (AIDS) (no, yes, and unknown); Diabetes (no and yes); and Behavioral factors: Alcoholism (no and yes), Smoking (no and yes), and use of illegal substances (no and yes).

Data analysis

For data analysis, the multiple logistic regression model was used. For the selection of the explanatory variables used in the adjustment of the logistic regression model, it was considered an inclusion criterion that there was a relationship between the explanatory variable and the outcome variable based on the univariate analysis with a significance level of 25%[7]. Variables above this cutoff point were excluded from the final model. In this analysis, crude odds ratio values were also estimated with a 95% confidence interval. The entry order of the variables in the models was determined based on the value of the Wald chi-square test, followed by the odds ratio, found in the univariate analysis.

The R software was used to estimate the logistic model[8]. The stepwise procedure was used to adjust the models. The final model was defined according to the Akaike information criterion (AIC). For the purposes of the analysis, a significance level of $p<0.05$ was considered.

Ethical approval

The information was collected in the SINAN database of the Tisiology Clinic of the Integrated Health Center of Presidente Prudente. All variables that could identify the individuals were excluded, safeguarding the confidentiality of the identification data of each case. This work was approved by the Research Ethics Committee (protocol nº 48932315.6.0000.5515).

RESULTS

A total of 356 cases of TB were treated at the Tisiology Outpatient Clinic of the Integrated Health Center of Presidente Prudente between 2010 and 2016. Among the cases, the majority obtained cure, followed by treatment default, death by TB, death by other causes, and treatment failure. The overall treatment success rate was 85.96%, with a range between 80.33% (2010) and 97.65% (2016) (Table 1). Of these, eight were DR/MDR-TB, resulting in the inclusion of 348 patients to analyze the factors associated with the treatment outcomes (Table 1).

Table 1. Treatment outcomes and inclusion in the study of patients with tuberculosis followed at one reference service in Brazil, 2010–2016.

Year	Total patients n	Cure n (%)	Default n (%)	Death by TB n (%)	Death by other causes n (%)	Failure n (%)
2010	61	49 (80.33)	5 (8.20)	1 (1.64)	6 (9.84)	0
2011	49	43 (87.76)	4 (8.16)	0	2 (4.08)	0
2012	69	60 (86.96)	6 (8.70)	3 (4.35)	0	0
2013	51	43 (84.31)	3 (5.88)	2 (3.92)	2 (3.92)	1 (1.96)
2014	44	36 (81.82)	3 (6.82)	1 (2.27)	4 (9.09)	0
2015	41	35 (85.37)	1 (2.44)	2 (4.88)	2 (4.88)	1 (2.44)
2016	41	40 (97.56)	1 (2.44)	0	0	0
Total	356	306 (85.96)	23 (6.46)	9 (2.53)	16 (4.49)	2 (0.56)
DR/MDR-TB patients excluded from the study	8	6 (75)	0	0	0	2 (25)
Total patients included in the study	348	300 (86.21)	23 (6.61)	9 (2.59)	16 (4.59)	0

DR/MDR-TB: resistant or multidrug-resistant tuberculosis.

The distribution of the sociodemographic characteristics of the patients showed that most cases were male, aged 20–49 years, with white skin color and education less than 8 years, and employed. The evaluation of clinical characteristics showed that about half of the cases had bacteriological confirmation, with 137 cases of positive sputum smear microscopy. Among the patients with TB, only 25 cases were classified as retreatment, and there was a predominance of the pulmonary form of the disease, with 87 cases associated with cavitation. Regarding comorbidities, most patients were not associated with diabetes. Only 87.36% of the patients had a record for HIV/AIDS in their medical records, with the majority being negative for co-infection. Substance use evaluation demonstrated that most TB patients did not use alcohol, tobacco, or illicit substances (Table 2).

In the univariable analysis, education less than 8 years, people living with HIV/AIDS, and unknown HIV status were found to be significantly related to unfavorable treatment outcomes (Table 2). In the final logistic regression model analysis, education less than 8 years and people living with HIV/AIDS were found to be significantly related to unfavorable treatment outcomes (Table 3).

DISCUSSION

This study demonstrated that individuals with less than 8 years of schooling and living with HIV/AIDS are more likely to have an unfavorable outcome of anti-TB treatment.

The overall treatment success rate of this study was above the national rate of 72% in 2016[9]. Although there was an improvement in the service to achieve TB cure, the evaluation of factors associated with an unfavorable outcome of the anti-TB treatment could help build strategies to keep the high rate of cure.

Tuberculosis is a public health problem that is directly related to poverty and has been associated with low body mass index[10]. This could be due to more precarious living conditions, which include lower incomes and more limited access to health services, a common reality among the Brazilian black and "pardo" population[11]. In Brazil, the "mixed" ethnic category is called "pardo", which means a mixture of European, black, and Amerindian[12]. The Brazilian health indicators from 2014/2015 demonstrated that the black and "pardo" populations presented higher rates of TB incidence than those presented by the white population[13]. A Brazilian study demonstrated that the black population exceeded the average TB incidence rate in the general population more than three times[12].

The aforementioned precarious conditions could influence the level of education of TB patients. Low education can indicate a lower adherence to treatment, making it difficult to sterilize the bacilli, which facilitates their survival in a dormant form, suggesting that it would mask the effectiveness of the treatment[14]. Our results demonstrated an association between individuals who dropped out of the treatment and poor education, which agrees with other Brazilian studies[14-16]. A study with the Turkish population also demonstrated this association, highlighting the importance of educational actions for TB control[17].

Other studies showed an association between other social characteristics and the unsuccessful anti-TB treatment outcome,

Table 2. Univariate analysis of clinical and sociodemographic characteristics according to the treatment outcome of patients with tuberculosis followed at one reference service in Brazil, 2010–2016.

Characteristics	Successful treatment n (%)	Unsuccessful treatment n (%)	OR (95%CI)	p
Sociodemographic				
Gender (n=348)				
Male	188 (54.02)	35 (10.06)	1	0.1721
Female	112 (32.18)	13 (3.74)	0.62 (0.31–1.21)	
Age (n=348)				
≤19 years	19 (5.46)	1 (0.29)	1	
20–49 years	154 (44.25)	30 (8.62)	3.70 (0.72–67.75)	0.2105
50–69 years	101 (29.02)	8 (2.3)	1.50 (0.25–28.74)	0.7076
≥70 years	26 (7.47)	9 (2.59)	6.57 (1.09–126.57)	0.0858
Skin color (n=332)				
White	198 (59.64)	22 (6.63)	1	0.1690
Non-white	95 (28.61)	17 (5.12)	1.611 (0.81–3.17)	
Education (n=322)				
<8 years	166 (51.55)	28 (8.70)	1	**0.0081**
≥8 years	122 (37.89)	6 (1.86)	0.30 (0.11–0.68)	
Occupation (n=341)				
Unemployed	44 (12.91)	9 (2.64)	1	0.3377
Employed	253 (74.19)	35 (10.26)	0.68 (0.31–1.58)	
Clinical				
Bacteriological confirmation (n=348)				
No	148 (42.53)	23 (6.61)	1	0.8554
Yes	152 (43.68)	25 (7.18)	1.06 (0.57–1.96)	
Smear acid-fast bacilli (n=181)				
Negative	38 (21.00)	6 (3.31)	1	0.9325
Positive	119 (65.75)	18 (9.94)	0.96 (0.37–2.79)	
Retreatment (n=348)				
No	278 (79.89)	45 (12.93)	1	0.7875
Yes	22 (6.32)	3 (0.86)	0.84 (0.19–2.56)	
Pulmonary form (n=347)				
No	71 (20.46)	11 (3.17)	1	0.9686
Yes	229 (66.00)	36 (10.37)	1.01 (0.50–2.18)	
Cavitação (n=276)				
No	165 (59.78)	24 (8.69)	1	0.9899
Yes	76 (27.54)	11 (3.99)	0.99 (0.45–2.09)	
Comorbidities				
HIV/AIDS (n=348)				
No	238 (68.39)	19 (5.46)	1	
Yes	35 (10.06)	12 (3.45)	4.29 (1.88–9.54)	**0.0003**
Unknown	27 (7.76)	17 (4.88)	7.89 (3.66–17.08)	**<0.0001**
Diabetes (n=348)				
No	286 (82.18)	47(13.51)	1	0.4261
Yes	14 (4.02)	1 (0.29)	0.44 (0.02–2.24)	
Behaviour factors				
Alcoholism (n=348)				
No	285 (81.9)	46 (13.22)	1	0.8039
Yes	15 (4.31)	2 (0.57)	0.83 (0.13–3.06)	
Smoking (n=348)				
No	271 (77.87)	46 (13.22)	1	0.2290
Yes	29 (8.33)	2 (0.57)	0.41 (0.06–1.41)	
Illegal substance (n=348)				
No	282 (81.03)	44 (12.64)	1	0.5393
Yes	18 (5.17)	4 (1.15)	1.42 (0.40–4.03)	

Bold indicates statistically significant p-values.

Table 3. Final logistic regression model of clinical and sociodemographic characteristics according to the treatment outcome of patients with tuberculosis followed at one reference service in Brazil, 2010–2016.

Variables	OR_c	OR_a	95%CI*	p†	p‡
HIV/AIDS (n=348)					
No	1	1			
Yes	4.29	1.66	0.53–4.73	0.3567	0.0001
Unknown	7.89	9.91	3.41–29.82	<0.0001	
Age (n=348)					
≤19 years	1	1			
20–49 years	3.70	2.97	0.49–58.89	0.3296	0.1433
50–69 years	1.50	0.88	0.12–18.47	0.9151	
≥70 years	6.57	1.45	0.16–32.45	0.7669	
Education (n=322)					
<8 years	1	1			
≥8 years	0.30	0.23	0.07–0.59	0.0046	0.0046
Skin color (n=332)					
White	1	1			
Non-white	1.611	1.57	0.69–3.58	0.2800	0.2800

OR_c: crude odds ratio; OR_a: adjusted odds ratio; 95%CI*: 95% confidence interval of adjusted odds ratio; p†: category p-value; p‡: variable p-value.

such as male gender, age, and unemployment, as well as the influence of behavioral factors, such as the use of alcohol and illicit drugs, risks that did not show significance in our population[15,16]. A study conducted in Finland demonstrated that death was the main reason for a non-successful outcome, justified by the advanced age of the study population[18].

In our study, the only comorbidity that demonstrated the association with an unsuccessful anti-TB treatment outcome was HIV, a fact that has also been demonstrated by other authors, including the association with TB patients receiving antiretroviral drugs[19,20]. A concerning fact was the lack of HIV status from some patients, evidencing that not all TB patients are being investigated for HIV coinfection. A study conducted in Nigeria demonstrated the association of not knowing HIV status with a higher chance of treatment failure[19]. It is recommended to conduct an anti-HIV test for all patients with TB because of its ability to change the clinical presentation of the disease, duration of treatment, tolerance to TB drugs, and resistance to available drugs[21].

This study has the limitation of conducting a retrospective study of a single TB center which resulted in a reduced number of participants. The fact that we excluded patients belonging to the penitentiary system and that the treatment adherence was also not investigated could also be a bias to the distribution of the outcomes. Furthermore, the incompleteness of data available for each patient made other data analyses impossible.

CONCLUSION

Low education and being a person living with HIV/AIDS are vulnerability factors that can affect the successful outcome of anti-TB treatment. Health actions aimed at this group with social and medical support, focused on demystifying TB and better monitoring of patients, could contribute to the success of treatment.

AUTHORS' CONTRIBUTIONS

MCG: Data curation, Methodology, Writing – original draft. **AASA:** Data curation, Methodology. **APB:** Data curation, Methodology. **PJMM:** Data curation, Writing – review & editing. **MVPR:** Writing – review & editing. **RLP:** Formal Analysis, Writing – review & editing. **EPL:** Conceptualization, Data curation, Formal Analysis, Supervision, Writing – original draft, Writing – review & editing.

REFERENCES

1. World Health Organization. Global health TB report. 2019. Available from: https://apps.who.int/iris/handle/10665/329368
2. Ministério da Saúde do Brasil. Panorama da tuberculose no Brasil: diagnóstico situacional a partir de indicadores epidemiológicos e operacionais. Brasília. 2018. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/tuberculose_brasil_indicadores_epidemiologicos_operacionais.pdf
3. Governo do Estado de São Paulo. Plano estadual pela eliminação da tuberculose: 2018 A 2021. Programa de controle da tuberculose do estado de São Paulo. São Paulo. 2017. Available from: https://docs.bvsalud.org/biblioref/2020/06/1100721/tb17_plano_eliminacao.pdf
4. Bortoluci AB. Avaliação da distribuição espacial e dos aspectos epidemiológicos dos casos notificados de tuberculose na região do Pontal do Paranapanema. Thesis (Master's degree). Presidente Prudente: Universidade do Oeste Paulista; 2018. Available from: http://bdtd.unoeste.br:8080/jspui/handle/jspui/1068
5. Instituto Brasileiro de Geografia e Estatística. Estimativas populacionais (IBGE). 2019. Available from: https://www.ibge.gov.br/cidades-e-estados/sp/presidente-prudente.html
6. Brasil. Vigilância epidemiológica da tuberculose: Análise de indicadores operacionais e epidemiológicos a partir da base de dados do Sinan versão 5.0. 2016. Available from: http://portalsinan.saude.gov.br/images/documentos/Agravos/Tuberculose/Apostila_Curso_Sinan_2016.pdf
7. Hosmer D, Lemeshow S, Sturdivant R. Applied logistic regression. 3rd ed. New York: John Wiley & Sons; 2013. p. 528.
8. R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing;. 2020. Available from: https://www.R-project.org/
9. World Health Organization. Global health TB report. 2018. Available from: https://apps.who.int/iris/handle/10665/274453.
10. Oxlade O, Murray M. Tuberculosis and poverty: why are the poor at greater risk in India? PLoS One. 2012;7(11):1-8. https://doi.org/10.1371/journal.pone.0047533
11. Chiavegatto Filho ADP, Laurenti R. Disparidades étnico-raciais em saúde autoavaliada: Análise multinível de 2.697 indivíduos residentes em 145 municípios brasileiros. Cadernos de Saúde Pública. 2013;29(8):1572-82. https://doi.org/10.1590/0102-311X00139012
12. Viana PVS, Gonçalves MJF, Basta, PC. Ethnic and racial inequalities in notified cases of tuberculosis in Brazil. PLoS One. 2016;11(5):1-16. https://doi.org/10.1371/journal.pone.0154658
13. Ministério da Saúde do Brasil. Indicadores de Vigilância em Saúde descritos segundo a variável raça/ cor, Brasil. Boletim Epidemiológico. 2017;48(4):1-35. https://doi.org/10.1590/S1415-790X2004000400010
14. Vieira AA, Leite DT, Adreoni S. Recorrência de tuberculose em município prioritário do estado de São Paulo. J Bras Pneumol. 2017;43(2):106-12. https://doi.org/10.1590/S1806-37562016000000002
15. Silva TC, Matsuoka PFS, Aquino DMC, Caldas AJM. Fatores associados ao retratamento da tuberculose nos municípios prioritários do Maranhão, Brasil. Cien Saude Colet. 2017;22(12):4095-103. https://doi.org/10.1590/1413-812320172212.20612015
16. Oliosi JGN, Reis-Santos B, Locatelli RL, Sales CMM, Silva Filho WG, Silva KC, et al. Effect of the Bolsa Familia Programme on the outcome of tuberculosis treatment: a prospective cohort study. Lancet Glob Health. 2019;7(2):e219-26. https://doi.org/10.1016/S2214-109X(18)30478-9
17. Sengul A, Akturk UA, Aydemir Y, Kaya N, Kocak ND, Tasolar FT. Factors affecting successful treatment outcomes in pulmonary tuberculosis: a single-center experience in Turkey, 2005-2011. J Infect Dev Ctries. 2015;9(8):821-8. https://doi.org/10.3855/jidc.5925
18. Holden IK, Lillebaek T, Seersholm N, Andersen PH, Wejse C, Johansen IS. Predictors for pulmonary tuberculosis treatment outcome in Denmark 2009–2014. Sci Rep. 2019;9(1):6-13. https://doi.org/10.1038/s41598-019-49439-9
19. Sariem CN, Odumosu P, Dapar MP, Musa J, Ibrahim L, Aguiyi J. Tuberculosis treatment outcomes: a fifteen-year retrospective study in Jos-North and Mangu, Plateau State, North - Central Nigeria. BMC Public Health. 2020;20(1):1-11. https://doi.org/10.1186/s12889-020-09289-x
20. Khunthason S, Kaewkungwal J, Pan-Ngum W, Okascharoen C, Apidechkul T, Lawpoolsri S. Factors associated with the unsuccessful tuberculosis treatment of hill tribe patients in Thailand. J Infect Dev Ctries. 2020;14(1):42-7. https://doi.org/10.3855/jidc.12029
21. Ministério da Saúde do Brasil. Manual de recomendações para o controle da tuberculose no Brasil. Brasília. Secretaria de Vigilância em Saúde, Departamento de Vigilância das Doenças Transmissíveis. 2019. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/manual_recomendacoes_controle_tuberculose_brasil_2_ed.pdf