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Factors associated with the outcomes in the treatment of tuberculosis in people monitored by Primary Health Care

Fatores associados aos desfechos no tratamento da tuberculose em pessoas acompanhadas pela Atenção Primária à Saúde

Factores asociados a resultados en el tratamiento de la tuberculosis en personas seguidas por Atención Primaria de Salud

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ABSTRACT

Introduction: Tuberculosis (TB) represents a challenge that go through the history of mankind. The monitoring in the Primary Health Care (PHC) consists in an important mechanism of accomplishment of the policies on TB, since it provides greater longitudinal care relationship (longitudinality) and closeness to the infected individual. **Objective:** To analyze TB cases attended by the PHC in Sergipe. **Outline:** It was performed a retrospective cohort of the TB cases attended by the PHC in Sergipe between 2014 and 2018. **Results:** 2,172 TB cases attended by the PHC in Sergipe were included, of which 283 (13.0%) abandoned the treatment, 1813 (83.5%) progressed to cure and 76 (3.5%) to death. The factors associated with treatment abandonment were: male, age range of 20 to 29 years, alcoholics, people with diabetes mellitus and persons deprived of liberty. In relation to the mortality, higher rates were found in: male, age range of 70 years and above, illiterate and people with diabetes mellitus. **Implications:** Conditions of social vulnerability and comorbidities impacted mortality, as well as abandonment of TB treatment.

DESCRIPTORS

Tuberculosis; Primary Health Care; Epidemiology.

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INTRODUCTION

Tuberculosis (TB) has as main etiologic agent the *Mycobacterium tuberculosis*, which has already infected around 2 billion people around the world.[1] One of the most ancient death records due to the TB was evidenced through forensic examination of the mummified body of the Egyptian pharaoh Tutankhamun.[2] Among the infectious diseases caused by only one agent, it is the first cause of death, exceeding HIV ones.[3]

Besides that, one third of world population carries the TB bacillus and has the risk of developing the active disease.[1] Generally, it is associated with the economic vulnerability, such as living in precarious housing, having low educational status, using alcohol and other drugs.[3] It is mainly airborne, causing pathological manifestation of slow and chronic course in individuals with lowered immunity.[4]

With a view to facing this disease, the World Health Organization created, in 2014, the End TB Strategy, which establishes goals to reduce deaths by 90% and incidence by 80% until 2030 and the end of tuberculosis in 2035.[5-6] This Strategy is composed of three pillars: integrated, patient-centered TB care and prevention; bold policies and integrated information systems, including social protection and universal health coverage policy; intensified research and innovation, and the incorporation of new technologies.[7]

Accompanying this need to combat TB more intensely, Brazilian Ministry of Health issued, in 2017, a document structuring a plan for tuberculosis elimination (the National Plan for the End of Tuberculosis as a Public Health Problem) that was designed to reduce, until 2035, the incidence of tuberculosis to less than 10 cases/100,000 inhabitants and the mortality by tuberculosis to less than 1 death in 100,000 inhabitants.[6]

In this context, the Primary Health Care (PHC) has fundamental a role since it consists in the individuals' entry point for health systems. Denominated Basic Care in Brazil, it has four essential attributes, that are: first-contact access, integrality, the longitudinal care relationship (longitudinality) and coordination of the care.[8] This type of health care has low technological density resources and must fulfill three functions: solvability, communication and accountability for sanitary micro-territories.[9]

TB treatment can have different outcomes such as discharge due cure, death and treatment abandonment, besides the possibility of therapeutical failure by resistance to the drugs of the basic scheme.[4] By virtue of the reach and proximity to the citizens, this study aims to analyze the factors associated with the outcomes in the treatment of tuberculosis monitored by the PHC.

METHOD

An epidemiological study was conducted, of retrospective cohort nature, of the new cases of tuberculosis admitted in Basic Care in Sergipe between 2014 and 2018.

Sergipe is one of the nine states that compose Brazilian Northeast region, has 2,298,6996 inhabitants according to estimates of IBGE for 2019 and is subdivided into 7 health regionals: Aracaju, Estância, Lagarto, Propriá, Itabaiana, Glória and Socorro. It has a territorial extension that configures it as one of the smallest federative units, being bigger only than Distrito Federal. In terms of population, it ranks 22nd among Brazilian states.

The data were extracted from the database of the *Sistema de Informação de Agravos de Notificação* (SINAN) of the State Health Secretariat of Sergipe and exported by means of application developed by the Computing Department of SUS (Datasus), tabulator for Microsoft Windows® (TabWin).

The following were included: all the new TB cases occurred in Sergipe between 2014 and 2014, which had primary care as place of monitoring. The following were excluded: the cases closed as change of scheme, death and multidrug-resistant tuberculosis, since this monitoring shall be continued in the

specialized network. The ones with loss of segment were also excluded.

The following were evaluated as valid outcomes, after one year: start of the treatment, progression to cure, treatment abandonment, or death. The demographic, clinical and epidemiological variables were the exposure evaluated as to the association with different outcomes.

The statistical analysis was performed in the OpenEpi software (https://www.openepi.com/Menu/OE_Menu.htm), the relative risk (RR) was calculated as association measure, the chi-square test (and the exact Mid-P test when the variable is less than 5) was used, and a level of significance of $p < 0,05$ was adopted with confidence interval of 95%.

The ethical aspects concerning the Resolution 466/2012 of the Brazilian National Health Council were followed, and the principles of Declaration of Helsinki were respected in this study. The Project, due to using secondary data, not identifying patient names, dispensed with the need to utilize the Informed Consent Form (ICF) and ethics committee approval.

RESULTS

3,443 new TB cases were diagnosed in Sergipe, of these, 2,419 (70.25%) were monitored in Primary Health Care (PHC) unities, of which 2,172 (89.3%) were included in the cohort for analysis. Among these TB cases, 10,202 home contacts were recorded, of which 8,433 (82.7%) were examined. The anti-HIV was performed in 1,655 (76.2%) of cohort-included cases, being positive in 29 (1.8%).

Most cases were in male persons, and these had, in relation to women, significantly, lower cure rates, higher abandonment rates and progression to death (Table 1).

The most stricken age range was the one between 20 and 39 years, with 53% of the total. The range between 60 and 69 years and the one between 10 and 19 years were the ones with highest cure rates, with 88.8% and 90.6%, respectively. The highest abandonment rate was evidenced in the population of 20 to 29 years, with 18.4%, and the highest proportion of death occurred in the population 60 years or above (11%). As to the color/race criterion, brown and black represented 78.6% of the total. The abandonment reduced as the educational level increased. The illiterates had the highest death rates, with 6.7% (Table 1).

Table 1 – Relation among the sociodemographic variables and the outcomes in the cohort in the treatment of tuberculosis in Primary Health Care, Sergipe, 2014–2018.

Sociodemographic Variables	Abandonment			Cure			Death			Total	
	n	%	RR	n	%	RR	n	%	RR	n	%
Sex											
Female	56	9	-	552	88.7	-	14	2.3	-	622	28.6
Male	227	14.6	1.6*	1261	81.4	0.9*	62	4	1.7*	1550	71.4
Age range											
0–9 years	0	0.0	-	9	100.0	-	0	0.0	-	9	0.4
10–19 years	15	8.3	0.6*	163	90.6	1.1*	2	1.1	0.3*	180	8.3
20–29 years	124	18.4	1.7*	533	79.1	0.9*	17	2.5	0.6	674	31.0
30–39 years	63	12.9	1.0	413	84.5	1.0	13	2.7	0.7	489	22.5
40–49 years	37	12.0	0.9	262	85.1	1.0	9	2.9	0.8	308	14.2
50–59 years	34	13.5	1.0	203	80.9	1.0	14	5.6	1.7*	251	11.6
60 years and above	10	3.8	0.3*	230	88.1	1.1*	21	8.0	2.8*	261	12.0
Raca/color											
Black/brown	243	14.2	1.6*	1402	82.1	0.9*	63	3.7	1.3	1708	78.6
Yellow/indigenous	3	8.1	0.6	34	91.9	1.1	0	0.0	-	37	1.7
Caucasian	32	9.1	0.6*	314	89.0	1.1*	7	2.0	0.5	353	16.3
Without information	5	6.8	0.5	63	85.1	1.0	6	8.1	2.5*	74	3.4

Education level											
Illiterate	16	11.9	0.9	109	81.3	1.0	9	6.7	2.0*	134	6.2
Middle School	187	16.2	1.7*	936	80.9	0.9*	34	2.9	0.7	1157	53.3
High School	37	9.4	0.7*	346	87.8	1.1*	11	2.8	0.8	394	18.1
Higher Education	1	1.5	0.1	65	98.5	1.2*	0	0.0	-	66	3.0
Without information	42	10.1	0.7	352	84.6	1.0	22	5.3	1.7*	416	19.2
Not applicable	0	0.0	-	5	100.0	-	0	0.0	-	5	0.2
Total	**283**	**13.0**		**1813**	**83.5**		**76**	**3.5**		**2172**	**100.0**

* *p < 0.05* When the variable was equal zero, relative risk was not calculated. RR = relative risk.

The place of diagnosis occurred in 83.5% of the cases was in the PHC. Among the monitored cases in the PHC, most of them had its diagnosis in unities of the PHC itself, these had, significantly, higher cure and lower abandonment rates (Table 2).

Aracaju's regional responded by 46.7% of the cases, besides that, it obtained the highest abandonment rate, with 16.8%. Meanwhile, Itabaiana's regional obtained the highest percentage of deaths, 8.2%. The urban zone comprehended 73.2% of the cases and had a higher abandonment rate, 14.2% (Table 2).

Table 2 – Relation among the epidemiological variables and the outcomes in the cohort in the treatment of tuberculosis in Primary Health Care, Sergipe, 2014–2018.

Epidemiological Variables	Abandonment			Cure			Death			Total	
	n	%	RR	n	%	n	%	RR	n	n	n
Place of diagnosis											
PHC	225	12.4	0.7*	1530	84.3*	1.1*	59	3.3	0.7	1814	83.5
Non-PHC	58	16.2	-	283	79.1*	-	17	4.7	-	358	16.5
Regional of residence											
Aracaju	170	16.8	1.7*	814	80.3	0.9*	30	3.0	0.7	1014	46.7
Estância	8	4.1	0.3*	183	93.4	1.1*	5	2.6	0.7	196	9.0
Glória	5	5.7	0.4*	80	92.0	1.1*	2	2.3	0.6	87	4.0
Itabaiana	13	6.7	0.5*	166	85.1	1.0	16	8.2	2.7*	195	9.0
Lagarto	20	10.4	0.8	163	84.9	1.0	9	4.7	1.3	192	8.8
Propriá	17	12.6	0.9	115	85.2	1.0	3	2.2	0.6	135	6.2
Socorro	50	14.2	1.1	292	82.7	1.0	11	3.1	0.8	353	16.3
Area of residence											
Urban	225	14.2	1.4*	1312	82.7	1.0	50	3.2	0.7	1587	73.1
Rural/peri-urban	39	8.3	0.6*	408	86.6	1.1*	24	5.1	1.7*	471	21.7
Without information	19	16.7	1.3	93	81.6	1.0	2	1.8	0.5	114	5.2
Total	**283**	**13.0**		**1813**	**83.5**		**76**	**3.5**		**2172**	**100.0**

* *p < 0.05* When the variable was equal zero, relative risk was not calculated. RR = relative risk.

Most of TB cases (94.6%) monitored by the PHC were pulmonary, which had the lower cure rates and the highest abandonment proportion, besides a significantly higher lethality in relation to the extrapulmonary ones (Table 3).

29 cases of TB and HIV coinfection occurred, which, despite presenting worst outcomes, with abandonment rate significantly higher than in non-HIV-infected people (Table 3).

Alcoholism was significantly associated with higher abandonment and death rates, and lower cure rate. Persons deprived of liberty had significantly higher abandonment rates, as well as the homeless ones, who also had lower cure rates. Higher cure rates were significantly associated with the patients who received government monetary aid *Bolsa Família* and the ones who were underwent directly observed treatment (Table 3).

Table 3 – Relation among the clinical variables and the outcomes in the cohort in the treatment of tuberculosis in Primary Health Care, Sergipe, 2014–2018.

Clinical Variables	Abandonment			Cure			Death			Total	
	n	%	RR	n	%	n	%	RR	n	n	n
Clinical Form											
Extrapulmonary	12	10.3	-	103	88.8	-	1	0.9	-	116	5.3
Pulmonary	271	13.2	1.2	1710	83.2	0.9	75	3.6	4.2*	2056	94.6
PVHIV											
No	276	12.9	-	1792	83.6	-	75	3.5	-	2143	98.7
Yes	7	24.1	1.8*	21	72.4	0.8	1	3.4	1.0	29	1.3
Alcoholism											
No	179	10.5	-	1470	86.5	-	51	3.0	-	1700	78.3
Yes	104	22	2.1*	343	72.7	0.8*	25	5.3	1.8*	472	21.7
Diabetes											
No	273	13.6	-	1669	83.3	-	62	3.1	-	2004	92.3
Yes	10	6	0.4*	144	85.7	0.9	14	8.3	2.7*	168	7.7
Mental disease											
No	273	12.8	-	1778	83.6	-	75	3.5	-	2126	97.9
Yes	10	21.7	1.7*	35	76.1	0.9	1	2.2	0.6	46	2.1
Persons deprived of liberty											
No	239	12.5	-	1599	83.6	-	74	3.9	-	1912	88.0
Yes	44	16.9	1.3*	214	82.3	1.0	2	0.8	0.2*	260	12.0
Homeless population											
No	270	12.7	-	1788	83.8	-	76	3.6	-	2134	98.3
Yes	13	34.2	2.7*	25	65.8*	0.8*	0	0.0	-	38	1.7
Migrant population											
No	282	13.0	-	1807	83.5	-	76	3.5	-	2165	99.7
Yes	1	14.3	1.1	6	85.7	1.0	0	0.0	-	7	0.3
Bolsa Família											
No	270	13.5	-	1657	82.8	-	74	3.7	-	2001	92.1
Yes	13	7.6	0.6	156	91.2	1.1*	2	1.2	0.3	171	7.9
Directly Observed Treatment											
No	220	16.5	-	1068	79.9	-	48	3.6	-	1336	61.5
Yes	63	7.5	0.5*	745	89.1*	1.1*	28	3.3	0.9	836	38.5
Total	**283**	**13.0**		**1813**	**83.5**		**76**	**3.5**		**2172**	**100.0**

* $p < 0.05$ When the variable was equal zero, relative risk was not calculated. RR = relative risk.

DISCUSSION

In this study, despite most of the cases progress to cure, a considerable part (13%) dropped out of treatment, which may be related to several factors. A structured interview conducted in Indonesia identified as barriers the difficult access to the health care and the lack of knowledge about TB,[10] while in Ethiopia the main hindrances were the distance, the lack of awareness on the importance of concluding the treatment and the cost of transportation.[11] In Porto Alegre/RS, abandonment rate of 25% was evidenced. The related factors were the low-income, drugs abuse, previous treatment abandonment, and smoking.[12]

The lethality of 3.5% found in the study has correspondence with data of developing countries. A study performed in Spain between 2006 and 2013 found lethality of 3.5%, being the most during the intensive part of the treatment, and the following factors associated with the death were listed: to be over 50 years, being retired; to have visited the emergency department, infection by HIV, initial standard treatment either with 3 medicaments or non-standard treatments, difficulty understanding, and positive sputum bacilloscopy.[13]

The gender questions are equally worthy of highlighting. In Manaus, a 58.3% incidence rate was found in men,[14] in São Paulo, 67% in 2013.[15] Systematic review of 2018 with works from 24 countries concluded that men are 2.2 times more likely to have this disease than women. Besides that, generally, among men, the

following occur: higher abandonment rates and a higher delay among between first symptoms and treatment start.[16]

In a literature review from 2011, mortality of 9.2% was found in people living with HIV (PLHIV) and 3% among non-infected individuals.[17] One international cohort involving Europe and Latin America found a rate of 13% among HIV/TB coinfected who died due to tuberculosis. The high mortality linked to that coinfection was due to the disseminated tuberculosis, low CD4 cell count and reduced percentages of treatment using antiretrovirals, since 18% of the patients were receiving Antiretrovirals Therapy after tuberculosis diagnosis in Eastern Europe, 44% in Western Europe and 39% in Latin America.[18]

The abuse of alcohol impacts on the incidence and in the outcome by altering the pharmacokinetics of the medicaments used in TB treatment, favors social marginalization, higher reinfection rate, higher discontinuation rate and developing resistance to medicaments.[19] Consumption greater than 60g of ethanol per day is associated with a 68% increase in the risk of having tuberculosis compared to those who do not use it.[20]

Another determinant factor is the presence of Diabetes Mellitus, which can increase three times the risk of falling ill with TB in relation to the general population. There is evidence that the decompensated diabetes increases the risk of infections, so it can end up harming both innate and adaptive immune responses, favoring the reactivation of latent tuberculosis. An *in vitro* study evidenced that diabetics have higher levels of glycated hemoglobin and of fasting glucose, which makes the identification of the Mycobacterium by monocytes be smaller, enabling the replication of bacteria.[21-22]

The infection by TB in persons deprived of liberty is often neglected and is an important problem of public health, especially in countries with high incidence of this disease. A meta-analysis that involved works from 1997 to 2016, from several countries, found a 2% estimated prevalence of tuberculosis among prisoners, being 14 times greater than the one found in the general population (0.14%). The incidence and the mortality also are greater in persons deprived of liberty than the ones found in the general population.[23-24]

In the prison system, there is the acting of the Prison Basic Care Teams. A study carried out with these teams in the State of Rio Grande do Sul contained reports which exposed the particularities of this care network. The teams mentioned difficulties in filling out the forms due to constant changes, absence of professional reference, inadequacy/non-existence of records, lack of technical knowledge and absence of protocols for the TB bacteriological diagnosis. Also, the following were proclaimed: the insufficient number of professionals, inadequate physical structure for care and the dependence on security staff.[25]

Homeless population represents a part of people with peculiarities which negatively interfere with disease outcome as well. The Doctor's Office in the Street strategy, instituted by PNAB in 2011, seeks to reach this population. A study performed with teams of Doctor's Office in the Street in the municipality of São Paulo/SP, health professionals reported difficulty of acting in the context of poverty, difficulties in how to deal with unexpected situations, the prejudice, the stigma attached to the population living in the streets, as well as the need of that persons to be supported by social assistance and by the health services.[23]

Moreover, personal perception of the process is different for each individual, what has direct influence in treatment adherence, and the understanding that this process is essential to enable cure and the networked work. The frequent impossibility of changing the context of poverty in which sick persons live and the scarcity of institutional resources for both patients and professionals regarding TB control demotivate professionals. Among the reported cases in Brazil in 2015, only 36.8% of the homeless population diagnosed with TB progressed to cure.[23-26]

Among the protective measures, there are the social benefits. Evidence suggests that the government

monetary aid *Bolsa Família* reduced extreme poverty, reduced socioeconomic inequalities, improved nutritional status, reduced child mortality and the incidence of leprosy, increasing income and providing other benefits to the health. Although *Bolsa Família* is not specifically for families affected by TB, the program focuses on poor families, reducing risk factors which promote the progression to active disease and potentiating the adherence to the treatment of people in a situation of social vulnerability.[9-28]

The Directly Observed Treatment (DOT) positively impacted on the outcome. This strategy strengthens the bond, an important principle in the care of the sick person with TB, as it determines dialogues, confidence and respect between the health professional and patient, who begins to understand the relevance of properly following his/her treatment.[29] A 2017 systematic review concluded that DOT increased the chance of cure and completed treatment by 22%, the results showed no significant difference in mortality.[30]

As limiting factor to the study, it is the fact of due to having retrospective cohort outline, the data collection is linked to the appropriate record of the epidemiological, clinical data and those from the outcomes in the notification forms, being only these variables analyzed.

The challenges remain huge for Brazil and for the State of Sergipe. The United States, for instance, shows a rate of incidence of 2.8 cases per 100,000 inhabitants, being that almost all occurred in people who were not born in the country.[30]

The treatment of TB in Primary Care assumes that the proximity to the individual is greater, with longitudinal character. The decentralization of diagnosis and treatment of TB for primary health care with measures of social protection for patients must be considered as priorities for disease control strategies, in order to reduce the impact of these barriers on adherence to treatment.[31] Only when there is an indication or signs of seriousness, these cases should be treated at other levels of care. In addition, in this study, mortality and abandonment rates have shown a steady trend over the years, which indicates the need for more actions to implement the strategy for the end of tuberculosis.

CONCLUSION

Despite being a well-studied disease, easily diagnosed for most of its kinds and with treatment available in SUS able to cure almost all cases, in practice TB remains a big challenge.

The study demonstrated that several factors directly affect the possible outcomes of TB cases, and the care scenario in the PHC, with a unique look at the individual and his whole context. The use of well-stablished protocols and standardized schemes to achieve greater success must consider the uniqueness of each individual, recognizing that there are individual and social factors.

RESUMO

Introdução: A Tuberculose (TB) representa um desafio que atravessa a história da humanidade. O acompanhamento na Atenção Primária à Saúde (APS) consiste em um importante mecanismo de cumprimento das políticas voltadas para a TB, já que proporciona maior longitudinalidade e proximidade com o indivíduo infectado. **Objetivo**: Analisar os casos de TB atendidos pela APS em Sergipe. **Delineamento**: Foi realizada uma coorte retrospectiva dos casos de TB atendidos pela APS em Sergipe entre 2014 e 2018. **Resultados**: Foram incluídos 2172 casos de TB atendidos pela APS em Sergipe, dos quais 283 (13,0%) abandonaram o tratamento, 1813 (83,5%) evoluíram para cura e 76 (3,5%) a óbito. Os fatores associados ao abandono foram: sexo masculino, faixa etária de 20 a 29 anos, etilistas, portadores de diabetes mellitus e população privada de liberdade. Já em relação à mortalidade, foram encontradas taxas mais elevadas em: sexo masculino, faixa etária de 70 anos ou mais, analfabetos e portadores de diabetes mellitus. **Implicações**: Condições de vulnerabilidade social e comorbidades impactaram na mortalidade, bem como no abandono ao tratamento da TB.

DESCRITORES

Tuberculose; Atenção Primária à Saúde; Epidemiologia.

RESUMEN

Introducción: La tuberculosis (TB) representa un desafío que atraviesa la historia de la humanidad. El monitoreo en Atención Primaria de Salud (APS) es un mecanismo importante para el cumplimiento de las políticas de TB, ya que brinda mayor longitudinalidad y proximidad al individuo infectado. **Objetivo:** analizar los casos de TB atendidos por la APS en Sergipe. **Delineación:** Se realizó una cohorte retrospectiva de casos de TB atendidos por APS en Sergipe entre 2014 y 2018. **Resultados:** Se incluyeron un total de 2172 casos de TB atendidos por APS en Sergipe, de los cuales 283 (13,0%) abandonaron el tratamiento, 1813 (83,5%) evolucionaron a curación y 76 (3,5%) fallecieron. Los factores asociados al abandono fueron: sexo masculino, 20 a 29 años, consumidores de alcohol, personas con diabetes mellitus y personas privadas de libertad. En relación a la mortalidad, se encontraron tasas más altas en: sexo masculino, grupo de edad de 70 años o más, analfabetos y con diabetes mellitus. **Implicaciones:** Las condiciones de vulnerabilidad social y las comorbilidades afectaron la mortalidad, así como el abandono del tratamiento de la TB.

DESCRIPTORES

Tuberculosis; Atención Primaria de Salud; Epidemiología.

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CONFLICTS OF INTEREST

There are no conflicts of interest to declare.