J Young Pharm, 2018; 10(4): 476-480
A multifaceted peer reviewed journal in the field of Pharmacy
www.jyoungpharm.org | www.phcog.net

Original Article

Predictors of Mortality among Individuals with Tuberculosis and Human Immunodeficiency Virus Coinfection at a Reference Center in Southeastern Brazil: A Retrospective Cohort Study

Dirce Ines Silva[1,2]*, Maria das Graças Braga Ceccato[1,3], Michelline Rosa Silveira[1,3], Silvana Spíndola Miranda[4], Rosângela Maria Gomes[1], João Paulo Amaral Haddad[5], Wânia Silva Carvalho[1,3]

[1]Postgraduate Program in Medicines and Pharmaceutical Assistance, Faculty of Pharmacy, Federal University of Minas Gerais, Belo Horizonte, MG, BRAZIL.
[2]Hospital Foundation of the State of Minas Gerais/Eduardo de Menezes Hospital, Belo Horizonte, MG, BRAZIL.
[3]Department of Social Pharmacy, Faculty of Pharmacy, Federal University of Minas Gerais, Belo Horizonte, MG, BRAZIL.
[4]Department of Clinical Medicine, Faculty of Medicine, Federal University of Minas Gerais, Belo Horizonte, MG, BRAZIL.
[5]Veterinary School of the Federal University of Minas Gerais – Department of Preventive Veterinary Medicine of the Federal University of Minas Gerais, Belo Horizonte, MG, BRAZIL.

ABSTRACT

Background: Tuberculosis (TB) remains an important cause of morbidity, the leading cause of death in patients with human immunodeficiency virus (HIV) infection, and a challenge to global public health. This study aimed to analyze the predictors associated with mortality among individuals coinfected with TB/HIV at a reference center in southeastern Brazil. **Method:** This retrospective cohort study used the data obtained from clinical records and information systems from 2007 to 2014. The data were analyzed using Cox proportional hazards model to identify the independent predictors. **Results:** Among the 924 individuals studied, 72.7 % were men. The median age was 38 years (range: 16–78 years). The mortality rate was 21.6%. The predictors associated with mortality were as follows: age over 50 years (Adjusted Hazard Ratio [AHR] : 2.52, 95% confidence interval [CI]: 1.39–4.59), CD4+ T lymphocyte count ≤200 cells/mm3 [AHR]: 1.40, 95% [CI]: 0.86–2.27), detectable viral load [AHR]: 1.73, 95% [CI]: 0.98–3.01), and non-use of antiretroviral therapy [AHR]: 2.91, 95% [CI]: 1.71–4.93). **Conclusion:** Results demonstrated that patients coinfected with TB/HIV have high mortality rates. Therefore, it is necessary to address the social determinants of health to provide every individual an equal opportunity to gain access to healthcare to cope with TB/HIV coinfection.

Key words: Tuberculosis/HIV, Mortality, Retrospective cohort, Brazil.

Correspondence

Ms. Dirce Ines Silva, Postgraduate Program in Medicines and Pharmaceutical Assistance, Faculty of Pharmacy, Federal University of Minas Gerais, BRAZIL.

Phone: +55-031-999411770

Email: dirceines68@gmail.com

DOI: 10.5530/jyp.2018.10.103

INTRODUCTION

HIV infection is one of the risk factors for tuberculosis (TB) in individuals infected with *Mycobacterium tuberculosis* (*M. tuberculosis*).[1] The synergy between *M. tuberculosis* and human immunodeficiency virus (HIV) has an impact on the natural history, epidemiology, economy, politics, molecular biology and clinical evolution of both diseases and poses a challenge for public health.

TB is the leading cause of morbidity and mortality in people living with HIV/AIDS (PLWHA).[2] Individuals infected with HIV are 21 to 34 times more likely to develop TB than are those without HIV.[3] HIV promotes the reactivation of latent *M. tuberculosis* infection for active TB owing to the patients' poor immune responses.[4]

The initiation of antiretroviral therapy (ART) during TB treatment has significantly improved the survival of this population. Studies have shown that ART reduces the individual risk of developing TB by 65%, regardless of the number of CD4+ T lymphocytes.[5] However, people living with HIV/AIDS coinfected with TB have complexity in pharmacological treatment due to frequency of doses, long duration and toxicity of the drugs,[6-7] as well as the behavioral factors of this population.[8] These factors may cause inadequate adherence to therapies, leading to therapeutic failure and decreased survival of these individuals.

In Brazil, the average survival time of PLWHA after diagnosis has been altered because of several factors, such as access to treatment and the inclusion of new pharmacological groups and formulations such as fixed-dose combinations. During the 1980s and 1990s, the average survival time of PLWHA was 5 months.[9] This average increased to 18 months and 58 months in 1995 and 1996, respectively.[10] In 2002, the average survival time was reported to be 7 years.[11] Different factors affect the survival rate of individuals with TB/HIV coinfection in developing countries such as Brazil. These factors include age, sex, marital status, education level, religion, occupation, residence, body weight, clinical presentation of TB,[12-13] abandonment of TB treatment, CD4+ T lymphocyte count ≤200 cells/mm^3, low wages, smoking, alcohol consumption, previous TB treatment and illiteracy.[5,14-16]

However, the average survival time of individuals coinfected with TB/HIV has not been well studied in Brazil. Thus, knowledge on survival time in this population can provide indicators for control actions and planning interventions that can reduce the mortality in this population. This study aimed to analyze the mortality rate of patients coinfected with TB/HIV and its associated factors.

MATERIALS AND METHODS

Study design

This retrospective cohort study used the data obtained from clinical records and notifications from January 1, 2007 to December 31, 2014.

The study was performed at the Eduardo de Menezes Hospital (EMH), which belongs to the public health network of Minas Gerais, southeastern Brazil. EMH provides specialized care services and is a reference center for the care of PLWHA. The services provided by EMH have regional and state strategic importance at the secondary and tertiary levels of complexity. This is the only hospital located in Belo Horizonte that plays an important role as part of the program for adequate integration of PLWHA in the Department of IST/HIV/AIDS and Viral Hepatitis of the Ministry of Health.

Study population

We included all individuals with concomitant TB and HIV/AIDS, regardless of their initial diagnosis, who were reported in the Epidemiology Hospital Center (EHC) and who received care in EMH within the study period.

We considered TB cases, individuals who had a smear and/or culture positive for *M. tuberculosis* or those in whom the physician established a diagnosis of TB on the basis of the clinical and/or epidemiological data and the results of complementary tests regardless of its clinical form, according to the case definition recommended by the National Tuberculosis Control Program in Brazil.[17]

We considered HIV infection cases, individuals who had positive screening and confirmatory tests from January 1, 2007, to December 31, 2014, according to the guidelines of the Brazilian Ministry of Health.[18]

The database was constructed based on the data recorded in the EHC/EMH, data obtained from the Medical File and Statistics Service (MFSS), records of patients being followed up in the reference hospital and data recorded in the following information systems: 1. Computerized System of Hospital Management, 2. System of Logistic Control of Medicines (SLCM) and 3. Laboratory Tests Control System of the National Network for CD4/CD8 T Lymphocyte Count and Viral Load (LTCS). We performed the analysis of inconsistencies after the construction of the database.

Variables

The survival time in months and occurrence of death or censoring were considered as response variables. The survival time was calculated in months, on the basis of the date of entry into the cohort and the date of death or censoring. For the analysis of death, the cases recorded in the EHC, MFSS and SLCM and confirmed in the Mortality Information System were considered.

The explanatory variables were age, sex, skin color, municipality of residence, date of TB diagnosis, type of TB, use of anti-TB drugs, year when the patient was diagnosed with HIV, CD4+ T lymphocytes count, viral load count and ART use. For the variables CD4+ T lymphocyte count and viral load, the initial results of these tests were considered in the follow-up period.

Statistical analysis

A descriptive analysis of the population was performed using frequency distributions, central tendencies and dispersion measurements. Student's *t*-test was used to compare the mean differences of continuous variables, whereas Pearson's chi-square test was used to compare the proportions of categorical variables.

The Kaplan-Meier nonparametric method was used to compute for the accumulated probability of survival times in patients coinfected with TB/HIV.

The significance level was considered as <0.05. The magnitude of the association between the selected explanatory variables and the death event was estimated by the adjusted hazard ratio (AHR) with 95% confidence interval (CI), which was obtained using the Cox proportional hazards model for both univariate and multivariate analyses. To adjust the main confounding factors, the significance level considered for the final model was 0.05.

Multivariate modeling was performed, initially, for each explanatory variable separately. The explanatory variables were sequentially deleted and only those statistically associated (p <0.05) with the event remained in the final model. The software used for statistical analysis was Statistical Package for the Social Sciences (SPSS®) 20.

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki of 1975 and the protocol was approved by the Research Ethics Committee of the Federal University of Minas Gerais - Certificate of Presentation for Ethical Consideration (CAAE) number: 31192914.3.0000.5149) and Eduardo de Menezes Hospital/Hospital Foundation of the State of Minas Gerais (FEMHIG) (CAAE number: 31192914.3.3001.5124).

RESULTS

The cohort included 924 individuals coinfected with TB/HIV from January 1, 2007 to December 31, 2014. The majority of the participants were men (72.7%), aged 20 to 79 years (median: 38 years); 48.2% lived in the urban area of Belo Horizonte; and most were brown (33.9%). Approximately 41.8% of the participants had pulmonary TB, 31.9% had extrapulmonary TB and 15.9% had mixed TB. In total, 46.4% of the participants had a CD4+ T lymphocyte <200 cells/mm^3, 49.4% of the coinfected individuals had a detectable viral load (<40 copies/mm^3) and 17.3% had an undetectable one.

With regard to treatment, 81.7% of the individuals used ART, whereas 82.5% used anti-TB drugs. In 2014, the largest TB/HIV coinfection registry occurred. The highest number of deaths occurred in 2007 (36.1%), followed by the year 2010 (29.3%). The demographic and clinical characteristics of the study participants are presented in Table 1.

During the study period, 1,603 person-years were at risk (1,135 and 468 for men and women, respectively) and 200 died. The mortality rate of the cohort was 21.6%. The death toll ratio was 12.5/100 person-years, that is, 8.48/100 person-years for men and 3.99/100 person-years for women. The average survival time was 83 months (95% CI: 79.3–86.1).

The Kaplan-Meier survival curves according to age, CD4+ T lymphocyte cell count, viral load and ART used are shown in Figure 1.

In the adjusted multivariate analysis (Table 2), the mortality risk was 2.5 times higher among individuals aged over 50 years. Individuals with a CD4+ T cell lymphocyte count of <200 cells/mm^3 had a 1.4-fold greater risk of mortality than those with CD4+ T lymphocytes >200 cells/mm^3. Regarding the viral load, the risk was 1.73 for detectable individuals (>40 copies/mm^3). Individuals who did not use antiretroviral therapy had a 2.9-fold higher risk than those who used it.

DISCUSSION

This study showed a high mortality rate among individuals with TB/HIV coinfection at a reference center that specialized in the treatment of patients with infectious diseases in the State of Minas Gerais, Brazil. The mortality rate was higher among men and was positively associated with age above 50 years, CD4+ T lymphocyte count ≤200 cells/mm^3, detectable viral load (>40 copies/mm^3) and non-use of ART.

TB/HIV coinfection poses a challenge for developing countries with a high prevalence of TB.[19] In this study, TB remained the major caused of severe morbidity and death in individuals with HIV infection. Unlike other opportunistic diseases, TB may occur in individuals with HIV infection regardless of the degree of immunodeficiency.[20]

Table 1: Demographic and clinical characteristics of HIV coinfected patients at the Eduardo de Menezes Hospital, Minas Gerais, Brazil, from 2007 to 2014 (n = 924).

Variables	Category	Censored (n, %)	Death (n, %)	Total (n, %)
Sex	Male	536 (79.8)	136 (20.2)	672 (72.7)
	Female	188 (74.6)	64 (25.4)	252 (27.3)
Age (years)	10–19	11 (91.7)	1 (8.30)	12 (1.30)
	20–29	132 (82.0)	29 (18.0)	161 (17.8)
	30–39	274 (80.8)	65 (19.2)	339 (36.5)
	40–49	205 (79.5)	53 (20.5)	258 (27.9)
	50–59	78 (65.0)	42 (35.0)	120 (12.8)
	60–59	21 (77.8)	6 (22.2)	27 (2.90)
	70–79	3 (42.9)	4 (57.1)	7 (0.80)
Residence	Urban	361 (81.2)	84 (18.8)	445 (48.2)
	Others	267 (76.1)	84 (23.9)	351 (38.0)
	Ignored	96 (75.0)	32 (25.0)	128 (13.8)
Race/color	White	112 (15.5)	31 (15.5)	143 (15.5)
	Brown	254 (35.1)	59 (29.5)	313 (33.9)
	Black	75 (10.4)	28 (14.0)	103 (11.1)
	Ignored	281 (38,8)	80 (40,0)	361 (39,1)
	Yellow	1 (0.10)	1 (0.50)	2 (0.22)
	Indigenous	1 (0.10)	1 (0.50)	2 (0.22)
Form of TB	Pulmonary	301 (41.6)	85 (42.5)	386 (41.8)
	Extrapulmonary	240 (33.1)	55 (27.5)	295 (31;9)
	Pulmonary/ Extrapulmonary	113 (15.6)	34 (17.0)	147 (15.9)
	Ignored	70 (9.70)	26 (13.0)	96 (10.4)
CD4 (cell/mm³)	<200	335 (78.1)	94 (21.9)	429 (46.4)
	≥200	209 (87.1)	31 (12.9)	240 (26.0)
	Ignored	180 (70.6)	75 (29.4)	255 (27.6)
Viral charges (copy/mm³)	Detectable	370 (51.1)	86 (43.0)	456 (49.4)
	Undetectable	143 (19.8)	17 (8.50)	160 (17.3)
	Ignored	211 (29.1)	97 (48.5)	308 (33.3)
Use of ARV medications	Yes	626 (82.9)	129 (17.1)	755 (81.7)
	No	95 (58.3)	68 (41.7)	163 (17.6)
	Ignored	3 (50.0)	3 (50.0)	6 (0.70)
Use of antituberculosis medications	Yes	600 (78.7)	162 (21.3)	762 (82.5)
	Ignored	124 (76.5)	38 (23.5)	162 (17.5)
Year of diagnosis	2007	76 (63.9)	43 (36.1)	119 (12.9)
	2008	102 (85.0)	18 (15.0)	120 (13.0)
	2009	105 (86.1)	17 (13.9)	122 (13.2)
	2010	58 (70.7)	24 (29.3)	82 (8.87)
	2011	63 (78.7)	17 (21.3)	80 (8.66)
	2012	75 (75.8)	24 (24.2)	99 (10.7)
	2013	111 (83.5)	22 (16.5)	133 (14.4)
	2014	134 (79.3)	35 (20.7)	169 (18.3)

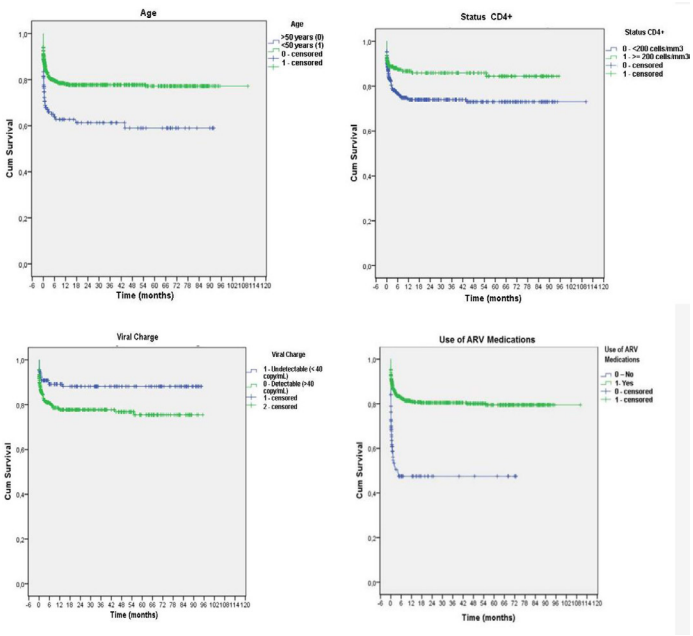

Figure 1: Kaplan-Meier survival function curve by age, status CD4+, viral charge and use of ARV medications.

Table 2: Univariate and multivariate analyses of factors associated with HIV/TB coinfected mortality reference center in southeastern Brazil from 2014 to 2017 (n = 924).

Description	Analyses univariate		Analyses multivariate	
	AHR (95% CI)	p value	AHR (95% CI)	p value
Years of diagnosis				
2007	1		1	
2008	0.39 (0.23–0.68)	<0.01	0.51 (0.18–1.44)	<0.01
2009	0.33 (0.19–0.59)		0.68 (0.29–1.56)	
2010	0.72 (0.44–1.19)		0.74 (0.28–1.97)	
2011	0.52 (0.30–0.91)		0.79 (0.32–1.99)	
2012	0.61 (0.37–1.01)		0.85 (0.36–2.01)	
2013	0.39 (0.24–0.66)		0.48 (0.20–1.13)	
2014	0.58 (0.37–0.91)		0.94 (0.44–1.99)	
Age				
<50 years	1		1	
≥50 years	2.03 (1.48–2.78)		2.52 (1.39–4.59)	0.01
CD4 (cells/mm³)				
>200	1		1	
≤200	1.78 (1.19–2.67)	<0.001	1.40 (0.86–2.27)	<0.001
Viral charges (copy/mm³)				
Undetectable	1		1	
Detectable	2.05 (1.22–3.45)	<0.001	1.73 (0.98–3.01)	<0.001
Use of ARV				
Yes	1		1	
No	3.71 (2.75–5.00)	<0.001	2.91 (1.71–4.93)	<0.001

AHR, adjusted hazards ratio; ARV, antiretroviral therapy

There was a clear predominance of male patients in this study, which agrees with the findings other studies in the Brazilian context that observed a higher incidence and prevalence of TB/HIV among male patients.[5,21] In addition, our findings showed a prevalence of coinfection among individuals aged 20–59 years, which is similar to the results of other studies.[22] Currently, the increase in the number of individuals with HIV infection, aged over 50 years, both in Brazil and in the world, can be detected and evaluated on the basis of demographic data, increase in the number of notifications and aging of the infected population.[23]

The differences in skin color mentioned in the study population, with a higher prevalence of brown color, should be highlighted. This variable may have limitations in the self-perception of the individual and in the reliability of this information to fill out the notification forms. This result differs partially from other studies where the highest prevalence was in the black and brown population. Analysis of this variable has contributed to the understanding of the disadvantages and inequalities faced by the black population in accessing health care resources.[24]

Moreover, about 48.2% of the individuals lived in urban regions; this may be due to the increased urbanization and the social and economic habits of the population in the last decades. Previous studies have showed that the predominant clinical form of TB was pulmonary and this result is consistent with that of other studies.[25]

In this study, most of the participants used ART. Since the introduction of ART, a significant reduction in the progression of AIDS and the burden of opportunistic infections has been observed globally.[26] In this cohort, the risk of death in individuals who did not use ART was three times higher than that among individuals who used it. The use of ART reduces the incidence of TB by 65% in individuals with HIV infection.[27] The majority were using ART (81.7%), a similar result found in the study by Cunha *et al*.[28]

In our cohort, 49.4% presented detectable viral load (>40 copies/mm^3). Recent studies have reported that viral suppression rates range from 65% to 80% according to different antiretroviral regimens.[29]

Adherence to the treatment regimen is of paramount importance to achieve viral suppression. Viral suppression is greater in individuals with greater than 95% treatment adherence. Adherence to treatment greater than 95% results in reduction of viral resistance and an increase in the quality of life as well as survival.[30]

The mortality rate (21.6%) reported in this study was higher than that reported in studies conducted in Europe (4.0%), Uganda (10.5%), Argentina and Latin America (11.0%) and Nigeria (16.6%).[31-33] Furthermore, between 2002 and 2012, the incidence of TB/HIV coinfection in Brazil increased by 3.8%, indicating a growing importance of HIV in TB epidemiology.[34]

In our cohort, 49.4% presented detectable viral load (>40 copies/mm^3). Recent studies have reported that viral suppression rates range from 65% to 80% according to different antiretroviral regimens.[29]

Adherence to the treatment regimen is of paramount importance to achieve viral suppression. Viral suppression is greater in individuals with greater than 95% treatment adherence. Adherence to treatment greater than 95% results in reduction of viral resistance and an increase in the quality of life as well as survival.[30]

The mortality rate (21.6%) reported in this study was higher than that reported in studies conducted in Europe (4.0%), Uganda (10.5%), Argentina and Latin America (11.0%) and Nigeria (16.6%).[31-33] Furthermore, between 2002 and 2012, the incidence of TB/HIV coinfection in Brazil increased by 3.8%, indicating a growing importance of HIV in TB epidemiology.[34]

CD4+ T lymphocyte count is a strong predictor of HIV progression and patient survival. This study showed that individuals with a CD4+ T lymphocyte count lesser 200 cells/mm^3 were more likely to die, which is similar to the results of other studies.[5,35] A low CD4+ T lymphocyte count in patients with TB/HIV indicates that these patients were probably diagnosed late. Even with the incentive for the early diagnosis of HIV in Brazil, this is not yet the case and late diagnosis is a public health problem.[35]

This study had some limitations. The study was conducted in a single reference hospital that provides treatment to patients with infectious diseases and outpatient care. The database included secondary information from notifications, medical records and information systems, which may lead to under- or overestimation of the analyses performed; additionally, some data were missing.

CONCLUSION

Although Brazilian patients have access to TB/HIV treatment, this study demonstrated a high proportion of TB/HIV coinfection and mortality. Factors associated with mortality risk were age above 50 years, count CD4+ T lymphocyte less than 200 cells/mm^3, detectable viral load and non-use of ART. These factors should be monitored to improve the survival of this population. Moreover, early diagnosis and treatment, as well as provision of continuing healthcare, can reduce the mortality rate among individuals with TB/HIV coinfection.

ACKNOWLEDGEMENT

We thank the Hospital Foundation of the State of Minas Gerais (FEMHIG)/Eduardo de Menezes Hospital (EMH) for their assistance and permission to perform the data collection; the Researcher Support Center (FEMHIG), especially Fernando Madalena Volpe, Marcelo Militão and Flávio Capanema, for the training and incentives; the Teaching and Research Promotion Center (FEMHIG), especially Rita de Cássia Nogueira Mota, for the support and incentives; and the Foundation for Research Support of the State of Minas Gerais (FAPEMIG) for the financial support.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

ART: Antiretroviral Therapy**; HIV:** Human immunodeficiency Virus; **PLWAS:** Peoples Living with HIV/AIDS; **TB:** Tuberculosis.

REFERENCES

1. Prado TN, Caus AL, Marques M, Maciel EL, Golub JE, Miranda AE. Epidemiological profile of adult patients with tuberculosis and AIDS in the state of Espírito Santo, Brazil Cross-referencing tuberculosis and AIDS databases. J Bras Pneumol. 2011;37(1):93-9.
2. Yen CN, Weuenga HO, Kim AA, Malika T, Muttai H, Katana A, *et al*. Comparison of trends in tuberculosis incidence among adults living with HIV and adults without HIV - Kenya, 1998–2012. PLoS One. 2014;9(6):e99880.
3. World Health Organization. WHO news release. Saudi Med J. 2013;34(11):1205-7.
4. Hino P, Takahashi RF, Bertolozzi MR, Egry EY. Coinfecção de TB/HIV em um distrito administrativo do Município de São Paulo. Acta Paul Enferm. 2012;25(5):755-61.
5. Maruza M, Albuquerque MFPM, Coimbra I, Moura LV, Montarroyos UR, Miranda FDB, *et al*. Risk factors for default from tuberculosis treatment in HIV-infected individuals in the state of Pernambuco, Brazil: a prospective cohort study. BMC Infect Dis. 2011;11(1):351.
6. Rodrigues AMS, Scatena ML, Vendramini SHF, Canini SRMS, Villa TCS, Gir E. Assessment of tuberculosis treatment accessibility for patients co-infected or not with the human immunodeficiency virus. Rev Esc Enferm USP. 2012;46(5):1163-9.
7. World Health Organization. Global tuberculosis report 2014. Geneva: WHO; 2014.
8. Brazil Ministry of Health. Health Surveillance Department. Department of STD, AIDS and Hepatitis. Clinical protocol and therapeutic guidelines for management of HIV infection in adults. Brasília. 2013.

9. Chequer P, Hearst N, Hudes ES, Castilho E, Rutherford G, Loures L, *et al*. Determinants of survival in adult Brazilian AIDS patients, 1982-1989. The Brazilian State AIDS Program Co-ordinators. AIDS. 1992;6(5):483-7.
10. Marins JR, Jamal LF, Chen SY, Barros MB, Hudes ES, Barbosa AA, *et al*. Dramatic improvement in survival among adult Brazilian patients. AIDS. 2003;17(11):1675-82.
11. Gadelha AJ, Accacio N, Costa RLB, Galhardo MC, Cotrim MR, Souza RVD, *et al*. Morbidity and survival in advanced AIDS in Rio de Janeiro, Brazil. Rev Inst Med Trop. 2002;44(4):179-86.
12. Domingos M, Caiaffa WT, Colosimo E. Mortality, TB/HIV co-infection and treatment dropout: predictors of tuberculosis prognosis in Recife, Pernambuco State Brazil. Cad Saúde Pública. 2008;24(4):887-96.
13. Català L, Orcau A, Olalla GP, Millet JP, Mondragón RA, Cavlà JA, *et al*. Survival of a large cohort of HIV-infected tuberculosis patients in the era of highly active antiretroviral treatment. Int J Tuberc Lung Dis. 2011;15(2):263-9.
14. Muture BN, Keraka MN, Kimuu PK, Karibu EW, Ombeka VO, Oguya F. Factors associated with default from treatment among tuberculosis patients in Nairobi province, Kenya: a case control study. BMC Public Health. 2011;11(696):1-10.
15. Zhang Q, Gaafer M, Bayoumy IE. Determinants of default from pulmonary tuberculosis treatment in Kuwait. Sci World J. 2014;14:672825.
16. Matida LH, Ramos ANJ, Heukelbach J, Sañudo A, Succi RC, Marques HH, *et al*. Improving survival in children with AIDS in Brazil: results of the second national study, 1999-2002. Cad Saúde Pública. 2011;27(Sup1):93-103.
17. Ministry of Health. Secretariat of Health Surveillance. Department of Epidemiological Surveillance. Manual of recommendations for the control of tuberculosis in Brazil / Ministry of Health, Secretariat of Health Surveillance, Department of Epidemiological Surveillance. - Brasília: Ministry of Health. 2011;284 p. il. - (Series A. Norms and Technical Manuals) ISBN 978-85-334-1816-5.
18. Ministry of Health. Secretariat of Health Surveillance. Department of STD, AIDS and Viral Hepatitis. Clinical Protocol and Therapeutic Guidelines for Management of HIV Infection in Adults. Brasilia. 2015.
19. Ribeiro SR, Luz PM, Campos DP, Moreira RI, Coelho L, Japiassu A, *et al*. Incidence and determinants of severe morbidity among HIV-infected patients from Rio de Janeiro, Brazil, 2000–2010. Antivir Ther. 2014;19(4):387-97.
20. World Health Organization Global Tuberculosis Report 2012. Geneva, Switzerland: WHO; 2012. http://www.who.int/iris/handle/10665/75938.
21. Batista Jd, Albuquerque MDEDF, Maruza M, Ximenes RA, Santos ML, Montarroyos UR. Incidence and risk Factors for Tuberculosis in People Living with HIV: Cohort from HIV Referral Health Centers in Recife, Brazil. Plos One. 2013;8(5).
22. Barbosa IR, Costa ICC. Epidemiological study of tuberculosis-HIV co-infection in northeastern Brazil. Rev Patol Trop. 2014;43(1):27-38.
23. Sousa ACA, Suassuna DSB, Costa SML. Clinical-epidemiological profile ofAIDS patients. DST J Bras Diseases Sex Transm. 2009;21(1):22-6.
24. Melo MC, Donalísio MR, Cordeiro RC. Survival of patients with AIDS and co-infection with the tuberculosis bacillus in the South and Southeast regions of Brazil. Ciência and Saúde Coletiva. 2017;22(11):3781-92.
25. Coelho AB, Bilberg CA. Tuberculosis / HIV coinfection profile in the municipality of São Luís, Maranhão, Brazil. Cadernos ESP, Ceará. 2015;9(1):19-26.
26. UNAIDS. The Gap Report. UNAIDS. 2014.
27. Suthar AB, Law SD, Del AJ, Getahun H, Dye C, Sculier D, *et al*. Antiretroviral therapy for prevention of tuberculosis in adults with HIV: a systematic review and meta-analysis. PLoS Med. 2012;9(7):e1001270.
28. Silva EROD, Velasque L, Ribeiro SR, Cardoso SW, Marins LMS, Grinsztejn E, *et al*. Mortality in patients with HIV-1 and tuberculosis co-infection in Rio de Janeiro, Brazil- associated factors and causes of death. BMC Infect Dis. 2017;17(1):373.
29. Guest JL, Weintrob AC, Rimland D, Rentsch C, Bradley WP, Agan BL, *et al*. A Comparison of HAART Outcomes between the US Military HIV Natural History Study (NHS) and HIV Atlanta Veterans Affairs Cohort Study (HAVACS). PLoS One. 2013;8(5):e62273.
30. Chesney MA. The elusive gold standard. Future perspectives for HIV adherence assessment and intervention. J Acquir Immune Defic Syndr. 2006;43(Suppl 1):S149-55.
31. Podlekareva DN, Mocroft A, Post FA, Riekstina V, Miro JM, Furrer H, *et al*. Mortality from HIV and TB coinfections is higher in Eastern Europe than in Western Europe and Argentina. AIDS. 2009;23(18):2485-95.
32. Podlekareva DN, Efsen AMW, Schultze A, Post FA, Skrahina AM, Panteleev A. TB/HIV study group in EuroCoord. Tuberculosis-related mortality in people living with HIV in Europe and Latin America: an international cohort study. Lancet HIV. 2016;3(3):e120–e131.
33. Adamu AL, Gadanya MA, Abubakar IS, Jibo AM, Bello MM, Gajida AU. High mortality among tuberculosis patients on treatment in Nigeria: a retrospective cohort study. BMC Infect Dis. 2017;17(1):170.
34. Gaspar RS, Nunes N, Nunes M, Rodrigues VP. Temporal analysis of reported cases of tuberculosis and of tuberculosis-HIV co-infection in Brazil between 2002 and 2012. J Bras Pneumol. 2016;42(6):416-22.
35. Cunha R, Maruza M, Montarroyos UR, Coimbra I, Miranda FBBD, Albuquerque MDF, *et al*. Survival of people living with HIV who defaulted from tuberculosis treatment in a cohort, Recife, Brazil. BMC Infect Dis. 2017;17(1):137.

Article History: Submission Date : 08-04-2018; Revised Date : 02-07-2018; Acceptance Date : 06-08-2018.
Cite this article: Silva DI, Ceccato MDGB, Silveira MR, Miranda SS, Gomes RM, Haddad JPA, Carvalho WS. Predictors of Mortality among Individuals with Tuberculosis and Human Immunodeficiency Virus Coinfection at a Reference Center in Southeastern Brazil: A Retrospective Cohort Study. J Young Pharm. 2018;10(4):476-80.